Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

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Dédicace:

A mon pays

A mes grands parents

A qui qu'il se concerne

Roza
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Abstract

The objective of this study was to study and investigate the efficacy and pharmacotoxicity of some trypanocidal: Cymelarsan®, quinapyramine and homidium bromide, and also oxytetracycline at single and multiple dosages, in addition to their pharmacotoxicity of interaction of each other. A trial for the treatment of *T. evansi* with Cymelarsan supplemented with zinc and copper was also conducted. Parasitological, clinical and pathological investigations were also made. Drugs under experimentation were also studied for their residual status. The study consisted of 10 experiments conducted in 380 Nubian goats and 65 camels (*Camels dromedarius*), divided randomly into different groups of both sexes each of ten goats and five camels. Three groups were defined as control groups such as uninfected, untreated group, infected with *T. evansi* or *T. vivax* were also used. The infection was done first in 5 albino rats in both sexes, and then the animals were infected after many passages with rats’ blood each experiment was taken from 79-86 days. These ten experiments targeted:

1. Toxicity and efficacy of Cymelarsan® in goats infected with *T. evansi* at single and multiple doses.
2. Toxicity and efficacy of oxytetracycline in goats infected with *T. evansi* and given single and multiple dosages of oxytetracycline.
3. Efficacy and clinicopathological effects of Cymelarsan and oxytetracycline in goats infected with *T. evansi*.
4. Clinicopathological effects and efficacy of Cymelarsan in Nubian goats infected with *T. evansi*, supplemented with zinc and copper.
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(5) Toxicity and efficacy of quinapyramine in goats infected with *T. evansi*

(6) Toxicity and efficacy of ethidium bromide in goats infected with *T. vivax*

(7) Efficacy and clinicopathological effects of quinapyramine and ethidium bromide combination in goats infected with *T. evansi* or *T. vivax*

(8) Toxicity and efficacy of Cymelarsan in camels (*Camelus dromedaries*) naturally infected with *T. evansi* and given single and multiple dosages of Cymelarsan

(9) Toxicity and efficacy of oxytetracycline in camels (*Camelus dromedaries*) infected with *T. evansi* and given single and multiple dosages of oxytetracycline

(10) Efficacy and clinicopathological effects of Cymelarsan and oxytetracycline in camels (*Camelus dromedaries*) infected with *T. evansi*.

Various parameters pertaining to existence or removal of parasites from blood as well as survival or death and the experimental animals have been recorded with respect to the drug given alone singular or in combination. Liver impression smears indicated parasitaemia in the different experimental groups.

A number of clinical signs were observed in goats in different groups with respect to hypothermia and various manifestations and thriftiness or posture and state of health.

Post treatment all goats dosed with Cymelarsan showed swelling at injection site which disappeared after 1-2 days in a few goats but never in other majority of the groups. Severity of the clinical signs developed with the high dosing of the drugs. Some goats showed decrease in body temperature, respiratory rate, pulse rate, body weight and blood pressure, others showed severe signs, including lacrimation, nasal discharge, shivering, and pyrexia, loss of appetite, keratitis, diarrhoea, weak respiration and pulse rate. Some camels exhibited crying sounds
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) and restlessness with episodes of diarrhoea whereas in goats most prevalent lesions were congestion, oedema and haemorrhage and frothing at the mouth plus necrosis of livers and kidneys in addition to nephritis, gastritis, enteritis, peritonitis and hydroperitoneum, splenomegaly, and orchitis post infection. Post treatment these signs disappeared in some groups while in other groups they remained with different severities. Similar observations were made with respect to histopathological findings pre and post dosing.

Minor effects were noticed with respect to haematocrit parameters and minerals and enzymatic activity.

Residues of Cymelarsan were measured by determination of arsenic. The residue of Cymelarsan, OTC and quinapyramine was measured in serum, organs (liver, kidney, heart, lung, spleen, cerebellum, cerebrum, fat, site of injection, leg muscle, uterus, ovary and testis), bile and urine. Generally the drug concentration increased when the dose is increased.

The residual status of Cymelarsan, quinapyramine and OTC was studied and relevant data obtained. Serum arsenic (for Cymelarsan) values were monitored under the various circumstances. Kinetics of these drugs was studied with respect to different manipulations.
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Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

The first experiment: Treatment of trypanocidal agents in Nubian goats and camels.

The second experiment: Treatment of trypanocidal agents in Nubian goats and camels.

The third experiment: Treatment of trypanocidal agents in Nubian goats and camels.

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The ninth experiment: Treatment of trypanocidal agents in Nubian goats and camels.

The tenth experiment: Treatment of trypanocidal agents in Nubian goats and camels.

The eleventh experiment: Treatment of trypanocidal agents in Nubian goats and camels.

The twelfth experiment: Treatment of trypanocidal agents in Nubian goats and camels.

The thirteenth experiment: Treatment of trypanocidal agents in Nubian goats and camels.

The fourteenth experiment: Treatment of trypanocidal agents in Nubian goats and camels.
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 análisis de algunos tratamientos tritánicos en animales de consumo (corderos nubios y camellos)

La evaluación del toxicidad de algunos tratamientos tritánicos en animales de consumo, como los greges nubios y camellos, es un tema de interés. Los tratamientos incluyen la administración de diferentes tipos de fármacos en el momento del tratamiento y controlando los efectos a largo plazo.

Los resultados muestran que algunos tratamientos son efectivos en el control de la enfermedad, mientras que otros pueden tener efectos tóxicos a largo plazo. Es importante continuar investigando para encontrar tratamientos seguros y efectivos.

Además, se recomienda realizar pruebas de toxicidad antes de utilizar cualquier tratamiento en animales de consumo para asegurar la seguridad y la salud de los animales.
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INTRODUCTION

Camels (*Camelus dromedarius*) play an important role in arid and semi-arid zones where they are used by pastoral societies as a source of meat, milk and, for drought and transport purposes (Shwarts and Dioli,1992).

In Sudan, the one-humped camel (*Camelus dromedarius*) plays an important role in the national income and constitutes a major proportion of foreign currency revenue. Sudanese camels are affected by three major diseases namely mange (Jereb), internal helminthiasis mainly haemonchosis (Holaa), and trypanosomosis (Guffar). The latter is the most important health problem of all (Wilson, 1984).

The goat is one of the small-domesticated ruminants, which have served mankind since early times and longer than cattle and sheep. In the Sudan people keep goats for several purposes including food. Goats need mainly natural grazing, at low cost management and they are a form of investment (meat and milk products) but the productivity of goats will be low if they are not kept healthy.

Trypanosomosis (Surra) encompasses about 9 – 10 million square kilometers of Savannah area (Atang, 1982) and is widespread in East Africa (Ethiopia, Sudan, Somalia, and Kenya) and West Africa (Chad, Mali, Mauritania, and Niger). It has also been described in the Middle East, India and Asia (Wilson, 1984). The disease is well known by camel’s herder but not far small ruminants (Rötcher and Heising1980).

*T. vivax* causes the most important form of trypanosomosis of cattle in West Africa, Sahel and Sudan zones of territories of Chad. Niger, Mali, Northern Senegal and Northern Nigeria which are relatively free of Tsetse. The cattle migrate yearly south into Guinea zone which were heavily infested with Tsetse flies, also in East Africa cause infection and disease but the course is mild(Anosa and Isoun, 1976).
ElKarib, (1961) reported that only sheep showed clinical episodes of the disease with loss of weight and abortion during 220 days after inoculation of \textit{T. evansi} (strain isolated from dairy camels) in sheep and goats.

There is little information about the distribution and the economic importance of the disease caused by the \textit{T. congo\ls{}lense} in small ruminants. The infection and the disease, however, are known to occur in both West and East Africa. Pecaud, (1909and1910) recorded a 1.3% incidence of infection by the \textit{T. congo\ls{}lense}, \textit{T. vivax} and \textit{T. evansi} in a large number of animals. In a more recent but much smaller survey, 13.8% were infected with either \textit{T. congo\ls{}lense} or \textit{T. vivax} (Kramer, 1966). Mornet, (1954) considered that goats and sheep made up 4% of all the animals infected with \textit{T. congo\ls{}lense}. Lewis, (1949) reported that goats can be infected if kept close to infected cattle. Yesufu, (1975) exposed pregnant female rates infected with \textit{T. brucei}, \textit{T. congo\ls{}lense}, \textit{T. gambiense} to various stresses and noted a high rate of abortion and two litter survived, also Ige and Amdou observed that infection with \textit{T. vivax}, \textit{T. congo\ls{}lense}, \textit{T. brucei brucei} and mixed infection had a severe effect on the fertility of the cattle.

The pathology of animal trypanosomosis was summarized in more details by Ikede, (1975) although the disease caused by the various species of trypanosomes has certain features in common, the types and mechanisms of injury done to the host may vary considerably with the species.

Human sleeping sickness influences physical, sexual maturity and academic performance of children (Khonde \textit{et al.}, 1997). Control of the vector is not feasible and the production of vaccine is still remote due to the problem of antigenic variation. Thus chemotherapy is the only method available for controlling trypanosomosis in camels and other animals (Bujon, 1990). Treatment in camels is dependent on one of two drugs suramin and quinapyramine (Bujon, 1990). However, suramin has become less effective (Gadel Mwla and Fayed, 1979). In addition, suramin has disadvantages related to its route of administration (Zelleake \textit{et al.}, 1989) and quinopyramine sulphate is no longer available from the original manufacturer. On the other hand isometamidium chloride (samorin) only removes the parasites from the blood-stream for 21 hours.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) followed by relapse. And causes some serious adverse effects (Ali et al., 1986). Diminazine aceturate (Berenil) was found to be toxic at a dose of 10 or 20 mg/kg in camels (Leach and Robert, 1981).

Mwambu, (1975) re-evaluated the value of ethidium for the treatment of *T. brucei* subgroup infection in cattle and concluded that the use of this drug as a curative in *T. brucei* infection of cattle should be restricted. Ethidium bromide was recorded as carcinogenic and mutagenic drug.

Extensive use of these compounds led to the appearance of drug resistance, which is becoming more widespread (Leach and Robert, 1981). This drug resistance poses a great problem (Mahmoud and Gray, 1980, Bujon, 1990) thus highlighting the need for newer trypanocidal drugs (Bujon, 1990).

Since 1961 no additional drugs for use against animal trypanosomosis have gone beyond the experimental stage. Drug resistance between diamidines and isometamidium group seems to exist (Finelle, 1975).

Cymelarsan® is a new trypanocide for treatment of camel trypanosomosis presented in the market by Rhône Mérieux – France and is indicated for the treatment of acute, sub-acute and chronic *T. evansi* infections, which are resistant to other drugs (Bujon, 1990).

Trypanosomosis may sometimes be associated with other infections such as internal parasites and bacterial infection. Of the commonly used antibiotics, a tetracycline group is a broad spectrum toxic, bacterio-static, have effect against virus, mycoplasma, protozoa of blood (Thielirea, Anaplasma) (Giovani and warren, 1983), and have high concentration in the kidney, spleen, lung and liver (Bywater et al., 1991).

It is well known that the vast majority of livestock in the Sudan are kept under extensive systems of husbandry pasturolists. Accordingly under such extensive systems one would expect that mineral nutrition problem would been in countered since nomadic cares don't stay in any one place for a long time where mineral deficiency areas would be expected and also areas of adequacy and
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) toxicity also would be expected however, mineral nutrition problem in nomadic herds and great in addition, the tremendous physical extension of nomadic movement may lead to even more salt losses through increased sweating, micturition, defecation and other avenues of minerals escape of the animals body. In addition these herds expose environmental factors that stressed the camels through starvation, lack of water, prevalence of diseases and management of the lack of trace element which aggregate the stimulation.

At the recommended dose Cymelarsan® has been shown to be well tolerated (Bujon, 1990 and Fairouz, 2000). It is well known that drug combined is used mainly to overcome resistance or any undesirable side effects. Drugs are often given in combination with potentially beneficial or adverse effect results. When two drugs are given together, their effects may be additive, the final being the sum of the individual effects. Alternatively, the interaction may be synergistic, the effect then being greater when two drugs are given together than one would expect from their effect when given alone (Girdwood, 1979). Interaction may be the result of pharmacokinetic (absorption, distribution, metabolism and excretion), pharmacodynamic (antagonism, additive interaction, synergism and potential) changes or a combination of both (Bentram and Anthony, 1993). The combination Cymelarsan® OTC gave best results in infected T. evansi Nubian goats, with correction of the haemogram, and some biochemical changes such as liver enzymes, thyroxin and progesterone levels were more quickly revealed with combined action than in Cymelarsan® alone (Fairouz, 2000).

This study describes the efficacy, toxicity, drug interaction and residues of some trypanocidal drugs in infected goats and camels of the Sudan. Thus, the main objectives of this study are:

1- A trial to use Cymelarsan against T. evansi in Nubian goats.

2- To study pharmacotoxicity of some trypanocidal drugs Cymelarsan®, quinapyramine and homidium bromide.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

3- To study the pharamcotoxicity of oxytetracycline at different doses.
4- To study the pharamcotoxicity of interaction between these drugs at different doses.
5- To study the efficacy of different doses of the above mentioned drugs.
6- A trial for the treatment of infected goats with Cymelarsan supplemented with zinc and copper.
7- A trial for intermittent treatment of infected camels and goats with the above mentioned drugs.
8- To study the residual effects of the drugs experimented with, in tissue, urine, serum and bile of camels and goats.

CHAPTER ONE
LITERATURE REVIEW

1.1 Classification

As described by Soulsby, (1982):
Phylum Protozoa
Subphylum Sarcomastigophora
Super class Mastigophora
Class Zoomasigophorea
Order Kinetoplastida
Suborder Trpanosomatida
Family Trypanosomatidae
Genus Trypanosoma
Subgenus Pycnomas Nanomas Duttonella Trypanozoon
Species suis congolense simiae vivax brucei
Subspecies vivax uniforme viennei brucei rhodesiense gambesiense equiperdum equinum evansi

1.2 Description of trypanosomes

Trypanosomes are microscopic elongated unicellular flagellates. They move forwards with the help of a single flagellum, which arises from the flagella pocket, near the kinetoplast that is situated at the posterior end of the cell. They are obligate parasites, which multiply in the body fluids, especially blood stream and tissue fluid of the vertebrate host, and live in the digestive tract of the invertebrate host, which is generally a biting fly (Solusby, 1982).

1.3 Trypanosomosis in Africa

In Africa, the disease occurs in 37 countries extending over one third of the continent and covered about 9 – 10 million square kilometers of Savannah area (Atang, 1982). An estimated 50 million cattle constituting
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

30% of Africa total cattle are exposed to the risk of infection (FAO, WHO, and OIE, (1982) – Muarray and Gray, 1984). The sleeping sickness is found only in Sub-Saharan Africa (WHO, 1998). Trypanosomosis in camels (Surra) is widespread in East Africa (Ethiopia, Sudan, Somalia, and Kenya) and West Africa (Chad, Mali, Mauritania, and Niger). It has also been described in the Middle East, India and Asia (Wilson, 1984).

1.3 Transmission of trypanosomes

There are three major types of transmission of trypanosomes:

1- Cyclical transmission: Is restricted to *Glossina* species only.

2- Mechanical transmission: Materialized by two means firstly biting insect (Uilenberg, 1998) e.g *Tabanids, Stomoxys* and tsetse flies themselves (Jordon, 1974), secondly by latrogenic means, these caused by the careless operators and one induced involuntarily by operators using unhygienic procedures, such as contaminated instruments like surgical instrument and needle (Uilenberg, 1998).

3- Transmission by other means:

   a) Carnivores were reported to be infected with *T. evansi* and *T. burcei* by ingesting meat or organs from infected animals, as long as these are still sufficiently fresh to contain live trypanosomes (penetration through the mucous membranes).

   b) Transmission of *T. evansi* in Latin American by the bites of vampire bats is common.

   c) Congenital transmission from the mother to the offspring, either through placenta, while the foetus still in the uterus or when bleeding occurs during birth.

   d) Venereal transmission is the normal means by which dourine of equines, caused by *T. equiperdum* is propagated (Uilenberg, 1998).

*Trypanosoma evansi* belongs to the brucei group of trypanosomes and is morphologically identical with the long slender form of the polymorphic tsetse transmitted *T. brucei* (Soulsby, 1982). It has been reported to be transmitted mechanically with body fluids from camel to camel by a number
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) of haematophagous biting flies: Tabanus, Stomoxys and Haematobia. The transmission of *T. evansi* and *T. equiperdum* in horses and cattle in South America by the bite of vampire bat was described by Hoare (1939 and 1967).

### 1.4 Trypanosomosis outside the tsetse belt in Africa

Wells (1972) stressed that the occurrence of *T. vivax* in areas where tsetse flies are absent is widely attributed to mechanical transmission. Ford (1964 and 1972) found that, in Rhodesia *T. congolesense* culminated in cattle adjacent to the tsetse area whereas *T. vivax* was found in areas further. The same result was found in Uganda (Ford and Cliford, 1968) and in Nigeria (Folkers and Jones, 1966).

### 1.5 Trypanosomosis in the Sudan

In Sudan, trypanosomosis has been recognized as an important disease of livestock since 1904 when it was recorded that 87 cattle were sick of trypanosomosis when they came to Khartoum from Upper Nile province (Annual Veterinary Department). In 1908 Dr. Wenyon reported the disease in camels in Bahr Elgazal province. In 1914 cattle trypanosomosis caused by *T. perccorum*, *T. brucei* and *T. cazalboui* in Southern provinces and camel trypanosomosis to be widespread throughout the Northern Sudan, high mortality in equines, cattle and camels due to *T. brucei* in Bahr ElGazal Province was reported by the Wellcome Tropical Research Laboratories in Khartoum as *T. sudanese*. (Elkarib, 1961). In the study of Kheir *et al.* 1992 along Sudan Ethiopian border in an area from Khor Yabous (lat.9° 45’ long 43° 10’) in the South to River Setit in the North included areas of Rivers Rashad, Dinder, the Blue Nile and Kurmuk district *T.congolesense*, *T. brucei* and *T.vivax* were found. Five strains from *T.vivax* isolated from Sennar
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) 
(Blue Nile State), Gedid (40km from Khartoum state), Jabal Awlia(50km from Khartoum State) and from Soba(20km from Khartoum State) and they were infective to white mice (Abdoon et al., 2001).

Bovine trypanosomaisis is mainly a problem of mechanical transmission by the genera tabanids, stomoxys and possibly others. The main cattle-rearing zone lies north of the tsetse zone, in Bahr El Gazal, Darfur, Kordofan, Upper Nile and the Blue Nile province (Elkarib, 1961). T. congolense occurs throughout, and in areas just north of the tsetse zone. It may also occur in areas farther north. T. vivax occurs in the tsetse zone and extends farther north than T. congolense east from parallel 15th north on the east T. brucei affects cattle in the tsetse zone and possibly immediately north of it and in the latter case it is probably of tsetse origin. Outside the tsetse zone T. congolense is widespread in Bor, Central Nuer Province and Malakal district of the Upper Nile province. T. brucei is commoly found in tsetse areas and T. vivax outside the tsetse zone. (Elkarib, 1961).

1.6 Trypanosomosis outside the tsetse belt in the Sudan

Ismail and Shomain (1975) reported the presence of T. vivax in Damazin (Blue Nile). Homeida, (1993) recorded T. vivax in Sennar, Kosti and El Deuim. Surveys conducted in South Darfour area along Bhar El Arab site the tsetse fringe and in South Kordfan revealed that the species of trypanosomes prevalent to be T. vivax, T. brucei and T. congolense (Hall et al., 1990) T. evansi was recorded in camels comming from El Gadadarif State (Eastern Sudan) to El-Mwelh market (Khartoum State) (Fairouz, 2000).

1.7 Distribution of the vectors

Lewis made a first major review of the tsetse fly problem in the Sudan in 1949, and studied the genus Glossina as a full description. The various
species of tsetse in the Sudan, *Glossina fuscipes fuscipes* together with *G. moristans* were found east of the Nile in the Sudan Blue Nile area around Kurmuk district. *G. tachiniodes*, *G. palidipes*, *G. longipennis*, *G. fuscipleuris* and *G. fusca fusca*. In addition to the four mentioned above. Records and maps of tsetse flies and their distribution in the Sudan are well documented (Elkarib, 1961 and Razig and Yagi, 1973) and changes in fly belt with a northward spread beyond the previously was noted (Yagi and Abdel Razig, 1972). Two distinct zones are recognized viz the tsetse fly zone and tsetse free zone. The tsetse zone covers an area of about 90,000 square miles, which lies south of a diagonal line extending from the point on the western border at 10° north parallel to a point on the Southern border at 32° longitude.

Tsetse infested area in Sudan, where owner’s spend the dry season, is estimated at 250,000 km² in South Western Sudan (Razig and Yagi, 1973), Jur narrow (Yagi and Razig, 1972).

Lewis, (1954) reported seventy species of tabanidae flies and Yagi (1968) added four species, *Atylotus agrestis*, *A. fuscipes*, *T. taeniola*, *T. sufis*, *T. biguttatus*, *T. gratus*, *philoliche magretti*, *Ancala latipes* and *A. africana* were the main species known in Sudan (Razig and Yagi, 1975 and Khier and Majid, 1999).

Mechanical transmission by tabanids and their contribution to the seasonal outbreaks to of *T. evansi* infections are well outlined (Yagi and Abdel Razig, 1972; Mahmoud and Gray, 1980). Results of surveys on tsetse and trypanosomal infection and their rates in Darfour, Kordofan, Eastern Region, and Central and Southern Sudan were reported (Hall et al., 1983 and 1984).

A camel normally live immediately north of the cattle zone and biting flies chiefly tabanids and the zone where this combination exists extends from 15th north parallel on the west to 18th north parallel on the east. North of these line camels exist but no flies occur and south of the cattle zone flies are abundant but normally no camels live there (Elkarib, 1961) and it was between lat. 13°-18°N in (Kheir et al., 1999) report.
Southern Darfur province is situated on the northern edge of the main African tsetse belt and was first surveyed by Yagi and Abdel Razig (1972) who captured tsetse north of these assumed limits. The seasonality of tsetse catches at Radom on the Bahr ElArab (9° 47’ N, 24° 47’ E) and female tabanids at the provincial capital Nyala (12° 02’ N, 24° 53’ E), at Radom and at Qoz Dango up to about 10° 15 N, a line from Birka Khadra to Fereidi to Gileizan were determined by examination of monthly records. The greater densities are found in the South-west of the province particularly along and south of the Wadi Umbelasha. Flies were not found around the area of umm Dafog nor at several camps southwards along the Wadi Khadra until Birka Khadra. (Hall, et al 1984)

Tabanids have long been considered as pests of cattle in Sudan (Lewis, 1953). In southern Darfur the tsetse fly as a vector of tryanosomosis it is more important than tabanids (Lewis, 1953).

Bovine trypanosomaisis is mainly a problem of mechanical transmission by the genera tabanids, stomoxys and possibly others. The main cattle-rearing zone lies north of the tsetse zone, in Bahr El Gazal, Darfur, Kordofan, Upper Nile and the Blue Nile province (Elkarib, 1961). T. congolense occurs throughout, and in areas just north of, the tsetse zone. It may also occur in areas further north. T. vivax occurs in the tsetse zone and extends further north than T. congolense east from parallel 15th north on the east T. brucei affects cattle in the tsetse zone and possibly immediately north of it and in the later case it is probably of tsetse origin. Outside the tsetse zone T. congolense widespread in Bor, Central Nuer Province and Malakal district of the Upper Nile province. T. brucei is commonly found in tsetse areas and T. vivax outside the tsetse zone. (Elkarib, 1961).

In the study of Kheir et al. (1992and 1995) along Sudan Ethiopian border in an area from Khor Yabous (lat.9° 45’ long 43° 10’) in the South to River Setit in the North included areas of Rivers Rashad, Dinder, the Blue Nile and Kurmuk district, in this survey G. morsitans and G. fuscipes were
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

found except in North El-Kurmuq and the Bank of the Blue Nile Dinder, Rashad and Setit River. Also *Tabanus taeniola, T. gratus, T. biguttatus, A. agrestis* and *A. fuscipes* were found.

No pathogenic species were detected in several hundreded specimens of blood samples examined but only a few nonpathogenic species were seen. (Elkarib, 1961).

Lewis (1954) reported two species of Stomoxys in Sudan *S. cacitrans* and *S. nigra*. The peak of this fly coincides with high trypanosomosis incidences (Mohamed *et al.*, 1989 and Mohamed, 1989). They are three speics of Haematobia. The Hippoboscidae is wide spread in the Sudan but not well studied(Kheir and Majid, 1999).  

1.8 Importance of the animals in Sudan

Sudan has an immense animal wealth, which satisfies all local needs of meat and produces an export surplus constituting 20% of foreign currency earnings. It satisfies 80% of total milk needs in Sudan. (AOAD, 1992).

In the Sudan people are dependent on animals as a first source of food, milk and foreign currency. The population of the livestock in the Sudan was 128,523,000 animals (3,342,000 head of camels, 41,485,000 head of goats, 48,136,000 head of sheep and 39,479,000 head of cattle and 370,056,000 head of poultry). (MARF, 2002). The greater number was found in Blue Nile state (11,642,942 head of animals), then Western of Darfur state (10,753,521 head of animals) and Southern Darfur state (10,155,074 head of animals)(MARF, 2001).

The exported livestock was (155,710,000 head of camels, 53,164,000 head of goats, 160,263,800 head of sheep and 2,655,000 head of cattle), the exported of meat was (6.6 ton of camels, 353.8 ton of goats, 347.1 ton of sheep and 7113.8 ton of cattle)(MARF, 2002). The production from meat was 1628 ton, 7298 ton of milk, 60 ton of fish, 18 ton of poultry meat, 22 ton of eggs and 60 ton of hide and skin.(MARF, 2002). The gross domestic product was 16088S.D at constant prices of 1981-1982(MARF, 2002). It is well
known that diseases have a negative influence of feed intake, growth rate and body gain, production and feed conversion efficiency.

1.9 The economy of trypanosomosis

The habitat of the dromedary camel is Northern Africa (The Mediterranean) the Sahelian States of West Africa, Sudan, Ethiopia, Somalia and Northern Kenya (Wilson, 1984). The camel has been used as a pack animal by Northern Arabian tribes since 3000 BP; the South Arabian tribes used it as a source of milk.

In general terms, the camel is considered as an animal of the tropics but, much of the present day normal range is extra-tropical. World total of 15 million camels about 20% spread thinly over a vast area not found within the tropics (Wilson, 1984). Somalia and Sudan contain about 50% of all old world Camelidae and 55% of all dromedaries. In Africa these countries account for 70% of camels, while Ethiopia, Chad and Kenya contain a further 12.5%. Apart from these countries Mauritania, Niger and Mali has important camel populations (as de Maghreb countries) (FAO, 1978). Sudan has the second largest number of camels in the world and almost 1.5 million km² of territory suitable primarily or solely for their raising. The proximate southern limit suitable for breeding is about 14°N in the west (in Darfur and Kordofan) and about 16°N in the east. Seasonal movements take camels considerably to the south of these limits, in ever increasing number and over longer distances. The common classification of camels is into riding and pack types. It should be remembered that camels are the basis of the family economy over very large areas and for a considerable number of people (Wilson, 1984). They are most important as a source of meat, for human consumption, source of milk and for export. Economically, and probably
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

ecologically a family might do better to sell protein (meal) and fat and buy in exchange energy (grain) to fulfill its annual food needs, hides, wool, hair and work (Wilson, 1984). In modern world, after some 40 to 50 centuries of domestication, the camel seems to be an anachronism.

Trypanosomosis is by far the most important protozoan disease of camels and is probably the most important health problem of all. The chronic form of the disease is a more common than the acute. The acute form commonly affects the adults. Real immunity is never acquired although premunition may be attained through dams. An infection level of 20% in areas where the disease occurs is not uncommon and up to 70% is common.

Death may reach 3%, declining milk production; abortion and chronic poor condition are the classic symptoms of the disease in camels (Wilson, 1984). An estimated 50 million cattle constituting 30% Africa total cattle are exposed to the risk of infection (FAO, WHO, OIE, 1982 and Murray and Gray, 1984). Due to this widespread incidence of this disease, Africa produces about 70% less animal proteins per hectare than Europe (ILRAD, 1987).

Wild animals can also be infected with trypanosomes but generally adversely they do not suffer from it. They serve instead as reservoirs as the source of infection. Goats and sheep become infected with various species of pathogenic trypanosomes when kept close to infected cattle (Lewis, 1949) or to infected camels (ElKarib, 1961).

There are direct and indirect impacts on trypanosomosis in Africa. The direct impacts are aggregated into three groups: impacts on livestock productivity, impacts of migration and settlement and impacts on livestock management. The indirect impacts are aggregated into four groups: crop
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

production, land use, ecosystem structure and function and human welfare. Animal trypanosomosis has serious economic consequences including the loss of meat and milk protein to the population, a subsequent demand for imports of dairy products, further potential export earnings. Agricultural communities are denied the benefits of draught animals, in addition the concentration of cattle as a result of overgrazing and subsequent erosion. There are also the costs of treatment and planning, execution and evaluation of vector control program (Uilenberg, 1998). In Sub-Saharan Africa for example, in addition to the enormous direct losses, more than US $20 million are spent per annum on trypanocides, accounting for 44% of the total expenditure in veterinary drugs (Solano et al., 1999).

1.10 Trypanosomosis in different animals

The parasite *T. evansi* causes Guffar in camels, commonly known as Surra (Wilson, 1984) Nagana in livestock mainly cattle, sheep and goats is caused by *T. vivax*, *T. congolense* and *T. brucei*. *T. equiperdum* causes dourine and *T. equinum* causes mal de caderas. (Soulsby, 1982)

1.10.1 Trypanosomosis in camels

In camels *Trypanosoma evansi* causes a disease known as Guffar in Sudan. Commonly the disease is known as Surra, can result in infection rates of 20%, in affected areas. In some instances infection may be as high as 70% have been detected (Wilson, 1984). The disease in camels is usually chronic, and is characterized by recurrent pyrexia and anaemia. In *T. evansi*- infected camels an acute form is also reported (Bujon, 1990).

1.10.2 Trypanosomosis in goats and sheep
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

The disease in small ruminants is caused by the *T. congolense*. Infection and disease, however, are known to occur in both West and East Africa. Pecaud, (1909; 1910) recorded a 1.3% incidence of infection by the *T. congolense*, *T. vivax* and *T. evansi* in a large number of animals. In a more recent but much smaller survey, 13.8% were infected with either *T. congolense* or *T. vivax* (Kramer, 1966). Mornet, (1954) considered that goats and sheep made up 4% of all the animals infected with *T. congolense*. Lewis, (1949) reported that goats could be infected when kept close to infected cattle. None of 381 blood smears and none of the 187 sera (109 goats, 78 sheep) were positive in south Mauritania (Jacquiet *et al.*, 1993).

There is no detailed information on the distribution of the disease in small ruminant (Bruce *et al.*, 1910). In Africa, about 9-10 million km$^2$ is Savannah (Atang, 1982).

There are reports on the incidence of infection in sheep with *T. congolense*, *T. vivax* and *T. Brucei* of 2.5% (Pecaud, 1910), 10.4% (Delonoe, 1914) and 17% (Krampitz, 1970) respectively.

1.10.3 Trypanosomosis in cattle

Pathogenic species affecting cattle are *Trypanosoma congolense* (*T. congolense*) and *T. vivax* and they have a significant impact on cattle production. The landmass of Africa, south of the Sahara, over which tsetse flies are distributed, and which is virtually devoid of cattle because of trypanosomosis, is about 4 million square miles. It is estimated that if this area is reformed, 125 million cattle could be raised, and this would be more than double the present cattle population of Africa. *T. congolense* produces the most important form of animal trypanosomosis in East Africa, *T. vivax*
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) causes trypanosomosis in West Africa. (Wilson et al, 1963). Natural infections with *T. brucei* are common, and an incidence of 20 to 30% has been reported in West Africa in both zebu and humpless cattle. Infections are usually mixed with *T. congolense* and *T. vivax*, which are present in larger numbers than *T. brucei*. Cattle can naturally be infected with *T. rhodesiense* (Onyango et al, 1966), *T. gambiense* was less infective than either *T. brucei* or *T. rhodensiense* (Kleine and Fischer 1911) and with *T. evansi* in South America, India and South East Asia (Atange,1982).

1.10.5 Trypanosomosis in wild animals

Wild animals can also be infected with trypanosomes but generally; they do not suffer from the disease. They serve as the source (reservoir) of infection from which the trypanosomes are transmitted to the domestic animals by several species of tsetse flies and by other biting insects (Atange,1982).

1.10.6 Trypanosomosis in other animals

There are very few descriptions of either infection or disease in the horse (Hornby,1952).

West African donkeys and horses make up 8% of the animals infected with *T. congolense* and 10% with *T. vivax* (Mornet, 1954). *T. brucei* causes an important and severe disease, which is considered to make up 48% (Mornet, 1954) , *T. evansi* in horses in South America, India and South East Asia (Atang,1982). *T. evansi* effects in Asia and horses and domestic buffalo in South America, India and South East Asia (Atang,1982).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Mornet, (1954) reported that dogs and cats make up 2% of the animals infected with *T. congolense*. No reports exist about natural infection with *T. vivax* (MacFie, 1913) and 48% with *T. brucei* (Mornet, 1954).

No record of natural infection in monkeys (Bruce *et al*., 1910) but can be infected with *T. brucei* (Bruce *et al*., 1911).

In rodents, infection with *T. brucei* and *T. rhodesiense* was different from that of *T. gambiense* and no natural infection with the other species. (Andrews *et al*., 1927).

1.10.7 Infection with mixed species

Mixed infections by *T. congolense*, *T. vivax* and *T. brucei* are very common in cattle than in other species. (Mettam, 1933; 1934)

1.10.8 Trypansomosis in human (Human sleeping sickness)

There are two subspecies of *T. brucei*, which cause chronic sleeping sickness in West and Central Africa *T. brucei rhodesiense*, which causes acute sleeping sickness in East Africa and *T. brucei gambiense*. They are transmitted to humans by the various species of Glossina (tsetse). Molyneux *et al*. (1984) indicated that, in the sleeping sickness the disease was characterized by three stages, the chancre in the primary lesion of the site of the infection seldom in *T. b. gambiense* disease(stage one), haematolymphatic and meningoencephalitic stage(stage two) and the severity of the pathological lesions that arise during the haematolymphatic stage (e.g. anemia, immunodepression and IgM and IgG hyperglobulinaemia) only partly correlates with the level of parasitaemia (stage three)( WHO, 1998).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Sleeping sickness was first recorded from Nimuli in 1915. Different areas in Southern Sudan were known as endemic foci. It had been predominantly of the Gambian type and has always been maintained by the palpalis group of flies particularly *G. fuscipes*, the major vector of *T. b. gambiense* (Hutchinson, 1975; Snow, 1983).

The sleeping sickness is found only in Sub-Saharan Africa between latitudes 14°N and 25°S, within the limits of the geographical distribution of the tsetse. There are around 200 discrete endemic foci in 36 countries so, 60 million people are at risk with an estimate of 300000 new cases each year (WHO, 1998).

### 1.11 Diagnosis of Trypanosomosis

#### 1.11.1 Parasitological examination

##### 1.11.1.1 Microscopic examination

There are four methods of microscopic examination of trypanosomosis: viz examination of:

1. fresh drop of blood under cover slip (wet mount).
2. stained thin
3. thick blood film

##### 1.11.1.2 Microhaematocrit centrifugation (m-HCT) technique

Capillary tube centrifugation or microhaematocrit centrifugation (m-HCT) was described by Woo (1970) as a rapid and reliable method when parasitaemia was low. It was satisfactory for *T. brucei* subgroup, while it was not sensitive for *T. congolense* (Walker, 1972).
1.11.1.3 Aspiration technique

Lymph node aspirate and cerebrospinal fluid examination are widely used in the diagnosis of human African trypanosomosis at a magnification of 10x40. Examination of the cerebrospinal fluid is used to determine the stage of the disease. Parasites can sometimes be seen in the cerebrospinal fluid. Examination of the deposits after a single centrifugation increases the likelihood of finding trypanosomes but the double centrifugation technique is substantially more sensitive (WHO, 1998).

1.11.1.4 Biological examination

Inoculation of animals especially rodents was of some diagnostic value.

1.11.1.5 Biochemical tests

There are two types of tests first one for animals trypanosomosis this chemical tests depend on increased serum globulin and it is used for T. evansi infection they are include the mercuric chloride test (MCT) (Bennett and Kenny, 1929), the formol-gel test (FGT) (Plantureux, 1923) and the thymol turbidity test (TTT) (Abdel Gaaffar, 1960).

Second one for sleeping sickness, they are including the dye binding protein assay (WHO, 1998) for the second stage infection of human African trypanosomosis, which is characterized by an increase in protein content of the cerebrospinal fluid. Lejon et al. (1999) detected light subunit neurofilament (NFL) and glial fibrillary acidic protein (GFAP) in cerebrospinal fluid of patients infected with T. b. gambiense.

1.11.1.6 Serological tests
Serological test or diagnosis is of great help when few parasites are present in the body fluid of infected host (WHO, 1979). It is assessing the level of circulation antigen and/or antibodies including complement fixation test (CFT) (Schoening, 1924 and Sabanshiev, 1973), indirect haemoagglutination test (Jatkr and Singh, 1971), precipitation test, latex fixation test (Mohamoud and Kreier, 1972), indirect immunofluorescent antibody test, enzyme linked immunosorbent assay, capillary tube agglutination and indirect immunofluorescent antibody (Sabanshiev, 1973; Wilson, 1969; 1979).

Parasite DNA detection technique, has a high sensitivity and specificity when coupled with amplification of the DNA by the polymerase chain reaction (PCR) it is used for research purposes only at present (WHO, 1998).

1.12 The pathogenesis of trypanosomosis

The success of the trypanosomes as pathogens is due to their ability to undergo antigenic variation; this enables them to establish persistent infection by evading host immunoresponse (Solusby, 1982).

The prepatent period is 3 – 5 days in *T. evansi*-infected goats (De-Villa et al., 1991) 2 – 30 days Elmalik, (1983) 4 – 9 days Fairouz, (2000) in *T. evansi* infected goats and 4-5 days in *T. vivax* (Kyewalabye et al, 1988). In both goat and cattle infected with *T. vivax* parasitaemia was detected 6-7 days after inoculation with $1 \times 10^5$ but not in *T. congolense* infection (Maxie et al., 1979).


In infection of goats with *T. evansi* loss of body weight were noticed Elmalik (1983), Mutayoba et al. (1989), Negeranwa et al. (1993) and Fairouz (2000).

Amodu and Ige, (1975) elucidated the mechanism of development of anaemia in rabbits experimentally infected with *T. brucei* and concluded that the anaemia is possibly a
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)
result of an auto reaction together with anaemia and specific organ damage, a wider range
of immunological abnormalities appear to character the pathology of the disease.

Pyrexia, inappetance, respiratory and pulse rate and anaemia were observed in trypanosomosis *T. evansi* infected goats (Elamin, 1980). Emaciation, rapid loss of body condition, scrotal swelling, kertitis, nervous signs followed by prostration and death was observed in goats infected with *T. evansi* (De-Villa *et al.*, 1991 and Fairouz, 2000). In addition muscle wasting, lethargy and paleness of mucous membranes was observed in Olaho *et al.* (1996) Lacrimation, shivering, weakness, diarrhea, weak respiratory and pulse rate and in some animals muscle spasm, neck back position, nasal discharges and nervous signs followed by death while others animals showed nasal discharge and loss of hair. (Fairouz, 2000).

(Elamin, 1980) noticed haemorrhages and congestion in the lungs, liver, spleen, kidney and brain of infected *T. evansi* goats. The pericardial sac contained straw coloured fluid and pulmonary emphysema and congestion were seen in some infected groups.

Yesufu, (1975) exposed pregnant female rates infected with *T. brucei*, *T. congolense*, *T. gambiense* to various stresses and noted a high rate of abortion and only two litter survived, also Amdou and Ige, (1975) observed that infection with *T. vivax*, *T. congolense*, *T. brucei brucei* and mixed infection had a severe effect on the fertility of the cattle.

West Africa Dwarf goats were allotted to a diet of Lucerne pellets or a diet of chopped grass straw, and infected with *T. vivax*, caused an increased weight of the liver and prescapular lymph nodes in animals from both feed treatments, but lymph nodes were more enlarged in infected animals that had been fed Lucerne (Dam *et al.*, 1998b).
Enlargement of lymph nodes, spleen, liver and oedema of the lung, kidneys, flabby heart, accumulation of sero-sanguineous fluid in the peritoneal, thoracic cavity, and pleura and intestinal-mucosa oedematous brain, brain congestion and meningial petechiation was observed in *T. evansi* infected goats (Olaho *et al.*, 1996). Fairouz (2000) studied *T. evansi* infected goats treated with Cymelarsan®, Cymelarsan® OTC treated goats. Enlargement of spleen, kidneys lymph nodes oedema in lungs and kidneys, flabby heart, petechial haemorrhage on the serosa, pleura, and intestine, congestion in brain, emaciation and serous atrophy of fat, hydropericardium, pseudocysts were observed in the infected group. In addition multifocal encephalitis, pesudocysts in the cortex of cerebral and cerebellum, whereas, it was absent post-treatment.

Focal degeneration of the myocardial fibers and haemorrhage were seen, liver congestion, mononuclear wall infiltration especially around blood vessels, Cytoplasmic fatty vacuolation of the centrilobular hepatocyte, deposits of haemosidrin in the hepatic sinusoids and red pulp and haemorrhage, mononuclear cell infiltration was more prominent in the interstitial tissue of the kidney, increase in the number of endothelial cells and mild cellularity in the renal glomeruli, haemorrhage, degeneration of cells of the proximal convoluted tubules, and its human contained desquamated epithelial cells, lung congestion and increase in the number of endothelial cells of alveoli were observed in Elamin (1980) on *T. evansi* infected goats. No apparent structural damage in the thyroid gland observed in *T. conglense* infected cattle (Abebe and Eley, 1992). In female goats the thyroids glands were extensively degenerated and atrophied (Mutoyoba *et al.*, 1988).
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Negeranwa et al. (1993) studied the histological changes in goats infected with *T. evansi* and found lymphatic tissue hyperplasia, muscular atrophy focal necrosis foci in the liver, kidney, spleen and lungs and also bronchopneumonia. There was a decrease of lymphocytes in lymphatic tissues, destruction of hepatocytes. Infiltration by inflammatory cells was been in the liver, spleen and kidney.

The pathology of *T. vivax* in East African goats Frisian cattle showed major changes in the lymph nodes, spleen, eyes, pituitary gland, testicles and heart (Masake, 1980).

*T. vivax* infected cattle showed fever, increased in heart rate, anorexia, emaciation, elevation of body temperature, anaemia, leukopenia and thrombocytopenia (Maxie et al., 1979).

The acute form of *T. vivax* infection in mice was characterized fibrin thrombus formation in the blood vessels of heart, lung, spleen and brain (Anosa and Isoun, 1976).

Anaemia, muscle mass atrophy, generalized oedema and petechial to ecchymotic haemorrhages, swollen oedematous lymph nodes, oedema in lung, spleen, proliferative interstitial pneumonia and lobular pneumonia, were seen, hyperplasia of the bone marrow, localized extra medulary hemopoiesis, haemosiderosis in various organs, and monoclear cell infiltration in the heart and skeletal muscle were observed (Anosa and Isoun, 1976).

Increase in blood plasma volumes and decrease in RBC and PCV values indicating anaemia were observed in *T. vivax*-infected goat and sheep (Anosa and Isoun, 1976).

*T. vivax* and *T. congolense* infection caused significant fall in Hb, PCV and RBC values and slight reduction in WBC (Ugochukwu, 1986).

Certain indigenous breeds of cattle in west and Central Africa can also better tolerate exposure to trypanosomosis (Murray et al., 1982). There is also evidence for similar breeds in East Africa e.g *Orma boran* (Njogu et al., 1985). These naturally resistant (trypanotolerant) livestock breeds offer a potential means for improving agricultural productivity in tsetse-infested areas of
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Africa. It has been shown both in field and experimentally, that trypanotolerant cattle are capable to varying extent of resisting the pathogenic effects of trypanosomosis (Murray et al., 1982), they remain productive despite the infection and often spontaneously recover from infections. There is another breed of cattle from West Africa, the N’Dama, which is known to be naturally resistant to effects of trypanosomosis (Paling et al., 1987). Even under field conditions trypanotolerant livestock can be productive under trypanosome challenge depending on nutrition status (ILCA, 1979).

Serum potassium level was decreased in camels infected with *T. evansi* (Anosa, 1988b) and also in infected *T. evansi* goats. (Fairouz, 2000) while no changes recorded in serum sodium level were seen post infection (Anosa, 1988b, Otsile et al., 1991; Fairouz, 2000).

The serum calcium was normal in acute *T. rhodesiense* infection of mice, but reduced in *T. evansi* infection of camels and buffalo calves and during relapse in *T. congolense* in cattle (Anosa, 1988b) and decrease in *T. evansi* infected goats (Elamin, 1980 and Fairouz, 2000).

The serum phosphorus was decreased in *T. evansi* infection of camels and goats (Fairouz, 2000). *T. congolense* infection of cattle and it was normal in *T. rhodesiense* infection of mice and *T. evansi* infection of buffalo calves (Anosa, 1988b).

A depletion of zinc and copper values was obtained in six New Zealand white rabbits infected with *T. b. brucei*. Also, in *T. evansi* infected goats.

Plasma levels of iron and zinc were measured in *T. vivax* and *T. congolense* infected goats. They declined post-infection the reduction being
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) much less pronounced as compared with the values found with, bacterial pyrogen – induced fever (Amole et al., 1990 and Fairouz, 2000).


Serum globulin levels were increased post-treatment in infected goats (Igbokwe and Mohammed, 1992; Dam et al., 1998a) and in infected sheep and goats (Anosa, 1988b). However, it was decreased post-infection (Kalu-Au et al., 1989; Arunsi et al., 1989; Otsile et al., 1991 and Fairouz, 2000).

Raina et al. (1988) observed in 24 male buffalo calves infected with T. evansi, blood urea nitrogen values were significantly increased in one group and decreased in the two other infected groups, also in goats subjected to restricted feeding regimen of pelleted Lucerne and infected with T. vivax (Dam et al., 1997). It was lower in infected goats with T. vivax (Dam et al., 1998a), and with T. evansi (Fairouz, 2000).

In T. brucei infected goats no significant changes were seen in the serum creatinine (Igbokwe and Kohammed, 1992). In goats infected with T. vivax serum creatinine concentration was higher in grass straw fed than in Lucerne fed animals, infected animals had a lower creatinine levels post-infection (Dam et al., 1998a). In infected T. evansi goats it was lower in Cymelarsan® and Cymelarsan® OTC treated groups (Fairouz, 2000).
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In *T. evansi* infected goats they positive for ketone bodies test (Fairouz, 2000).

The serum alkaline phosphatase was increased in *T. cruzi* infected dogs (Barr-s *et al*., 1986), also, in *T. evansi* infected goats (Fairouz, 2000). The serum bilirubin concentration in *T. evansi* infected goats was increased post-treatment with Cymelarsan and Cymelarsan-OTC(Fairouz, 2000).

The serum aspartate amino transferase (AST) and alanine amino transferase (ALT) activities was increased post-infection in infected donkeys (Aliyu *et al*., 1997), and in infected *T. evansi* goats (Fairouz, 2000). Infection with *T. congolense* in cattle caused hypothyroidism (Abebe and Eley, 1992), also, infection with *T. vivax* in goats (Dam *et al*., 1998a) and in infected *T. evansi* goats (Fairouz, 2000).

The serum progesterone was lower in ewes infected with *T. congolense* (Osaer *et al*., 1998) and in infected *T. evansi* goats (Fairouz, 2000).

The leukocytes counts were normal pre, post infection (Elamin, 1980; Elmalik, 1983; Damayanti *et al*., 1994); were reduced in infected cattle (Naylor, 1971b). In Moulton and Sollod (1976) study it was increased early in infection in calves, also in Fairouz, (2000) study in infected *T. evansi* goats.

The basophils and eosinophils cells disappeared post-infection in infected goats (De-Villa *et al*., 1991 and Fairouz, 2000). Monocytes levels showed little change post-infection (Naylor, 1971b; De-Villa *et al*., 1991) two groups of five showed monocytes post-infection with *T. evansi* in goats (Fairouz, 2000). Lymphocytes disappeared from the circulation post-infection (De-Villa *et al*., 1991) it was decreased during the infection.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) (Fairouz, 2000). Neutrophils count were depressed (Naylor, 1971a) whereas, De-Villa et al. (1991) observed sudden increase, also increase were seen in Fairouz, (2000)

In infected *T. evansi* goats there was a greater reduction in RBC counts (Elmalik, 1983; De-Villa et al., 1991; Fairouz, 2000).

There was a drop in PCV values in goats post-infection (De-Villa et al., 1991; Negeranwa et al., 1993; Elamin, 1980; Elmalik, 1983, Mutayoba et al., 1989; Dam et al., 1998b and Fairouz, 2000).

There was a decline in Hb levels post-infection (Naylor, 1971a; Elamin, 1980; Damayanti et al., 1994 ; Fairouz, 2000).

No clear difference in Mean corpuscular volume (MCV) was observed between infected and control buffaloes (Damayanti et al., 1994). Whereas, there was a decrease in MCV post-infection in buffalo calves infected with *T. evansi* (Raina et al., 1988 ; Fairouz, 2000).

No changes were observed in Mean corpuscular haemoglobin (MCH) post-infection in infected *T. evansi* buffaloes (Damayanti et al., 1994). It was decreased in infected *T. congolense* cattle (Naylor, 1971a) and infected *T. evansi* buffalo calves (Raina et al., 1988). But it was increased in *T. evansi* infected goats (Elamin, 1980 and Fairouz, 2000). Mean corpuscular haemoglobin concentration (MCHC) was normal infected *T. evansi* buffaloes calves (Raina et al., 1988).

1.13 Drugs

Parasitic protozoa are responsible for a wide range of diseases in both animals and man, diseases which are of world importance but are difficult to eliminate as these are frequently transmitted by ticks, tsetse flies and tabanids which abide in many of the under developed parts of the world.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Wide ranging research for new drugs in the area of protozoa control, apart from coccidiosis, is inhibited by the absence of any financial incentive; without WHO or FAO financial support it is difficult for pharmaceutical companies to justify the very large research effort that is necessary to support both the basic research and the large-scale field trials. In addition the drugs used in the field of trypanosoma, babesia and histomonas control are frequently chemically unrelated.

Generally four groups of antitrypanosome were used: Dimidines compounds (Diminazine aceturate -Berenil, phenanmidine, isothionate, stilbomidine and pentamidine), Aminophenanthridium compounds (homidium bromide, homidium chloride and isometamidium chloride), quinapyramine compounds (quinapyramine chloride, quinapyramine sulphate and quinapyramine prosalt (chloride and sulphate)) and others compounds (Suramin, Samorine, Nitrovinylfuran, some arsenical compounds (Melarsorpol and Cymelarsan) and antipyrtic agents). (Bywater et.al. 1991).

1.13.1 Chemotherapy of trypanosomosis

Chemotherapy is the treatment of disease by the use of chemical drugs. Such drugs are curative. They disrupt or block one or more of the vital processes which are essential to the invading micro-organism. Certain compounds have specific effects on some enzyme system or block essential metabolic pathway, but the exact way in which they work is often not known or only incompletely understood, and this is true of most of the trypanocides (chemotherapeutic drugs which kill trypanosomes or inhibit their development).

Chemotherapeutic drugs are toxic to the trypanosome, because they interfere with one or more of its vital processes. An ideal drug is one which kills the parasite but, at the same time, causes no or minimal harm to host cells. The toxicity of drugs differs in different species of the animals.

The application of antitrypanosomal drugs has been the mainstay of controlling animal trypanosomosis since the early 1950s (Kinabo, 1993). It is important to release that drugs alone will not treat trypanosomosis. Trypanosomosis overwhelm the immune system of the host, they are
immune suppressive. Chemotherapy, by stopping the multiplication of the trypanosomes helps the immune system to overcome the infection. Treatment will be more effective in well-fed and rested animals, in which the immune system is not adversely affected by stress and lack of food. The management of African animal trypanosomosis (AAT) at farmer’s level has been predominately dependent on the use of the trypanocidal drugs (Diminazine, Homidium and Isometamidium). It is estimated that, about 35 million doses per year are used in Africa to cure the disease (Geerts, Holmes, 1997).

There is another problem in the treatment of animal trypanosomosis, because of the variety of domestic livestock, which are susceptible to trypanosome infection and the diversity of trypanosome species, which are pathogenic to animals of economic importance.

The problems of chemotherapy and chemoprophylaxis are even more complicated and formidable than human trypanosomosis (Muligan, 1970). Other complimentary measures aimed at tsetse eradication using insecticides have been successful only to a limited extent. Despite the fact that chemotherapy is the major means of disease controls.

Development of new anti-trypanosomal drugs have been more or less static over the last three decades, due to lack of interest by the pharmaceutical industry to invest into research and development of anti-trypanosomal drugs (Gutteridge, 1985). Consequently, this has been a major stimulus to intensive research into the few existing drugs. It is well known that developing an effective drug for chemotherapy of protozoan infections and particularly effective against *T. brucei evansi*, is a difficult task (Bourdichon and Zhang, 1999). *Trpanosoma evansi* is an economically
important; infection affecting a variety of domestic animals such as horses, cattle and camels (Lun et al., 1993).

1.13.2 Quinapryamine (Antrycide)

1.13.2.1 Chemistry and mode of action
It is available as the chloride and as methyl sulphate, the latter being quickly absorbed and the chloride slowly absorbed from sites of injection. It was introduced in the 1950s for field use as a therapeutic (Antrycide sulphate\textsuperscript{R}) and prophylactic drug (Antrycide prosalt\textsuperscript{R}) for animal trypanosomosis chemistry. It is 4 – amino – 6(2 – amino – 6 – methylquinoline – 1, 1 di – metho) (methyl sulphate) (C\textsubscript{19}H\textsubscript{28}N\textsubscript{6}O\textsubscript{6}S\textsubscript{2}, molecular weight 532.6) (Curd and Davey, 1950). Quinapyramine inhibits the groth and cell division (Alexander, 1985).

Its local name in Sudan (Eljazy) and (Elroby) for quinapyramine chloride and quinapyramine sulphate respectively.

1.13.2.2 Adverse effects and toxicity
Severe and immediate general reaction resulting in collapse is of common occurrence when the drug is administered to horses; these symptoms usually subside after a short time but are sometimes fatal (Mulligan, 1970). It is advisable a suitable antidote at hand and to divide the amount of the drug into two or three equal doses at six hourly intervals subcutaneous, at different sites. This will also reduce the tendency to abscess formation at the injection site (Mulligan, 1970).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Quite severe and sometimes fatal general reaction may sometimes be seen in dogs with doses in excess of 4.5 mg/kg (Mulligan, 1970). However, due to the development of drug resistance, the drug was withdrawn from the market in many parts of Africa in the 1970s, in cattle trypanosomosis and is associated with cross resistance to the other entire trypanocidal drugs in use (Uilenberg, 1998). It is now produced for treatment of surra in camels and horses, where there is resistance of *T. evansi* to suramin.

1.13.3 Amino Phenanthridium compounds

1.13.3.1 Homidium bromide (Ethidium)

1.13.3.1.1 Chemistry and mode of action

It is known as Ethidium bromide (Homidium bromide) and is 3,8 diamino – 5 ethyl – 6 phynyl – phenantheridium bromide. It is dark purple, almost odourless crystalline or amorphus powder with persistent bitter taste and is available as the bromide salt. Solution is stable for several days at 20°C. And it must be difficult in hot or boiling water, but this practical disadvantage was overcome by the use of the chloride salt of the drug (NovidiumR), which is soluble in cold water. It’s mode of action not understood; the compounds are fixed by the trypanosomes in small amounts. This small amount inhibits the factor required for division of the trypanosomal cytoplasm. When the store of this factor has been exhausted, the trypanosomes cease to multiply and disappear. They are active mainly against *T. congolense* and *T. vivax* (Alexander, 1985). Its local name in Sudan is Alhabba Alhamraa. It has been used primarily as a curative drug in cattle, intramuscular injection was advised by the manufactures (Bailey, 1967). On the basis of trials in the Sudan, Kenya, Tanganyika and Nigeria against *T. congolense* and *T. vivax* a therapeutic dose of 1.0 gm/kg was recommended (Leach and Ropers, 1981). Kalu *et al.* (1983) observed complete disappearance of trypanosome from the blood 3days after treatment with homidium bromide. Mwambu, (1975) re-evaluated the value of ethidium for the treated of *T. brucei* subgroup infection in cattle and concluded that the use of this drug as a curative in *T. brucei* infection of cattle should be restricted.
De-Deken et al. (1989) have reported success in protecting rabbits for more than 300 days against seven challenges of *T. congolense* use a slow release device implanted subcutaneously, this finding suggests that the commonly used drug products, lack prolonged prophylactic activity because the active principle, homidium is rapidly eliminated from the body, should this field it will undoubtedly be widely accepted in many areas with a yearlong high incidence of trypanosomosis (Kinabo, 1993). The period of protection recorded in South West Kenya was 4 – 6 weeks over twelve months (Stevenson et al., 1995).

Infected Zebu cattle with *T. vivax* and *T. congolense* and treated 12\textsuperscript{th} week post infection with Novidium and slaughtered for histological evidence of healing of the genital lesions (Sekoni, 1990).

### 1.13.3.1.2 Adverse effect and toxicity

Sings of acute toxicity were reported in several countries such as photosensitivity, necrosis and sloughing of extensive areas of unpigmented skin, followed by death. Severe local reaction can result from subcutaneous injection, so that deep intramuscular route should be used, when local swellings and allergic reaction were observed. Dividing the dose between two sites may also reduce the local reaction in the horse (Stephen, 1963).

#### 1.13.3.2 Isometamidium chloride (Samorin)

It is used against *T. brucei*, *T. vivax*, and *T. congolense*. It shows its effect after latent period of trypanosome division. Also it is used for prophylaxis for six to eight months (Alexander, 1985). Kalu et al. (1983) observed complete disappearance of trypanosome from the blood 3days after treatment with samorin. It causes weight loss in poorly nourished cattle if administered at short months intervals.

#### 1.13.4 The Diamidines

They are as equally effective trypanocide *in vitro* thus demolishing the hypothesis of trypanocidal activity being related to hypoglycaemia. They are not well absorbed from the gut. The toxic effect is attributed to involving the CNS. It has been used against *T. congolense* and *T. vivax* (Alexander, 1985). Kalu et al. 1983 observed complete disappearance of trypanosome from the blood 3days after treatment with berenil. Cattle treated with diminazine aceturate after several isometamidium treatments suffer from hepatic damage and may even die.

The diminazine aceturate in Sudan is known as Berenil.
Suramin

It is a polyanionic drug that has been used for Africa trypanosomosis before CNS involvement. It causes skin rashes, gastrointestinal distress, and neurological complications. (Bentram and Anthony, 1993). It is known as Naganol in Sudan and used against *T. evansi*, *T. brucei*, *T. equinum* and *T. equiperdum*. It shows its effect after latent period of trypanosome division. Also it used for prophylaxis for six months (Alexander, 1985).

Use of arsenical compound in veterinary medicines and as a trypanocide

The first widely used member of the Melaminyl Thioarsentie family was Arosbal® as a combination of melarsenoxide and dimercaptopl BAL (for British Anti Lewisite), MeIB or Melarsorpol was invented in (1949) by Dr. Friedheim presented as a solution in propylene glycol for strict intravenous perfusion. The product is very effective on phase 1 human sleeping sickness, when the parasite multiply in lymph fluid or blood, at a dose of 10 mg/kg/four days. In the same family he invented in (1963) a water soluble product used by intramuscular injection Trimelarsan® MelW. This product had a relative short commercial use and Arsobal® remained as the only arsenical used for about 50 years. None of the products were developed for veterinary medicine. Melasony potassium (MelW), has also been synthesized, but showed little improvement over MelB. Treatment of the cerebral stage of trypanosomosis has relied primarily on the melamino phenylarsine melarsorpol (Mel B) (Friedheim, 1949). Mel B induced encephalopathy (Pepin and Milord, 1991; Friedheim and Distefano, 1989), thrombophlebitis (Apted, 1970). In 1985, in the same family (Melaminyl Thioarsenite) Friedheim discovered a combination of melarsenoxide and cysteamine, the product was named Cymelarsan® (MelCy) (Bujon, 1990).
Melasamine hydrochloride (MelCy) is very effective against *T. brucei*, *T. evansi* and *T. equiperdum* in camels, buffalo, cattle, pigs, goats and *in vitro* (Lun *et al.*, 1991; Otsulya *et al.*, 1992). Also, it is effective against diminazine aceturate resistant *T. brucei* and *T. evansi* (Zhang *et al.*, 1992). It is more effective than MelW (Zweygarth, and Kaminsky, 1990) this result has an important for the use of Mel Cy as a therapeutic agent and it is theorized melarsenoxide is the active form of all melamine-phenyl arsine and that it acts by binding trypanosomal thiols, such as trypanothione (Fairlamb *et al.*, 1989; Zweygrath *et al.*, 1992).

However, melarsenoxide is generally considered to be too toxic for direct administration (Friedheim, 1989) and is therefore, administered as less toxic dithiol conjugates. These compounds must first convert to melarsenoxide to have direct. MelCy, which more readily converted than MelB and MelW to melarsen solution, might be expected to have greater activity (Bradley and Fairlamb, 1994b). Pentavalent melarsen is much less active than trivalent melarsenoxide (Fairlamb *et al.*, 1992). Because it enters the CNS it is the drug of choice in African sleeping sickness. It causes gastrointestinal irritation thus it is given parenterally and it has caused a reactive encephalopathy that may be fatal.(Bentram and Anthony, 1993).

**1.13.6.1 Cymelarsan®**

This is based on a trypanocide launched nearly 30 years ago, its an arsenical, patented in (1985), discovered by Friedheim. It is introduced to the market by Rhône, Mérièux – (France). It is a combination of Melarsenoxide and cysteamine. It is related to the drug Arsobal®, which is the only treatment available for the late-stage sleeping sickness in human. It is a new compound from a group that has not previously been used against
animal trypanosomosis. The product is a white powder highly soluble in water. It is described chemically as: bis (aminoethyl thio – 4 melamino phenyl arsine dihydrochloride), used as an aqueous solution at 0.5% prepared at the time of use, it is presented as a sterile freeze – dried powder, (Bujon, 1990). It is very good in both local and general tolerance (Bujon, 1990), injectable I.M. or S.C and a very effective (more than the two predecessors) on parasites of the *T. brucei* group. Its qualities merit its development as a trypanocide in veterinary medicine (Code No. RM110) with a curative dose as a single treatment and at a rate of 0.25 to 0.5 mg/kg, against trypanosomosis especially *T. evansi* infection which are resistant to other drugs commonly used in the field, vis Quinapyramine and suramin (Raynaud *et al.*, 1989a, b and Bujon, 1990).

### 1.13.6.1.1 Chemistry

The drug was made by conjugation of one equivalent of melarsenoxide and two equivalents of cysteamine. Immediately after it has been dissolved in water, it exists as a mixture in equilibrium containing Cymelarsan® (Mel Cy) 43%, which had lost one cysteamine moiety 1.24% melarsenoxide 38% and free cysteamine. Small amounts, 2% of the oxidation products derived from the last two components also form cysteamine and sodium melarsen. On incubation at room temperature, the Mel CY content decreased steadily, associated with an increase in arsenical agent melarsenoxide, oxide and sodium melarsan. (Bujon, 1990)

### 1.13.6.1.1.2 Characteristics

Cymelarsan® has a rapid trypanocidal activity. Trypanosomes are destroyed within a few hours; it achieves a peak plasma concentration by about 15 min. post-injection, irrespective of the route of injection, after which plasma levels decline rapidly. The
absolute bioavailability is a 100% when given by the intramuscular route. In view of the short duration of trypanocidal levels in plasma, Cymelarsan® should not be regarded as a therapeutic product that has no preventive or long acting effect. After injection, complete recovery occurs rapidly (Bujon, 1990). The bioequivalence of the S/C and I/M routes was studied in infected dromedary, the area under the curve for I/M route was 12% greater than that for S/C route, no significant difference between the pharmacokinetics of the routes of administration or the different formula. (Toutain, 1991).

1.13.6.1.1.3 Mode of action

Cymelarsan® inhibits the metabolism of trypanothion reductase (TTR), an enzyme which is present in the parasite and absent from the host (Chouchane and Snow, 2001); Bujon, 1990). In 1909 Paul Ehrlich first proposed that trivalent arsenical compounds exert their lethal effect against trypanosomes and spirochetes by chemical reaction with sulphahydroxylal groups. However, the first definitive evidence in favour of this theory was obtained by Voegtline et al. (1923) observing that arsenicals had a propensity to combine more avidly with vicinal dithiols than with simple monothiols ultimately leading to development of 2,3-dimercaptopropanol [British Anti Lewisite (BAL)] as an antidote to the arsenical nerve gases subsequently (Friedheim, 1949) used this compound in the development of MelB although the mode of action of the trivalent arsenical drugs such as melarsen oxide and melarsorpol remains to be determined.

One primary effect of exposing trypanosomes to these compounds is the formation of stable MelT (Fairlamb et al., 1989) between melarsen oxide and the unique intracellular dithiol, dihydro trypanthione (Fairlamb et al., 1985) the other dithiol found in most organisms is dihydrolipomaide, which along with dihydrolipomaide dehydrogenase forms part of the exo-decarboxylase complexes for pyruvate and ketoglutarate in mammalian
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)
cells. These two enzymes are absent from long-slender blood stream forms of *T. brucei* (Fairlamb *et al.*, 1989). Therefore, dihydrolipomaide dehydrogenase has never been seriously considered as possible target for arsenical drugs. However, this organism does in fact contain significant amounts of dihydrolipomaide dehydrogenase, which has an unusual localization in plasma membrane (Fairlamb *et al.*, 1992). This enzyme and its substrate may be involved in the transport of maltose in the cell. (Richarm, 1985 ; Fairlamb *et al.*, 1992) hypothesized that D, L-dihydrolipomaide and D, L-dihydrolipoic acid react to form stable complexes with melarsen oxide. These complexes are 10 fold less stable than that found in trypanocidal drugs melarsorpol and trimelarsen, but 500 fold more stable than the complex formed between melarsen oxide and dihydrotrypanothione.

Arsenical resistant strain of *T. brucei* was found to contain significantly less lipoic acid than the sensitive strain. However, since the enzyme dihydrolipomaide dehydrogenase, dose not appear to be a target for inhibition, its substrate, lipoic acid, could be involved in either the mechanism of uptake or being the ultimate target for the drug (Fairlamb *et al.*, 1992).

1.13.6.1.1.4Safety

At the recommended dose, Cymelarsan® has been shown to be well tolerated, (Bujon, 1990 and Fairouz, 2000). No adverse systemic effects were observed and only a slight, transient local reaction like a tennis ball at the site of injection was seen in a small number of animals. This transient local reaction resolves in a few days. Cymelarsan® is safe for target animals. RM 110 was rapidly and completely absorbed after S/C injection 24h. when 0.1, 0.15, 0.2 or 0.3 mg/kg was injected in Morocco dromedaries. (Toutain, 1991).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

It must be stored in dry cool place. It has been shown not to be mutagenic, teratogenic or embryotoxic by standard procedures. It can be used in animals in poor condition or in pregnant females (Bujon, 1990).

1.13.6.1.1.5 Toxicity and adverse effects

General toxicity with a maximum tolerated dose in the range of 3-4 mg/kg gave a large safety margin when therapeutic dose is used (Bujon, 1990). 3.75 mg/kg induced a significant necrosis of the tissue of the point at inoculation whether the injection was subcutaneous or intramuscularly (Tagerkagan and Clair 1989). Often a depot of drug is formed at the site of the injection where it is retained and slowly released into circulation to maintain a concentration in the blood at a level at which no trypanosome can exist. Other drugs are not maintained in the form of such a local depot, but are found loosely attached to blood proteins and become slowly available to act the parasite.

Necrosis at the site of injection was also reported in buffaloes treated with 3.0 mg/kg Cymelarsan®, in order to avoid problem, dosages 1 – 2 mg/kg were recommended (Lun et al., 1991).

In human, avoid contact of the product with the mucus membrane especially the ocular mucous (Bujon, 1990).

The comparison the kinetics between camel and other species at doses of 1 – 0.2 or 0.3 mg/kg and for the two routes of administration (I/M and I/V) was made. The absolute bioavailability was 70 – 80% in camels, from 0 to 10 hours kinetic were similar in all species. Trypanocidal activity was apparently higher in horses than in cattle or camels, which are equivalent (Raynaud et al., 1989a).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

1.13.6.1.1.6. Residues

The product has a short half-life in the animals, and the toxicological profile or a residue is low. The proposed withdrawal time for meat, milk and edible tissue is provisionally recommended at 2 weeks (Raynaud et al., 1989b). Cymelarsan® has a short-life in horses and monkeys and the toxicological profile or residues is low (Raynaud et al., 1989b).

Seven infected camels in Kenya were treated with 0.25 mg/kg of Cymelarsan I/M and slaughtered either 7 days, 14 or 21, residues of total arsenic were noted in fat, liver and kidney all results of assay for total As were less than 2 mg/kg, no residues were observed in plasma, but were observed on 4 occasions in milk on one camel, in 3 occasions in one camel, no residues in one camel, seven days after treatment no residues of As were observed in the milk of any treated camel (Sones, 1991). Also Rahman et al., (2001) mentioned that about 1/3 of total tubewells in Bangladesh contained arsenic on average of 500 µg/l also Mir Misbahuddin and Kamaluddin, (2002) found that water of some tubewells contains 1500 µg/l of arsenic and people are drinking that As contaminated water unknowingly and recommended that one should be careful to prescribed Zn supplementation unless he is in sure that the patient is not taking As at the same time

1.13.6.1.1.7. Use of Cymelarsan® infected animals

No trypanosomes were detected by any of the method in either of the groups of camels treated with 0.3 mg/kg or 0.6 mg/kg (Zelleake et al., 1989). All parasites disappear within 3 – 24 hours after injection with a dose of 0.625 mg/kg and 1.25 mg/kg, in infected camels none relapsed for more than 65 days (Tagerkagan et al., 1989). Musa,(1990) and Musa et al., (1990) used the recommended dose of 0.25 mg/kg with 100% efficiency to cure the disease in infected camels.

Cymelarsan® eliminates T. evansi, T. equiperdum and T. equinm in acute and sub acute or chromic infection. Therapeutic dose of 0.25 – 0.5 mg/kg gives safety margin in the range of x6 to x2 times, with few or no local reaction I.M.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Evidence from parasitological and serological assay confirmed the effectiveness of Cymelarsan® for the treatment of *T. evansi* infection of Friesian Holstein cattle. The infection appeared to be eliminated most effectively when the drug was administrated intramuscularly at dose between 0.50 and 0.70 mg/kg. Cymelarsan® cleared *T. evansi* population and resistant to suramin from the circulation within 24 hours after treatment (Payne et al., 1994b). All infected *T. evansi* buffaloes treated with a single dose of 0.5 to 3.5 mg/kg were cured and no relapses could be observed with one to three years, at a dose of 0.25 mg/kg, relapse occurred in two out of four treated buffalo within two months after treatment, indicating that the lowest effective dosage to treat *T. evansi* in buffalo might be between 0.25 to 0.50 mg/kg (Lun et al., 1991). Goats infected with *T. evansi* were cured after a single injection of 0.3 mg/kg Cymelarsan® and above (Zewygarth et al., 1992 and Fairouz, 2000). In contrast, all animals infected with the least sensitive stock of *T. brucei* and subsequently treated with one I.M injection of Cymelarsan® at 0.625 or 2.5 mg/kg parasitaemic between 11 to 17 days after treatment, and lower dose of 0.037, 0.075 and 0.17 mg/kg did not provide a cure (Zewygarth et al., 1992). Two – four 0.5 – 2.0 mg/kg Cymelarsan® could cure the mice the infected with *T. evansi* and *T. equiperdum* (Zhang et al., 1992).

1.13.6.1.1.8 Antigen and antibody level

Olaho et al., (1992) reported that antigen detection could be used to evaluate the success of therapeutic trials when trypanosome detection tests fail to pick patent infection. In 14 infected camels treated with Cymelarsan®, 0.5 mg/kg and 1.2 mg/kg, thereafter, no trypanosomal antigen could be
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) detected in the animals, while two out of three camels treated with 0.4 mg/kg showed no trypanosomal antigen by day 90 post-treatment. However, there was evidence of trypanosomal antigen in camels treated with 0.2 mg/kg and untreated positive controls, 90 day post-treatment. Antibody levels were still high in all 14 camels, 90 day post-treatment.

In another group of 55 field camels, of which 47 were parasite-positive and 8 negative, trypanosomal antigens could not be detected in 42 of the camels, 28 and 49 days post-treatment with quinapyramine prosalt. However, antigen levels were still high in five parasite-positive camels, 48 days post-treatment.

1.13.7 Other trypanocidal drugs

1.13.7.1 Antirovinylfuran

It has trypanocidal activity when given by mouth in mice infected with *T. rohesiense* intramuscular single injection had prophylactic properties. It inhibits various nucleic acid and carbohydrate metabolic pathways (Alexender, 1985).

1.13.7.2 The effect of antipyretic agents

Flurbiprofen (1 mg/kg) i.v twice daily inhibited the febrile reactions during the acute phase of *T. congolense* or *T. brucei* infections. Again parasitaemia of a progressive type could be observed during drug treatment. All infected *T. congolese* goats treated with flurbiprofen died. However, a number of the *T. brucei* infected goats treated with the drug survived, this was also the case during long-standing trypanosome infections.

Suprofen, an antipyretic agent, which is less potent than flurbiprofen, induced parasitaemia of a progressive type as compared with the control when tested in *T. vivax* infected goats.

Treatment of *T. vivax* infected goats with sodium salicylate or flunixine meglumine only had a partial inhibitory effect upon the febrile reactions, no effect upon the number of circulating trypanosomes could be seen. Both flurbiprofen and suprofen induce a
progressive increase in the number of circulating trypanosomes, which often terminated in early death (Newton, 1974).

**1.13.7.3 Nitrofurazone derivative**

It inhibits the unique enzyme trypanothione reductase. It has an effect on mucocutaneous leishmaniasis. It causes severe toxicity, including allergies, gastrointestinal irritation, and central nervous system (CNS) (Alexander, 1985)

**1.13.8 Tetracyclines group**

The tetracyclines were discovered as a result of a search for antibiotics active against a wider range of bacteria than penicillin. They are bacteriostatic acting on the bacterial ribosome and they have a chelating action in binding the metallic ions, calcium, magnesium and manganese. They also inhibit a number of essential enzyme systems. It is found in the market in the form of an odourless, yellow base, insoluble in water, soluble in hydrochloride. Solutions lose their activity in a few days. They inhibit a wider range of Gram-positive and negative bacteria and act against certain protozoa such the Anaplasma, Mycoplasma spp. and also act against, Reckettsia and Theileria. They may be given by mouth and take 3-4 days to be excreted. (Alexander, 1985)

**1.13.8.1 Oxtetracycline (OTC)**

**1.13.8.1.1 Isolation and synthesis**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

This broad spectrum antibiotic has been isolated from a culture of *Streptomycyes reimosus*. It could be obtained by extracting the culture filtrate with BuOH and then extracting the organism phase with dilute mineral where an aqueous extract obtained. Purification is carried out by chromatography on an alumina column followed by repetitive solvent and dilute acid extractions. Final purification is done by dissolving in dilute acid and then neutralization to give crystals of the dehydrated form of the antibiotic known. (Anon, 1985).

1.13.8.1.2 Characteristics

The free antibiotic sodium salt and hydrochloride are all soluble in polar organic solvents. The dehydrate is laevorotatory with specific rotation of $[\alpha]_{D}^{25} = 196.6^\circ$C) (0.9, 0.1 N – HCl) and $[\alpha]_{D}^{25} = 2.1 (^\circ$C(0.9, 0.1 N - NaOH) among the crystalline salts and derivatives that have been prepared are the hydrochloride, which form (CH$_3$OH, m.p 208 – 213$^\circ$C, $[\alpha]_{D}^{25} + 214^\circ$C CH$_3$OH) and the sodium salt as lemon-yellow crystals from CH$_3$OH. The latter decomposes in aqueous solution at room temperature and the acid salt hydrolyses slowly in solution above pH 1.0 to yield crystal of OTC (Glasby, 1978).

1.13.8.1.3 Chemistry

The tetracycline antibiotics differ from each other as a result of differing molecules or atoms being attached to R$_1$, R$_2$ and R$_3$ positions as noted in Fig. 2. However, relatively few modifications can be made on the structure without loss of antibacterial activity (Giovani *et al.*, 1983). It is named chemically: 4 – (dimethylamino) – 1, 4, 49, 5, 59, 6, 11, 129 – octahydro – 3, 5, 6, 10, 12, 12a – hexahydroxy – 6 – methyl – 1, 11 – dioxo – 2 – nepthacene carboxamide (Anon, 1985).
1.13.8.1.4 Mode of action

Oxytetracycline is indicated for the treatment and control of a wide range of bacterial infections caused by, or associated with OTC – sensitive organisms, a large number of gram positive (Farca and Nebbia, 1984; A non, 1985) and Gram negative bacteria (A non, 1985) certain large viruses, rickettsiae, protozoa and chlamydia are sensitive to OTC (A non, 1985). Also, it is effective against certain species of Mycoplasma such as *M. gallinarum* and *M. orginini*, and against theileriosis (Mishra *et al.*, 1983). Tetracyclines block protein synthesis by the organism (Dineen, 1980).

1.13.8.1.5 Absorption and excretion

Giovani *et al.* (1983) found tetracycline groups in significant amounts in the bile of most animals after treatment with tetracycline. It can be excreted by hepatic cells into bile and eventually pass into the intestines. A cycle (enterohepatic) can result in which the drug is continually re absorbed from the intestines after biliary secretion until enough of the drug passes through the liver to render it sufficiently water soluble for urinary excretion (Giovani *et al.*, 1983 and Bywater *et al.*, 1991).

Varma and Paul (1983) reported a very slow rate of absorption of OTC-LA from I/M site and the drug remains ionised over the entire pH range. The slow absorption of the drug from I/M site as well the delayed appearance of the drug in milk as compared to plasma may be chiefly attributed to the greater ionized fraction of the drug at pH of the body fluids, since it is the unionized fraction of a drug that usually passes across a cell membrane.

All tetracyclines including OTC-LA form a stable calcium complex in any bone-forming tissue. A decrease in the fibula growth rate has been observed in premature
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) infants given oral tetracycline in dosages of 25 mg/kg every 6h this reaction was shown to be reversible when the drug was discontinued. (Pfizer, 2005). OTC-LA and its salts are readily absorbed orally and are 10-40% bound to plasma proteins. Between 40-70% is excreted unchanged in the urine via glomerular filtration. A serum half life of 6-10 h. has been reported for OTC-LA in patients with normal renal function. (Pfizer, 2005). Tetracyclines as a class, are widely distributed in the body, including to the heart, kidney, lungs, muscle, pleural fluid, bronchial secretions, sputum, bile, saliva, urine, synovial fluid, ascetic fluid, and aqueous and vitreous humor. Only small quantities of tetracycline and oxytetracycline are distributed to the CSF and therapeutically may not be attainable. (Susan and Donald2003-2005).

While all tetracyclines distribute to the prostate and eye, doxycycline or minocycline penetrate better into these and most other tissues. Tetracyclines cross the placenta, enter fetal circulation and are distributed into milk. The volume of distribution of oxytetracycline is approximately 2.1 L/kg in small animals, 1.4 L/kg in horses, and 0.8 L/kg in cattle and the amount of plasma protein binding is about 10-40% for oxytetracycline. (Susan and Donald2003-2005).

All tetracyclines readily distributed to most body fluids, including bile, sinus secretions, and synovial, pleural, ascitic, and gingival crevicular fluids. Cerebrospinal fluid (CSF) concentrations vary and may achieve 10 to 25% of plasma concentrations following parenteral administration. Concentrations in gingival crevicular fluid may be three to seven times the serum concentrations. Tetracyclines tend to localize in bone, liver, spleen, tumors, and teeth; tetracyclines also cross the placenta and distribute into breast milk. (Ziv and Suliman, 1974, Susan and Donald 2003-2005; Pfizer, 2005).

1.13.8.1.6 Safety

Oxytetracycline is safe in the recommended doses of 15 – 50 mg/kg but must be given in divided doses (Varma and Paul, 1983; Davey et al., 1985 and Radwan et al., 1989).

1.13.8.1.7 The half-life and the long-acting formulation
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

In Xia et al. (1983) study on OTC-IA (long acting) as compared OTC-C the half-life is 6 hours, after I.V and I.M injection.

The long-acting formulation was an effective way to administer OTC and remove the need for repeated daily treatment (Toutain and Raynaud, 1983). The long-acting formulation gave a lower serum concentration and showed longer half-life as compared with conventional formulation (Davey et al., 1985). In buffaloes the half-life after I.V was shorter than after I.M administration – (Varma and Paul, 1983). The half-life was shorter after conventional preparation than in long acting preparation when OTC 10 mg/kg L.A preparation and 20 mg/kg OTC-C at the therapeutic levels is given (Luthman and Jacobsson, 1982). OTC suspended in milk replacer was responsible for low serum concentration whereas the greater absorption form glucose glycine electrolyte solution was responsible for improved uptake of antibiotic. This was observed in Palmer et al. (1983) study when OTC was suspended in milk replacer, water or glucose glycine electrolyte solution given orally to 64 calves. Bertzalf et al. (1982) observed that OTC when administered I.V attained concentrations in the wall of the uterus of the cow, equivalent to its plasma concentration.

The long-acting formulation gave a lower serum concentration and showed longer half-life as opposed to the conventional formulation (Davey et al., 1985) OTC given intraperitoneal 250, 500, 1000 mg/6 weeks daily to ewes infected with Brucella melitensis, after 16 weeks they were Brucella free with 52, 69 and 100, respectively (Radwan et al., 1989).

1.13.8.1.9Adverse effects and toxicity
Drug concentration may accumulate in developing bones, teeth and other organs of the young, since their detoxification enzyme systems are not fully developed (Alexander, 1985).

Gross et al. (1981) observed that, OTC causes increase in pulmonary arterial pulse and decreased in heart rate, pulmonic and systemic resistance were increased and no direct effect on the left ventricular contractility was observed also glossitis, diarrhoea, idiosyncrasy and photodynamic reactions were observed in rabbits when administered orally at dose of 10-100mg/kg/day for 20 days there were regeneration of blood cells, proliferation and maturation of bone marrow elements, together with atrophy of the gastric and intestinal mucosa and dystrophic changes in the kidney, liver and myocardium.

The toxic effect is observed in the gastrointestinal tract, producing diarrhea, nausea and vomiting. The degradation product of tetracyclines namely epianhydrot and unhydrot are toxic. The degradation can result from improper storage. Also, it may produce symptoms of acute proteinuria, glycosuria and acidosis. The inclusion of lactose in oral tetracycline capsules prevents this decomposition (Cluff, 1980).

1.13.8.1.12 The residues

Residues of OTC may therefore be expected in milk, milk products, and meat products of livestock. With help of pharmacokinetic research in target animals and toxicological investigation, it is possible to establish (qualitatively and quantitatively) what residues are present in milk and meat after several intervals of time and what amounts of residue may be acceptable in milk or meat. The toxicological investigation includes a long list of toxicity tests like biotransformation, mutagenicity, neurotoxicity
…etc, for establishment of the quantitative toxicity. Special investigations involve establishment of acceptable drug residues in milk and meat and these involve pharmacokinetic, teratogenicity and mutagenicity tests.

Pharmacokinetic research might give the information needed with respect to the interval needed pertaining non-detectable residues and the required information about the profile of the metabolites. Teratogenicity tests on the other hand will point to the non-toxic levels, being the most sensitive to toxicological criteria. Mutagenicity tests which address potential quantitative toxic profile of substances make it possible to establish an acceptable daily intake for the consumer of food products of animal origin (Koenen-Dierick, et al., 1995).

Bywater et al., (1971) mentioned that the lowest therapeutic serum concentration is considered to be 0.5 µg/ml while Salte, (1982) mentioned that this limit of serum concentration was mentioned for about 48hr after I/M injection of OTC-LA in cattle. Xia et al., (1983) mentioned that I/M injection of OTC-LA resulted in plasma concentration with big values after 6-8 hr with100%, bioavailability about 60% of the dose was excreted in the urine during the first week and plasma concentration above 0.5µg/ml was mentioned for approximately 60 hr indicating normal effect of OTC-LA. The maximum allowable tolerance for OTC-LA in cattle is 6ppm in the liver and 2ppm in muscle tissue (FDA, 2003).

If residues are found, serious economic sanctions may follow at great cost to the livestock producer (Mercer et al.,1978). In addition, public health regulatory authorities usually legally define withdrawal times and limitation for use of certifiable antibacterial in food-producing animals. Once again the presence of disease process can substantially alter the normally accepted withdrawal times.

The elimination half-life of oxytetracycline is approximately 4-6 hours in dogs and cats, 4.3 - 9.7 hours in cattle, 10.5 hours in horses, 6.7 hours in swine, and 3.6 hours in sheep.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) and in high concentrations, tetracyclines can also inhibit protein synthesis by mammalian cells. (Susan and Donald, 2003-2005).

In the committee for veterinary medical products (CVMP) of the European Agency for the evaluation of medicinal products (EAEMP, 1995) evaluated OTC-LA in the past an established an acceptable daily intake (ADI) of 0-0.003 mg/kg bw based on the human gut flora. Based on this ADI and taking into account the typical residue distribution of OTC-LA in tissues, the following maximum residue limits (MRLs) established by 36th joint FAO/WHO expert committee on food additive (JECFA) were adopted: kidney 600 µg/kg, liver 300 µg/kg, eggs 200 µg/kg, muscle 100 µg/kg and milk 100 g/kg. It was concluded that the antimicrobial potency of chlortetracycline and tetracycline is comparable to that of OTC-LA, the JECFA established a group ADI of 0-3 µg/kg bw for OTC-LA, tetracycline and chlortetracycline alone or in combination, the highest levels are in the kidneys and liver but, they are not detectable in fat to any great extent. For the complete recovery compounds, the 4-epimers of OTC-LA, tetracycline and chlortetracycline, have to determine. The 4-empires of the compounds occur in samples and are formed during sample preparation. The 4-empires are in equilibrium with the parent compound. Therefore, the marker residue is the sum of the parent drug and its 4-empires (EAEMP, 1995).

Suitable and well validated HPLC methods are available which can be used in the surveillance of residues of tetracycline, OTC-LA and chlortetracycline in tissues of cattle, sheep, pig, turkey, trout, carp, and in milk and eggs. This method takes into account the 4-epimers of OTC-LA, tetracycline and chlortetracycline. (EAEMP, 1995).

1.13.8.1.13 Use of OTC in production animals

Because of their relatively low toxicity, tetracyclines have been used extensively as animal feed additives in animal production due to their stability in dry form. When administered in the feed at the onset of clinical signs at a dose of 15 mg/kg reduces the symptoms but does not prevent the development of lesion (Betts and Campbell, 1956).

Larson and Stowe (1981) studied OTC residues when injected I.V at dose of 10 mg/kg to 3 horses, after 4 hours mean concentration of OTC of
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

kidney tissue, in lung, plasma and diluted bronchial fluid, respectively. In lung, OTC concentration was high enough for cambering bacterial infections. In infected *T. evansi* goats and negative-control Fairouz, (2000) observed that OTC late the death of goats when compared with untreated control and the goats had gained a high body weight.

1.13.9 Drug resistance

Malaria, Trypanosomosis, Lieshmaniasis and Amoebiasis are the most serious of the diseases caused by protozoa. Satisfactory drugs exist for all these diseases. However, there is increasing evidence of resistance to most of the drugs used to cure trypanosomosis in Africa where, in an area of nearly four million square miles South of the Sahra Desert, many millions of people are affected either in health or by the illness of their animals. The disease is confined to under developed areas, and is complicated by under nutrition. (Adrien, 1973).

One of the major problems in the chemotherapy and chemoprophylaxis of animal trypanosomosis is resistance to trypanocides (Joshua, 1988). Repeated passage (83) through mice treated with sub-therapeutic concentration of Cymelarsan® induced complete resistance in the subclones whether they were derived from very sensitive or more resistant to the compound. During induction of resistance to Cymelarsan®, *T. evansi* subclones develop cross-resistance to both berenil and pentamidine. Berenil resistant clones display two different types of resistance:

1- Single drug resistance demonstrated by those that remained sensitive to Cymelarsan.

2- Cross-resistance (Zhang et al., 1992).
The relapse of the *T. brucei* in mice after treatment was attributed to trypanosomes in the brain beyond the action of tryanocides, and which subsequently replicate and reinvade the circulation (Jennings and Gray, 1983). Mice infected with *T. evansi* were cured with lower doses of Cymelarsan® if treated early, (< 24 hours post-infection) than if treated late (< 48 hours post-infection) (Dennings *et al.*, 1989). This implies failure of treatment or prevention, and if no other active drugs are available the animal has to rely on its immune defenses alone to combat the disease (Uilenberge, 1998). In trypanosome strain to survive, despite the administration of drug given in doses equal to higher than, those usually recommended (El Rayah, 1997).

Drug resistance was found to develop, when trypanosomes were exposed to sub-curative doses of trypanocidale (El Rayah and El Malik, 1990).

The usefulness of isometmedium has been greatly reduced due to widespread resistance over the years (Scott and Pegram, 1974), but it has remained essentially a curative drug in the field despite claims that the drug has some prophylactic properties (Dolan *et al.*, 1990).

1.13.10 the combined action of the drugs

1.13.10.1 The interactions of tetracyclines

Interactions are due to the displacement of drugs like barbiturates from plasma proteins by other drugs, such as phenylbutazone and doxycycline. A problem is to differentiate disease effects from drug effect, e.g. in nephrotoxicosis by oxytetracycline during azotemin or to identify the drug involved in behavioral reactions, e.g. egg restiveness due to predinsolone and metoclopramide.
Fatal shock and edema were reported after a second injection of neomycin, OTC, trimethoprim sulfadimethoxine 3-6 days. Dyspnoea and recumbency following intrauterine administration of polymixin and OTC for 15 days after calving. In heifers by ptyalism and blooding, for 6 hr, 30 min following chlorotetracycline and bullocks by dyspnoea and pulmonary edema (within 2 min following i.v OTC and phenylbutazone).

1.13.10.2 Combination chemotherapy possibilities in trypanosomosis

Some infectious diseases are routinely treated with drug combinations (Keiser et al., 2001). Trypanosomosis may sometimes be associated with other parasites such as hemonchus and bacteria (Bywater et al., 1983). Additional studies investigated the susceptibility of T. brucei infections to diminazine aceturate in combination therapy with non-steroidal anti-inflammatory drugs and lithium chloride (Abatan, 1991). The effect of combination of calcium antagonists with standard trypanocidal against T. evansi was described (Anene et al., 1996). One drug may damage macromolecules and the other inhibits the availability of precursors for synthesis (diamidine plus cordycepin), drugs, which bind to DNA, appear to be of the kinds which are expected to be synergetic. The demonstration specific inhibitors of RNA synthesis are powerfully trypanocidal (Williamson and Scott-finnigan, 1975), may indicate a potential source of ancillary agents, which if not too toxic might be used to reinforce existing drugs. In certain instance a combination of drug may prove to be toxic whereas either may be used safely if administered alone. Some compounds used at the correct dosages are non-toxic, but are excreted so slowly from the organism that repeated administration at relatively short intervals may result in accumulation until a level is reached which will result in the appearance of toxicity.
Synergetic effects with less active drugs have produced lightened activity and showed inhibited drug- resistance development, so for this approach has not been looked at extensively trypanosomosis, a part from the prophylactic suramin complexes, the demonstration of potentiative synergism between suramin and tryparsamide (Williamson, 1966; Williamson ;Scott-Finnigan, 1975; Gill, 1971).

Complexes of suramin with cationic drugs especially quinapyramine have been found to be more effective in prophylaxis than suramin alone but such complexes have not been widely acceptable for field use because of the high cost of the complex formulations and the severe tissue reaction that occur in the injection sites (Williamson, 1970 and Williamon et al., 1982). It is unclear whether the improved prophylactic activity is due to pharmacodynamic or pharmacokinetic factor, which is now suramin have been shown to be synergistic with a number of drugs, including trypansamide, puromycin, and diminazine aceturate (Williamson et al., 1982). More studies on the synergistic activity seem justified considering the potential of Cymelarsan® and oxytetracycline combination. It was the best treatment of *T. evansi* infection in Sudanese Nubian goats. (Fairouz, 2000).

### 1.13.10.3 Use of Cymelarsan and OTC in normal animals

In Nubian goats infected with *T. evansi*, Fairouz, (2000) studied the effect of Cymelarsan and OTC intramuscularly and found that Leucocytes numbers, lymphocytes were increased after injection of the combination, monocytes appeared at 1 – 3% but neutrophils were decreased. The serum sodium, potassium, calcium, phosphorus, total protein, albumin, globulin, urea, creatinine, thyroxin, progesterone, bilirubin concentration and alanine amino transferase, aspirate amino transferase and alkaline phosphatase activities were increased after injection with combination. The ketone bodies were negative to the test except one animal in day one after injection with the combination.
CHAPTER TWO
MATERIALS AND METHODS

2.1 Animals

The study was done in two species of animals:

2.1.1 Nubian Goats

2.1.2 Camels (Camelus dromedarius)

2.2 Adaptation period of goats

Three hundred and eighty five (175) Nubian goats, 8 – 10 month old, weighing 9-10 kg, and of both sexes were purchased from Sheikh Abu Zeed Market (Omdurman -Khartoum State). Animals were housed in pens at the College of Animal Production and Veterinary Medicine – Sudan University-Hillat Koko. Each animal was fed daily on green forage consisting of 3kg Lucerne (Medicago sativa), 1.5 kg sorghum (Sorghum vulgar) and 2 kg millets (Pearl millet) one time weekly as a concentrate, and with free access to water.

The goats were kept for 14 days before commencement of the study for acclimatization. General health examinations were done daily and samples of urine; faeces, blood and serum were taken for determination of normal base-line data. The goats, giving abnormal data were excluded.

Twenty goats were chosen randomly, divided into two groups each of ten. Group (1) was uninfected-un-treated (control negative group), while group 2 was infected-untreated (control positive group). The remaining animals were infected either with T. evansi or T. vivax and were used in ten experiments each experiment was divided into groups, each group consisted of 10 goats.

2.3 Parasite and infection

Two species of the parasite were used for precipitating the infection in goats excepting group 1:

2.3.1 Trypanosoma evansi (T.evansi)
Albino rats of two month old, weighing 250gm, were inoculated intraperitoneal with 0.2ml camel’s blood containing 3-5 parasite/field, (These camels were infected naturally with *Trypanosoma evansi* strain Gad trip (1) which was obtained from El Gadarif State, Eastern Sudan) when parasitaemia developed in rats, each goat (except goats in group 1) was injected intravenously with 0.75 ml rat's blood containing $5 \times 10^5$ organisms. The parasites were activated by adding phosphate glucose solution (PGS) buffer before inoculation.

### 2.3.2 *Trypanosoma vivax* (*T. vivax*)

*Trypanosoma vivax* obtained from Western Sudan (Gebeesh town), the strain being designated as vivax west (1). It was inoculated in goat intravenously using 0.5ml containing 2.3 parasites/field till parasitaemia developed. Experimental goats each goat injected with 0.75ml-inoculated goat's blood intravenously which contained $5 \times 10^5$ organisms. Before inoculation activation of the parasites was made by adding PGS buffer.

### 2.4 Drugs used

1. Cymelarsan® 0.25mg/kg (Rhône – Mérieux – France).
2. Oxyteracycline (Remacyline®) 20mg/kg (Coophavet – France).
3. Quinapyramine (Trypanil®) 5mg/kg (Agropharm – U.K).
4. Homidium Bromide (Ethidium®) 1mg/kg (Laprovet – France).

Each animal in each experiment was subjected to the following investigations:

**a/ Clinical examination:**

Which included body temperature (°C), body weight (kg), respiratory rate (movement/min.), pulse rate (pulse/min.) and blood pressure(mmHg) and were examined daily.

**b/ The efficacy** of the drugs is determined by the detection of the parasites daily in peripheral blood with thin or thick smears, or whole blood by wet films and
The detection of the parasite by the above methods was done daily until the animals died or slaughtered.

c/Blood analysis:

Blood from jugular vein was withdrawn in two plain test vacutainers one containing anticoagulant and used for examination of complete haemogram, packed cell volume (PCV), haemoglobin (Hb), red blood cell count (RBC), white blood cell count (WBC), differential WBC count, reticulocytes count, platelets count in addition to calculation of blood indices (MCV, MCH, MCHC). Tubes contain no anticoagulant were left to clot, centrifuged at 3000rpm for examination, sera collected and kept at -20°C until analyzed for the activity of glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), creatine kinase (CK), pyruvate kinase (PK), succinate dehydrogenase (SDH), amylase and lipase and for the concentrations of sodium, potassium, chloride, calcium, phosphorus, magnesium, manganese, zinc, copper, iron, arsenic, urea, creatinine, total protein, albumin, globulin, total cholesterol, glucose, triglycerides and phospholipids.

d/Pathology:

Animal that have died or slaughtered underwent immediately: post mortem examination and findings were recorded. Specimens of heart, brain, kidney, spleen, liver, lung, colon, small intestine, ovary, testis, thyroid gland, and muscle, site of
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Injection, nerve, tendon, spinal cord and tongue were taken and fixed in 10% formal saline for histopathology.

e/ Residues:

Other specimens of heart, brain, kidney, spleen liver, lung, ovary, testis, muscle and site of injection, were kept in plastic containers kept in a deep freezer for determination of residues of Cymelarsan, oxytetracycline and quinapyramine after the withdrawal period 14, 21,28 days respectively in slaughtered animals two goats/week or one camel/week or after death.

2.5 Experimental design of goats

Ten procedures were conducted:

2.5.1 Experiment 1: Toxicity and efficacy of Cymelarsan® in goats infected with T. evansi

Two experiments were conducted:

2.5.1.1 Single-dose experiment

Each goat in groups 3, 4,5 and 6 was given single intramuscular (I/M) dose of Cymelarsan® at the rate of 0.125 mg/kg (half-therapeutic dose), 0.25 mg/kg (therapeutic dose), 0.625 mg/kg (two and half times the therapeutic dose), 1.25 mg/ml (five-times the therapeutic dose) respectively.

2.5.1.2 Multiple-dose experiment.

Each goat in groups 7 and 8 was given intramuscularly (I/M) a dose of Cymelarsan® at rate of 0.125 mg/kg (half-therapeutic dose) twice/week for two weeks, 0.125 mg/kg (half-therapeutic dose) daily for 8 days, respectively. Goats in groups 9 and 10 were each given the drug (I/M) at the rate of 0.25 mg/kg (therapeutic dose) twice/week for two weeks and 0.25 mg/kg (therapeutic dose) daily for 8 days respectively.

Goats in groups 1 and 2 were not given the drug but used as control negative and control positive, respectively

2.5.1.2 Experiment 2: Toxicity and efficacy of oxytetracycline in goats infected with T. evansi
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Two experimental procedures were conducted:

2.5.1.2.1 Single dose experiment
Each goat in group 3, 4, and 5 was given the single (I/M) dose of the drug at the rate of 20 mg/kg (therapeutic dose), 50 mg/kg (two and half therapeutic dose), and 100 mg/kg (five-therapeutic dose) respectively.

Goats in group 6 were each given the drug weekly at dose rate of 200 mg/ml for three weeks intramuscularly.

2.5.1.2.2 Multiple dose experiment.
Each goat in groups 7 and 8 was given the drug intramuscularly (I/M) at dose rate of 20 mg/kg (therapeutic dose) twice/week for two weeks or repeated daily for 8 days respectively.

Goats in groups 1 and 2 were not given the drug but used as control negative and control positive respectively.

2.5.1.3 Experiment 3: Clinicopathological effect and efficacy of Cymelarsan® and oxytetracycline in goats infected with *T.evansi*.

Goats in groups 3 and 4 were each given single intramuscular dose of Cymelarsan® at the rate of 0.125 mg/kg (half therapeutic dose) followed by single intramuscular dose of oxytetracycline at rate of 10 mg/kg (half therapeutic dose) while goats in group (4) were also each given single intramuscular dose of Cymelarsan® 0.125 mg/kg (half therapeutic dose) followed by single dose of oxytetracycline (intramuscular I/M) at rate of 50 mg/kg (two and half therapeutic dose). Group(5) was given Cymelarsan 0.125 mg/kg (half therapeutic dose) followed by oxytetracycline 20 mg/kg (therapeutic dose) intramuscularly twice/week for two weeks. Group (6) was given the drugs similar to group (5), but daily for 8 days.

Goats in groups 1 and 2 were not given the drug but used as control negative and control positive respectively.

2.5.1.4 Experiment 4: Clinicopathological effect and efficacy of Cymelarsan® in goats infected with *T.evansi* supplemented with zinc & copper.
Zinc (98%) and copper (98%) (The British Drug Houses Ltd. BDH-Laboratory Chemicals Division. Poole- England) were dissolved in distilled water with (1g in 100ml distilled water). Goats in group (3) were each given a single intramuscular dose
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)
of Cymelarsan at the rate of 0.125 mg/kg, goats in group (4) were each given a single intramuscular dose of Cymelarsan at the rate of 0.125 mg/kg followed by zinc (12 µmol/l) intramuscular and copper (1g in 100ml distilled water) orally. While goats of group (5) was given Cymelarsan at the rate of 0.125 mg/kg the same dose daily and goats in group (6) were each given a single intramuscular dose of Cymelarsan at the rate of 0.125 mg/kg followed by zinc (12 µmol/l) intramuscular and copper (1g in 100ml distilled water) orally daily for 8 days.
Goats in groups 1 and 2 were not given the drug but used as control negative and control positive respectively.

2.5.1.5 Experiment 5: Efficacy and toxicity of quinapyramine in goats infected with
T. evansi:
Two experimental procedures were conducted:

2.5.1.5.1 Single dose:
Each goat in groups 3, 4, 5 and 6 was given single intramuscular doses of quinapyramine at the rate of, 5mg/ kg (therapeutic dose), 10 mg/ kg (two and half-therapeutic dose), 25mg/ kg (five-therapeutic dose) and 50mg/kg(ten therapeutic dose) respectively.

2.5.1.5.2 Multiple doses:
Each goat in groups 7 and 8 was given the drug intramuscular at the rate of 5 mg/ kg (therapeutic dose) weekly for three successive weeks or daily for 8 days respectively.
Goats in groups 1 and 2 were not given the drug but used as control negative and control positive respectively

2.5.1.6 Experiment 6: Toxicity and efficacy of Homidium bromide in goats infected with T. vivax:
Two experimental procedures were conducted:

2.5.1.6.1 Single dose:
Each goat in groups 3, 4 and 5 was given single intramuscular dose of homidium bromide at the rate of 1 mg/ kg (therapeutic dose), 2.5 mg/ kg (two and half therapeutic dose) and with 5 mg/ kg (five-therapeutic dose) respectively.

2.5.1.6.2 Multiple doses:
Goats in groups 6 and 7 were given the drug at the rate of 1mg/ kg (therapeutic dose) weekly for three successive weeks and 1 mg/ kg (therapeutic dose) daily for 8 days respectively.

Goats in groups 1 and 2 were not given the drug but used as control negative and control positive respectively.

2.5.1.7 Experiment 7: Clinicopathological effect and efficacy of quinapyramine and homidium bromide interaction in goats infected with *T. vivax* or *T. evansi*

*a/ T. evansi* infection

Each goat in group 3 was given single intramuscular dose of quinapyramine at the rate of 5 mg/ kg (therapeutic dose) followed by 1 mg/ kg of homidium bromide (therapeutic dose) while, goats in group 4 were each given single intramuscular dose of quinapyramine at 12.5 mg/kg (two and half-therapeutic dose) followed by 1mg/ml (therapeutic dose) of homidium bromide.

*b/ T. vivax* infection

Each goat in groups 5 and 6 was given 5mg/ kg (therapeutic dose) of quinapyramine followed by 1mg/ml (therapeutic dose) of homidium bromide, 5 mg/kg (therapeutic dose) of quinapyramine followed by 2.5 mg/kg (two half-therapeutic doses) of homidium bromide respectively.

Goats in groups 1 and 2 were not given the drug but used as control negative and control positive respectively.

2.5.2 Camels (*Camelus dromedarius*)

Sixty one- humped camels (*Camelus dromedarius*) 1 – 3 years-old, of both sexes weighing (250-300 kg) were obtained from El Gadarif State and were stabled in Elmewelh Market pens (Omdurman-Khartoum State). Each camel was fed daily on 4kg Lucerne (*Medicago sativa*), 3.5 millets (*Pearl millet*) and 2.5kg sorghum (*Sorghum vulgare*); with free access to water. The camels were kept for 14 days before the study was commenced for acclimatization. General health examinations were done such as urine, faeces, blood and serum samples taken for analysis to determine normal base-line
data. The camels, recording abnormal data, were eliminated from the study. All experimental animals chosen were clinically healthy giving data with normal ranges for all parameters. They were divided randomly into three experiments, each experiment consisting of groups of 5 camels each.

Ten camels were chosen randomly and divided into two groups, each of five. Group 1 was uninfected-untreated (control negative group), while group 2 was infected-untreated (control positive group). The remaining animals were infected with *T. evansi* naturally as they came from a trypanosomosis region (El Gadarif State-Eastern Sudan). They were used in three experiments each experiment being divided into groups, group consisted of 5 camels each.

Three experimental procedures were conducted:

**2.5.2.1 Experiment 1: Efficacy of Cymelarsan® in camels infected with *T. evansi***

Each camel in group 3 and 4 was given a single intramuscularly dose of the drug at the rate of, 0.25 mg/ kg (therapeutic dose), and 0.6125 mg/ kg (two and half-therapeutic dose), respectively. Camels in group 5 were each given a single dose of Cymelarsan at rate of 0.125mg/ kg (half-therapeutic dose) weekly for three successive weeks.

Camels in groups 1 were used as un- infected-untreated (control negative), while camels in group 2 were infected-untreated (control positive).

**2.5.2.2 Experiment 2: Toxicity and efficacy of Oxytetracycline in camels infected with *T. evansi***:

Two experimental procedures were conducted:

**2.5.2.2.1 Single doses experiment**

Each camel in group 3, 4 and 5 was given a single intramuscular dose of the drug at the rate of 20 mg/ kg (therapeutic dose), 50mg/kg (two and half therapeutic dose), and 100 mg/ kg (five-therapeutic dose) respectively.

**2.5.2.2.2 Multiple doses**

Each camel in groups 6 and 7 was given the drug intramuscularly at the rate of 20 mg/ml (therapeutic dose) twice /week for two weeks or repeated daily for 8days respectively. Camels in groups 1 were used as un- infected-untreated (control negative), while camels in group 2 were infected-untreated (control positive).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

2.5.2.3 Experiment 3: Clinicopathological effect and efficacy of Cymelarsan and oxytetracycline interaction in camels infected with T.evansi:

Each camel in group 3 was given single intramuscular dose of Cymelarsan® at the rate of 0.250mg/ kg (therapeutic dose) followed by 20 mg/ kg of oxytetracycline, (therapeutic dose) while animals in group 4 were given a single intramuscular dose of Cymelarsan® at 0.125 mg/ kg (half therapeutic dose) followed by oxytetracycline at 50 mg/ kg (two and half therapeutic dose). A single dose of Cymelarsan® at 0.125 mg/ kg (half-therapeutic dose) followed by a single intramuscular dose of oxytetracycline at 100mg/ kg (five therapeutic) were given to each camel in the groups.

Camels in group 1 were used as un-infected-untreated (control negative), while camels in group 2 were infected-untreated (control positive).

2.6 Collection and preservation of samples

A weekly slaughter program for survival animals studied after the cessation of the drugs in Cymelarsan 14 days, 21 days in oxytetracycline and 28 day in ethidium and quinapyramine. Urine samples were collected from urinary bladder, bile from the gall bladder after the death or slaughter (two animals/week) of the animals in plain containers (Wols – U.K) and were preserved under -20°C until use. Specimens (5-7mm) for histopathology were taken from heart, brain, kidney, spleen liver, lung, colon, small intestine, ovary, testes, thyroid gland, muscle, site of injection, nerve, tendon, spinal cord and tongue. Two specimens were taken one (9g) from heart, brain, kidney, spleen, liver, lung, ovary, testis, muscle, site of injection for the determination of residues of the drugs and were preserved under -20°C until use.

2.7 Postmortem changes and Histopathology

At necropsy, animals were examined for postmortem lesions and specimens (5 – 7 mm), of heart, brain, kidney, spleen liver, lung, colon, small intestine, ovary, testes, thyroid gland, muscle, site of injection, nerve, tendon, spinal cord and
tongue were fixed in 10% formal saline, according to (Carleton, 1976; Culling, 1974).

2.8 Methods

2.8.1 Clinical examination

2.8.1.1 Clinical signs were closely observed daily and recorded regularly.

2.8.1.2 Body temperature (BT)  
Rectal temperature was obtained daily by using a Digital Thermometer (Astro Temperature, Marshall, Elec.). (Kelly, 1986).

2.8.1.3 Body weight (BW)  
Body weight was measured twice a week by the Poked Balance (Original Rebüre – Germany) (Kelly, 1986).

2.8.1.4 Respiratory rate (RR)  
Respiratory rate was done daily by counting the movements of the nose per second (Kelly, 1986).

2.8.1.5 Blood pressure rate (BPR)  
Blood pressure rate was measured twice a week using Electronic Apparatus (Digital Blood Pressure Meter, Seinex Electronics Ltd. Jenny Mount Court, North Derby Street Belfast BT IS 3HN – UK).

Principle  
Blood pressure is a measurement of the force of blood flowing against resistance along the walls of arteries. Arterial blood pressure is constantly changing during the course of the cardiac cycle. The highest pressure in the cycle is called the systolic blood pressure; the lowest is the diastolic pressure; both pressure readings are necessary to enable evaluation of status of blood pressure. World Health Organization (WHO) has established standards for assessment of high and low blood pressure. (MHSS, 1971).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

**Procedure**

Wrap the cuff around the left femur; turn the power and adjust the zero in one second the cuff pressurizes after the zero displayed on the display window and when the pressurization is complete, the (heart mark) will appear indicating that measurement is in progress.

**Calculation**

Read from the display window as systolic pressure/diastolic pressure.

**2.8.1.6 Pulse rate**

Pulse rate of the femoral artery was measured using Electronic Apparatus (Digital Blood Pressure Meter, Seinex Electronics Ltd. Jenny Mount Court, North Derby Street Belfast BT 15 3HN – UK).

**Principle**

Pulse rate is a measurement of the force of blood flowing against resistance along the walls of arteries. World Health Organization (WHO) has established standards for assessment of pulse rate. (MHSS, 1971).

**Procedure**

Wrap the cuff around the left femur; turn the power and adjust the zero . in one second the cuff pressurizes after the zero displayed on the display window and when the pressurization is complete, the (heart mark) will appear indicating that measurement is in progress.

**Calculation**

Read from the display window as pulse rate pulses/min.

**2.9 Parasitological methods**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

The parasitological methods are done to detect the parasites *T. evansi* and *T. vivax* in blood (peripheral or whole blood) or liver tissues in rats, goats and camels in the daily using different techniques:

### 2.9.1 Wet blood film

A drop of blood was taken from the ear vein on a glass slide covered with cover slip and examined under light microscope (CH20- Olympus Germany) using 10 x 40 of magnification (Soulsby, 1982).

### 2.9.2 Thin film

A drop of blood was spread on a glass slide fixed with methanol 70 % and stained with Giemsa’s stain then the slide was examined under light microscope (CH20- Olympus Germany) using an oil immersion lens 10 x 100 (Soulsby, 1982).

### 2.9.3 Thick film

A drop of blood was spread as a thick smear on a glass slide, stained with leishman’s stain, and examined under light microscope (CH20- Olympus Germany) using 10 x 40 magnification (Soulsby, 1982).

### 2.9.4 Buffy coat technique

Samples of blood were taken at the every three days post infection for 15 days, then 1 hour, 3 hours post-treatment, 24 hours, 3 days, 7, 14, 21, 28, 35, 42 and/or 49 days post-treatment). A centrifuge capillary tube (Becton and sons- France) was filled with ear vein blood and centrifuged at 5000rpm. The tube was broken in a buffy coat area and squeezed on glass slides to prepare a wet smear and examined under light microscope (CH20- Olympus Germany) using 10 x 40 magnification (Soulsby, 1982).

### 2.9.5 Liver impression smears
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

This method was done after death or slaughter of the animals. The specimens of the liver (3-5mm) were pressed between two slides then a drop of distilled water was added and examined under the microscope as described by Soulsby, (1982).

2.10 Collection of the blood

Animals were bled from the jugular vein (at the first day after infection, and then three days post infection then 1 hour, 3 hours post-treatment, 24 hours, 3 days, 7, 14, 21, 28, 35, 42 and/or 49 days post-treatment). Two plain vaccutainer test tubes were used (Becton and sons-France) the tube containing no anticoagulant was left to clot, centrifuged at 3000 rpm and serum was collected and kept at -20°C until analyzed for the concentration of sodium, potassium, chloride, calcium, phosphorus, magnesium, manganese, zinc, copper, iron, arsenic (as Cymelarsan), urea, creatinine, total protein, albumin, globulin, total cholesterol, glucose, triglycerides, phospholipids, and for the activity of glutamic oxaloacetic transaminase (GOT), and glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), creatine kinase (CK), pyruvate kinase (PK), succinate dehydrogenase (SDH), amylase, lipase, determination of oxytetracycline and quinapryamine.

The other tube containing ethylene diamine tetra acetic acid (EDTA) was used for the determination of red blood cells (RBC), white blood cell (WBC) count, haemoglobin concentration (Hb), platelets counts, reticulocytes counts, packed cell volume (PCV) and differential white blood cell (WBC) count.

2.11 Haematological methods

The haematological methods for RBC (x10⁶), WBC (x10³), Hb (g/dl), differential WBC count, blood indices (MCV, MCH, MCHC) and PCV% were done in Khartoum North Human Hospital by using an instrument called Cell-DYN®,
2.11.1 Cell-DYN® Diff screen

### 2.11.1.1 Calibration

The most efficient way to calibrate the open sample mode of the cell-DYN 1700 system is to use calibrator and the auto-Cal method. When a control is used as a calibrator, a different lot or brand of control must be used for Daily Quality Control (DQC) the procedure as the following:

Return each control at 2 – 8°C for 1 min then shake the DOQ and allow to rest and warm for 50 min.

### 2.11.1.2 Procedure, principle and reagents

The apparatus can suck 2 ml of the blood and 2 ml of screen reagent, computerized the data and the result were given in the screen. The screen reagents consist of diluents, lytic agent, detergent and enzymatic cleaner:

#### 2.11.1.2.1 Diluents:

Cell-DYN® Diluents are formulated to meet following the requirements: WBC, RBC, PCV and Hb.

- Rinse the sample probe and maintain the cell volume of RBC during the count.
- Sizing portion of the measurement cycle.

And it consists of: Sodium sulfate anhydrous < 1%, Sodium chloride < 0.5%, Anti-microbial agent, <0.5%, Buffer, < 0.1% and Stabilizer < 0.1%.

#### 2.11.1.2.2 Lytic agent

It is formulated to meet the following requirements:

- Rapidly lyses the RBC and minimize the result out cell stroma.
- Alters the WBC membrane to allow the cytoplasm to slowly diffuse and allow the membrane to shrink around the nucleus and any granules that may present.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

-Converts the Hb to a modified the hemoglobin cyanide complex that is measurable at 540 nm.

It consists of: Quaternary ammonium salt 50% (< 4.50%) and Potassium cyanide < 0.08%.

### 2.11.1.2.3 Detergent

Detergent is formulated to meet the following requirements:

- Provide an optically clear solution that is used to obtain the zero preference during the Hb measurement cycle.

- Provides proper meniscus formation in both metering tubes and maintain it during each run cycle and rinse both chambers, both metering tubes, and the HGB flow cell with minimal bubble formation.

And it consists of: Sodium sulfate anhydrous < 1.50%, Sodium chloride < 0.60%, Anti-microbial agent < 0.10% and Poly oxyethylene ether < 0.25%.

### 2.11.1.2.4 Enzymatic cleaner

Enzymatic cleaner is formulated to effectively remove protein build up within the instrument.

### 2.11.2 Staining and counting reticulocytes

New methylene blue 0.5g, and potassium oxalate 1.6g were dissolved in distilled water 100.0 ml. 2 drops of blood with an equal quantity of stain mixed and left for 15 – 20 minutes, blood films were made and reticulocytes were counted under light microscope x40 (number of reticulocyte cells x 10⁶ µml/l) (Brecher, 1949).

### 2.11.3 Thrombocytes count

Dissolve sodium citrate 3.8g, formaldehyde (40%) 0.2 ml and brilliant crystal blue 0.1 g in distilled water 100.0 ml.1.0 ml from the diluting fluid
was taken by the RBC pipette; 0.5 ml of blood was added; mixed and shaken; expel a third of the fluid, fill both sides in haemocytometer. Place the haemocytometer in Petri dish containing filter paper keep it without touch. Count in erythrocytes counting area. The number of erythrocytes x 1.0 = No. of erythrocytes/µl = thrombocyte cells x10³µml/l. (Schalm et al. 1981)

2.12 Serobiochemical analysis
Serobiochemical analysis was carried out using commercial kits (Randox Laboratories Ltd. U.K.) or (Plastic Laboratory Product Ltd. U.K) or (Linear chemicals, S.L.-Spain) or chemical– using absorption spectrophotometer (Unicam 8625/U.V. Vis U.K.), atomic absorption (Cornning EEL 197Spectra- Evans Electroselenium Ltd., England) and (400 flame photometer corning – England).

2.12.1 Enzymes activity

2.12.1.1 Determination of serum lactate dehydrogenase (LDH) (L-Lactate: NAD oxidoreductase (1.1.1.27)).

Lactate dehydrogenase was determined according to the method described by King (1965) using commercial kits (Linear chemicals, S.L.-Spain).

Principle
Lactate dehydrogenase catalyzes the reduction of pyruvate by NADH. The rate of decreasing in concentration of NADH is proportional to the concentration of LDH present in the sample.

\[
\text{NADH} + H^+ + \text{Pyruvate} \rightarrow \text{LDH} \rightarrow \text{Lactate} + \text{NAD}^+
\]

Reagents
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Phosphate buffer, pH 7.4, 100 mmol/l, nicotinamide adenine dinucleotide and sodium pyruvate, 22.4 mmol/l

**Procedure**

Measure 2.4 ml phosphate buffer with spectrophotometer, then add 0.1 ml serum and 0.1 reagent 2, mix well, allow to stand for 20 min at 25°C, then add reagent 3, monitor the rate of change extinction at 340 nm.

**Calculation**

Serum LDH (U/l) = \( \frac{E_{340}/\text{min} \times 1000 \times 2.7}{0.1 \times 6.3} \)

### 2.12.1.2 Determination of serum creatine kinase (CK) (ATP: Creatine phosphotransferase(2.7.3.2 C))

It was measured according to Swanson and Wilkinson (1972) method using commercial kits (Linear Chemicals, S.L.-Spain).

**Principle**

Creatine kinase (CK) catalyzes the transfer of a phosphate group from phosphocreatine to ADP. This reaction is coupled to those catalyzed by hexokinase and glucose-6-phosphate dehydrogenase. The rate of NADPH formation is proportional to the concentration of CK present in the sample.

\[
\text{Phosphocreatine + } \text{CK} \text{~creatinine + ATP} \\
\text{ATP + Glucose } \text{HK} \text{~glucose-6-phosphate + ADP} \\
-\text{Glucose-6phosphate + NADP}^+ \text{~G6DH~phosphogluconate +NADPH + H}^+
\]

**Reagents**

Consist of Tris buffer, 50 mmol/l, pH 6.8, reagent mixture containing adenosine diphosphate, 1.25 mmol/l (60.5 mg) + creatine phosphate, 12.5 mmol/l (408 mg) + glucose, 25 mmol/l (450 mg) + magnesium, 25 mmol/l (760 mg) + adenosine monophosphate 12.5 mmol/l (456 mg), make to 100
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

ml, IVADP+, 12 mmol/l. Dissolve a 2 mg of the monosodium salt in 10 ml tris buffer, pH 6.8 with 1 mol/l hydroxide stored frozen, cysteine, 74mmol/l. Prepare freshly each day. Dissolve 131 mg cysteine hydrochloride monohydrate in 10 ml deionside water, pH 6.8 with 1 mol/l sodium hydroxide and enzyme solution consisting of: glucose – 6 – phosphate dehydrogenes (9 units/ml) + 18 units/ml hexokinase in Tris buffer.

**Procedure**

Mix 2.4 ml reagent solution with 0.2 ml NADP+, 0.2 ml cysteine and 0.1 ml enzyme solution place in 37°C for 10 min, then add 0.1 ml serum and mix and read in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at 340 nm over a period of 10 – 15 min against blank.

**Calculation**

Serum creatinine kinase (U/l) = \(\frac{\Delta E_{340/\text{min}} \times \text{total volume in the cuvette (ml)} \times 10^3}{603 \times \text{volume of serum taken (ml)}}\)

**2.12.1.3 Determination of serum pyruvate kinase (PK) (ATP:pyruvate phosphotransferase (2.7.1.40C))**

It was measured according to method described by (Gutmann and Berit,(1974).

**Principle**

Less trouble is experienced from colour in the blanks with this technique, due to its appearance in the earlier method to the hydrogen peroxide used.

Pyruvate kinase (PK) catalyses the interconversion of phosphoenolpyruvate (PEP) and pyruvate:
For the determination of PK activity the above reaction is coupled with the reduction of pyruvate by lactate dehydrogenase in the presence of NADH. PK is activated by potassium ions and inhibited by sodium.

Reagents

Consist of: Triethanolamine buffer: PH 7.5, 160 mmol/l containing 120 mmol/l KGI, 21 mmol/l MgSO4, 7H2O, 40 mg EDTA. Dissolve 2.2 g triethanolamine, 0.7 g KGI, 0.4 g MgSO4, 7H2O, 40 mg EDTA (disodium salt), in about 50 ml water, adjust to pH 7.5 with 100 mmol/l sodium hydroxide and dilute to 75 ml, NADH-PEP: 6 mmol NADH/l and 32.5 mmol PEP/l. Dissolve 2.2 g 10mg NADH (disodium salt) and 45 mg PEP (trihexylamine salt) and 10 mg sodium bicarbonate in 3 ml water, lactate dehydrogenase, 0.5 mg/ml. Dilute stock suspension with 2.2 mol/l ammonium sulphate solution, adenosine diphosphate, 100 mmol/l, 162 mg ADP (disodium salt) plus 30 mg sodium bicarbonate in 3 ml water and Sodium chloride solution, 9 g/l.

Procedure

Collect blood without stasis. Determine the red cell count. Serum should be free from haemolysis. For haemolysis wash the red cell from 0.20 ml finger blood three times with 2 ml sodium chloride solution, centrifuging red after each wash for 10 min at approx. 3000 rpm. then suspend the centrifuged red cell in 2 ml redistilled water, allow to stand for 15 min at +4 °C, centrifuge again and use the supernatant for the determine. Take 2.5 ml buffer (and 2.0 ml for haemolysate) and 0.1 ml NADH-PEP. 0.5 ml serum, 0.9 redistilled water, 0.1 ml NADH-PEP and 0.1 ml supernatant, then add 50µl LD suspension, NADH-Pep, mix, incubate 5 min at 25 °C, pour into a
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)
cuvette, read at 340nm against air (E1) or a dilute picric acid solution, prepare a diluent 1 or 2 drops of a 12g/l solution to 100ml with water, incubate at 25 °C and read again at 340 nm (E2) within 10min from the first reading, add 0.1ml ADP mix and read again (E3) and Incubate at 25°C and read again at 340nm within 10 min. (E4).

Calculation

E340 due to PK activity = (E3 – E4) – (E1-E2)

PK activity (U/l) = E340 x 104.5.

2.12.1.4 Determination of serum glutamic oxalocetic transaminase (GOT) (Asparate: 2-oxoglutarate aminotransferase or Asparate aminotransferase (AST) or glutamic oxaloacetic transaminase (2.6.1.1)) and glutamic pyruvic transaminase (L- Alanine : 2-oxoglutarate aminotransferase or Alanine aminotransferase (ALT)(2.6.1.2))

Their activities measured according to the method described by (Young et al., 1975) using commercial kits (Randox Laboratories Ltd. U.K.).

Principle

Alanine aminotransferase catalyzes the transfer of an amino group from alanine to 2-oxoglutarate forming glutamate and pyruvate. The pyruvate produced is reduced to lactate dehydrogenase and NADH. The rate of decrease in concentration of NADH is proportional to the concentration of ALT present in the sample.

\[
\text{Alanine} + 2\text{-oxoglutarate} \xrightarrow{\text{ALAT}} \text{Glutamate} + \text{pyruvate} \\
\text{NADH} + H^+ + \text{Pyruvate} \xrightarrow{\text{LDH}} \text{Lactate} + \text{NAD}^+ 
\]

Reagent
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Reagents (1) consist of: TRIS pH 7.3, 100mmol/l, and alanine, 500mmol/l.

Reagent (2) consists of: 2-oxoglutarate, 0.18 mmol/l, LDH, 1200U/L and NADH, 15mmol/l.

In GPT 2-oxoglutarate, 0.18 mmol/l act as Starter and Reagent 3.

Procedure
Mix reagent (1) with (2) (working reagent), then add 100 µl sample and 1.0 ml from working reagent. And 100µl from reagent (3) in GPT measurement. Read in in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength at 340 nm against blank.

Calculation
Serum AST U/L = Reading x1750
Serum ALT U/L = Reading x 1905

2.12.1.5 Alkaline phosphatase (ALP)((3.1.3.1))

It was measured according to the method described by (Young et al. 1975) it was done using commercial kits (Linear Chemical-).

Principle
Alkaline phosphatase catalyzes the hydrolysis of p-nitrophenyphosphate, in the presence of magnesium ions, liberating inorganic phosphate and p-nitrophenol. The rate of p-nitrophenol to the concentration of ALP present in the sample.

\[
\text{4-nitrophenilphosphate} \xrightarrow{\text{ALP}} \text{4-nitrophenol formation} + \text{Inorg. Phosphate}
\]

Reagents
Reagent (1) consists of: DEA buffer pH 9.8, 1 mmol/l and reagent(2)consists of 4-nitrophenylphosphate, 10mmol/l.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

**Procedure**

Mix reagent (1) with (2) (working reagent). Add 20µl sample and 1.2ml from working reagent, read in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 405nm against blank at I min. then after 3 min.

**Calculation**

Alkaline phosphatase (ALP)(U/L) = Mean of reading x 3300

2.12.1.6 Determination of serum α-amylase (α-1,4-glucan 4 glucanohydrolyase (3.2.1.1C))

Activity was measured according to the method described by (Young *et al.* 1975) using commercial kits (Linear Chemicals, S.L.-Spain).

**Principle**

α–amylase catalyzes the hydrolysis of blocked p-nitrophenylmatoheptaoside liberating oligomaltosides. The enzymes amyloglucosidase and α-glucosidase hydrolyse completely the oligomaltosides, liberating p-nitrophenol. The rate of p-nitrophenol formation is proportional to the concentration of α-amylase present in the sample.

\[
\begin{align*}
\text{PNPG7bl.} & \xrightarrow{\alpha\text{Amylase}} \text{PNP-oligomaltosides} \\
\text{PNP-oligomaltosides} & \xrightarrow{\alpha\text{glucosidase}} \text{Glucose} \\
\text{PNP-oligomaltosides} & \xrightarrow{\alpha\text{amyloglucosidase}} \text{Glucose}
\end{align*}
\]

**Reagent**

Reagent(1) consists of: pipes pH 7.0 50 mmol/l and reagent (2) consists of: PNPG7bl. 1.6 mmol/l, amyloglucosidase 10 U/L and glucosidase 25 U/L. Dissolve a tablet of reagent 2 with one bottle of buffer reagent 1 and mix gently to dissolve contents.

**Procedure**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Mix reagent (1) with (2) (working reagent): add to 100µl, 2.0ml from the working reagent at 25/30°C or add to 50µl, 2.0 ml from the working reagent at 37°C.

**Calculation**

When measured under 25/30°C the formula is:

\[
\text{Serum } \alpha\text{- amylase} = \frac{A}{\text{min}} \times 2690 \text{ U/L}
\]

When measured under 25/30°C the formula was:

\[
\text{Serum } \alpha\text{- amylase} = \frac{A}{\text{min}} \times 5125 \text{ U/L}
\]

2.12.1.6 **Determination of serum lipase (glycerol ester hydrolyase (3.1.1.3))**

Activity was measured according to method described by Tietz and Fiereck, (1972)

**Principle**

As the enzyme acts on substrates in emulsified form, the preparation of a stable emulsion is important. The most appropriate substrate is olive oil.

**Reagent**

It consists of: Purified olive oil 300 ml, remove the fatty acid by adding, whilst stirring, 60g; substrate emulsion. Mix 100 ml water plus 0.2g sodium benzoate plus 7g gum acacia till dissolved; add slowly 100ml purified olive oil mix for 10 min. keep at 4°C; Tris stock solution, 800mmol/l. Dissolve 48.55g tris (hydroxyl methyl) aminomethane in water. Make to 500ml, Tris working buffer, 200mmol, pH 8 at 27°C to 50ml; Tris
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

stock solution in a 200ml. Add 21.5ml, 1mol/l HCl and make up to the mark, sodium hydroxide solution, 50mmol/l; Aqueous ethanol, 950 ml ethanol/l and thymolphthalein solution, 1g in 100ml reagent 7.

Procedure

Boil tube and keep it to cool then add 2.5 ml water, 10 ml emultion and 1 ml Tris buffer and bring to 37°C in a bath then add 1ml serum, cover the tubes and shake well, replace in the bath for 3 hours then add 3ml ethanol to both tubes to stop the reaction and bring the fatty acid into solution, then add 5 drops of indicators to each and titrate with sodium hydroxide, till definite blue colour then add the alkali quickly and shake well.

Calculation

Serum lipase (U/L) = Titration of the test ml – titration of blank ml

2.12.1.7 Determination of serum succinate dehydrogenase (SDH) (succinate dehydrogenase –succinate: accepter oxireductase (1.3.99.1))

Activity was measured according to method described by McComb et al. (1976 or1975).

Principle

The reduced NAD⁺ and NADP⁺ has an absorption peak at 340nm and the oxidized form has little absorption at that wavelength.

Calculation

Serum SDH U/L = reading at 340nm x \( \frac{1000}{\text{total volume in the cuvette ml}} \)
2.12.2 Other Biochemical change

2.12.2.1 Determination of Serum creatinine

Concentration was measured according to the method described by Balets and Bohmer (1972) using commercial kits (Randox Laboratories Ltd. U.K.).

Principle
Creatinine in the sample reacts with alkaline picrate forming a red complex. The rate at which the red complex develops is measured quickly to avoid interference from other serum constituents.

Working reagents consists of:
- Picric acid: 35 mmol/l and sodium hydroxide 0.32 mmol/l

Standard:
- 2 mg/dl (177 mmol/l) creatinine

Add to 200l of the samples and standard 2 ml of the working reagent, read in spectrophotometer (Unicam 8625/U.V. Vis U.K) at wavelength 420-510nm. Incubate at temperatures: 25°C/30°C/37°C for 30-60 sec. against air and were measured as A standard and A samples

Calculation

Serum creatinine concentration (mg/dl) = \[ \frac{A_{\text{sample}}}{A_{\text{standard}}} \times 2 \]

2.12.2.2 Determination of serum urea

Concentration was measured according to the method described by Patton and Crowch (1977) using commercial kits (Randox Laboratories Ltd. U.K.).

Principle
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Urea in the sample is hydrolyzed enzymatically into ammonia and carbon dioxide. Ammonia reacts with salicylate and hypochlorite, in the presence of the nitroprusside, to form a green indophenol. The colour intensity is proportional to the concentration of urea present in the sample.

\[
\text{Urea} + \text{H}_2\text{O} \xrightarrow{\text{Urease}} \text{CO}_2 + 2\text{NH}_3
\]

\[
\text{NH}_3 + \text{Salicylate} + \text{Hydro} + \text{Nitroprusside} \xrightarrow{\text{OH}} \text{Indophenol}
\]

**Reagent (1)**

Consists of 60 mmol/L phosphate buffer, 1.5 mmol/L EDAT, 60 mmol/L sodium salicylate and sodium nitroprusside 5.2 mmol/L.

**Enzyme reagent**

Reagent (2) consists of hypochloride solution consisting of: 18 mmol/L sodium hypochloride and 450 mmol/L sodium. Reagent (3) consists of 75000/urease.

**Standard**

Urea 50mg/dl

**Procedure**

Add 1ml of reagent 1 and 3 to 10µl of the sample and standard, incubate for 5min. then add 1ml of reagent 2. Read in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 580 nm – 600 nm and measurement against blank and were measured as A standard and A samples

**Calculation**

Serum urea concentration (mg/dl) = \( \frac{A_{\text{sample}}}{x \times 30/50} \)
2.12.2.3 Determination of serum direct bilirubin

Measured according to (Young et al. 1975) using commercial kits (Linear chemicals, S.L.-Spain).

**Principle**

Bilirubin in the sample reacts with diazotized sulfanilic acid in the presence of DMSO. The formed coloured azobilirubin is measured photometrically.

There are two Bilirubin fractions in serum, Bilirubin-glucuronide and free Bilirubin which bind with albumin.

The term total or direct Bilirubin refers exclusively to the reaction characteristic in the presence or absence of an accelerator or solubilizer and are only approximate equivalents of the two Bilirubin fractions.

**Reagent**

Reagent (1) consists of: Sulfanilic ac. 50mmol/l, DMSO 7mol/l and HCL 50 mmol/l. Reagent (2) consists of: Sodium nitrate 29 mmol/l.

**Procedure**

Add to 100µl of the samples 1.5ml of the reagent 1 and 50µl from reagent 2. Mix and allow to rest at room temperature for 5 min. and measure the absorbance in a spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 555 nm against blank and were measured as A blank and A samples.

**Calculation**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Direct serum bilirubin (mg/dl) = Reading (A sample - Absor. blank) x 7

(A standard- A standard blank)

2.12.2.4 Determination of serum total bilirubin

Measured according to (Young et al. 1975) using commercial kits (Boehringer Mannheim GmbH Diagnostics, West Germany).

**Principle**

Bilirubin is coupled with diazothized sulphonilic acid in the presence of caffeine to give an azo dye. No caffeine is added when direct bilirubin is determined. The formed coloured azobilirubin is measured photometrically. There are two bilirubin fractions in serum, bilirubin-glucuronide and free bilirubin which is bind with albumin. The term total or direct bilirubin refers exclusively to the reaction characteristic in the presence or absence of an accelerator or solubilizer and are only approximate equivalents of the two bilirubin fractions.

**Reagent**

Reagent (1) consists of: Sulfanilic ac. 50mmol/l and HCL 50 mmol/l, Reagent (2) consists of: Sodium nitrate 29 mmol/l, Reagent (3) Caffeine 9mmol/l and Reagent (4) consists of Sodium tartarate and hydroxide 50mmol/l.

**Procedure**

Add to 100µl of the samples 1.5ml of the reagent (1) and 50µl from reagent (2) and (3). Mix and allow to rest at 20-25° for 10 min. and add reagent (4) and allow to rest at 20-25° for 5-30 min. and measure the absorbance in a spectrophotometer (Unicam 8625/U.V. Vis U.K.) at
wavelength 578 nm against blank and were measured as A blank and A samples.

**Calculation**

Serum total bilirubin (mg/dl) = Reading x 10.8

### 2.12.2.5 Determination of serum total protein

Concentration was measured according to the method described by King *et al.* (1956) with Biuret reagent using commercial kits (Randox Laboratories Ltd. U.K.).

**Principle**

Proteins in the sample give an intense violet – blue complex with copper salts (II) in an alkaline medium. The intensity of colour is proportional to the amount of total proteins present in the sample.

**Reagent**

**Biuret reagent**

It consists of 100 mmol/L sodium hydroxide, 16 mmol/L sodium and potassium tartrate, 15 mmol/L potassium iodide and curpic sulphate 6 mmol/L.

**Blank**

It consists of 100 mmol sodium hydroxide and sodium – potassium tartrate 16 mmol.

**Standard**

It consists of Protein 60 g/l

**Procedure**

Add 5ml of the working reagent, then add 100µml of the standard and samples, mix and incubate at 37°C for 20min. read in spectrophotometer
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) (Unicam 8625/U.V. Vis U.K.) at wavelength 540 nm against blank. and they were measured as A standard and A samples

**Calculation**

Serum total protein concentration (g/dl) = \( \frac{A\text{ sample}}{A\text{ standard}} \times 60 \)

**2.12.2.6 Determination of serum albumin**

It was measured according to Barthlomew and Delany (1966) using commercial kits (Randox Laboratories Ltd. U.K.).

**Principle**

Albumin in the sample produces, in the presence of Bromocresol green, a colour change of the indicator from yellow – green, to yellow – blue at a slightly acidic pH.

**Reagents**

BCG concentrate: 75 mmol/L, pH 4.2 succinate buffer and 0.15 mmol/L Bromocresol green.

**Standard**

Serum albumin 45 g/l.

**Procedure**

Add to 20\(\mu\)l of the standard and samples, 4 ml from the working reagent then read in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 623 nm against blank and were measured as A standard and A samples

**Calculation**

Serum albumin concentration (g/dl) = \( \frac{A\text{ sample}}{A\text{ standard}} \times 45 \)

**2.12.2.7 Determination of serum globulin**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

It was done by deduction of the total protein values from albumin values.

### 2.12.2.8 Determination of serum phospholipids

Phospholipids were measured according to the method described by Connerty et al. (1961) using commercial kits (Linear chemicals, S.L.-Spain).

**Principle**

The technique used mostly for phospholipids has been to extract them into a suitable solvent, for example ethanol-ether, to digest an aliquot of the extract with sulphuric acid and hydrogen peroxide to oxidize the phosphorus to inorganic phosphate and determine this by one of the methods used to inorganic phosphate.

**Reagents**

Consist of Trichbrcetic acid solution, 50 g/l, 50 ml water + 25 ml concentrated sulphuric acid + 25 ml perchloric acid, Sodium acetate solution, 500 g trihydrate, Ammonium molybdate solution 25 g/l and Metol, 1 g/100ml/sodium hydrogen sulphite solution (30 g/l).

**Standard situation**

It consists 4.085 g anhydrous KH$_2$PO$_4$/l and 2 ml concentrated sulphuric.

**Working standard**

0.12 mmol dilute the stock standard to 250 with water.

**Blank**

It consists of 0.25 ml concentrated sulphuric acid, 1 ml sodium acetate, 1 ml molybdate, 1 ml metol and 8.75 ml water

**Procedure**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Add serum sample 0.2 ml + 5 ml trichoracetic, then filtered, then add reagent 2, 1 ml, then heat gently until becomes colorless, Allow to cool, add 1 ml water and boil, dd 1 ml sodium acetate and make it to 10 ml with water, add 1 ml ammonium molybdate, 1 ml metol, and mix well and after 15 min read at 700 mm against blank in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 555 nm against blank. and they were measured as A standard and A samples

Calculation

Serum phospholipids (mmol/l) = Reading of unknown x 3.0
Reading of standard

The reading was expressed in (mg/dl)

2.12.2.9 Determination of serum triglycerides

Measured according to (Bucolo and David (1973) using commercial kits (Linear chemicals, S.L.-Spain).

Principle

The triglycerides in the sample are hydrolyzed enzymatically to glycerol phosphate by Glycerol kinetic. Glycerol phosphate is oxidized to dihydroxyacetone phosphate by Glycerol phosphate oxidase. The liberated hydrogen peroxide is detected by a chromogenic acceptor, chlorophenol-anpyrone, in the presence of peroxidase. The red quinine formed is proportional to the amount of triglycerides present in the sample.

Triglycerides + H2O lipase $\rightarrow$ Glycerol+fatty acids
Glycerol + ATP $\rightarrow$ Glycerol-3-P + ADP
Glycerol-3-P + O2 $\rightarrow$ Dihydroxyacetone + H2O2
H2O2 + P-chlorophenol + 4-AP $\rightarrow$ Quinone + H2O

Reagents
Reagent (1) consists of: buffer pH7.5, 50mmol/l and p-chlorophenol, 2mmol/l.

Reagent (2) consists of: lipase, 150000U/L, GK, 500U/L, GPO 2500 U/L, POD, 440 U/L, 4-AP, 0.1mmol/l and ATP 0.10.1mmol/l.

**Procedure**

Mix reagent (1) with reagent (2) (working reagent). Add to 20µl sample and 20µl standard; 2.0ml from working reagent. Read in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 505 nm against blank and they were measured as A standard and A samples.

**Calculation**

Triglycerides (mg/dl) = \( \frac{A_{\text{sample}}}{A_{\text{Standard}}} \times 10 \)

**2.12.2.10 Serum Total cholesterol**

Concentration was measured according to the method described by (Trinder et. al. 1969) using commercial kits (Linear Chemicals, S.L.-Spain).

**Principle**

In the presence of cholesterol esterase, the cholesterol esters in the sample are hydrolyzed to cholesterol and free fatty acids. The cholesterol produced is oxidized by cholesterol oxides to cholestenone and hydrogen peroxide is detected by a chromogenic of peroxidase. The red quinine formed is proportional to the amount of cholesterol present in the sample.

\[
\text{Cholesterol esters} + \text{H}_2\text{O} \xrightarrow{\text{CHE}} \text{Cholesterol} + \text{Fatty acid} \\
\text{Cholesterol} + \text{O}_2 + \text{H}_2\text{O} \xrightarrow{\text{CHOD}} \text{cholestenone} + \text{H}_2\text{O}_2 \\
\text{H}_2\text{O}_2 + \text{phenol} + 4\text{-AP} \xrightarrow{\text{POD}} \text{Quinone} + \text{H}_2\text{O}
\]

**Reagents**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Reagent (1) consist of: pipes buffer pH 6.9, 90 mmol/l, phenol 26 mmol/l.

Reagents (2) consist of: CHE, 300 U/L, CHOD, 300 U/L POD, 1250 U/L and 4-AP, 0.4 mmol/l.

Procedure
Mix reagent (1) with (2) (working reagent): then add 20 µl sample, 20 µl standard and 2.0 ml from working reagent. Read in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 505 nm against blank and they were measured as A standard and A samples.

Calculation
Serum cholesterol (mmol/L) = \frac{\text{Reading of unknown}}{26} \times \frac{\text{Reading of standard}}{	ext{Reagents}}

2.12.2.11 serum glucose

It was measured according to (Trinder, 1969)) using commercial kits (Randox Laboratories Ltd. U.K.).

Principle
Glucose in the sample is oxidized to gluconic acid in the presence of Glucose oxidase. The liberated hydrogen peroxide is detected by a chromogenic oxygen accepter, phenol-ampyrene. The red quinone formed is proportional to the amount of glucose present in the sample.

Glucose + 1/2 O_2 + H_2O \xrightarrow{\text{GOD}} \text{Gluconic acid} + H_2O_2

2H_2O + phenol + 4-AP \xrightarrow{\text{POD}} \text{Red Quinone} + 4H_2O

Reagents
Reagent (1) consist of: TRIS Buffer pH 7.4, 92 mmol/L, buffer Solution Phenol 0.3 mmol/L
Reagents (2) consist of: Glucose Oxidase 15000u/l, Enzymes Peroxidase 1000 U/L, 4 Aminophenazone 2.6 mmol/L.
Standard Glucose Sol. 100 mg/dL
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

**Procedure**

Add to 10µl of the standard and samples 1.0ml from the reagents. Mix, incubate 10 min at 37°C or 30 min at room temperature. The colour is stable 30 min at room temperature. Read in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 505 (490 – 550) nm against blank. at temperature 25/30/37°C and they were measured as A standard and A samples.

**Calculation**

Serum glucose (mg/dL) = \( \frac{A_{\text{sample}}}{A_{\text{standard}}} \times 100 \)

2.12.3 Minerals and trace elements change

2.12.3.1 Serum Sodium and Potassium

Concentration were measured according to the method described by Varley (1975) using flame photometer (400 flame photometer Corning – England).

**Stock standard**

Dissolve 58.45 g NaCl in litre of distilled water.

**Working standard**

**High standard** for: 8.0 of the stock, made up to 1 litre with distilled water.

**Low standard**: 7.0 ml of the stock, made up to 1 litre with the distilled water.

Dissolve 7.4g potassium chloride in 1 litre of distilled water.

**High standard**: 7ml of the stock made up 1 litre with the distilled water.

**Low standard**: 5ml of the stock, made up to 1 litre with the distilled water.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Mix the two high standards together and the two low standards together.

**Procedure**

It is based on passing under controlled conditions, a dilute serum (1:100) as a very fine spray in the air supply to a burner where the solution evaporates and the salt dissociates to give neutral atoms. Light of characteristic wavelengths was emitted and passed through a specific filter for sodium (or potassium) on to a selenium cell and the amount of current produced was read on a galvanometer. The air pressure was adjusted to 10 Lb/square inch and compressed air through the flame, passing compressed air through an atomizer into which the diluted serum was drawn by suction and then entered the burner with its air supply formed the spray. The gas and the air pressured were carefully regulated in order to maintain a constant and steady flame. Changes in the galvanometer reading were recorded in mmol/l and were measured as A standard and A samples.

**Calculation**

\[
\text{Sodium concentration (mmol/l) = } \frac{A\text{ sample}}{A\text{ standard}} \times 140
\]

\[
\text{Potassium concentration (mmol/l) = } \frac{A\text{ sample}}{A\text{ standard}} \times 5
\]

2.12.3.2 Determination of chloride

Concentration was measured by the method described by Schales and Schales (1941) using commercial kits (Linear chemicals, S.L.-Spain).

**Principle**

Chloride ions in the sample react with mercuric nitrate forming a coloured complex proportional to the amount of chloride ions present in the sample.

**Reagent**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Consists of 8.5 mmol/l Mercuric nitrate solution, dissolve 2.9 to 3g (Hg(NO3))2 H2O in 100ml water, made up to litre with distilled water, diphenylcarbazone indicator, dissolve 100mg in 100 ml ethanol, store at 4°C in dark place and standard chloride solution 100 mmol/l.

Procedure
Add 0.2ml serum sample + 1.8 ml water, and then add 60 µl of the indicator. The mixture was titrating with mercuric nitrate solution, which calibrated to 0.01 ml/l. Repeat the titration on 2 ml of the standard chloride solution. And they were measured as A standard and A samples.

Calculation
Serum chloride (mmol/l) =
\[
\frac{\text{ml titrant needed for A sample}}{\text{ml titrant needed for A standard}} \times 100
\]

2.12.3.3 Serum Magnesium

Measured according to the method described by Gindler et al. (1971) using commercial kits (Linear Chemicals, S.L.-Spain).

Principle
Magnesium in the sample forms a coloured complex when it reacts with a calmagite solution in the presence of EGTA at alkaline pH. The intensity of coloured formed is proportional to the amount of magnesium present in the sample.

Reagents
Reagent (1) consists of aminomethylpropanol1 mmol/l and EGTA0.21mmol.
Reagent (2) consists of calmagite0.3mmol/l

Procedure
Mix reagent (1) with (2)(working reagent). Add to 10µl of the sample and of the standard, 1.0ml incubate for 5min. at 28°C and read the result as
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

A sample and A standard in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 520nm.

**Calculation**

Serum magnesium (mg/dl) = \( \frac{A\text{ sample}}{A\text{ standard}} \times 0.73 \)

**2.12.3.4 Serum Calcium**

It was measured according to Stern *et al.* (1957) using commercial kits (Linear Chemicals, S.L.-Spain).

**Principle**

Calcium in the sample reacts with o-cresolphtaleine at alkaline pH. The coloured complex formed is proportional to the amount of calcium present in the sample.

**Reagents:**

Reagent (1) consists of: Ethanolamine 500mmol/l.

Reagent (2) consists of: o-cresolphtalein 0.62mmol/l and 8-hidroxyquiinoline 69mmol/l.

**Procedure**

Add 1ml from reagent (1) and (2) to 20µl mix, incubate for 5min. at room temperature. Read the result as A sample and A standard in in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 570nm.

**Calculation**

Serum calcium (mg/dl) = \( \frac{A\text{ sample}}{A\text{ standard}} \times 0.25 \)

**2.12.3.5 Serum Inorganic Phosphorus**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

It was measured according to (Young, 1975) using commercial kits (Linear Chemicals, S.L.-Spain).

**Principle**

Inorganic phosphate reacts with sodium molybdate forming a phosphomolybdate complex. Its subsequent reduction in alkaline medium originates a blue molybdenum complex. The density of colour formed is proportional to the amount of phosphorus present in the sample.

**Reagent**

Reagent (1) consists of molybdate-borate 1.21 mmol/l.

Reagent (2) consists of 1,2 diphenyldiamine

**Procedure**

Mix reagent (1) with (2) (working reagent).

Add 3.0 ml of the mixture of the reagent 1 and 2 to 100 µl standard solution and also to 100 µl to the test; read each at the wave length 710 nm in spectrophotometer (Unicam 8625/U.V. Vis U.K.). Measurement was done against blank and they were measured as A standard and A samples.

**Calculation**

Serum inorganic phosphorus mg/dl = \[
\frac{A_{\text{sample}}}{A_{\text{standard}}} \times 2.59
\]

2.12.3.6 Serum Zinc

It was measured according to the method described by to Dawson and Walker (1969).

**Principle**

About a third of the plasma zinc is bound loosely to albumin with the rest more firmly bound to globulin. Zinc is a component of a number of enzymes, particularly carbonic anhydrase, carboxypeptidase A, dehydrogenase acting on alcohol, glutamate, glyceraldehydes-3-phosphate and lactate. Zinc activates many enzymes including dipeptidases and aminopeptidase.

Stock solution (100 mg/L): Dissolve 0.1g pure zinc in 10 ml of 5 hydrochloride acids, made up to 1 liter with water.

Stock solution (10 mg/L): 10 ml of stock (1) was pipetted into 100 ml volumetric flask, made up to 100 ml with water.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Stock solution (100 mg/L): 10 ml of 2 was made up to 100 ml with water.

Sodium stock solution (140 m/L): 8.2 g of dry NaCl (zinc free) was dissolved in 1 liter water.

Calibration

0, 10, 20 ml of zinc stock solution 3 were each pipetted into 100 ml flask each flask was made up to 20ml with water.

Corresponding to 0, 100, 200 ml in the sample solutions, 200 ml of serum was made up to a 20 ml with water and they were measured as A standard and A samples

Calculation

\[
\text{Zinc in serum} = \text{reading} \times \frac{10}{0.2} \times \frac{100}{1000} \text{mg/100 ml}
\]

The result was expressed in (µmol/)

2.12.3.7 Copper

Copper was measured according to Ventura and King (1951) method.

Principle

After releasing the copper from protein by hydrochloric acid, the proteins are precipitated by trichloroacetic acid, and the copper extracted into amyl alcohol and ether as a golden yellow coloured complex with sodium diethylthiocarbamate for colorimetric determination. Sodium pyrophosphate is added to prevent interference from iron.

Reagents and procedure

To each 3ml add 1ml 100mmol hydrochloric acid, worm in boiling water until begun to cloud cool, then add 1.5ml hydrochloric acid 6mol/l, stand for 10 minutes, then add 3ml trichloracetic acid, 200g/l, mix, stand for minutes, centrifuge the mixture, remove the supernatant fluid; wash the precipitate with 3ml trichloracetic acid, 50g/l, centrifuge again, remove the
supernatant, then add 1ml sodium pyrophosphate + 2ml ammonia; then add 5ml amyl alcohol-ether, remove the organic layer and dry shaking with a little powdered anhydrous sodium sulphate and then read in spetrophotometr (Unicam 8625/U.V. Vis U.K.) at wavelength 440nm. and they were measured as A standard and A samples.

**Stock standard solution**
Dissolve 500mg copper sulphate in water, then add 0.1 ml concentrated sulphuric acid and make up to 1 litre (2mmol/l).

**Standard work solution**
Dilute the above 1 to 100 to obtain a solution containing 20 nmol/l. Treat 5ml standard, (100 nmol of copper) in the same way as the serum.

**Calculation**
Serum copper (mmol/l) = \( \frac{A_{\text{sample}}}{A_{\text{standard}}} \times 33.3 \)

The result was expressed in (µmol/l)

2.12.3.8 Serum Manganese

**Principle**
The serum was dissolved with distilled water as 2ml to 8ml according to (Jeffery et al., 1989). Read the sample in atomic absorption (Cornning EEL 197Spectra- Evans Electroselenium Ltd., England) at wavelength 279.5nm or 1-4 air acetylene/l (fuel lea).

**Calculation:** read the result from the standard curve as mmol/l.

2.12.3.9 Serum Iron
Iron was measured according to the method of (Caraway, 1959 and 1963) using commercial kits (Linear chemicals, S.L.-Spain).

**Principle**

Iron in the sample is dissociated from transferring-iron complex in weakly acid medium and the liberated iron is reduced into ferrous ions by means of ascorbic acid. The reduced form reacts with Tripyridil – Triazine (TPTZ) forming a blue complex. The coloured intensity is proportional to the iron concentration present in the sample.

**Reagent**

Reagent (1) consists of citrate pH 2.2 50mmol/l; reagent (2) consist of ascorbic acid 113.5mmol/l, while reagent (3) consists of Tripyridil – Triazine (TPTZ) 9.6mmol/l

**Procedure**

Mix reagent(1) and (2) (working reagent), then add 2.0 ml from the mixture of 1 and 2 and one drop from reagent 3 to 500 µl, sample and 500 µl standard, keep at 20-50 °C for 5 min., read in spectrophotometer (Unicam 8625/U.V. Vis U.K) at wavelength 595 nm. and they were measured as A standard and A samples

**Calculation**

Serum iron (µg/dl) = A sample x 40

A standard

**2.13 Determination of serum hormones**

**2.13.1 Determination of serum total T₄ serum total T₃**

It was done using Amersham, international, Amersham, Bucks, UK, in gamma counter (Nuclear Enterprises, NE, 1612, Turbo) at RIA lab. Of Sudan Atomic Energy Commission (SAEC)-Khartoum. The results were analyzed using the WHO Immunoassay Programme (A5.2).

**Principle**

Antigen (Ag) and tracer (Agt) compete with a limited amount of antibody (Ab) to form Ab-Agt complexes. When this reaction reached an
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Equilibrium, the free fraction of both antigen and tracer are removed using appropriate separating agent, then the Ab-Agt comlex is counted for radioactivity using appropriate gamma counter.

\[
\text{Ag}^+ + \text{Ab} + \text{Agt} \rightarrow (\text{Ab} - \text{Ag}) + (\text{Ab} - \text{Agt}) + \text{Ag} + \text{Agt} = \text{separation (to give)}
\]

1. Counted in gamma counter deposit (Ab-Agt) + (Ab- Ag)
2. Decanted supernatant Agt + Ag

2.13.1.1 Determination of serum total T4

Reagents

It consists of: Assay phosphate buffer (0.05 M, pH 7.4): 7.13 g Na₂HPO₄.2H₂O and 1.53 g NaH₂PO₄.2H₂O were dissolved in one litre of distilled water and stored at 4°C with the addition of 0.1% NaN₃; wash buffer: 0.1% triton X-100 in 0.05 M phosphate buffer; I¹²⁵-T₄: the high radioactive hormone was diluted by addition of assay buffer to give a solution of 20,000 counts/minutes (c.p.m.); quality control sera (Q.C): provided by SAEC and labeled (A) high, (B) normal and (C) low; standards: reconstitution of T₄ standards gives concentrations of 300, 150, 85, 37.5, 18.75 and 0.0 nmol/L; donkey Anti-Sheep Serum (DASS); sheep anti-T₄ serum and T₄/ANS assay buffer 4 g of 8-anilino-1-naphthalene sulfonic acid (ANS) dissolved in 100ml of assay phosphate buffer.

Procedure

The assay is performed by using tubes containing: samples standards, quality control (Q.C) and non-specific binding (N.S.B); the total control count tube contains only 100 ul of the tracer; 50 µl of the sample, standard and Q,C, were pipetted, then to all tubes 100 µl ofANS (0.4%), 100 µl of DASS and 100 µl of I¹²⁵-T₄ were added, 100 µl of sheep anti-T₄ antiserum were added to the tubes containing samples, standards and Q.C, all tubes
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

were vortexed and incubated for one hour at 37°C (water bath), one ml of wash buffer was added to all tubes, all tubes were centrifugated at 3000 rpm for 5 minutes at room temperature (20-26°C).

**Calculation**

The supernatant was decanted and the deposit was counted for 60 seconds in a gamma counter, all tubes were prepared in duplicates and they were mixed after each addition.

**2.13.1.2 Determination of serum total T3**

**Reagents** It consists of Assay phosphate buffer (0.05 M, pH 7.4): 7.13g Na₂HPO₄.2H₂O and 1.53 g NaH₂PO₄.2H₂O dissolved in one litre of distilled water and stored at 4 °C with the addition of 0.1% NaN₃, wash buffer: 0.1% triton X-100 in 0.05 M phosphate buffer; ¹²⁵-T₃: the high radioactive hormone was diluted by addition of assay buffer to give a solution of 12,000 counts/minutes (c.p.m.); quality control sera (Q.C): provided by SAEC and labeled (A) high, (B) normal and (C) low; standards: reconstitution of T₃ standards gives concentrations of 0.00, 0.6, 1.25, 1.25, 5 and 10 noml/L; donkey Anti-Sheep Serum (DASS); sheep anti-T₃ serum and T₃/ANS assay buffer 2 g of 8-anilino-I-naphthalene sulfonic acid (ANS) dissolved in 100ml of assay phosphate buffer.

**Procedure** The assay is performed by using tubes containing: samples standards, quality control (Q.C) and non-specific binding (N.S.B), The total control count tube contains only 100 µl of the tracer to 50 µl of the sample, standard and QC, were pipetted then to all tubes 100 µl of ANS (0.4%), 100 µl of DASS and 100 µl of ¹²⁵-T₃ were added and 100 µl of sheep anti-T₃ antiserum were added to the tubes containing 50 µl samples, standards and Q.C. All tubes were well vortexed and incubated for one hour at 37°C (water bath) then add 1 ml of wash buffer was added to all tubes except that of the
total count then all tubes were centrifuged at 3000 rpm for 5 minutes at room temperature (20-26°C).

**Calculation**

The supernatant was decanted and the deposit was counted for 60 seconds in a gamma counter to all tubes were prepared in duplicates and they were mixed after each addition.

**2.13.1.3 Progesterone radio immuno assay (PRI)**

The kits (Agriculture Laboratory, Austria) were used and assembled by the Animal Production Unit, International Atomic Energy Agency (IAEA). The procedure was done according to FAO/IAEA assay protocol version 3-1 (1996).

**Principle**

The method depends on the competition between progesterone in serum samples and I-labeled for a limited number of binding sites on a progesterone specific antibody immobilized (coated) on the internal walls of the test tubes (solids phase). The proportion of the I-labeled progesterone bond to the antibody is inversely related to the concentration of the progesterone present in the serum. After completion of the reaction and separation of hormone, it is possible to calculate blood progesterone concentration from a standard curve, using serum standard.

**Reagents and technique**

Progesterone antibody coated tubes, buffered I-labelled progesterone (iodine tracer), and store at 2-8°C in glass bottles of 110 ml covered with a rubber stopper, progesterone standard (sodium azide and gentamicin as preservatives).

**Procedure**
At room temperature, labeled antibody-coated tubes for standards (STD), internal quality control (QC), add 100µl of STD, QC and samples, then add 1ml of I-progesterone was pipetted into each tube within five min., cover the tubes with parafilm and incubated for 4 h. at room temperature, hold the tubes upside-down to remove the residual droplets, read at gamma counter.

**Calculation**

The maximum binding percentage in the assay (B max) was calculated by dividing the average counts per minute(cpm) of the two zero standard tubes (B0) by the average (cpm) of the total count tubes(TC) and then multiplied by 100 as in the following equation:

\[
B_{\text{max}} = \frac{\text{average cpm of zero STD}}{\text{Average cpm of TC}} \times 100
\]

The percentage binding values for all, standards, samples and QC tubes were calculated by dividind each cpm of these tubes with that of zero STD tubes and then multiplied by 100 as in the following equation:

\[
B = \frac{\text{Average cpm of STD( samples/ QC)}}{\text{Average cpm of B0}} \times 100
\]

Where the \(B/B_0\) was the percentage of the STD, samples or QC bound by the antibody in comparision with B max.

Using the logit-log graph paper provided with the kits, the average percentage bound(\(B/B_0\)) was plotted on the vertical Y axis and the progesterone standard concentraion on the horizontal X axis in nmol/l.

**2.14 Total arsenic (as residues of Cymelarsan) in animal tissues, urine and bile**

Arsenical compounds were detected by measurement of total arsenic. Cymelarsan\(^R\) in milk and meat was measured by measurement of the total arsenic in infected camels in Kenya using recommended route (Sones, 1991)
and in camel’s serum in Morocco (Toutain, 1989) using intravenous route. Groups of arsenical compounds (phynyle arsenoxides, arsphenamines, arsionic acids, acid-substituted phenylearsenoxides and inorganic arsenicals) in plasma were elucidated by detection of total arsenic in urine, stool, blood and tissues (Ralph et al., 1944). The RM340, immicide in infected dogs with (*Dirofilaria immitis*) with doses 2.5 mg/kg twice at 24h. intervals (Toutain, 1990) or 2.2 mg/kg twice at 3h. intervals (Toutain, 1990) or using intravenous rout in dogs (Sundlof et al., 1986 and Guisppin, 1986).

CymelarsanR is an arsenical, patented in (1985) and discovered by Friedheim. It is introduced to the market by Rhône, Mérièux – (France). It is a combination of Melarsenoxide and cyseamine. The residues of Cymelarsan were measured by the total arsenic according to (AOAC, 1995) method. Tissues were ashed, but bile, serum and urine were used as such.

2.14.1 Total arsenic in tissue

**Dry ashing**

Blend tissue specimens in high-speed blender then pass fibrous tissue through meat grinder, weigh 10g tissue; add 3g MgO + 20 ml cellulose powder only 10 ml cellulose powder to muscle sample, mix well, then cool, add 3 g Mg (NO₃)₂. 6H₂O, place in 55°.* Reach, operating temperature, ash for 2h, cool, moisture ash with 10 ml H₂O, make to 250 ml and Add 90 ml 6N HCl (Erlenmeyer) dilute to 175 ml with H₂O.

**Reagents**

These consist of Silver diethyl dithiocarbamate and Chill 200 ml AgNO₃, 0.1 M in 10°C (or lower); 200 ml sodium diethyl dithiocarbamate solution in 10; Add 1 to 2, filter; Dissolve salt in pyridine, chill, add cold water slowly, filter, wash with H₂O; Dry pale yellow crystals under reduced
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

pressure (185 – 187°); Recrystallize; Store in refrigerator; Silver diethyl dithiocarbamate solution and Dissolved 0.5 g in colorless pyridine 100 ml.

**Procedure**

Add 2 ml KI solution 15%, swirl then add 1 ml SnCl₂ solution, swirl, cool for 45 min in 4°C, prepared blank containing 90 ml 6N HCl and 85 ml H₂O, treat; Trapping solution it consists of: 3 ml silver diethyl dithiocarbamate, place in ice bath and add 10g Zn to cooled Erlenmeyer.

Determine reagents and samples in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 450 nm against blank.

**Arsenic standard solutions (stock)**

Dissolve 0.66 AS₂O₃ in 25 µl 2N NaOH, dilute to 1 litre with H₂O; working solutions (0 – 2 ppm) before use and dilute with H₂O

**Preparation of standard curve**

Add 2 ml working standard solution to 10 g tissue to provide curve desired range (0 – 2 PPAS) then carry samples through ashing and distillation and determine best fitting straight line from ≥4 sets of determination for each tissue by method of least squares.

**Calculation**

Determine As content from standard curve.

**2.14.2 Total arsenic in urine, serum and bile**

To 5ml of the sample; add 3g MgO + 20 ml cellulose powder mix well then cool, add 3 g Mg (NO₃)₂. 6H₂O, place in 555°. Reach, operating temperature, ash 2h, cool, moisture ash with 10 ml H₂O, make to 250 ml and Add 90 ml 6N HCl (Erlenmeyer) dilute to 175 ml with H₂O.

**Reagents**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Consist of Silver diethyl dithiocarbamate and Chill 200 ml AgNO₃, 0.1 M in 10°C (or lower); 200 ml sodium diethyl dithiocarbamate solution in 10; Add 1 to 2, filter; Dissolve salt in pyridine, chill add cold H₂O slowly, filter, wash with H₂O; Dry pale yellow crystals under reduced pressure (185 – 187°); Recrystallize; Store in refrigerator; Silver diethyl dithiocarbamate solution and Dissolved 0.5 g from a in colorless pyridine 100 ml.

Procedure

Add 2 ml KI solution 15%, swirl then add 1 ml SnCl₂ solution, swirl, cool for 45 min in 4°C, prepared blank containing 90 ml 6N HCl and 85 ml H₂O, treat; Trapping solution it consist of : 3 ml silver diethyl dithiocarbamate, place in ice bath and add 10g Zn to cooled Erlenmeyer.

Determine reagents and samples in spectrophotometer (Unicam 8625/U.V. Vis U.K.) at wavelength 450 nm against blank.

Arsenic standard solutions (stock)

Dissolve 0.66 AS₂O₃ in 25 µl 2N NaoH, dilute to 1 litre with H₂O; working solutions (0 – 2 ppm) before use and dilute with H₂O

Preparation of standard curve

Add 2 ml working standard solution to 10 g tissue to provide curve desired range (0 – 2 PPAS) then carry samples through ashing and distillation and determine best fitting straight line from ≥4 sets of determination for each tissue by method of least squares.

Calculation

Determine As content from standard curve.
2.15 The residues of oxytetracycline (OTC) in serum, urine, and tissue

OTC was measured by two methods: Microbiology and with high pressure liquid chromatography (HPLC) assay as follows:

2.15.1 The residues of oxytetracycline in serum, urine, bile and tissue

**microbiologically**

OTC was measured according to the method described by (Koenen-Dierick et al. 1995).

**Procedure of Culture medium**

Nutrient agar (Merck 7883) was prepared with dextrose 0.4% w/v; then sterilized by autoclaving at 121°C for 20 min; pH 7 ± 0.05 1N NaOH and 1N HCl cool at 50°C; spore suspension (Merck 10649) containing 10^4 Bacillus subtilis BGA spores; 40 ml of the culture medium was poured into 9 cm Petri dishes; keep at 4°C upside down in plastic bags; used between 1 – 7 days.

**Control samples**

Four paper disks of 12.7mm diameter containing 1µg oxytetracycline.

**Preparation of standard curve**

Paper disks containing 0.5, 1.0, 2.0, and 4.0 µg of pure oxytetracycline (Glaxo Lab. Cairo, Egypt) was spotted on the agar medium in duplicate. The zones of inhibition were measured after incubation at 30°C. Then the standard curve was made.

**Samples of tissues**

6 – 8 mm diameter and 2mm thick of tissues was taken by cork and pored in the solidified agar medium then it was incubate overnight at 30°C.

**Samples of bile, urine and serum**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Paper disks of 12.7mm diameter saturated with urine, bile and serum then pored in solidified agar medium.

**Calculation**

Measure the inhibition zone and read from the standard curve then it was incubating overnight at 30°C.

2.15.2 The residues of oxytetracycline (OTC) in serum, urine, bile and tissue using (HPLC)

**Material agents:**

Chromatograph: LDC Model 4000.

Wavelength: SM 4000 and LDC IC 4000 integrator.

Column: Hypersil 10 MOS (octylsilyl silica gel). Length 250 mm.

Mobile phase: sodium dihydrogen orthophosphate 0.1 75v. Acetonitrile 25v.

Add 7.8 g/l tetrabutylammonium bromide and adjust pH to with 2N sodium hydroxide solution.

**Isocratic program**

Flow: 1.5 ml/mn

**Injected volume**

20l

**Sensitivity of the detector**

0.2 AUFS.

**Preparation of solution**

**Reference solution:**

Dissolve a 40 mg (4000IU) sample Ss (g) accurately weighted of oxytetracycline in 100 ml mobile phase. Dilute 5 times with same solvent.

**Test solution**

Dilute a 1.0 ml sample S of Remacycline L.A. in 100 ml of mobile phase. Dilute 25 times with same solvent.
Calculation

The retention time of oxytetracycline contained in the test solution should be concordant with the retention time of the standard OTC.

Determine the peak areas:
A: peak area of OTC contained in the test solution.
B: peak area of OTC contained in reference solution.

The OTC content (g/ml) of the sample being examined is:
\[ \frac{A \times S_s \times 500}{B \times S} \]

2.16 Detection of quinapyramine

It was measured according to (Agropharm limited Buckingham House-England)

Identity

The infrared spectrum between 2.5 and 15u of a 0.1% dispersion of the sample in potassium bromide should not be significantly different from that of an authentic specimen of quinapyramine sulphate. Mix 0.1g sample in 10ml water, add 2 drop concentrated HCl, boil for 5min., cool and filter. Add 2 drops 10%w/v barium chloride solution to the filtrate and mix; a white precipitate should be produced.

Reagent

Sodium hydroxide thiosulphate reagents:
Mix 200 ml 50% w/v with 50 ml 16% w/v sodium thiosulphate and cool.

Sample

0.25g

Procedure
Weigh about 0.25g sample, add 6g anhydrous sodium sulphate, 0.6g yellow mercuric oxide, 13ml concentrated sulphuric acid and a few carborundum granules. Then heat, continue the digestion for 2 h. allow cool, adding continually 175 ml water, swirling to dissolve any solid and cool.

Add 65 ml of the sodium hydroxide thiosulphate reagent carefully without mixing connect to an ammonia distillation apparatus, mix and distill into 50.0 ml 0.05M. sulphuric acid containing 3 drops screened methyl red indicator solution until bumping commences, wash down the condenser and delivery tube with a little water, collect the washing in the flask containing the sulphuric acid and titrate the excess acid with 0.1 M sodium hydroxide.

Blank

12 ml concentrated sulphuric acid and distilling into mixture of 10.0 ml of the 0.05M. sulphuric acid and 40 ml water.

Microbial Contamination

Carry out the determination in duplicate.

Aseptically weigh 1g samples into 100ml of quarter strength Ringers solution in a jar, and shake vigorously to dissolve then filter through a 0.45um porosity hydrophobic edged membrane. Wash the filter with 200ml sterile distilled water, place face up on a Trypton Soya Agar plate, incubate at 23°C for 7 days then count the number of colonies.

Hi performance liquid chromatography (HPLC) examination

Examine under the following condition: column 25cmx4.6mm i.d. Parlisil 5, mobile phase0.5%w/v ammonium acetate and 0.25%viv glacial acetic acid in methanol/water (9:1 by volume), flow rate 2.0ml/min., sample solution a 0.1%w/v solution in methanol/water(1:1 by volume), reference solution a 0.1%w/v solution of an authentic specimen of quinapyramine sulphate in methanol water (1:1 by volume)., detector U.V. at 254nm,
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) injection volume 10ul, attenuation 0.5 a.u. f.s for quinapyramine and 0.05 a.u.f.s for impurities.

**Calculation**

Quinapyramine sulphate % =

\[
\frac{40 \times f_1 + (B - A) \times f_2}{W \times (100 - L)} \times 88.77
\]

Where:

- A: ml 0.1M sodium hydroxide used in sample titration
- B: ml 0.1M sodium hydroxide used in blank titration
- \( f_1 \): factor of 0.05M Sulphuric acid.
- \( f_2 \): factor of 0.05M Sodium hydroxide.
- W: weight of sample used.
- L: loss on drying (1.5%) 

2.17 The effect of oxytetracycline on *T. evansi* in phosphate glucose buffer solution (PGS):

**The stock:**

0.59g of PGS
9.5ml (0.1%) NaOH

Complete to 100 ml with distilled water.

**The buffer**

29.4g sodium citrate
Complete to 100ml with distilled water.

**Citric acid**

21g citric acid.
Complete to 100 ml with distilled water.

**Working solution:**

6 ml of the stock, 32 ml of the buffer and 17.3 ml of citric acid and complete to 1 liter with distilled water.

The *trypanosoma evansi* added to the working solution and preserved in liquid nitrogen.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Oxytetracycline (100%) added to the work solution when there is a live trypanosomes in
different concentration (0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1, 1.5 µg/ml) the live
trypanosomes examined every hour for 72 hrs.

Chapter Three

Results

Experiments with Nubian goats

3.1 Experiment 1: Toxicity and efficacy of Cymelarsan\textsuperscript{R} in goats infected with \textit{T. evansi} at single and multiple doses

The study included two control groups group (1)(uninfected untreated) and group 2(infected untreated).

3.1.1 Parasitaemia

3.1.1.1 Parasitaemia in peripheral blood

\textit{a/ post-infection:}

Table (1) summarizes the parasitaemia in the peripheral blood of the goats infected with \textit{T. evansi} and treated with single and multiple dosages of Cymelarsan \textit{T. evansi} is
detected in the peripheral blood of goats in group (2) which is mild on days4-5 (+),
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

 moderate on day 6 (+++) and severe on days 7-10 (++++) until the animals are died on
days 9-11. Goats in groups (3-10) also showed mild parasitaemia on day 4 and the
severity gradually increased till day 11 (+++++).

b/ post treatment:

Parasitaemia disappeared completely post treatment of goats of groups (5, 6, 9 and
10) until they died or slaughtered but it appeared 3-4 days post treatment in goats of
groups (7 and 8) then disappeared completely until they died or were slaughtered. The
parasitaemia in goats of group (3) was mild but animals died on day 13-15 post

treatment.

3.1.1.2 Parasitaemia in liver impression smears

Parasites detected by the liver impression smears in goats infected with *T. evansi* and
treated with single and multiple dosages of Cymelarsan are summarized in table (2).
No parasites were detected in goats of group (1) while; goats of group (2) showed
moderate parasitaemia (++) throughout the period of 9-11 days post infection. Goats
in groups (4-10) subjected to the slaughter program weekly for 5 weeks after the
cessation of the drug treatment have not shown the parasites in their livers. It is
noticed that livers of goats in group (3) showed mild parasites (+) at weeks 1, 2, 4 and
5 but negative in week 3.

3.1.2 Clinical signs and investigation

Table (3) and figures (1a and b) illustrate changes in the body weight, body
temperature, pulse rate, respiratory rate, blood pressure and fate of the animals in
Nubian goats infected with *T. evansi* and treated with single and multiple doses of
Cymelarsan.

No clinical signs were observed in goats of group (1). Goats in group (2) showed 4-7
days post infection hypothermia, watery lacrimation, frothy salivation, mucopurulent
conjunctivitis, mucopurulent nasal discharge, decrease in appetite, severe diffuse
alopecia (plate 1), diarrhoea, depression, apathy, muscle tremors, slight increase in the
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

respiratory rate, decrease in the pulse rate, convulsion and shivering. In the second week, the lymph nodes and testes were hot and swollen, and animal became off food, cachexia, recumbent with lateral kink of the neck for 1-2 days then the animals died.

Post treatment (pt), in the first week, all goats showed swelling at the site of injection, which disappeared after 1-2 days in goats of groups (3, 4, and 5) and never disappeared in other groups. Goats in group (3) showed mild clinical signs as that of group (2) and there was keratitis while goats of group (4) showed nasal discharge and mild diarrhoea. Goats of group (5) showed no apparent clinical signs except the diarrhoea, which stopped on day 3 pt. In contrast, goats in groups (6-10) showed watery lacrimation with mucopurulent conjunctivitis, accompanied with blindness in goats of groups (6 and 7) and in 75% of goats in groups (8-10), mucopurulent nasal discharge, frothy salivation, fever, depression, apathy, pressing the head against objects (plate 2), watery diarrhoea for 3-4 days then changed to bloody diarrhoea, bloody urine, muscle tremors, decrease in appetite, slight increase in the respiratory rate, decrease in the pulse rate. In the second week, groups (8-10) showed hot and swollen lymph nodes and testis, severe diffuse alopecia which is slight in the other treated groups, with no shivering or convulsion, weakness (tonic paralysis) in the forelimb (plate 3 and 4), in sternal recumbent, off food, emaciation and anuria. These sings continued until the death.

Goats in groups (6-10) showed skin lesions (plate 5) in the second week as red 3mm raised concave nodules which increased in size to 5mm then changed to a brown scab these scabs when removed by hand left white to yellowish ulcers, when excised a greasy white yellowish hard material was seen and remained until death. An increase in the body weight was observed in goats of groups (4-5) and it was decreased in groups (6-10).

3.1.3 Gross findings pathology

Table (4) summarizes the factually of the gross findings in goats infected with *T. evansi* and treated with single or multiple dosages of Cymelarsan. No gross findings
were observed in goats of group (1). The gross pathological findings in groups (2, 3 and 6) were moderate to severe lesions, while goats in groups (4 and 5) showed mild or no lesions. Lesions were congestion, oedema and haemorrhage in the different organs including lung (plate 6), froth on the trachea, and flabbiness and dilation of the heart (plate 7), while fatty change and or necrosis is investigated mainly in livers and kidneys. Haemorrhage under the liver capsule (atelectasis) were also observed (plate 8) in addition nephritis, gastritis, enteritis, peritonitis and hydroperitoneum, spleenomegaly (plate 9), myositis and peripheral nerve necrosis (plate 10) at the site of injection, lymphadenitis, orchitis (plate 11) and hypoatrophy of the left testis (plate 12) and the thyroid gland are also investigated. It was noticed that these lesions had disappeared by the fourth week post treatment in goats of groups (4 and 5). The goats, which were, received multiple dosages of the drug showed mostly same lesions but increased in severity.

3.1.4 Histopathological findings

Cerebellum: goats in groups (2-3 and 6-10) showed diffuse vacuolation around the neurons which were elongated in shape and with dark stain, some of them still maintained star-shapes with eccentric nuclei (plate 13), glial cell proliferation and widening of perivascular spaces (plate 14), congestion and haemorrhages (plate 15). Goats in groups (4 and 5) showed no significant lesions in cerebellum.

Cerebrum: slight congestion and haemorrhages were observed in goats of group (6) while, goats in groups (2-3 and 6-10) in addition showed vacuulations mainly around neurons (plate 16) and widened in perivascular spaces.

Group (3) showed in the first two weeks slight widened perivascular spaces in the brain. No significant changes were observed in goats of groups (4-5).

Spinal cord: showed proliferation of ependymal canal with glial cell around the central canal in goats of groups (2, 6 and 7), and vacuulations in white matter were seen in goats in groups (2 and 3-10) while; goats in groups (6-8) showed widening perivascular spaces. In goats of group (9) the spinal cord showed vacuulations,
irregular axons sheaths, and neurons degeneration, (rounded cells, and central chromatolysis) (plate17). No significant lesions were observed in the goats of groups (4and 5).

**Peripheral nerves:** were normal in goats of groups (2-5), but showed diffuse vacculations in goats of groups (6-10) and loss of nerve structure in goats of groups (8-10).

**Tongue:** Sections of goats in groups (2-7and 9-10) were normal. Some goats of group (8) showed melanosis.

**Thyroid glands:** goats in groups (2-10) showed congestion while in goats of groups (2, 6, 7,9and 10) the glands were atrophied with a loss of thyroid tissues. Some sections of goats in group (5) showed empty follicle.

**Lung:** the lungs of goats in groups (2, 3, 6-10) were emphysematous, oedematous, and congested. Exudates and RBC were seen in bronchioles of goats in groups (6-10). Alveoli were haemorrhagic and collapsed and focal pneumonitis was observed in groups (2, 3, 6, and 7). Goats in group (10) showed mononuclear cell infiltration (lymphocyte, and macrophage) thickened alveolar septa, fibrinous exudation in alveoli and foci of interstitial pneumonia (plate 18).

**Heart:** congestion, moderate haemorrhages and lymphocyte infiltration in the cardiac muscle were noticed in goats of groups (2, 6-10). Focal or diffuse vacculations in the cardiac muscles were seen in goats of groups (6-10). Goats in groups(4,5,8 and 10) showed myodegeneration, with neutrophils infiltration, oedema and slight haemorrhage (plate 19).

**Liver:** goats in groups (2 and 6-10) showed congestion; sinusoidal dilatation, slight cetrilobular necrosis and some times scattered foci of lymphocytes and macrophages (plate20). Widened portal tracts were seen in goats of groups (2,6and 9). Haemosiderin, deposits were also observed in the liver of goats in groups (8and 9) while hepatic fibrosis was detected in goats of group (10).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

**Spleen**: congestion and haemosedrosis were noticed in spleens in goats of groups (2-5 and 10), while goat in groups (6-10) showed haemosiderosis thickened trabiculae, and follicle around the white pulp. Groups (9-10) showed congestion and haemorrhages of the red pulp with haemosiderosis and depletion lymphoid tissue.

**Kidney**: Goats of groups (2 and 3) showed dilatation of tubules, increase in glomerular cellularity, congestion and haemorrhage. Groups (4 and 5) showed slight congestion, and those of group (6) showed hypercellularity of glomerular tuft (extracted glomeruli), however, group (7) showed widened tubules and haemorrhage, group (8) showed pale tubule, absence of nuclei, hypercellularity of glomerular tufts, and goats in group (9) showed small lobulated glomerulai, thickened wall of glomerular and epithelial, diffuse interstitial tissue, glomerular, swollen vascular endothelium,, emptiness of glomerular capillaries and dilated tubules. Goats in group (10) showed dilated tubules and interstitial haemorrhage.

**Small intestine**: Congestion and loss of villus epithelium were seen in goats of groups (6-10). Goats in groups (2, 6 and 10) showed submucosal oedema. Also the blood vessel's walls were thickened, was observed in goats of group (10) while, groups (4, 5 and 7) showed no significant changes.

**Colons**: section of groups (2 and 3) showed congestion and haemorrhage, also slight congestion was observed in group (6) and no lesions were observed in goats of groups (4, 5 and 7-10).

**Tendon**: no obvious lesions were observed in goats of groups (2-10).

**Sites of injection** Goats of group (6) showed oedema and diffuse vacculations of peripheral nerves.

**Leg muscle**: Section from groups (2-5) was normal while the leg muscle in goats of groups (6-10) showed oedema and cellular infiltration (plate 21).

**Lymph nodes**: section from groups (4-5) showed no significant changes, while that of groups (2-3) were congested and hyperplastic the medullar part attached with big
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) contained abundant interstitial tissues, and dilated blood vessels specially in goats of groups (6, 8, and 9) while lymph nodes of groups (7 and 10) were haemorrhagic.

**Testis:** there were congestion and haemorrhages in the testis of groups (2-5 and 8). Goats of group (7) showed tubular atrophy. Some somniferous tubules in group (6) were necrotic and appeared as solid dark mass separated by a wide interstitial tissue (plate 22). However other tubules showed evidence of functional activity with few spermatogonia. Sections from group (9) showed congestion and evidence of slight activity while those of group (10) showed loss of some tubules and absence of activity (plate 23).

### 3.1.5 Hematological changes:

Tables (5 and 6) and figure (2a and b) summarize the haematological changes in goats infected with *T. evansi* and given Cymelarsan at single or multiple dosages. The haemoglobin concentration (Hb), packed cell volume (PCV) and red blood cell count (RBC) decreased significantly in goats of groups (2, 3, 6, 10) but were within reference interval in groups (4 and 5) compared to the control group (1). Slight and statistically insignificant increase was observed in white blood cell counts (WBC) in all groups. Moderate increase was observed in the reticulocytes count of group (2), which slightly increased in goats of groups (3 and 7-10). Significant increases were observed in platelets count, neutrophiles and eosinophiles of goats in groups (2, 6-10), but they were within reference interval in groups (3, 4 and 5) compared to control group (1). Basophiles were absent in control group (1) but showed an increase in other experimental groups; however monocyte counts fluctuated in the test animals. Lymphocytes count decreased significantly in all experimental animals compared to control group (1) and goats of groups (4 and 5). Significant increase was observed in the MCV of all groups tested except goats in groups (1, 2, 4 and 5) while the MCH decreased moderately in group (6) and sharply in group (3). No significant changes observed in the MCHC of all experimental animals.

### 3.1.6 Serobiochemical changes
Tables (7-9) summarize the serobiochemical changes in goats infected with *T. evansi* and treated with single or multiple doses of Cymelarsan. The serum sodium concentration increased slightly but not significantly in all groups except goats that group (6) where there was a significant decrease. Serum potassium concentration showed moderate increases in groups (2,5,7-10) but slight decreases in group (6). The serum chloride concentration increased in groups (2,3,6,7,9and10) but not in groups (1,4,5 and8). Sharp decrease was depicted in the serum concentration of calcium and phosphorus in goats of groups (3and6), however increase was observed in the serum magnesium concentration in the same groups.

No significant changes were observed in serum zinc and copper concentration among the experimental groups. Also no significant changes were detected in serum manganese except goats in groups (2 and 9) where it was increased in group (10) and decreased in the others Figure (3a and b). Slight decrease in serum iron concentration was observed in goats of groups (3,5 and6).

Significant increase was noticed in serum concentration of bilirubin and direct bilirubin of goats in groups (2,6-10). Another significant increase was also observed in serum cholesterol concentration except in groups (1,4 and6), however, the triglyceride and phospholipid serum concentration increased in all the experimental animals except goats of groups (4and5) compared to the control group (1). The changes in serum glucose concentration increased in groups (2, 3, 7,9and10).

An increase in total protein was noticed in goats of groups (2,3 and 6), however, the globulin concentration decreased in groups (7-10) and increased in groups (2and3). Generally there were decreases in the concentrations of urea and creatinine in most experimental groups compared to control group (1).

No significant changes in the activities of serum LDH, CK, PK, and GPT were observed in any of the experimental groups. But, an increase was noticed in the activity of SDH and GOT and decreases in ALP and the amylase in most of the experimental animals compared to group (1). It was noticed that serum lipase activity
decreased in groups (2-6) and increased in groups (7-10) compared to goats of control group (1).

3.1.7 The concentration of the Cymelarsan in different organs, serum, bile and urine

Goats in groups 6-10 showed increased amounts of arsenic in the tissues of liver, kidneys, heart, lung, spleen, cerebellum, cerebrum, fats, site of injection, leg muscle, uterus, ovary, testis, bile and serum figure (4a and b) and tables (10). The increase depends upon frequency of administration and dose dependent. While goats of groups (3-5) recorded values by the end of the slaughter program equal to that of goats in group (1). Values of arsenical concentration in urine increased slightly if compared to that of tissues.

3.2 Experiment 2: Toxicity and efficacy of oxytetracycline (OTC) in goats infected with *T. evansi* and treated with single and multiple dosages of oxytetracycline.

3.2.1 The parasitaemia

3.2.1.1 Parasitaemia in peripheral blood

Table (1) summarizes the parasitaemia in the peripheral blood of the goats infected with *T. evansi* and treated with single and multiple dosages of OTC.

a/ Post infection

*T. evansi* was detected in the peripheral blood of goats in group (2) where it was mild on day 4 (+), moderate on day 6 (++) and severe on day 7 (++++) until the animals were died on day 11.

b/ Post treatment

Goats in group (3) showed moderate parasitaemia (++) between days 1-3, mild (+) on days 4-8, moderate (++) between days 9-11 and animals died on days 10-11. Goats in group (4) showed moderate (++) between days 1-3, mild (+) on days 4-17, moderate
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(+++) between days18-24, and mild (+) on days 25-49. Goats of group (5) showed moderate parasitaemia (+++) on days 1-3, parasite -free between days 4-21, then mild parasitaemia (+) until day 49. Goats in group (6) showed moderate parasitaemia (+++) in the first four days, mild (+) between days5-10 and moderate (+++) for the three subsequent days followed by mild parasitaemia (+) till day14 -49. Goats in group (7) showed moderate parasitaemia (+++) on day1-5, mild (+) on days6-8, moderate (+++) on days9-12), then mild (+) on days13-19, parasite -free between days20-25 and mild parasitaemia till day 26-49. Goats in group (8) showed moderate parasitaemia (+++) between day1-2, mild (+) on days3-9, then moderate parasitaemia (+++), parasite -free between day10-13, mild between days 14-17 and animals are died between days16-18.

3.2.1.2Detection of the parasites in liver impression smears

Table (2) summarizes the detection of the parasites by liver impression smears. In dead goats in group (2) liver impression smears showed it is moderate parasitaemia. Group (3) also showed moderate parasitaemia (+++) when dead animals were subjected to liver impression smears, while that of group (4) were mild during the five weekly slaughter program. Goats in groups (5 and6) showed moderate parasitaemia (+++) in the first slaughters, mild parasitaemia in slaughter 2and 3 then parasites free on slaughters 4and 5 and goats in groups (7 and 8) were parasite -free during the five weekly slaughters program.

3.2.2Clinical signs and clinical investigation

No clinical signs were observed in goats of group (1). Goats in group (2) showed 4-7 days post infection hypothermia, watery lacrimation, frothy salivation, mucopurulent conjunctivitis, mucopurulent nasal discharge, decrease in appetite, severe diffuse alopecia (plate1), diarrhoea, depression, apathy, muscle tremors, slight increase in the respiratory rate, decrease in the pulse rate , convulsion and shivering. In the second week the lymph nodes and testes were hot and swollen and animals become off food, cachexia, recumbent with lateral curvature of the neck for 1-2days prior to death.
Goats in group (3) showed the same clinical signs as group (2). But these signs are disappeared in groups (4 and 5) and goats didn't regain their appetite. Animals in groups (6-8) showed weakness of the fore and hind limbs (plate 24), colic (plate 25), lacrimations, shivering, decrease of appetite, emaciation and over reflection in hind limb (plate 26 and 27) which appeared 14-21 days post treatment and death occurred in goats of group (8) on days 16-18 post treatment.

Goats of group (2) showed hypothermia although it was not significant while, the respiratory rate increased in goats of groups (2-7); it decreased sharply in goats of group (8). Generally there were decreases in the body weights compared to goats of group (1). The blood pressure was generally decreased in all experimental groups compared to group (1). However the pulse rate was also decreased sharply in goats of group (7). Figure (5a and b).

Death occurred in goats of groups (2, 3 and 8) while the other groups were slaughtered at the rate of two animals/week on days 21, 28, 35, 42 and 49. Table (3).

3.2.3 post-treatment findings

Table (4) summarizes the post mortem findings in goats infected with *T. evansi* and treated with single and multiple dosages of oxytetracycline. No gross findings were observed in goats of group (1). The gross pathological finding in groups (2, 3, and 8) were severe or moderate lesions, while goats in groups (4 and 5) had mild or no lesions. Lesions under investigation were congestion, oedema and haemorrhage, hyperaemia, froth on the trachea, and dilatation and flabbiness of the heart (plate 28). Fatty change or necrosis was seen mainly in livers (plate 29) and kidneys in addition nephritis, gastroenteritis, peritonitis, enteritis (plate 35) hydropertoneum, spleenomegaly, myocitis at the site of injection (plate 30), inflamed and swollen nerve (plate 31) lymphadenitis, orchitis and the thyroid glands were observed in the different groups. It was noticed that these lesions disappeared in the fourth week post treatment in goats of groups (5 and 6). Goats in group (6) showed greenish bile with white granules (plates 32 and 33). Goats in group (7) showed urine retention (plate
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34. Goats in groups (5-8) showed atrophy of the right cerebellum (plates 36 and 37) and stiff muscle.

3.2.4 Histopathological findings

**Cerebellum:** Goats in group (2) showed diffuse vacuulations mainly around neurons, which appeared elongated with dark staining, and glial cell proliferation. Goats in groups (5 and 7-8) showed vacuulations in white matter, atrophy, Goats of groups (3, 4 and 6) showed neuron degeneration with appearance of glial cells around some neurons (plates 38 and 39) and widened prevascular spaces (plate 42).

**Cerebrum:** Showed capillary proliferation and congestion, vacuulations in white matter, neuronal degeneration and proliferation of glial cells in goats of groups (5, 6 and 8). Four animals of groups (4 and 6-8) (plate 40 and 41) showed satellitosis. Proliferations of ependymal cells with glial cells around the central canal and vacuulations in white matter were recorded of goats in group (2).

**Spinal cord:** In all experimental infected and infected treated goats showed vacuulations in white matter and slight glial cells proliferation around central canal (plate 43).

**Peripheral nerve:** showed congestion in goats of groups (5, 7 and 8) while those of the rest groups showed no significant changes.

**Thyroid glands:** Sections of goats in groups (2, 3 and 6-8) were showed congestion and follicular atrophy. Interstitial infiltration by mononuclear cells was seen in goats of groups (3-8).

**Lung:** the lungs of goats in group (2) showed congestion, emphysema, collapse, and pneumonia. Goats of groups (3, 6 and 8) showed dilatation of alveoli and increase in the interlobular septa was observed in goats of groups (4-7).

**Heart:** goats in group (2) showed congestion and haemorrhage.

**Liver:** goats in group (2) showed congestion, sinusoidal dilatation was observed. Slight centrilobular necrosis and sometime scattered foci of lymphocytes and macrophage, hyperplasia of portal tract, congestion and haemocedrein were seen in
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going of groups (3, 5 and 7) (plate 44 and 45). Haemorrhages also seen in goats of
groups (4, and 6-8) (plate 46 and 47).

**Kidney:** Goats of group (2) showed dilatation of medulla and dilation of tubules,
increase glomerular cellularity, haemorrhage and congestion. Oedema was seen in
goats of groups (3 and 6-8) and congestion were seen in goats of groups (3, 7 and 8)
(plate 48).

**Small intestine:** showed congestion, loss of villi submucosal oedema in goats of
group (2). Goats of groups (4, 6 and 8) showed losses of villi epithelium and
intestinal glands were few and separated from each other (plate 49). Oedema of the
submucosa and hypercellularity of lamina propria were observed in goats of groups
(3 and 8).

**Colon:** Congestion and haemorrhage were seen in goats of group (2).

**Site of injection:** Purulent inflammatory changes were seen only in goats of groups
(3, 5 and 8).

**Testis:** the testis of goats in group (2) showed congestion and haemorrhage.

**Tongue, spleen, leg muscles and lymph nodes:** No significant changes were
observed.

### 3.2.5 Haematological changes

Tables (5 and 6) summarize the haematological change in goats infected with *T.
evansi* and treated with single and multiple dosages of oxytetracycline. Decreases
were seen in the Hb concentration, PCV and RBC in tested animals compared to
group (1) while, an increase in the reticulocyte, platelets and WBC counts were
absence. Figures (6a and b). The differential count of WBC demonstrated an increase
in the basophiles and neutrophiles while the lymphocytes decreased and the
eosinophiles and monocytes are fluctuated as compared to group (1).

No significant changes were seen in MCV, MCH and MCHC in goats of groups (2-8),
but generally an increase was seen in the MCV and MCH, while the MCHC follows a
decreasing trend, compared to the control group (1). Figures (7a and b).
3.2.6 Serobiochemical changes

The serobiochemical changes are summarized in table (7-9) in goats infected with *T. evansi* and treated with single and multiple dosages of oxytetracycline. There were no significant changes in the serum concentration of sodium, potassium chloride, zinc, copper and iron. Decrease in serum calcium and phosphorus concentrations and also an increase in serum magnesium and manganese concentrations were observed. Changes were observed mostly in goats of groups (7 and 8).

Generally no prominent changes were observed in serum concentration of urea, creatinine, cholesterol, phospholipids and triglyceride in the experimental animals compared to group (1). Figure (8a and b). Slight increases were observed in serum concentration of bilirubin, direct bilirubin, total protein, albumin and globulin were observed in experimental goats compared to group (1).

No apparent changes were detected in serum activity of LDH, CK, PK, GOT, GPT, ALP, SDH, amylase and lipase in the experimental goats compared to control group (1).

3.2.7 The concentration of the oxytetracycline in different organs

The concentration of oxytetracycline in serum, organs (liver, kidney, heart, lung, spleen, cerebellum, cerebrum, fat, site of injection, leg muscle, uterus, ovary and testis), bile and urine are summarized in tables (10-12).

The concentration of oxytetracycline increased significantly in the serum in goats of groups (3-8). The concentration of OTC was not recorded in serum after week four (second slaughter) in goats of groups (3, 4 and 5) and avis versa in goats of groups (6-8). Residues were also detected in the heart, kidney, liver, testis, lungs, spleen, leg muscle, fat, site of injection, cerebellum, cerebrum, uterus, ovary, bile and in urine goats of groups (3-8) during the (1-5) slaughters. Generally any changes in concentration recorded in the treated groups were compared to those of groups (1 and 2).
3.2.8 The effect of oxytetracycline on *T. evansi* in phosphate glucose buffer solution (PGS):

Table (13) summarizes the effect of oxytetracycline on *T. evansi* in phosphate glucose buffer solution (PGS). The effect of oxytetracycline (100%) in different concentrations (0.1-1 and 1.5 - 15.5 µg/ml) on *T. evansi* was examined every hour for 72 hr. The working solution after examination inoculated in rats. No trypanosomes were detected in the solution or rats when 4.4-15.0 µg/ml were added while, in the concentrations of 0.1-0.9 µg/ml the trypanosomes were still alive and 50% of the trypanosomes died when the concentration of 1-3 µg/ml examined.

3.3 Experiment 3: Efficacy and clinicopathological effect of Cymelarsan and oxytetracycline combination in goats infected with *T. evansi*

3.3.1 The parasitaemia

3.3.1.1 The parasitaemia in the peripheral blood

Table (1) summarizes the parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* and treated with single or multiple doses of Cymelarsan and oxytetracycline combination.

**a/ post infection**

Goats in groups (2-6) showed mild parasitaemia on days 4-5 (+), moderate on day 6 (++) and severe on day 7-14 (+++). Animals of group (2) died on day 11.

**b/ post treatment**

Goats in group (3) showed moderate parasitaemia (+) on days 1-3, mild (+) on day 4-6, then moderate (++) on days 7-14. The group died on days 13-15.
Goats of group (4) were clear of the parasites on days 1-6, then mild parasitaemia (+) on day 7, they showed severe parasitaemia (++++) on day 8, mild parasitaemia (+) on day 9, all the goats were negative on day 10-20 and they showed mild parasitaemia (+) on days 21-35 then the animals were free of the parasite until day 49.

Goats of group (5) showed mild parasitaemia (+) on days 1-8, moderate (++) on days 9-11 then they were free from the parasites until day 49 however, goats in group (6) were mild (+) on days 1-3, then they were negative until death on days 25-28.

3.3.1.1.2 Detection of the parasites in liver impression smears

Table (2) summarizes the parasites in the liver impression smears of Nubian goats infected with *T. evansi* and treated with single or multiple doses of Cymelarsan and oxytetracycline combination within the withdrawal period. *T. evansi* was detected goats’ livers of groups (2) where they showed moderate parasitaemia (++) until they death on day 11.

Goats of group (3) which died 13-15 days post treatment showed no parasites in week 1 and 2 then they were mild and moderate. However, goats in group (4) are free of the parasites in the first and second slaughter, moderate in the third week and mild in the fourth and fifth slaughter while goats in groups (5and 6) were free of the parasites during the withdrawal period but goats of group (6) died after the second slaughter.

3.3.2 Clinical signs and Clinical investigation

Table (3) summarizes the clinical changes in goats infected with *T. evansi* and given Cymelarsan and oxytetracycline combination.

No clinical signs were observed in goats of group (1). Goats in group (2) showed 4-7 days post infection hypothermia, watery lacrimation, frothy salivation, mucopurulent conjunctivitis, mucopurulent nasal discharge, decrease in appetite, severe diffuse alopecia (plate1), diarrhoea, depression, apathy, muscle tremors, slight increase in the respiratory rate, decrease in the pulse rate, , convulsion and shivering. In the second week the lymph nodes and testis were hot and swollen, were become off food, cachexia, recumbent with lateral curvature of the neck for 1-2 days prior to death.
Post treatment all goats showed swelling at the injection site which disappeared after one day. Goats of groups (3 and 5) showed the same clinical signs of group (2), but mild and consistent throughout the experimental period while group (4) behaved similarly to group (3 and 5) but signs were disappeared after 14 day post treatment and started to improve however, goats of groups (6) showed hyperthermia, decrease in pulse rate, body weight and blood pressure was severe bloody diarrhoea without colic, bloody urine, and mild skin lesions weakness followed by paralysis of hind limbs without fetlock over reflection and died 25-28 day post treatment. In addition no swollen lymph nodes and testis, no alopecia, no pressing head against objects and no blindness were observed in all experimental groups.

3.3.3 Gross findings post-treatment

Table (4) summarizes the gross findings in Nubian goats infected with *T. evansi* and treated with single or multiple doses of Cymelarsan and oxytetracycline-LA in combination. Atrophy of the brain (plate 50), inflammation of the peripheral nerves and myositis (plate 51) were observed in goats of groups (5 and 6). The flabbiness, dilatation of the right ventricle, and degeneration of the heart in groups (2-5), (plate 52) with hydropericardium in groups (2, 3 and 6) (plate 53) were observed. Slight to moderate fatty change, congestion and haemorrhage in the liver with distended gall bladder (plate 54) were also observed in groups (2, 3 and 6-10) and no granules observed in gall bladder. There were various degrees of congestion in different organs specially that of the lungs, heart, kidneys (plate 55), liver, and intestine in most of the experimental animals, but mild in groups (5 and 6). However pneumonia and atrophy of the testes (plate 56) were observed in most goats tested. Slight to moderate haemorrhages were observed in most groups tested. No gross findings were observed in goats of group (1).

3.3.4 Histopathological findings

**Cerebellum**: Goats in groups (2-3) showed diffuse vacculations mainly around the neurons which were elongated in shape and with dark staining and some of them still
with star shape with nuclei in one side (plate 57) glial cell proliferation, and neuronal degeneration. Haemorrhages and congestion were seen in goats of group (4).

**Cerebrum**: Vacuulations with widened prevascular and perineuronal spaces, and glial cells proliferation were noticed in goats of groups (2, 3, 5 and 6).

**Spinal cord**: The spinal showed recorded proliferations of ependyma with glial cell proliferation around the central canal in goats of groups (5 and 6) and vacuulations in white matter of goats in groups (2).

**Peripheral nerves**: showed slight congestion in goats of groups (4 and 5) and no significant changes were seen in other groups.

**Tongues**: No significant changes were seen in all experimental goats.

**Thyroid glands**: Goats in groups (2-4) showed congestion while those of groups (2) exhibited follicular atrophy. In group (6) some follicles were obviously dilated. No significant changes were seen in group (5).

**Lungs**: The lungs showed congestion (group 2), emphysema in groups (2, 3 and 6) and areas of collapse and pneumonia in groups (2, 4 and 5).

**Heart**: All experimental goats showed congestion and haemorrhages.

**Liver**: Congestion, sinusoidal dilatation in groups (2-4) (plate 58), slight cetrilobular necrosis and scattered foci of lymphocytes and macrophages (plate 59) were observed. Portal tracts are widened in goats of groups (2).

**Spleen**: Congestion and haemosiderosis were noticed in goats of groups (2 and 3) and no obvious lesions were seen in the rest groups.

**Kidneys**: Goats of groups (2 and 3) had haemorrhagic and congestion while, goats in groups (2 and 4-6) showed dilatation of renal proximal tubules and increase in glomerular cellularity.
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Small intestines: showed congestion, loss of villus epithelium in groups (2 and 3), while goats in groups (2, 5 and 6) showed submucosal oedema and no significant changes were observed in goats of group (4).

Colon: congestion and haemorrhages were observed in goats of groups (2, 5 and 6),

Leg muscles, lymph nodes and tendon: no abnormalities are detected in all experimental goats.

Sites of injection: showed congestion in goats of groups (5 and 6).

Testis: Congestion and haemorrhage were seen in animals of groups (2, 5 and 6), histological evidence of active spermatogenesis was seen in sections of group (3) while few spermatogonia were seen in tubules of section from groups (2, 4 and 6) (plate 60).

3.3.5 Haematological Changes

Tables (5 and 6) summarize the haematological changes in Nubian goats infected with *T. evansi* and treated with single or multiple doses of Cymelarsan and oxytetracycline combination. Generally it was depicted that the Hb concentration, PCV, RBC and lymphocytes values declined although some of them were not statistically significant, also the reticulocytes, WBC, platelet, basophiles and neutrophiles counts increased significantly compared to group (1).

Table (6) and figure (9) depicted the MCV, MCH and MCHC of Nubian goats infected with *T. evansi* and treated with single or multiple doses of Cymelarsan and oxytetracycline combination. The tables showed insignificant statistical difference in these parameters, but increase in MCV was noticed in groups (3 and 4) while, increases in MCH and MCHC were noticed in groups (4 and 5).
3.3.6 Serobiochemical Changes

Tables (7-9) summarize the changes in serobiochemistry of Nubian goats infected with *T. evansi* and treated with single or multiple doses of Cymelarsan and oxytetracycline combination. No significant changes were observed in the serum concentration of sodium, potassium, phosphorus, magnesium, zinc, copper and iron in all infected and treated groups compared to group (1). There was a slight increase in the serum manganese in most of the groups while that of the calcium concentration showed slight decrease compared to group (1).

It is noticed that although some parameters in the different group showed statistical significance, but still values remained within the normal ranges. figure (10).

Also it was clear that most changes in serum activities of the serum LDH, CK, PK, GOT, GPT, SDH, amylase and lipase were normal and some slight significant variations were seen.

3.3.7 The concentration of Arsenic (Cymelarsan) and oxytetracycline

Tables (10) summarizes the concentration of Cymelarsan in serum (figure (11)), organs; bile and urine in the goats increased with *T. evansi* and treated with single and multiple dosages of Cymelarsan and oxytetracycline combination. The arsenic concentration were found at the range above 100 µg/g in the liver, kidney, fat, site of injection and leg muscle of goats in group (6) while, the same group had a range of 70-99 µg/g in heart, lung, cerebellum, testis, and urine, the rest of the organs were less than 60 µg/g. also organs in goats of group (5) showed 70-99 µg/g in liver and fat, while that less than 60 µg/g was noticed in the rest of the organs. However, records of arsenic in most different organs of the goats in groups (3 and 4) were ≤0.07.

The concentration of oxytetracycline in serum, organs, bile and urine increased significantly in the goats of groups (6-3) respectively in organs, bile and urine. It increased in site of injection, fat, kidney, liver, spleen, ovary, leg muscle, cerebellum, cerebrum, bile, uterus, urine, testis, heart, lung respectively. Oxytetracycline
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Concentration was not detected in liver, kidney, heart, and cerebellum. Cerebrum, ovary, testis and urine in goats of group (4) in the third slaughter, in the spleen, cerebellum, cerebrum, leg muscle, uterus, ovary, testis in goats of group (5) whereas it was detected in the rest organs in the same groups and it was also detected in organs, bile and urine till days 15 and 28 in goats of groups (3 and 6) respectively. The oxytetracycline concentration increased in goats’ serum in groups (7 and 8) to 20±0.01 and to 10.3±0.05 respectively, it was 5±1.10 on day 14 in goats of group (3) and 1.5±0.02 on day 21 in goats of group (4). Generally any changes in concentration recorded in the treated groups compared to that of group (1 and 2). This was summarized in tables (11 and 12).

It was noticed that when Cymelarsan administered at single I/M 0.250 mg/kg combined with OTC at 10mg/kg or at 0.125mg/kg with 50mg/kg OTC the residual pattern in the different organs and serum, urine and bile is not different from that recorded when those drugs are given alone and single dosages but, a surprising observation was noticed when Cymelarsan had been given at 0.250 mg/kg with combination of OTC given twice/week for two weeks or daily for 8 days where the concentration of Cymelarsan is decreased and that of OTC increased when compared to results which were obtained when these drugs were administered alone at the same frequencies.

3.4 Experiment (4): Clinicopathological effect and Efficacy of Cymelarsan in Nubian goats infected with *T. evansi* and supplemented with zinc and copper.

3.4.1 The parasitaemia

3.4.1.1 The parasitaemia in the peripheral blood

Table (1) summarizes the parasitaemia in the peripheral blood in the Nubian goats infected with *T. evansi* and treated with single and multiple dosages of Cymelarsan and supplemented with zinc and copper.

a/ post infection
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Goats in groups (2-6) showed mild parasitaemia (+) on days 4-5, moderate (++) on day 6 and severe (++++) on days 7-10. Animals of group (2) died on day 11.

b/ post treatment

Goats of group (3) showed mild parasitaemia (+) until animals died on day 13-15. Goats of group (4) showed moderate parasitaemia (+++) until day 9, and they were negative till the end of the experiment. Goats of group (5) showed mild parasitaemia (+) during the first three days post treatment and they were negative until the animals died on day 15 post treatment. But it appeared 3-4 days post treatment in goats of group (6) then disappeared completely until they died 15-18 day post treatment.

3.4.1.2 Detection of the parasites in liver impression smears

Table (2) summarizes the parasites in the liver impression smears in the Nubian goats infected with *T. evansi* and treated with single and multiple dosages of Cymelarsan and supplemented with zinc and copper.

The goats of group (2) died 11 days post infection and the parasite was detected in the liver in the range of 4-6 parasites/field. Goats in group (3) showed mild parasitaemia (+) at weeks 1, 2, 4 and 5 but were negative in week 3. While goats of groups (4-6) showed no parasites in the liver during the withdrawal period which started at 14 days post dosing and continued for other 5 weeks.

3.4.2 Clinical signs and clinical investigation

No clinical signs were observed in goats of group (1). Goats in group (2) showed 4-7 days post infection hypothermia, watery lacrimation, frothy salivation, mucopurulent conjunctivitis, mucopurulent nasal discharge, decrease in appetite, severe diffuse alopecia (plate 1), diarrhoea, depression, apathy, muscle tremors, slight increase in the respiratory rate, decrease in the pulse rate, convolution and shivering. In the second week, the lymph nodes and testis were hot and swollen, animal become off food, cachexia, recumbent with lateral curvature of the neck for 1-2 days before death.
At post treatment in the first week goats of groups (3-6) showed swelling at the site of injection, which disappeared after 1-2 days, goats of group the group showed mild clinical signs as those of group (2). Goats of group (4) showed no clinical signs post treatment. Goats in group (5) showed watery lacrimation with mucopurulent conjunctivitis accompanied with blindness (75% of the goats), mucopurulent nasal discharge, frothy salivation, fever, depression, apathy, pressing the head against objects, watery diarrhoea for 3-4 days then changed to bloody diarrhoea, bloody urine, muscle tremors, decrease in appetite, slight increase in the respiratory rate, decrease in the pulse rate. In the second week this group showed hot and swollen lymph nodes and testis, severe diffuse alopecia which was slight in the other treated groups, no shivering and no convulsion, weakness in the forelimb, recumbent in sternal position, animals become off food, emaciation, a decreased in the body weight also was observed and anuria, these signs persisted until the death. Also the group showed skin lesions in the second week as red 3mm raised concave nodules which increased in size to 5mm then changed to a brown scab these scabs when removed by hand leave white to yellowish ulcer, when excised a greasy white yellowish hard material was seen and remain until death. While, goats of group (6) showed nasal discharge, pyrexia, bloody urine, bloody diarrhea, skin lesion and paralysis in hind limb.

Table (3) summarizes the clinical changes in the goats infected with T. evansi and treated with single and multiple dosages of Cymelarsan and supplemented with zinc and copper. The table showed normal values for goats of group (1). Goats of group (2) showed decreases in the body weight and, respiratory rate, blood pressure and in body temperature. A decreased in the body weight, body temperature, blood pressure was observed in goats of group (3) and the respiratory rate is within the reference interval. Results obtained from goats of group (4) as nearer those recorded in group (1). While a decrease in respiratory rate and pulse rate, normal body weight and blood pressure and hyperthermia, observed in goats of group (5), however, those of group (6) recorded hyperthermia, decrease in pulse rate, body weight and an increase in respiratory rate and blood pressure.
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3.4.3 Gross findings post-treatment

Table (4) summarizes the gross finding in the goats infected with *T. evansi* and treated with single and multiple dosages of Cymelarsan and supplemented with zinc and copper.

No gross findings were observed in goats of group (1). The gross pathological findings in groups (3 and 5) are moderate to severe lesions. Lesions under investigation were congestion, oedema and haemorrhage in the different organs and in the lung (plate 61) and heart (plate 63), pneumonia (plate 62), froth on the trachea, and flabbiness and dilation of the heart (plate 64), while fatty change and or necrosis is investigated mainly in livers (with whit bile)(plate 65) and kidneys(plate 67) in addition, gastroenteritis, peritonitis and hydroperitoneum, spleenomegally (plate 66), myositis and peripheral nerve (femoral), necrosis (plate 69 and 70) at the site of injection, swollen lymph node and testis and urinary retention(plate 68). The thyroid gland showed no apparent lesions. Generally the lesions observed in the dosed goats of groups (4) were mild or disappeared compared to group (2). Far away, lesions of goats in group (6) are more prominent in the intestine, site of injection as well as the congestion in the liver and kidneys and showed similarities as those of group (3).

3.4.4 The histopathological findings

**Cerebellum**: goats in groups (2, 3 and 5) showed diffuse vacculations mainly around the neurons which were elongated in shape and with dark stained. Some of them still maintained their star shape with nuclei. Glial cell proliferation, haemorrhage and congestion (plate 71) and widened in prevascular spaces.

**Cerebellum and cerebrum**: many neurons appeared small and oval in shape showing pyknotic nuclei. Vacculations and widened prevascular spaces were also seen in groups (2, 3, 5 and 6).

**Spinal cord**: recorded proliferations of ependymal cells with glial cells proliferation around the central canal in goats of group (2) and vacculations in white matter in goats of groups (2, 3 and 5) (plate 72), widened prevascular spaces were also seen in group (5).
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**Peripheral nerve:** showed in goats of group (6) slight congestion in goats of groups (2, 3 and 4). While, diffuse vaculation observed in goats in group (5) with loss of nerve structure in goats in group (6).

**Tongue:** in goats of groups (2-4) were normal. Some goats in group (5) showed melanosis.

**Thyroid glands:** goats in groups (2-5) showed congestion and the glands were atrophied with loss of thyroid tissues and goats in groups (4 and 6) has same follicles and dilatation were occurred.

**Lungs:** the lungs of goats in group (2) were congested; groups (2, 3 and 5) were emphysematous, edematous and congested. In groups (2, 3 and 4) areas of collapse, emphysema, pneumatic foci and haemorrhage in alveoli and bronchi were seen (plate 73).

**Heart:** all goats showed congestion and haemorrhages. However, lymphocytic infiltration in the cardiac muscle was noticed in goats of groups (2 and 5). But in goats of groups (4 and 6) the muscle fibers appeared thin with elongated nuclei. Focal or diffuse vaculations in the cardiac muscles were seen in goats of groups (5). Goats in group (5) showed myodegeneration, with neutrophils infiltration, oedema and slight haemorrhage.

**Liver:** goats in groups (2 and 5) showed congestion, sinusoidal dilatation, slight cetrilobular necrosis and scattered foci of lymphocytes and macrophage (plate 75). Widened of portal tract was seen in goats of groups (2 and 6). Haemosedrein, deposits are also observed in the liver of goats in groups (5).

**Spleen:** goats of groups (2, 3 and 4) showed congestion and haemosiderosis. Goat in group (5) showed haemosiderosis thickened trabicula, around the white pulp. In group (5) showed congestion and haemorrhages of the red pulp with haemocedrosis and depletion lymphoid tissue.

**Kidneys:** groups (2-6) showed varying degrees dilatation of renal tubules, increase in glomerular cellularity, haemorrhage and congestion.
Small intestine: showed congestion, loss of villus epithelium in goats of groups (2-6). Goats in groups (2 and 4) were showed intestinal glands while, widened in lamina propria and submucosal oedema are seen in group (6).

Colon: showed congestion and haemorrhages in goats of groups (2 and 3) and normal in goats of groups (4-6).

Site of injection: Purulent inflammatory reaction and congestion was noticed in goats of group (6).

Leg muscle: showed congestion in goats of groups (5 and 6) and normal in goats of groups (2-4).

Lymph nodes: Sections showed congestion and haemorrhage in goats of group (6) and were normal in goats of group (4). While that of groups (2-3) were congested and hyperplastic the medullar part contained abundant interstitial tissues, and dilated blood vessels specially in goats of group (5).

Tendon: in all goats no lesions were observed.

Testis: Section in goats of groups (2-3 and 5-6) showed congestion, abundant interstitial tissues, eosinophilic material in some semineferous tubules and some tubules showed loss of germinal cells with loss of activity haemorrhage. Semineferous tubules animals in group (4) showed many vacules and little activity (plate 74).

3.4.5 Haematological changes

Table (5 and 6) summarizes the haematological changes in the goats infected with *T. evansi* and treated with single and multiple dosages of Cymelarsan and supplemented with zinc and copper. The Hb, RBC, PCV and lymphocytes values decreased significantly in goats of groups (2-6) while, the count of WBC, reticulocyte, platelet, basophiles, eosenophiles, monocytes and neutrophiles increased significantly in goats of groups (2-6). However, no statistical significance was observed in MCV, MCH and MCH post infection and post treatment, but the MCH decreased sharply in goats of group (3). Figure (12).
3.4.6 The Serobiochemical changes

Tables (7-9) summarizes the serobiochemical changes in Nubian goats infected with *T. evansi* and treated with single and multiple dosages of Cymelarsan and supplemented with zinc and copper. No significant changes were seen in serum concentration of sodium, calcium, phosphorus, zinc, copper and in serum activity of LDH, CK, GOT, GPT and SDH with groups in under experiment. However, an increase in potassium, total bilirubin, direct bilirubin and decreased in globulin, lipase in group (5). An increase in chloride, glucose, protein and lipase and sharp decrease was seen in calcium, phosphorus, iron in group (3). No significant changes were observed the in serum activity of PK, and ALP in groups (1, 4 and 6) compared to that of group (1). Generally it was observed that changes in goats of group (6) is more towards that of group (2) while, that of group (4) is near to that of group (1) specially in the serum concentration of potassium, chloride, magnesium, manganese, iron, total bilirubin, direct bilirubin, total protein, albumin, globulin, cholesterol, glucose, phospholipids and triglycerides and serum activity of amylase and lipase. figure (13).

3.4.7 The concentration of Cymelarsan in serum, urine, bile and organs

Table (10) is summarize the concentration of Cymelarsan in serum (figure (14)), urine, bile and organs in Nubian goats infected with *T. evansi* and treated with single and multiple dosages of Cymelarsan and supplemented with zinc and copper. It is noticed that the serum arsenic amount of the serum, bile, urine and in the different organs of groups (1 and 2) <0.07. Goats of groups (5 and 6) which died 15 day post treatment and expressed to 7 days only withdrawal period recorded values ≤0.07 in the cerebellum, cerebrum, fat, leg muscle and testis and still high values recorded in the urine, site of injection, heart, kidney and liver in addition spleen, uterus, ovary is least (1-15). Samples in goats of groups (3 and 4) which taken the withdrawal period recorded ≤0.07 is kidney, heart, lung, spleen, cerebellum, site of injection, leg muscle, uterus, ovary, testis, bile and urine. While, the liver and fat were recorded ≤0.07 in the 2nd, 3rd, 4th and 5th week of the withdrawal period. The serum recorded a mean value
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

0.41µg/ml post treatment. Generally any changes in concentration recorded within the treated groups compared to that of groups (1 and 2).

3.5 Experiment 5: Toxicity and efficacy of quinapyramine in goats infected with T. evansi

3.5.1 The parasitaemia

3.5.1.1 The parasitaemia in the peripheral blood

Table (1) summarizes the parasitaemia in the peripheral blood of Nubian goats infected with T. evansi and treated with single or multiple doses of quinapyramine.

a/ post infection

Goats in groups (2-8) showed mild parasitaemia (+) on day 4-5 (+), moderate (++) on day 6 and severe (+++++) on day 7-14, but animals of group (2) died on day 11.

a/ post treatment

Goats of group (3) showed mild parasitaemia (+) on day 1-6, parasite-free on day 7-20, mild (+) on day 21-56, while goats of groups (4, 5, 6, 7 and 8) showed mild (+) on day 1-3, 1-8, 1-4, 1-6, 1-6 respectively, then they were free of the parasite thereafter.

3.5.1.2 Detection of the parasites in liver impression smears

Table (2) summarizes the parasite detected by liver impression smears of Nubian goats infected with T. evansi and treated with single or multiple dosages of quinapyramine. Goats in group (2) showed moderate parasite (++) until death on day 11 post infection.

Animal infected and treated with 0.1mg/km I/M (group 3) the first, third, fourth and fifth slaughter showed mild parasite (+) while the second slaughter was free from the
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parasite. On the other hand, animals in groups (4, 5, 6, 7 and 8) were negative throughout the 5 slaughters of withdrawal period.

3.5.2 Clinical signs and clinical investigation

No clinical signs were observed in goats of group (1). Goats in group (2) showed 4-7 days post infection hypothermia, watery lacrimation, frothy salivation, mucopurulent conjunctivitis, mucopurulent nasal discharge, decrease in appetite, Severe diffuse alopecia (plate1), diarrhoea, depression, apathy, muscle tremors, slight increase in the respiratory rate, decrease in the pulse rate, convulsion and shivering. In the second week the lymph nodes and testis were hot and swollen, off food, cachexia, recumbent with lateral curvature of the neck for 1-2 days then the animals died.

post treatment these signs were seen in goats of groups (3-8) but they were mild and disappeared 10-15 days then continued milder in goats of group (8), whereas in group (3) they are mild until the slaughter of the animals.

The body temperature, respiratory rate, pulse rate, body weight and blood pressure different recorded but not significant changes were seen, but that of group (6) recorded decrease and an increase in body temperature. Table (3).

3.5.3 Gross findings

Table (4) summarizes the gross pathologically findings in goats infected with *T. evansi* and treated with single and multiple dosage of quinapyramine. Varying degrees of congestion and haemorrhage were observed in the different organs examined such as heart, kidney (plate 77), and lungs fatty changes and/or necrosis were noticed in the liver and kidneys specially of those in groups (2, 6 and 8). The lungs showed congestion, haemorrhages, emphysema and small area of hepatization specially that of groups (2, 6 and 8) (plate 75). However, enteritis and hypoatrophy of the testis were mild but affected most of the animals in the different groups. The heart is flabby, soft and dilated specially the right side and the apex is round specially goats of group (2, 6 and 8) (plate 76). Generally lesions were more severe in group (2, 6 and 8). No changes were observed in group (1).
3.5.4 Histopathological changes:

Cerebellum and cerebrum: In cerebellum proliferation of glial cells in white matter was observed in groups (2, 3, 6, 5 and 8) and irregular of axon cheats, old neuron and central chromatolysis (plate 78). Cerebrum showed meningeal congestion, haemorrhages (plate 79), diffuse vacculations, infiltration and glial cell proliferation with satellitosis (plate 80 and 81) were seen in cerebral sections in groups (2, 3, 6, 5 and 8).

Spinal cord: proliferation of ependymal cells with glial cells around the central canal and vacculations in white matter were recorded in goats in groups (2 and 3); demyelenation, moderate dilatation of axons sheath and vacculations in white matter in groups (6-8) (plate 82).

Peripheral nerve: in goats of groups (2-8) were normal

Tongue: in goats of groups (2-7) were normal.

Thyroid glands: goats in groups (2, 3, 6 and 8) showed congestion and atrophy of thyroid follicles.

Lungs: the lungs of goats in groups (2-5) were congested and showed areas of emphysema and collapse, with focal pneumonitis. Goats in groups (6-8) showed emphysema, haemorrhage in alveoli and bronchi (plate 83).

Heart: goats in group (2) showed congestion and haemorrhages while goats of groups (6-8) the cardiac muscles were elongated with closely arranged nuclei and vacculations however, goats in group (5) the cardiac muscles were elongated with pyknotic nuclei.

Liver: goats in group (2 and 3) showed congestion and sinusoidal dilatation. Slight centrilocular necrosis (plate 84) and sometimes scattered foci of lymphocytes and macrophage but, haemorrhages and haemocedrosis (plate 85) were observed in goats of group (4-8) and portal areas were thickened with cellular infiltration (plate 86).

Kidney: goats in groups (2 and 3) showed dilatation of renal tubules, increase in glomerular cellularity, haemorrhage and congestion, but the lesions were slight in
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Goats of group (3). Goats in groups (5-8) showed hypercellularity of the glomerular tuft; congestion and swelling of tubules cells.

**Small intestine:** Congestion, loss of villus epithelium with submucosal oedema were seen in goats of groups (2, 3, 5, 6 and 7). Haemorrhages, few intestinal glands and infiltration of *lamina propria* villi macrophage, lymphocytes and submucosal oedema were seen in goats of groups (3, 5 and 7) (plate87).

**Colon:** showed congestion and haemorrhage in goats of groups (2, 3 and 6-8),

**Leg muscle** and **lymph nodes:** in goats of groups (2-8) were normal.

**Testis:** Section from goats of groups (2, 3, and 5-8) showed congestion and haemorrhage while that of group (4) appeared normal.

### 3.5.5 Haematological changes

Tables (5 and 6) summarize the haematological changes in Nubian goats infected with *T. evansi* and treated with single or multiple dosages of Quinapyramine. Significant lowering was seen in goats of groups (2, 3, 5 and 6) in the Hb, PCV, and RBC counts while there were no changes in lymphocyte and monocyte counts in all experimental animals except that of group (2). No significant changes were observed in the total WBC count and the eosenophile, slight increases were seen in the platelet count in groups (2 and 6) and also increases were observed in the basophiles of goats of groups (2, 5 and 6). Generally there was an increase in the reticulocyte and neutrophiles count.

In goats, which received multiple dosages of the drugs, no significant changes were observed in the lymphocyte and neutrophiles count in groups (7 and 8). Also it is noticed that goats of group (8) followed the same trend of those in group (1). No significant changes were observed in the MCV, MCH and MCHC values in all experimental groups. These findings were compared to that of goats in group (1). Figure(15a and b).

### 3.5.6 Serobiochemical changes:
Tables (7-9) summarize the serobiochemical changes in Nubian goats infected with *T. evansi* and treated with single and multiple dosages of quinapyramine. No significant changes were seen in serum iron and copper in all groups while significant decreases in serum zinc were observed only in group (8). Generally increases in serum manganese concentrations were observed in most of the treated groups compared to that of group (1). Increases in the phosphorus concentration were also detected in goats of groups (2, 6 and 8) while serum calcium values decreased significantly in goats of groups (2, 3 and 8). Generally the chloride serum concentration increased in all treated groups comparable to that of group (1), while the serum concentration of potassium and sodium increased in groups (2, 6 and 8).

Changes in the serum concentration of bilirubin, direct bilirubin, urea, creatinine were within the normal known levels, but significant increase in serum total protein, albumin and globulin in all goats except in goats of groups (4 and 7).

Significant decreases were observed in most treated groups in the concentration of the serum thyroxin hormone (T4) and serum progesterone (figure (16, 17a and b)) and in the activities of serum lipase, while slightly significant increase of SDH was observed in goats of groups (2 and 8). No significant changes were detected in the serum activities of LDH, GOT, GPT and ALP as they were within the normal levels.

### 3.5.7 The concentration of the quinapyramine in different organs in the goats

Table (10 and 11) summarizes the concentration of quinapyramine in Nubian goats infected with *T. evansi* and treated with single and multiple dosages of quinapyramine. The quinapyramine concentration increased in goats of groups (3-7) but decreased in the slaughtered animals, being nil in the last slaughtered animals and nil in the cerebrum and in the lung. Generally any changes in concentration of quinapyramine recorded within the treated groups comparable to that of group (1 and 2).
3.6 Experiment 6: Toxicity and efficacy of homidium bromide in goats infected with *T. vivax*

3.6.1 The parasitaemia

3.6.1.1 The parasitaemia in the peripheral blood

Table (1) summarizes the parasitaemia in the peripheral blood of Nubian goats infected with *T. vivax* and treated with single or multiple doses of ethidium bromide.

a/ post- infection

Goats in groups (2-7) showed mild parasitaemia (+) on day4-5, severe (++) on day6, very severe (++++) on day7-10, moderate on day11-12, severe on day 13-17 goats of group (2) died on day17.

b/ post treatment

The peripheral blood post treatment shows in the goats of group (3) showed mild parasitaemia (+) on day 1 then it disappeared on 2-7 days then appeared slightly on day 8-20 then disappeared on day 21-34 and appeared mildly on day 35, 3 goats died between day 16-20, where two were survived on day 28 and 35. , but that of goats in group (4) appeared mild on day 1-7 then became free on the following days. However, goats of group (5) showed slight parasitaemia on days 1-4 then disappeared for 3 days where the animals died. Goats in group (6) showed mild parasitaemia (+) until day 19, and then disappeared until the end of the experiment except mild parasitaemia (+) appearing on day 23-25. Goats of group (7) showed mild parasitaemia (+) on day 1-4 then the animals were free from parasites on day 6-16 and they were died on day 16-20.

3.6.1.2 Detection of the parasites in liver impression smears

Table (2) summarizes the parasitaemia in the liver impression smears of Nubian goats infected with *T. vivax* and treated with single or multiple doses of ethidium bromide. Goats in group (2) showed moderate parasitaemia (++).
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Goats in group (3) showed mild parasites (+) during the first, second, fourth and fifth slaughter whereas, in the third slaughter they were parasite -free also, goats in groups (4-7) were parasite -free throughout the slaughter time.

3.6.2 Clinical signs and clinical investigation

Goats in groups (2) started clinical signs at 7-10 days post infection, which included hypothermia, watery lacrimation with mucopurulent conjunctivitis, mucopurulent nasal discharge and frothy salivation. Lately week post infection decrease in appetite, depression, watery yellowish diarrhoea, muscle tremors, with lateral curvature of the head.

Post treatment goats of groups (3 and 5) showed the same clinical signs as that of group (2) but mild, death occurred between days 16-20 while the other two survived goats are slaughtered day 28 and day 35 while goats of group (5) were died 3-8 day. Goats of groups (4 and 6) showed the same signs but mild and disappeared after 7 days where the animals regain appetite and weight, alopecia improved and orchitis subsides. While that of group (7) were severe, there is colic and bloody diarrhoea and death occurred 16-20 days post treatment.

Tables (3) summarize the clinical investigation. The body temperature decreased significantly in goats of group (2), after treatment group (3) showed decrease in body temperature which increased in goats of group (5) but was normal in goats of groups (4, 6 and 7).

Significant increase was seen in respiratory rate in goats in all groups whereas significant decrease was seen in blood pressure in goats in all groups except goats in groups (4 and 6).

Goats in groups (4 and 6) were slaughtered after day 28 post treatment and two animals weekly, goats in group (2) died on day 9-11, goats in groups (3 and 7) died
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

between days 16-20, goats in groups (4 and 6) post dosing and goats in group (5) died between days 3-8 post dosing.

3.6.3 Gross findings

Table (4) summarizes the gross findings in goats infected with *T. vivax* and treated with single and multiple dosages of ethidium bromide. It is noticed that most of the lesions in the different organs were in groups (2, 3, 5 and 7). These lesions consist of varying degrees of congestion, haemorrhages, flabbiness of the heart observed in all groups (plate 88), froth in trachea, emphysema of the lungs (plate 89), fatty changes in the liver and kidneys (plate 90), hepatic atelectasis (plate 91) and enteritis. No apparent lesions are seen in goats of groups (4 and 6) compared to that of group (1). Other post mortem changes in the other groups were mild and goats of groups (3 and 5) showed dark with distended gall bladder greenish bile and urinary retention. Goats of group (7) showed swollen of the femoral nerve (plate 92).

3.6.4 Histopathological findings

**Cerebellum**: Sections from groups (2, 3 and 5) showed very diffuse vacculations mainly around the neurons where some of them were elongated in shape and with dark stained nuclei but, others were still maintained star shape with nuclei on one side and glial cell proliferation and neuronal degeneration (plate 93) however, goats of groups (4, 6 and 7) showed slight changes.

**Cerebrum**: goats in groups (2-5) showed vacculations (plate 94) and glial cells proliferation, congestion and degeneration changes (plate 95) while, that of groups (6-7) showed slight changes.

**Spinal cord**: Sections of groups (2, 3 and 5) showed proliferations of ependymal cells and glial cells around the central canal and vacculations of the white matter while, that of groups (4, 6 and 7) showed slight changes.

**Peripheral nerve**: slight vacuolated cytoplasm, slight segmental demyelination, aggregates of macrophages and slight oedema were observed in sections from groups (5-7) (plate 96).
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**Thyroid glands:** Section from groups (2, 3 and 5) showed congestion and follicular atrophy.

**Lungs:** Sections of lungs in groups (2, 3, 5 and 7) showed congestion, emphysema, areas of collapse, small foci of pneumonitis. Goats of groups (4 and 6) look normal.

**Heart:** goats in groups (2, 3, 5 and 7) showed congestion and haemorrhage. Muscle nuclei tended to be elongated in goats of groups (3, 4, 5 and 7) however while, that of groups (6) showed no changes.

**Liver:** goats in groups (2, 3 and 5) showed congestion, sinusoidal dilatation. Slight centrilobular necrosis, haemorrhages (plate 97) and sometimes scattered foci of lymphocytes and macrophages, widened of portal tracts in addition to haemosedrosis in goats of groups (5-7) while, that of groups (4 and 6) showed slight changes.

**Kidney:** goats in groups (2, 3, 5 and 7) showed dilatation of renal tubules (plate 98), increase in glomerular cellularity haemocedrosis (plate 99), haemorrhage and congestion.

**Small intestine:** showed congestion, loss of villus epithelium and submucosal oedema in goats of groups (2, 3 and 5) (plate 100) while, in groups (4 and 6) were normal.

**Colons:** congestion and haemorrhages in goats of groups (2, 3, 5 and 7) while, in groups (4 and 6) were slight.

**Peripheral nerve and lymph nodes:** in goats of groups (2-7) sections were normal.

**Leg muscle:** infiltration, myositis, dark staining fibers in groups (6-7) (plate 101) while, in groups (2-5) were normal.

**Testis:** goats of groups (2-5 and 7) showed congestion and haemorrhage while, in group (6) were normal.

### 3.6.5 Haematological changes

Tables (5 and 6) summarize the haematological changes. Most of the experimental groups showed decreases in the Hb concentration, PCV, RBC and lymphocyte count, increase in the reticulocytes, WBC, platelets, eosenophiles and neutrophiles count. However changes were observed in the basophiles count, the monocytes were increased in most of the groups tested except goats of groups (6 and 7). These values
were compared to those of the control group (1). It is clear that no significant changes were seen in MCV, MCH, MCHC values in test animals compared to goats of group (1) in addition the values recorded were with the normal levels. Table (6) and figure (18 a and b).

### 3.6.6 Serobiochemical changes

Tables (7-9) summarize the Serobiochemical changes in Nubian goats infected with *T. vivax* and treated with single and multiple dosages of ethidium bromide. No significant changes were observed in serum concentration of iron, copper and zinc. It is noticed that although some groups showed significant changes in serum concentration of sodium, potassium, calcium and phosphorus other were within the normal levels. Slight significant increase in serum concentration of cholesterol and magnesium in group (7) was seen while the serum concentration of the manganese increased in groups (2, 3, 5 and 7). These values were comparable to that of goats in group (1).

It is clear that most values of serum concentration of bilirubin, direct bilirubin, urea, creatinine, total protein, albumin, globulin, cholesterol and glucose were within normal level although some showed significant change.

Table (9 a and b) summarizes the serum activities, showing that most of the values of enzymes investigated were within normal levels; also it is clear that values of group (2) in most of the enzymes under examination changed significantly but some of them were within the normal levels. Slight changes were observed in serum concentration of thyroxin and progesterone where most values were within the normal levels. Biochemical changes under investigation were comparable with goats of group (1). Figure (19, 20a and b).

### 3.7 Experiment 7: Efficacy and clinicopathological effect of quinapyramine and homidium bromide combination in goats infected with *T. evansi or T. vivax*

#### 3.7.1 The parasitaemia
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

3.7.1.1 The parasitaemia in peripheral blood

Table (1) summarizes the parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* or *T. vivax* and treated with single dosages of quinapyramine and homidium bromide combination.

a/post infection

Goats in groups (2*, 3 and 4), which infected with *T. evansi* showed mild parasitaemia on day 4-5 (+), moderate on day 6 (++) and severe on day 7-14 (++++) but animals of group (2*) died on day 11. Goats in groups (2**, 5 and 6) which infected with *T. vivax* showed mild parasitaemia (+) on day 4-5, severe (+++) on day 6, very severe (++++) on day 7-10, moderate on day 11-12, severe on day 13-17 goats of group (2**) died on day 17.

b/ post treatment

Goats in group (3) showed mild parasitaemia (+) on day 1-6, they were negative on day 7-25, mild (+) on day 26-56, wile goats of group (4) wee showed mild (+) on day 1-5, parasite -free on day 6-35, mild (+) on day 36-49, parasite -free on day 56, goats in group (5) showed mild parasitaemia (+) on day 1-10, parasite -free on day 11-13, mild (+) on day 14-20, moderate (++) on day 21-22, mild (+) on day 23-25, parasite -free on day 26-56, also goats in group (6) showed mild parasitaemia (+) on day 1-4, parasite -free on day 5-17, mild (+) on day 18-23 an they were parasite -free on day 24-56.

3.7.1.2 The parasitaemia in liver impression smears

Table (2) summarizes the parasite in the liver impression smears of Nubian goats infected with *T. evansi* or *T. vivax* and treated with single dosing of quinapyramine and homidium bromide combination. *T. evansi* is detected in goats’ livers of groups (2*, 2** and 3) they showed moderate parasitaemia (++) whereas the other groups were parasite -free.
3.7.2 Clinical signs and clinical investigation

No clinical signs were observed in goats of group (1). Goats in group (2*) which were infected with *T. evansi* showed 4-7 days post infection hypothermia, watery lacrimation, frothy salivation, mucopurulent conjunctivitis, mucopurulent nasal discharge, decrease in appetite, Severe diffuse alopecia (plate1), diarrhoea, depression, apathy, muscle tremors, slight increase in the respiratory rate, decrease in the pulse rate, convulsion and shivering. In the second week the lymph nodes and testis were hot and swollen, off food, cachexia, recumbent with lateral curvature of the neck for 1-2days then the animals died. And goats in group (2**) which were infected with *T. vivax* started clinical signs at 7-10 days post infection, which included hypothermia, watery lacrimation with mucopurulent conjunctivitis, mucopurulent nasal discharge and frothy salivation. Lately week post infection decrease in appetite, depression, watery yellowish diarrhoea, muscle tremors, with lateral curvature of the head.

In goats of group (3-6) 4 days post treatment signs started to decrease in severity and started to regain the appetite, the diarrhoea stopped 10 days later. These animals became healthy and looked normal within the third week post dosing. Tables (3) summarize the clinical changes in Nubian goats infected with *T. evansi* or *T. vivax* and treated with single dosing of quinapyramine and homidium bromide combination. The body temperature, respiratory rate, pulse rate, blood pressure and body weight were within the normal range in all the groups although there were significant changes in some parameters under investigation compared to goats of group (1). However goats of groups (2* and 2**) showed decrease in body temperature, respiratory rate, pulse rate, body weight and blood pressure changes comparable to control or treated groups.

3.7.3 Gross findings

Table (4) summarizes the gross findings in Nubian goats infected with *T. evansi* or *T. vivax* and treated with single dosage of quinapyramine and homidium bromide combination. No gross findings were observed in goats of group (1). The gross
pathological findings in the different organs, which had been examined, which had been developed by trypanosomosis either, flabbiness of the heart in goats of groups (2*, 2**, 3, and 6) (plate 102), hepatic atelectasis especially in groups (2and3) (plate 103), fatty changes in liver and kidneys (plate 104) absent or mild lesions. Goats in groups (3-4) showed distended urinary and gall bladder (plate 105and 106).

3.7.4 Histopathological changes

Cerebellum and cerebrum: showed vacuulations, glial cells proliferation mainly in white matter with oval and pyknotic nuclei, widened in prevascular spaces (plate 108) in goats of groups (2*, 2**) which infected with *T. evansi* and *T. vivax* respectively, and also these lesions were observed in goats of groups (3 and4), irregular of axons cheats, degeneration were noticed in groups (5-6) (plate 107).

Spinal cords: Sections from groups (2*, 2** -6) showed vacuulations in white matter, proliferations of ependymal cells and glial cells around the central canal. Sections from groups (4-5) showed some widened of prevascular spaces.

Peripheral nerve: were normal.

Thyroid glands: goats of groups (2*, 2**, 3 and5) showed congestion and atrophy of some follicles.

Lung: Section of lungs of groups (2*, 2** and 4) showed congestion, emphysema, areas of collapse and pneumonitis. Goats in groups (5-6) showed alveolar and bronchial haemorrhages and emphysema while goats of groups (3and5) showed collapse and thickened interlobular septa (plate 109).

Heart: Sections from groups (2*, 2**, 3 and5) showed congestion and haemorrhages while, the cardiac muscles were thin and had elongated nuclei goats of groups (4-5) while, in groups (6) were normal.

Liver: In goats of groups (2*, 2** -5) congestion and sinusoidal dilatation were observed together (plate 110) with slight centrilobular necrosis and sometime scattered foci of lymphocytes and macrophages (plate111) in addition to haemocedrein deposits. Goats in groups (3 and5) showed areas of haemorrhage, widened portal tracts due to mononuclear cells infiltration and widened central and
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

portal veins. Goats in groups (5-6) showed multifocal areas of degeneration, dilation of hepatic veins and sinusoidal congestion.

**Spleen**: goats in groups (4-6) showed thickened capsule and the white pulp were depleted while, in groups (2*, and2**-3) were normal.

**Kidney**: goats of groups (2*, 2**, 4, 5and 6) showed dilatation of renal tubules, increase in glomerular cellularity (plate 112), haemorrhages and congestion while, in groups (3) were normal.

**Small intestine**: showed congestion, loss of villus epithelium with submucosal oedema in goats of groups (2*, 2**, 3 and6) while, in groups (4 and5) were normal.

**Colon**: showed congestion and haemorrhages in goats of groups (2*, 2** and 5) while, in groups (4 and6) were normal.

**Site of injection**: showed congestion, in goats of group (5) while, in groups (2*,2**-4and6)were normal.

**Peripheral nerve, leg muscle and lymph nodes**: were normal.

**Testis**: Sections from goats of groups (2*, 2** -5) showed congestion and haemorrhage, while goats of groups (5-6) showed little evidence of activity with vacculations in somniferous tubules (plate113).

### 3.7.5 Haematological Changes

The haematological changes are summarizes in tables (5-6) in Nubian goats infected with *T. evansi* or *T. vivax* and treated with single dosage of quinapyramine and homidium bromide combination. No significant changes were observed in the haemoglobin concentration, PCV, RBC counts, WBC counts, reticulocytes, platelet counts, eosenophiles counts, basophiles counts, neutrophiles counts, monocytes counts and lymphocyte counts compared to that of group (1). Significant changes observed in goats of groups (2*, 2**, 3, 4 and5). No significant changes observed in the MCV, MCH and MCHC in all animals. Generally any changes observed within the treated groups compared to that of group (1) still within the normal levels. Figure (21).

### 3.7.6 The Serobiochemical changes
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

The Serobiochemical changes summarize in tables (7-9) and figures (22-25) in Nubian goats infected with *T. evansi* or *T. vivax* and treated with single dosage of quinapyramine and homidium bromide combination. No significant changes were observed in the serum concentration of sodium, calcium, phosphorus, copper, zinc, iron bilirubin and glucose within the experimental groups. Significant changes were recorded in the serum chloride, magnesium, manganese, direct bilirubin, cholesterol, glucose, total protein, albumin globulin urea and creatinine. Significant increase was recorded in serum potassium only in goats of groups (2* and 2**).

No significant changes were observed in serum activity of LDH, GOT, GPT, SDH, amylase in any of the experimental groups, while significant increase was observed in the concentration of the serum thyroxin and progesterone of goats in groups (2*, 2** and 3). The serum lipase decreased significantly only in goats of group (1) while the serum ALP decreased slightly in goats of groups (2*, 2** and 3) comparable to that of group (1).

3.7.7 The concentration of the quinapyramine in different organs in the goats

Table (10 and 11) summarizes the concentration of quinapyramine in Nubian goats infected with *T. evansi* or *T. vivax* and treated with single and multiple dosage of quinapyramine and homidium bromide combination. The quinapyramine concentration increased in goats of groups (3-6) but decreased in the following slaughtered animals except in goats of group (6). It was nil in the cerebrum and in the lung in the last slaughtered animals. The quinapyramine concentration increased in the serum of goats in groups (3 and 6). Generally any changes in concentration recorded within the treated groups comparable to that of groups (1 and 2* or 2**).

Experiments of camels

3.8 Experiment 1: Toxicity and efficacy of Cymelarsan in camels (*Camelus dromedarius*) naturally infected with *T. evansi* and treated with single and multiple dosages of Cymelarsan
3.8.1 The parasitaemia

3.8.1.1 The parasitaemia in the peripheral blood

The parasitaemia in the naturally infected camels with *T. evansi* and treated with single and multiple dosages of Cymelarsan is summarizes in table (1).

post infection

No parasites were detected in camels of group (1). Camels in groups (2) showed mild (+) parasitaemia on day 1-7, moderate (++) on day 8-11, and severe (+++) on day 12-18, and very severe (++++) on day 19-22 until death on day 22.

b/Post treatment

Dosing was start on day 22 post infection. Camels of groups (3 and 4) showed mild parasitaemia (+) 2-3 days post treatment and then they were negative there after. However, camels in group (5) showed moderate parasitaemia (++) in the first 8 days post treatment, mild (+) on days 9-17, then negative parasitaemia on day 18-23, mild (+) on day 24-26 and then parasite-free thereafter till day 42.

3.8.1.2 Detection of the parasites in liver impression smears

Table (2) summaries the liver impression smears in camels naturally infected with *T. evansi* and treated with single and multiple dosage of Cymelarsan. Camels of group (2) showed severe parasites (+++) post infection while camels in groups (3-5) was clear from the parasites since day 14 post treatment.

3.8.2 Clinical signs

Camels of group (2) showed at the first week, which include lacrimation, nasal discharge which become purulent after the first week, shivering, hypothermia (33±0.02), decrease in the respiratory (7±0.01) and pulse rate (22±0.03). At the second week decrease of appetite, but, at week three these signs were severe and there were keratitis, diarrhoea, muscle tremor specially of the hind and forelimbs. Three
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)
camels were crying, kicking, and hyperesthesia, anxiety episodes of upward-backwards form, movement of the neck, loss of weight (plate114) and loss of appetite. These same signs were observed in camels of groups (3 and 4) during the treatment period but they were mild and disappeared 12-14 day post treatment while that of group (5) were also milder and which disappeared 21 day post treatment. All camels showed swollen at the site of injection disappeared after 1-2 days. These animals in groups (3-5) regain the appetite and the weight gradually thereafter.

3.8.3 Gross findings

The gross findings in the naturally infected camels with *T. evansi* and treated with single and multiple dosages of Cymelarsan are summarized in Table (3). Infected camels in group (2) showed enlargement of thyroid gland, spleen, kidney, lymph nodes, flabby heart with observable hydropericardium, gelatinization of fat and muscles, congestion in brain, nasal cavity, lung (plate 115), liver (plate 118), kidney (plate 120), and intestine (plate 121). Haemorrhages were observed in the heart (plate 117), pleura, lung (plate 115), liver (plate 118), kidneys (plate 120), intestines (plate 121) and emphysema, necrotic foci and pneumonia (plate 116), hypoatrophied and inflamed testes and spleenomegaly (plate 119). Camels under treatment in groups (3-5) either showed slight or absence of lesions mainly in lungs; heart and spleen (plate 122-125).

3.8.4 The histopathological findings

Cerebellum and spinal cords: showed vacculations, glial cell proliferation and neuronal degeneration in camels of group (2) while, the rest groups were normal.

Cerebrum: showed congestion, haemorrhage, and slight vacculations in camels of groups (2and3) while, the rest groups were normal.

Lung: Alveolar haemorrhages were observed in goats of groups (2and3), areas of collapse and haemorrhage in bronchi and alveoli were also observed in camels of groups (2and4) while, in group (5) were normal.

Heart: showed congestion and vacculations in camels of groups (2) while, the rest groups were normal.
Liver: showed congestion and haemorrhage in camels of groups (2and3), while proliferation of Coffle’s cells, sinusoidal congestion was noticed in camels of groups (2, 4 and 5).

Kidney: camels of groups (2and5) showed congestion, haemorrhage, dilatation of tubules and nephritis while, in groups (3and 4) were normal.

Small intestine: No obvious lesions are detected.

3.8.5 Haematological changes

Table (3and 4) summarize the haematological changes in camels naturally infected with *T. evansi* and treated with single and multiple dosages of Cymelarsan. Significant decreases were seen in the PCV, Hb concentration, and RBC count and an increase in the WBC count in camels of group (2) while no significant changes were observed in camels of groups (3, 4 and 5) as compared to group (1).

There are no significant changes in the MCV, MCH and MCHC in groups (3-5) but the MCV in camels of group (2) is increased and the MCH and MCHC are decreased. Figure (26).

3.8.6 Serobiochemical changes

Table (5and 6) summarize the serobiochemical changes in camels infected naturally with *T. evansi* and treated with single dosages of Cymelarsan. Significant decrease in serum concentrate of calcium and phosphorus and urea, is seen in camels of groups (2-4) they were within the reference interval in camels of group (5). The serum creatinine decreased significantly in camels of groups (2-3) and it was within reference interval in groups (4-5).

The serum total protein, albumin increased significantly in camels of groups (2-5) (the serum total protein was reference interval in camels of group 4) however, the serum globulins was within reference interval post – infection, it decreased significantly in camels of groups (3, 4 and5). The serum cholesterol, triglyceride concentration and GOT activity decreased in groups (2-5). The serum glucose
increased post – infection slightly and decreased significantly in camels of groups (2,3 and5). Figure (27).

The serum GPT is within reference interval in camels of groups (3-5); it was significantly increased in camels of group (2) however, the serum ALP activity decreased significantly in camels of groups (2and 4), it was raised in camels of group (3) and it within reference interval in group (5).

The serum progesterone was within reference interval in camels of group (5), it was significantly increased in camels of groups (2-4) while, the serum T3 decreased significantly post – infection, increased slightly in camels of groups (3, 4 and5). However, the serum T4was within reference interval in camels of groups (4 and5) and it decreased significantly in camels of groups (2 and3). figure (28-30).

3.8.7The concentration of Cymelarsan

Table (7) summarizes the concentration of arsenic in organs, serum, and urine in camels naturally infected with *T. evansi* and treated with single and multiple dosage of Cymelarsan. All groups of treated animals tend to record ≥0.07µg/ml arsenic in serum, urine or in the organs which include leg muscle, urine, liver, lung, spleen, cerebellum, cerebrum, fat, uterus, ovary, testis and the ≥0.07 were recorded 14-28 day since cessation of the drug except the kidneys, heart, site of injection record high values of 5µg/ml and which decreased gradually till ≥0.07 by 28-42 day after the cessation of the drug treatment.

3.9Experiment2: Toxicity and efficacy of oxytetracycline (OTC) in camels infected with *T. evansi* and treated with single and multiple dosages of oxytetracycline

3.9.1The parasitaemia

3.9.1.1The parasitaemia in the peripheral blood
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

The parasitaemia in the peripheral blood of naturally infected camels with *T. evansi* and treated with single and multiple dosages of oxytetracycline were summarizes in Table (1). No parasites were detected in camels of group (1). Camels in groups (2-7) showed mild parasitaemia on day 1-7 (+), which increased gradually until became very severe (++++) on day 14, then severe on day 15-18 and very severe (++++) on day 19-22 where the animals of group (2) died on day 22.

Post treatment camels in group (3) showed moderate parasitaemia (++) on day 1-3, mild (+) on day 4-16, then moderate (+++) on day 17-19 until they died on day 18-20, camels of group (4, 5, 6 and 7) showed moderate parasitaemia (++) until days 2, 3, 8 and 10 respectively then mild (+) until days 12, 8, 11 and 13 respectively. These groups were free of the parasite then for 14, 27, 15 and 25 days, the mild parasitaemia (+) occurred again in camels of groups (4, 5, 6 and 7) after the free-parasite period.

3.9.1.2 Detection of the parasites in liver impression smears

Table (2) summaries the parasites in liver impression smear of camels naturally infected with *T. evansi* and treated with single and multiple dosages of oxytetracycline. Camels in group (2) showed severe parasites (+++) while camels in group (3) were negative in the second slaughter 28 days after the prohibition of the drug dosages, moderate (++) in the fifth slaughter and mild (+) in the first, third and fourth slaughter. While camels in group (4) showed moderate parasites (++) in the second, third and fifth slaughter but they were negative in the first slaughter and mild in the fourth slaughter. However, camels in groups (5, 6 and 7) were parasite-free thought out the withdrawal period.

3.9.2 Clinical signs

Camels of group (2) showed at the first week, which include lacrimation, nasal discharge which become purulent after the first week, shivering, hypothermia (33±0.02), decrease in the respiratory (7±0.01) and pulse rate (22±0.03). At the second week decrease of appetite, but, at week three these signs were severe and there were keratitis, diarrhoea, muscle tremor specially of the hind and forelimbs. Three
camels were crying, kicking, hyperesthesia, anxiety episodes of upward - backwards form, movement of the neck, loss of weight (plate 114) and loss of appetite. Camels of group (3) showed clinical signs as group (2) but mild and persist until they are died 20day post treatment and no signs were in camels of groups (4and5), while camels of groups (6and7) showed the same signs as in group (2) but mild in addition to bloody diarrhoea, bloody urine, also the hoof was over reflected one week after cessation of the drug and continued for another two weeks then improved and the condition reversed to the normal until they are slaughtered. Alopecia did not recovered completely in all of the experimental tested groups but there is improved until they were died or slaughtered; all animals except group (3) improved the appetite and body weight gain.

### 3.9.3 Gross findings

Most of the finding which seen in camels in group (2) either became mild or absent, but the right cerebellum in camels under treatment were hypoatrophied. Tissue at the site of injection are stained yellow in groups (6and 7) small aggregates yellowish colour of the drug which can easily crushed by hand, serous fluids, congestion and haemorrhages mainly in the heart with congested blood vessels (plate 126), lung (plate 127) and the peripheral nerves (femoral nerves) were swollen, edematous, congested and haemorrhagic. No lesions observed in camels of group (1). Generally fever subside 10 days post treatment but it is continued in group (3). The site of injection in groups (6and 7) showed no swelling also no lameness in the two groups. Tables (3)

### 3.9.4 The histopathological findings

**Cerebellum and spinal cords**: showed vacculations, glial cell proliferation, neuronal in camels of groups (2, 5-7) while, in groups (3and 6) were normal.

**Cerebrum**: showed haemorrhages, congestion, slight vacculations in camels of groups (2, and5-7) while, in groups (3and 6) were normal.

**Lungs**: showed alveolar haemorrhage, in camels of groups (2, 3and6-7).areas of collapse, haemorrhage in bronchi and alveoli of camels in groups (2, 6-7) while, in groups (4and 5) were normal.
Heart: showed congestion, diffuse vacculations were detected in camels of groups (2,3,5and7) while, in groups (4and6) were normal.

Liver: showed congestion, haemorrhage in camels of groups (2and3), proliferation of Coffle’s cells, and sinusoidal congestion in camels of groups (2and3) while, in groups (4-7) were normal.

Kidney: showed congestion, haemorrhage, dilatation of renal tubules in camels of groups (2and7) nephritis with, unshaped renal tubular cells and due to indefinite proliferation, some of the cells had pyknotic nuclei, in camels of groups (2and5-7) while, in groups (3and6) were normal.

Small intestine: showed attachment of villi with creps due to regeneration in camels of groups (2,6and7) while, in groups (3,4and5) were normal.

3.9.5 Haematological changes

Table (4) summaries the haematological changes in camels naturally infected with *T. evansi* and treated with single and multiple dosages of oxytetracycline. There is no significant changes in the PCV and the WBC of camels under experiment, but the Hb concentration was generally decreased in camels of group (2) and moderately in groups (3and5) while it is insignificant in groups (4,6and7) compared to control group (1). The RBC count decreased in camels of groups (2,6and7) and were of insignificant changes in camels of groups (3,4and5) compared to control group (1). No significant changes are detected in the values of the MCV and MCH of camels in all groups, but the MCHC is significantly decreased in camels of group (2). Figure (31).

3.9.6 Serobiochemical and hormonal changes

Table (5-6) summarizes the Serobiochemical and hormonal changes in camels naturally infected with *T. evansi* and treated with single and multiple dosages of oxytetracycline. No significant changes in the serum concentration of calcium and phosphorus in different the groups except a decrease is noticed in groups (2and6). Changes in serum urea, creatinine, cholesterol, glucose and triglycerides were with
the normal level although same groups showed vice versa. Figure (32). Also there are no significant changes were recorded for serum activity GOT, GPT and for the concentration of progesterone, T3 and T4, values showed significant changes still within the normal level except there is an increase in the T3 and decrease in the T4 of camels in group (4). Also it is noticed that progesterone is high in camels of group (2), these results were compared statistically with the control camels of group (1). Figure (33-35).

3.9.7 The concentration of Oxytetracycline

Table (7 and8) summarizes the Serobiochemical and hormonal changes in camels naturally infected with *T. evansi* and treated with single and multiple dosages of oxytetracycline. The drug concentration reach the peak in the serum 3 hours post dosing then decrease gradually until 3 days post dosing and then nil in groups (3 and 4).

The drug concentration increased as the drug administration continued and then decreases as the withdrawal period progressed and recorded nil on day 21 post dosing (group 7). However, serum concentration of the drug in group of camels that received the drug intermittently recorded fluctuated values up and down where the increase follow the administration all days and vise versa and never recorded zero values until the end of the experiment. Generally any changes in concentration recorded within the treated groups compared to that of groups (1 and 2).

3.10 Experiment 3: Efficacy and clinicopathological effect of Cymelarsan and oxytetracycline combination in camels infected with *T. evansi*

3.10.1 The parasitaemia

3.10.1.1 The parasitaemia

The parasitaemia in the naturally infected camels with *T. evansi* and treated with single dosages of Cymelarsan and oxytetracycline combination is summarized in Table (1). No parasites were detected in camels of group (1).
a/ Post infection

Camels in groups (2-5) showed mild parasitaemia (+) on day 1-7, moderate (++) on day 8-11, and severe on day 12-13 (+++), very severe (++++) on day 14, severe on day (+++ 15-18, very severe (++++) on day 19-22 and the animals of group (2) died on day 22.

b/ Post treatment

The peripheral blood was free of the parasite 23, 18 and 11 days post treatment in groups (3), (4) and (5) respectively.

3.10.1.2 Detection of the parasites in the liver impression smears

Table (2) summarizes the parasite in liver impression smears in camels naturally infected with *T. evansi* and treated with single dosages of Cymelarsan and Oxytetracycline combination. Camels of group (2) showed severe parasites (+++) whereas the parasite was not detected in the liver tissue of camels in other groups (3, 4 and 5) in the five weeks slaughter program.

3.10.2 Clinical signs

Camels of group (2) showed at the first week, lacrimation, and nasal discharge which become purulent later, shivering, hypothermia (33±0.02°C), decrease in the respiratory (7±0.01/min) and pulse rate (22±0.03/min) and alopecia. At the second week decrease of appetite, but, at week three these signs were severe and there were keratitis, diarrhoea, muscle tremor specially of the hind and forelimbs. Three camels were crying, kicking, hyperesthesia, anxiety, episodes of upward - backwards, movement of the neck, in addition no over reflection of the hind limbs, no bloody diarrhoea or bloody urine, no alopecia, loss of weight (plate 114). The same signs
were observed in camels of groups (3-5) but they were mild and disappeared two weeks before the end of the experiment. The site of injection is swollen for 1-2 days.

3.10.3 Gross findings

The gross findings in the naturally infected camels with *T. evansi* and treated with single and multiple dosages of Cymelarsan and OTC-LA combination is summarized in table (3). Most of the lesions observed in tissues and organs of camels in group (3, 4 and 5) either disappeared or they were mild (plate 128 and 129).

3.10.4 The histopathological findings

**Cerebellum, cerebrum and spinal cords**: the cerebellum and spinal cords showed vacculations, glial cell proliferation, neuronal degeneration in camels of groups (2, 4-5) while, in groups (3) were normal while, the cerebrum showed haemorrhage, congestion, and slight vacculations in camels of groups (2-5) while, in groups (3 and 4) were normal.

**Lungs**: showed alveolar haemorrhage, in camels of groups (2 and 3). Areas of collapse haemorrhage in bronchi and alveoli of camels in groups (2-4) while, in group (5) were normal.

**Heart**: showed congestion, haemorrhage and diffuse vacculations in camels of groups (2 and 3) while, in group (4) were normal.

**Liver**: showed proliferation of Coffle’s cells, congestion of the sinusoids of camels in groups (2, 3 and 5). In addition to congestion and haemorrhage while, in group (4) were normal.

**Kidney**: showed congestion, haemorrhage, dilatation of renal tubules, nephritis with unshaped cells of renal tubules some of the cells were pyknotic in camels of groups (2-3) while, in groups (4 and 5) were normal.

**Small intestine**: the intestinal of villi were attached with creps due to regeneration in camels of groups (2, 3 and 5) while, in group (4) were normal.

3.10.5 Haematological changes
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Table (4 and 5) summarizes the haematological changes in camels naturally infected with *T. evansi* and treated with single dosages of Cymelarsan and oxytetracycline combination. There were no changes in Hb concentration, PCV, RBC and WBC count in camels of groups (3-5). No significant changes were observed in the MCH, MCHC and MCV on experimental camels. Also decreases in the MCV and an increase in MCHC were observed in camels of group (2) compared to control group (1). Figure (36).

### 3.10.6 The Serobiochemical changes and hormonal changes

Table (6 and 7) summarizes the serobiochemical changes in camels naturally infected with *T. evansi* and treated with single dosages of Cymelarsan and oxytetracycline combination. The serum activity GOT, GPT and ALP and serum concentration of urea, creatinine, total protein and cholesterol within the reference interval in the different groups tested. However, no significant changes were seen in serum concentration of globulins, triglycerides and glucose in groups (3-5). Compared to control group (1) Figure (37). However, a decrease in the globulin value was detected only in group (5). But significant increase in the progesterone was observed in group (2), while decrease in the level of T3, T4 and phosphorus was also detected in the same group. Figure (38-40).

### 3.10.7 The concentration of the Cymelarsan and Oxytetracycline

Table (8) summarizes the concentration of the Cymelarsan in camels naturally infected with *T. evansi* and treated with single dosages of Cymelarsan and oxytetracycline. Table (9-10) summarizes the concentration of the Oxytetracycline in camels naturally infected with *T. evansi* and treated with single dosages of Cymelarsan and oxytetracycline combination. It was noticed that in camels of groups (3-5) the concentration of Cymelarsan return to the control value group (1) when camels were slaughtered on day 21 post treatment, for the tissues organs, fluids investigated. High concentration of oxytetracycline were detected in group (5) which received five times the recommended dose compared to groups (3 and 4), in addition site of injection, kidneys, liver, cerebrum, fat, leg muscle, cerebellum and lungs.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) recorded high concentration. Also it is noticed that some organs do not release the drug rapidly such as the kidneys, heart, fat, site of injection and leg muscle. The least organs where the drug is concentrated after 21 days post treatment were urine, testis, ovary, spleen and the uterus. Table (9) summarizes the concentration of the Oxytetracycline in serum of camels naturally infected with T. evansi and treated with single dosages of Cymelarsan and oxytetracycline combination. Also when the residues amount of Cymelarsan studied in the different camels' tissues and urine it is noticed that when the concentration of OTC increased the residual amount of Cymelarsan decreased. No oxytetracycline residues were detected in the serum of camels in the different groups 10 days post treatment. Generally any changes in concentration recorded within the treated groups compared to that of group (1 and 2).

Table (1) The parasitaemia in the prepheral blood of Nubian goats infected with T. evansi and given single and multiple dosages of Cymelarsan.

<table>
<thead>
<tr>
<th>a/post infection</th>
<th>Post infection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Groups</strong></td>
<td></td>
</tr>
<tr>
<td>Days</td>
<td>1 2 3 4 5 6 7 8 9 10 11</td>
</tr>
<tr>
<td>Group (1)</td>
<td></td>
</tr>
<tr>
<td>Group (2) -ve</td>
<td>+ + ++ +++ +++ +++ +++ Died</td>
</tr>
<tr>
<td>Group (3) 0.125 mg/kg</td>
<td>+ + ++ +++ +++ +++ ++++</td>
</tr>
<tr>
<td>Group (4) 0.25mg/kg</td>
<td>+ + ++ +++ +++ +++ ++++</td>
</tr>
<tr>
<td>Group (5) 0.625 mg/kg</td>
<td>+ + ++ +++ +++ +++ ++++</td>
</tr>
<tr>
<td>Group (6) 1.25mg/kg</td>
<td>+ + ++ +++ +++ +++ ++++</td>
</tr>
<tr>
<td>Group (7) 0.125mg/kg twice/week for 2weeks</td>
<td>+ + ++ +++ +++ +++ ++++</td>
</tr>
<tr>
<td>Group (9) 0.25mg/kg twice/week</td>
<td>+ + ++ +++ +++ +++ ++++</td>
</tr>
<tr>
<td>Group (10) 0.25mg/kg daily for 8days</td>
<td>+ + ++ +++ +++ +++ ++++</td>
</tr>
</tbody>
</table>

+ = 1–4 parasite/field (milde), ++ = 5–8 parasite/field (moderate), +++ = 9–14 parasite/field (severe), more than++++ =15-20 parasite/field(very severe) and –ve = no parasite detected.
<table>
<thead>
<tr>
<th>Treatment</th>
<th>withdrawal period</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 g/kg</td>
<td>-</td>
</tr>
<tr>
<td>0.625 g/kg</td>
<td>-</td>
</tr>
<tr>
<td>0.5 g/kg</td>
<td>- Died</td>
</tr>
<tr>
<td>0.5 g/kg</td>
<td>- Died</td>
</tr>
<tr>
<td>0.1 g/kg</td>
<td>- Died</td>
</tr>
<tr>
<td>0.1 g/kg</td>
<td>- Died</td>
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<tr>
<td>0.1 g/kg</td>
<td>-</td>
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<td>0.1 g/kg</td>
<td>-</td>
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<td>0.1 g/kg</td>
<td>-</td>
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<tr>
<td>0.1 g/kg</td>
<td>-</td>
</tr>
</tbody>
</table>

Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan.

post treatment
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)
- = no parasites were detected  + = 1-4 parasites/field (mild), ++ = 5-8 parasites/field (moderate), +++ = 9-14 parasites/field (severe), more than++++ =15-20 parasites/field (very severe), and * = animals in group (2) died on day 11 post infection.

Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* and given single and multiple dosages of oxytetracycline.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Days</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
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</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group (2)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>Died</td>
</tr>
<tr>
<td>Group (3) 20mg/kg</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Group (4) 50mg/kg</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Group (5) 100mg/kg</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Group (6) 20mg/kg weekly for 3weeks</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>++++</td>
</tr>
<tr>
<td>Group (7) 20mg/kg twice/week for 2weeks</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Group (8) 20mg/kg daily for 8days</td>
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</tr>
</tbody>
</table>

- = no parasite was detected,  + = 1-4 parasite/field (mild)  ++ = 5-8 parasite/field (moderate)  more than +++ = 9-14 parasite/field (severe) and  more than++++ =15-20 parasite/field (very severe)
Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* an given single and multiple dosages of oxytetracycline.

post treatment

| Days | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 |
|------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Groups | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Group (1) | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Group (2) | * | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Group (3) | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 20mg/kg | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Died | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Group (4) | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 50mg/kg | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Group (5) | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 100mg/kg | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Group (6) | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 20mg/kg weekly for 3weeks | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Group (7) | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 20 mg/kg twice/week for 2weeks | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| Group (8) | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |
| 20mg/kg daily for 8days | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + |

* = animals in group (2) died on day 11 post infection.

+ = 1-4 parasites/field (mild), - = no parasite detected
Table (1) The parasitaemia in the peripheral of blood Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan and supplemented with zinc and copper.

<table>
<thead>
<tr>
<th>Days</th>
<th>1</th>
<th>2</th>
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<th>11</th>
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<tbody>
<tr>
<td>Groups</td>
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<td>Group (3)</td>
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</tr>
<tr>
<td>0.125mg/kg+Zn+Cu daily for 8 days</td>
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<td>Group (4)</td>
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<tr>
<td>0.125mg/kg+Zn+Cu daily for 8 days</td>
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</tbody>
</table>

- = no parasite was detected,  + = 1-4 parasite/field (milde)  ++ = 5-8 parasite/field (moderate)  +++ = 9-14 parasite/field (severe)  ++++ = 15-20 parasite/field (very severe)
Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan and supplemented with zinc and copper.

<table>
<thead>
<tr>
<th>Days post treatment</th>
<th>Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Days</td>
</tr>
<tr>
<td>Group (1)</td>
<td></td>
</tr>
<tr>
<td>Group (2)</td>
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</tr>
<tr>
<td>Group (3) 0.125 mg/kg</td>
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<tr>
<td>Group (4) 0.125 mg/kg + Zn + Cu</td>
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<tr>
<td>Group (5) 0.125 mg/kg daily for 8 days</td>
<td></td>
</tr>
<tr>
<td>Group (6) 0.125 mg/kg + Zn + Cu daily for 8 days</td>
<td></td>
</tr>
</tbody>
</table>

- = no parasite detected, + = 1-4 parasites/field (mild), ++ = 5-8 parasites/field (moderate) * = animals in group (2) died on day 11 post infection.
Table (1) The parasitaemia in the prepheral blood of Nubian goats infected with *T. evansi* an given single and multiple doses of Cymelarsan and oxytetracyclie.

a/ post infection

<table>
<thead>
<tr>
<th>Parameter</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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<th>8</th>
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</thead>
<tbody>
<tr>
<td>Groups</td>
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<td>Group (2)</td>
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<td>+++</td>
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<tr>
<td>Group (3) 0.125 mg/kg of MelCy+10mg/kg of OTC</td>
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<tr>
<td>Group (4) 0.125 mg/kg of MelCy+50mg/kg of OTC</td>
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</tr>
<tr>
<td>Group (5) 0.125 mg/kg of MelCy+20 mg/kg of OTC twice/Week</td>
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<tr>
<td>Group (6) 0.125 mg/kg of MelCy+20mg/kg of OTC daily for 8days</td>
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</tbody>
</table>

- = no parasite was detected, + = 1-4 parasite/field (milde) ++ = 5-8 parasite/field (moderate) more than +++ = 9-14 parasite/field (severe) and more than++++ =15-20 parasite/field (very (severe)
Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* an given single and multiple doses of Cymelarsan and oxytetracyclie combination. post treatment

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Groups</th>
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<th>2</th>
<th>3</th>
<th>4</th>
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<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>0.125 mg/kg of MelCy+10mg/kg of OTC</td>
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<tr>
<td>Group (2)</td>
<td>0.125 mg/kg of MelCy+10mg/kg of OTC</td>
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<tr>
<td>Group (3)</td>
<td>0.125 mg/kg of MelCy+50mg/kg of OTC</td>
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<tr>
<td>Group (4)</td>
<td>0.125 mg/kg of MelCy+20mg/kg of OTC twice/week for 2weeks</td>
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<tr>
<td>Group (5)</td>
<td>0.125 mg/kg of MelCy+20mg/kg of OTC daily for 8days</td>
<td>+</td>
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</tbody>
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- = no parasite was detected, + = 1-4 parasites/field (mild), + = 5-8 parasites/field (moderate), more than +++ = 9-14 parasites/field (severe) and more than ++++ = 15-20 parasites/field (very severe)
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* and given single and multiple dosages of Quinapyramine.

<table>
<thead>
<tr>
<th>Days</th>
<th>Post infection</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Groups</em></td>
<td>1</td>
</tr>
<tr>
<td>Group(1)</td>
<td>-</td>
</tr>
<tr>
<td>Group(2)</td>
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</tr>
<tr>
<td>Group(3) treated with 5 mg/kg</td>
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<tr>
<td>Group(4) treated with 12.5 mg/kg</td>
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<tr>
<td>Group(5) treated with 25 mg/kg</td>
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<tr>
<td>Group(6) treated with 1 mg/kg</td>
<td>-</td>
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<tr>
<td>Group(7) 50 mg/kg weekly for 3 weeks</td>
<td>-</td>
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<tr>
<td>Group(8) 5 mg/kg daily for 8 days</td>
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</tr>
</tbody>
</table>

-= no parasite was detected, + = 1-4 parasite/field (mild); ++ = 5-8 parasite/field (moderate) more than +++ = 9-14 parasite/field (severe) and more than ++++ = 15-20 parasite/field (very severe)
### Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* an given single dosages of Quinapyramine.

<table>
<thead>
<tr>
<th>Days post treatment</th>
<th>Group(1)</th>
<th>Group(2)</th>
<th>Group(3) treated with 5 mg/kg</th>
<th>Group(4) treated with 12.5 mg/kg</th>
<th>Group(5) treated with 25 mg/kg</th>
<th>Group(6) treated with 50 mg/kg weekly for 3 weeks</th>
<th>Group(7) mg/kg daily for 8 days</th>
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<tbody>
<tr>
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<td>20</td>
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<td>21</td>
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<td>22</td>
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<td>*</td>
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<td>23</td>
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<td>25</td>
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<td>26</td>
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<td>27</td>
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<td>28</td>
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<td>-</td>
<td>-</td>
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<td>*</td>
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<tr>
<td>31</td>
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<td>- ve</td>
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<td>-</td>
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<tr>
<td>32</td>
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<td>*</td>
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<td>- ve</td>
<td>-</td>
<td>-</td>
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<tr>
<td>33</td>
<td>-</td>
<td>*</td>
<td>- ve</td>
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<td>- ve</td>
<td>-</td>
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<tr>
<td>34</td>
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<td>35</td>
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<td>*</td>
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<td>- ve</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>36</td>
<td>-</td>
<td>*</td>
<td>- ve</td>
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<td>- ve</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>37</td>
<td>-</td>
<td>*</td>
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<td>- ve</td>
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<td>-</td>
</tr>
<tr>
<td>38</td>
<td>-</td>
<td>*</td>
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<td>- ve</td>
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<td>-</td>
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<td>39</td>
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<td>*</td>
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<td>- ve</td>
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<tr>
<td>40</td>
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<td>*</td>
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<td>41</td>
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<td>42</td>
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<td>*</td>
<td>- ve</td>
<td>+</td>
<td>- ve</td>
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</tr>
</tbody>
</table>

- = no parasite was detected,  + = 1-4 parasites/field (mild)
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Table (1) The parasitaemia in the prepheral blood of Nubian goats infected with *T. evansi* an given single and multiple dosages of Homidium Bromide.

<table>
<thead>
<tr>
<th>Days</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>13-17</th>
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<tbody>
<tr>
<td>Groups</td>
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<td>Group(1)</td>
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<tr>
<td>Group(2)</td>
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<td>+</td>
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<td>++++</td>
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<tr>
<td>Group(3) treated with 1 mg/kg</td>
<td>-</td>
<td>-</td>
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<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
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<td>++++</td>
</tr>
<tr>
<td>Group(4) treated with 2.5 mg/kg</td>
<td>-</td>
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<td>-</td>
<td>+</td>
<td>+</td>
<td>++</td>
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<td>++++</td>
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<tr>
<td>Group(5) treated with 5 mg/kg</td>
<td>-</td>
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<td>+</td>
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</tr>
<tr>
<td>Group(6) 1mg/kg weekly for 3weeks</td>
<td>-</td>
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<td>+</td>
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<td>++</td>
<td>+++</td>
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<td>++++</td>
</tr>
<tr>
<td>Group(7) 1mg/kg daily for 8days</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
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<td>++++</td>
</tr>
</tbody>
</table>

-= no parasite was detected, + = 1-4 parasite/field (mild), ++ = 5-8 parasite/field (moderate) more than +++ = 9-14 parasite/field (severe) and more than++++ =15-20 parasite/field(very severe)
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* and given single and multiple dosages of Homidium Bromide.

| Post treatment | Days | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 |
|----------------|------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Group(1)       | -    |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Group(2)       | *    |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Group(3) treated with 1 mg/kg | + | - |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Group(4) treated with 2.5 mg/kg | + |   | - |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Group(5) treated with 5 mg/kg | + | - |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    | Died |    |    |    |    |    |    |
| Group(6) 1mg/kg weekly for 3weeks | + |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Group(7) 1mg/kg daily for 8days | + |   |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    | Died |    |

- = no parasite was detected,  + = 1-4 parasites/field (mild)* = died 13-17 day post infection. ** = the three died animals were + and the rest as shown above.
Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* and given single dosages of quinapyramine and Homidium Bromide.

<table>
<thead>
<tr>
<th>Days</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groups</td>
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<tr>
<td>Group(1)</td>
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<tr>
<td>Group(2)</td>
<td>-ve</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>Died</td>
</tr>
</tbody>
</table>

*Group(3)* 5 mg/kg of quina. +1 mg/kg of eth.

*Group(4)* 12.5 mg/kg of quina. +1 mg/kg of eth.

**Group(5)** 5 mg/kg of quina. +1 mg/kg of eth.

**Group(6)** 5 mg/kg of quina. +2.5 mg/kg of eth.

- = no parasite was detected, + = 1-4 parasite/field (mild), ++ = 5-8 parasite/field (moderate), +++ = 9-14 parasite/field (severe), ++++ = 15-20 parasite/field (very severe). * = Infection was done by *T. evansi*. ** = Infection was done by *T. vivax*. quina. = quinapyramine. hom. = homidium bromide.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

### Table (1) The parasitaemia in the peripheral blood camels naturally infected with *T. evansi* and given single and multiple dosages of Cymelarsan.

a/Post infection

<table>
<thead>
<tr>
<th>Days</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
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</thead>
<tbody>
<tr>
<td><em>&lt;sup&gt;a&lt;/sup&gt; Post infection</em></td>
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<td>-</td>
<td>+</td>
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</tr>
</tbody>
</table>

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- = no parasite was detected, + = 1-4 parasites/field (mild), ++ = 5-8 parasites/field (moderate), * = Infection was done by *T. evansi*. ** = Infection was done by *T. vivax*. quina. = quinapyramine. hom. = homidium bromide.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (1)</th>
<th>-</th>
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</thead>
<tbody>
<tr>
<td>Group (2)</td>
<td>+ + + + + + ++ ++ ++ ++ +++ +++ +++ +++ +++ +++ +++</td>
</tr>
<tr>
<td>Group(3) 0.25mg/kg</td>
<td>+ + + + + + ++ ++ ++ ++ +++ +++ +++ +++ +++ +++ +++</td>
</tr>
<tr>
<td>Group (4) 0.625mg/kg</td>
<td>+ + + + + + ++ ++ ++ ++ +++ +++ +++ +++ +++ +++ +++</td>
</tr>
<tr>
<td>Group (5) 0.125 mg/kg weekly/3weeks</td>
<td>+ + + + + + ++ ++ ++ ++ +++ +++ +++ +++ +++ +++ +++</td>
</tr>
</tbody>
</table>

-= no parasite was detected,  + = 1-4 parasite/field (milde)  ++ = 5-8 parasite/field (moderate)  more than +++ = 9-14 parasite/field (severe) and  more than+++++ =15-20 parasite/field (very severe)

Table (1) The parasitaemia in the peripheral blood camels naturally infected with *T. evansi* and given single and multiple dosages of Cymelarsan.

<table>
<thead>
<tr>
<th>Days</th>
<th>1</th>
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<th>4</th>
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</table>

**Post treatment**
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) 0.25mg/kg</th>
<th>Group (4) 0.625mg/kg</th>
<th>Group (5) 0.125 mg/kg weekly for 3 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>+</td>
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</tbody>
</table>

- = no parasite was detected,  + = 1-4 parasites/field (mild), ++ = 5-8 parasites/field (moderate)

Table (1) The parasitaemia in the peripheral blood of camels naturally infected with *T. evansi* and given single and multiple dosages of Oxytetracycline.

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<th>15</th>
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<tbody>
<tr>
<td>Groups</td>
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</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (2)</th>
<th>+</th>
<th>+</th>
<th>+</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Group (3) 20 mg/kg</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
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<tr>
<td>Group (4) 50mg/kg</td>
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<tr>
<td>Group (5) 100 mg/kg</td>
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<tr>
<td>Group (6) 20mg/kg twice/week for 2weeks</td>
<td>+</td>
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</tr>
<tr>
<td>Group (7) 20mg/kg daily for 8days</td>
<td>+</td>
<td>+</td>
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<td>++</td>
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<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

-= no parasite was detected,  += 1-4 parasite/field (milde)  ++= 5-8 parasite/field (moderate) more
than +++ = 9-14 parasite/field (severe) and more than++++ =15-20 parasite/field(very severe)

Table (1) The parasitaemia in the peripheral blood of camels naturally infected with *T. evansi*
and given single and multiple dosages of Oxytetracycline.

<table>
<thead>
<tr>
<th>Post treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groups</td>
</tr>
<tr>
<td>Days</td>
</tr>
<tr>
<td>Group (1)</td>
</tr>
<tr>
<td>Group (2)</td>
</tr>
</tbody>
</table>
Table (1) The parasitaemia in the peripheral blood camels naturally infected with *T. evansi* and given single and multiple dosages of Cymelarsan and Oxytetracycline.

<table>
<thead>
<tr>
<th>Days</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
<th>17</th>
<th>18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groups</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group(1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group (2)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

| Group(3) | 0.25mg/kg of MelCY+20mg/kg of OTC | + | + | + | + | + | ++ | ++ | ++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ |
| Group(4) | 0.125mg/kg of MelCY+50mg/kg of OTC | + | + | + | + | + | ++ | ++ | ++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ |
| Group(5) | 0.125mg/kg of MelCY+100mg/kg of OTC | + | + | + | + | + | ++ | ++ | ++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ | +++ |

-= no parasite was detected,   += 1-4 parasite/field (milde)  ++ = 5-8 parasite/field (moderate)  more than +++ = 9-14 parasite/field (severe) and more than+++++ =15-20 parasite/field (very severe)

Table (1) The parasitaemia in the peripheral blood camels naturally infected with *T. evansi* and given single and multiple dosages of Cymelarsan and Oxytetracycline combination.

**Post treatment**

| Days | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
| Groups | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Group(1) | | | | | | | | | | | | | | | | | | | | | | | | | | | - |
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Parasitaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (2)</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Group (3)</td>
<td>0.250 mg/kg of MelCY + 20 mg/kg of OTC</td>
<td>++-+</td>
</tr>
<tr>
<td>Group (4)</td>
<td>0.125 mg/kg of MelCY + 50 mg/kg of OTC</td>
<td>++-+</td>
</tr>
<tr>
<td>Group (5)</td>
<td>0.125 mg/kg of MelCY + 100 mg/kg of OTC</td>
<td>++-+</td>
</tr>
</tbody>
</table>

- = no parasite was detected, + = 1-4 parasites/field (mild), ++ = 5-8 parasites/field (moderate)

Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. evansi* and given single dosages of quinapyramine and Homidium Bromide.

Post treatment

| Post treatment | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 35 | 42 |
|---------------|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Group (1)     | - |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Group (2)     | - |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |
| Group (3)     | + |   |   |   |   |   |   |   |   |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |    |

Note: Post treatment indicates the observed parasitaemia over time for each group.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group(4)</th>
<th>+</th>
<th>-</th>
<th>+</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5mg/kg of quina.</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

--- no parasite was detected, + = 1-4 parasites/field (mild), * = died on day 11. quina. = quinapyramine. hom. = homidium bromide.

Table (1) The parasitaemia in the peripheral blood of Nubian goats infected with *T. vivax* an given single dosages of quinapyramine and Homidium Bromide.

<table>
<thead>
<tr>
<th>Post treatment</th>
<th>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 35 42</th>
</tr>
</thead>
<tbody>
<tr>
<td>p (1)</td>
<td></td>
</tr>
<tr>
<td>p (2)</td>
<td></td>
</tr>
<tr>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>
### Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with \textit{T. evansi} and given single and multiple dosages of Cymelarsan.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Slaughter (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
</tr>
<tr>
<td>Group (1)</td>
<td></td>
</tr>
</tbody>
</table>

- no parasite was detected,  + = 1–4 parasites/field (mild)  ++ = 5–8 parasites/field (moderate), * = died on day 17. quina. = quinapyramine.  hom. = homidium bromide.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (2)</th>
<th>*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (3)**</td>
<td>+ + + -ve</td>
</tr>
<tr>
<td>0.125mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (4)</td>
<td>-ve</td>
</tr>
<tr>
<td>0.250 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (5)</td>
<td>-ve</td>
</tr>
<tr>
<td>0.625mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (6)</td>
<td>-ve</td>
</tr>
<tr>
<td>1.25mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (7)</td>
<td>-ve</td>
</tr>
<tr>
<td>0.125 mg/kg</td>
<td></td>
</tr>
<tr>
<td>twice/week for 2 weeks</td>
<td>(-ve) Died on day 17</td>
</tr>
<tr>
<td>Group (8)</td>
<td>-ve</td>
</tr>
<tr>
<td>0.125mg/kg daily</td>
<td>(-ve) Died on day 28</td>
</tr>
<tr>
<td>Group (9)</td>
<td>-ve</td>
</tr>
<tr>
<td>0.250 mg/kg twice/week for 2 weeks</td>
<td>(-ve) Died on day 21</td>
</tr>
<tr>
<td>Group (10)</td>
<td>-ve</td>
</tr>
<tr>
<td>0.250 mg/kg daily for 8 days</td>
<td>(-ve) Died on day 15</td>
</tr>
</tbody>
</table>

-ve = no parasite detected; += 1-3 parasites/field; ++ = 4-6 parasites/field; * = Died on day 11 post infection and showed ++ parasites/field.

**= Died on days 26-28 post infection. Week 1 (w1)=14 day post treatment (d.p.t), w2=21 d.p.t, w3=28 d.p.t, w4=35 d.p.t and w5=42 d.p.t.

Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with *T. evansi* and given single and multiple dosages of oxytetracycline.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Slaughter (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
</tr>
<tr>
<td>Group (1)</td>
<td>-ve</td>
</tr>
<tr>
<td>Group (2)</td>
<td>*</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

| Group (3)  
20mg/kg | (+++) Died on day 10 |
| Group (4)  
50mg/kg | + |
| Group (5)  
100mg/kg | ++ | ++ | + | + | + | -ve |
| Group (6)  
20mg/kg  
weekly 
for 3 weeks | ++ | ++ | + | + | -ve |
| Group (7)  
20 mg/kg 
twice/week | -ve |
| Group (8)  
20mg/kg daily | -ve | (-ve)  
Died on day 18 |

- ve = no parasite detected, += 1-3 parasites/field, ++ = 4-6 parasites/field. *= Died on day 11 post infection and showed ++ parasites/field.
**= Died on days 26-28 post infection. Week 1 (w1)=14 day post treatment (d.p.t), w2=21 d.p.t, w3=28 d.p.t, w4=35 d.p.t and w5=42 d.p.t.

Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with T. evansi and given single and multiple dosages of Cymelarsan and supplemented with zinc and copper.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Slaughter (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
</tr>
<tr>
<td>Group (1)</td>
<td>-ve</td>
</tr>
<tr>
<td>Group (2)</td>
<td>*</td>
</tr>
</tbody>
</table>
| Group (3)**  
0.125mg/kg | + | + | + | -ve | + | + | + |

Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with T. evansi and given single and multiple dosages of Cymelarsan and supplemented with zinc and copper.

- ve = no parasite detected, += 1-3 parasites/field, ++ = 4-6 parasites/field. *= Died on day 11 post infection and showed ++ parasites/field.
**= Died on days 26-28 post infection. Week 1 (w1)=14 day post treatment (d.p.t), w2=21 d.p.t, w3=28 d.p.t, w4=35 d.p.t and w5=42 d.p.t.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (4)</th>
<th>-VE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.250mg/kg+Zn+Cu</td>
<td>-VE</td>
</tr>
</tbody>
</table>

|-ve = no parasite detected , += 1-3 parasites/field, *= Died on day 11 post infection and showed ++parasites/field.
**= Died on days 26-28 post infection. Week1 (w1)=14d.p.t, w2=21d.p.t, w3=28d.p.t, w4=35d.p.t and w5=42d.p.t.

<table>
<thead>
<tr>
<th>Group (5)</th>
<th>-VE Died on day 15</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.250 mg/kg daily for 8 days</td>
<td>-VE Died on day 15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group (6)</th>
<th>-VE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.250mg/kg+Zn+Cudaily</td>
<td>-VE</td>
</tr>
</tbody>
</table>

| Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with T. evansi and given single and multiple dosages of Cymelarsan and oxytetracycline . |
|---|---|---|---|---|---|
| Groups | Slaughter (week) | W1 | W2 | W3 | W4 | W5 |
| Group (1) | -VE |
| Group (2) | * |
| Group (3)** 0.125 mg/kg of MelCy+10mg/kg of OTC | -ve | -ve | -ve | + | + | + |
| Group (4) 0.125 mg/kg of MelCy+50mg/kg of | -ve | -ve | ++ | ++ | ++ | + | + | + |
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>OTC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (5)</td>
<td></td>
</tr>
<tr>
<td>0.125 mg/kg of MelCy+20 mg/kg of OTC twice/week for 2 weeks</td>
<td>-Ve</td>
</tr>
<tr>
<td>Group (6)</td>
<td></td>
</tr>
<tr>
<td>0.125 mg/kg of MelCy+20 mg/kg of OTC daily for 8 days</td>
<td>(-Ve) Died on day 28</td>
</tr>
</tbody>
</table>

-ve = no parasite detected , ++ = 1-3 parasites/field, + = 4-6 parasites/field, * = Died on day 11 post infection and showed ++ parasites/field.
** = Died on days 26-28 post infection. Week 1 (w1)=14 day post treatment (d.p.t), w2=21 d.p.t, w3=28 d.p.t, w4=35 d.p.t and w5=42 d.p.t.

Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with T. evansi and given single and multiple dosages of Quinapyramine.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Slaughter (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
</tr>
<tr>
<td>Group (1)</td>
<td>-Ve</td>
</tr>
<tr>
<td>Group (2)</td>
<td>*</td>
</tr>
<tr>
<td>Group (3)**</td>
<td>+</td>
</tr>
<tr>
<td>5 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (4)</td>
<td></td>
</tr>
<tr>
<td>12.5 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (5)</td>
<td></td>
</tr>
<tr>
<td>25 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>

Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with T. evansi and given single and multiple dosages of Quinapyramine.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group(6) 1 mg/kg</th>
<th>(–ve) Died on day 12-18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group(7) 5 mg/kg weekly for 3 weeks</td>
<td>-ve</td>
</tr>
<tr>
<td>Group(8) 5 mg/kg daily for 8 days</td>
<td>(–ve) Died on day 16-20</td>
</tr>
</tbody>
</table>

-ve = no parasite detected, ++ = 1-3 parasites/field, +++ = 4-6 parasites/field, * = Died on day 11 post infection and showed ++ parasites/field.

** = Died on days 26-28 post infection. Week 1 (w1)=14 day post treatment (d.p.t), w2=21 d.p.t, w3=28 d.p.t, w4=35 d.p.t and w5=42 d.p.t.

### Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with *T. evansi* and given single and multiple dosages of Homidium Bromide.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Slaughter (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
</tr>
<tr>
<td>Group (1)</td>
<td></td>
</tr>
<tr>
<td>Group (2)</td>
<td></td>
</tr>
<tr>
<td>Group (3) ** 1 mg/kg</td>
<td>+</td>
</tr>
<tr>
<td>Group (4) 2.5 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (5) 5 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (6) 1 mg/kg weekly for 3 weeks</td>
<td>-ve</td>
</tr>
</tbody>
</table>

*ve = no parasite detected, ++ = 1-3 parasites/field, +++ = 4-6 parasites/field, * = Died on day 11 post infection and showed ++ parasites/field.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Group (7)
1mg/kg daily

-ve = no parasite detected . += 1-3 parasites/field. * = Died on day 11 post infection and showed ++parasites/field. **= Died on days 26-28 post infection. Week1 (w1)=14 day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4=35d.p.t and w5=42d.p.t.

Table (2): Detection of the parasites by the liver impression smears in Nubian goats infected with *T. evansi* and given single and multiple dosages of Quinapyramine and Homidium Bromide.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Slaughter (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
</tr>
<tr>
<td>Group (1)</td>
<td>-VE</td>
</tr>
<tr>
<td>Group (2)</td>
<td>*</td>
</tr>
<tr>
<td>*(Group(3) 5 mg/kg of quina. +1mg/kg of eth.)</td>
<td>-VE</td>
</tr>
<tr>
<td>*(Group(4) 12.5mg/kg of quina. +1mg/kg of eth.)</td>
<td>-VE</td>
</tr>
<tr>
<td>**Group(5) 5 mg/kg of quina. +1mg/kg of eth.)</td>
<td>-VE</td>
</tr>
</tbody>
</table>
**Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)**

<table>
<thead>
<tr>
<th><strong>Group(6)</strong></th>
<th>5mg/kg of quina.+2.5mg/kg of eth</th>
<th>-VE</th>
</tr>
</thead>
</table>

* = Infection was done by *T. evansi*. ** = Infection was done by *T. vivax*. quina. = quinapyramine. hom. = homidium bromid.

* = Died on day 11 post infection and showed ++parasites/field. Week1 (w1)=14 day post treatment (d.p.t), w2=21 d.p.t, w3=28 d.p.t, w4=35 d.p.t and w5=42 d.p.t.

Table (2): Detection of the parasites by the liver impression smears in camels naturally infected with *T. evansi* and given single and multiple dosages of Cymelarsan.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Slaughter (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
</tr>
<tr>
<td>Group (1)</td>
<td></td>
</tr>
<tr>
<td>Group (2)</td>
<td></td>
</tr>
<tr>
<td>Group (3) 0.250 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (4) 0.625 mg/kg</td>
<td></td>
</tr>
<tr>
<td>Group (5) 0.125 mg/kg weekly/3weeks</td>
<td></td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

* = Died on day 21 post infection and showed +++ parasites/field.
Week 1 (w1) = 14 days post treatment (d.p.t), w2 = 21 d.p.t, w3 = 28 d.p.t, w4 = 35 d.p.t and w5 = 42 d.p.t.

Table (2): Detection of the parasites by the liver impression smears in camels naturally infected with *T. evansi* and given single and multiple dosages of oxytetracycline.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Slaughter (week)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>W1</td>
</tr>
<tr>
<td>Group (1)</td>
<td></td>
</tr>
<tr>
<td>Group (2)</td>
<td></td>
</tr>
<tr>
<td>Group (3)**</td>
<td></td>
</tr>
<tr>
<td>20 mg/kg</td>
<td>+</td>
</tr>
<tr>
<td>Group (4)</td>
<td></td>
</tr>
<tr>
<td>50 mg/kg</td>
<td>-ve</td>
</tr>
<tr>
<td>Group (5)</td>
<td></td>
</tr>
<tr>
<td>100 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>

** *= Died on day 21 post infection and showed +++ parasites/field.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (6)</th>
<th>20mg/kg twice/week for 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (7)</td>
<td>20mg/kg daily for 8 days</td>
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-ve = no parasite detected,  + = 1-3 parasites/field,  ++ = 4-6 parasites/field,  +++ = 7-11,  * = Died on day 22 post infection and showed +++ parasites/field,

** = died on day 20. Week1 (w1)=14 day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4= 35d.p.t and w5=42d.p.t.

---

Table (2): Detection of the parasites by the liver impression smears in camels naturally infected with *T. evansi* and given single dosages of Cymelarsan and oxytetracycline combination within the withdrawal period.

<table>
<thead>
<tr>
<th>Slaughter (week)</th>
<th>W1</th>
<th>W2</th>
<th>W3</th>
<th>W4</th>
<th>W5</th>
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<tbody>
<tr>
<td>Groups</td>
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<td>(2) Group</td>
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<tr>
<td>Group (3) 0.250 mg/kg MelCY+20mg/kg of OTC</td>
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<tr>
<td>Group (4) 0.125mg/kg MelCY+50mg/kg of OTC</td>
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<td></td>
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<tr>
<td>Group(5) 0.125mg/kg MelCY+100mg/kg of OTC</td>
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<td>-ve</td>
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-ve = no parasite detected,  * = Died on day 21 post infection and showed +++ parasite/field.

Week1 (w1)=14 day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4= 35d.p.t and w5=42d.p.t.
Table (12) The effect of oxytetracycline on *T. evansi* in phosphate glucose buffer solution (PGS)

<table>
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<th>OTC concentration (µg/ml)</th>
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<th>Trypanosomes in rats</th>
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<tr>
<td>1-3</td>
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<tr>
<td>4-15</td>
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<td>- ve</td>
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* - ve= negative no parasite detected, + = 50% of the parasite added to PSG and ++ = all the parasites added to PSG
**Table (4): Postmortem findings in Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan**

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<tr>
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<td>+</td>
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Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

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</tbody>
</table>

| Site of injection | Damage | -   | -   | +   | +   | +++ | ++  | +++ | +++ |

| Site of injection | Damage | -   | -   | -   | +   | +   | +   | +   | +   |

- = no lesion, + = mild, ++ = moderate, +++ = severe.

Table(4) : Postmortem findings in Nubian goats infected with *T. evansi* and given single and multiple dosages of oxytetracycline

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### Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

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- = no lesion, + = mild, ++ = moderate, +++ = severe.

Table (4): Postmortem findings in Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan and oxytetracycline combination.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

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- = no lesion, + = mild, ++ = moderate, +++ = severe.

Table(4) : Postmortem findings in Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan supplemented with zinc and copper.
### Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

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- = no lesion, + = mild, ++ = moderate, +++ = severe.

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Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

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- = no lesion, + = mild, ++ = moderate, +++ = severe.

Table(4) : Postmortem findings in Nubian goats infected with *T. evansi* and given single and multiple dosages of Homidium Bromide.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

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</table>

- = no lesion , + = mild, ++ = moderate, +++ = severe.

Table(4) : Postmortem findings in Nubian goats infected with *T. evansi* and given single and multiple dosages of Quinapyramine and Homidium Bromide.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
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</table>

- = no lesion, + = mild, ++ = moderate, +++ = severe. *= infection done by *T. evansi*, **= infection done by *T. vivax*.

Table (4): Postmortem findings in camels naturally infected with *T. evansi* and given single and multiple dosages of Cymelarsan.
**Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)**

- Enlargement - +++ - - - +
- Congestion - +++ - - - -
- Haemorrhage - ++ - - - -
- Enteritis - + + - - -
- Peritonitis - - - - - -
- Hydroperitoneum - - - - - -
- Damage - - - - - -
- Damage and congestion - - - - - -
- Enlargement/lymph adenitis - + - - - -
- Atrophy and/or orchitis - + + - - -
- Hydropericardium - ++ - - - -
- Congestion - +++ - - - -
- Haemorrhage - + + - - - -
- Emphysema - - + - - - -
- Flabiness - ++ + - - - -
- Hepatization - + + - - - -
- Congestion - - + - - - -
- Haemorrhage - + + - - - -
- Oedema - - - - - - -
- Enlargement - +++ + + - -
- Hydropericardium - ++ - - - -
- Fatty change and/ or Necrosis - - - - - - -
- Haemorrhage - + - - - - -
- Congestion - - + - - - -
- Fatty change and/or necrosis - ++ - - + -
- Congestion - ++ - - - -
- Enlargement - +++ + + - -
- Congestion - +++ - - - -

- = no lesion, + = mild, ++ = moderate, +++ = severe.

**Table(4) : Postmortem findings camels infected naturally with *T. evansi* and given single and multiple dosages of Oxytetracycline.**

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Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

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</table>

- = no lesion, + = mild, ++ = moderate, +++ = severe.

Table (4): Postmortem findings camels naturally infected with *T. evansi* and given single and multiple dosages of Cymelarsan and Oxytetracycline combination.

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<tr>
<td></td>
<td>Oedema</td>
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<td>+</td>
<td>+</td>
<td>+</td>
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</tr>
<tr>
<td></td>
<td>Fatty change and/or necrosis</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
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<tr>
<td></td>
<td>Kidneys</td>
<td>Haemorrhage</td>
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<tr>
<td></td>
<td>Congestion</td>
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<td>+</td>
<td>+</td>
<td>-</td>
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<td>-</td>
</tr>
<tr>
<td></td>
<td>Fatty change and/or necrosis</td>
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<td>+</td>
<td>+</td>
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<tr>
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<td>Spleen</td>
<td>Congestion</td>
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<td>++</td>
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<tr>
<td></td>
<td>Enlargement</td>
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<td>Intestine</td>
<td>Haemorrhage</td>
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<td>++</td>
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<td>++</td>
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<td>Enteritis</td>
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<td>Peritonitis</td>
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<td>+</td>
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<tr>
<td></td>
<td>Hydroperitoneum</td>
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</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Site of injection</th>
<th>Damage</th>
<th>-</th>
<th>-</th>
<th>+</th>
<th>-</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral nerves</td>
<td>Damage and congestion</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Lymph node</td>
<td>Enlargement/lymph adenitis</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Testis</td>
<td>Atrophy and/or orchitis</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

- = no lesion, + = mild, ++ = moderate, +++ = severe.

Table (7) The Sodium, Potassium, Chloride, Calcium, Phosphorus, Magnesium, Zinc, Copper, Manganese, and Iron in Nubian goats infected with *T. evansi* and given Cymelarsan (M±SE).

<table>
<thead>
<tr>
<th>Parameter Groups</th>
<th>Sodium (mmol/l)</th>
<th>Potassium (mmol/l)</th>
<th>Chloride (mmol/l)</th>
<th>Calcium (mg/dl)</th>
<th>Phosphorus (mg/dl)</th>
<th>Magnesium (mg/dl)</th>
<th>Zinc (µmol/l)</th>
<th>Copper (µmol/l)</th>
<th>Manganese (µmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1) 145.0±0.50</td>
<td>3.8±0.02</td>
<td>125.4±0.19</td>
<td>9.5±0.04</td>
<td>4.9±0.04</td>
<td>2.3±0.08</td>
<td>12.4±0.01</td>
<td>10.7±0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group (2) 149.8±0.296</td>
<td>4.6±0.03</td>
<td>134.0±0.39</td>
<td>7.4±0.06</td>
<td>3.1±0.06</td>
<td>3.9±0.04</td>
<td>10.1±0.02</td>
<td>11.3±0.05</td>
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</tr>
<tr>
<td>Group (3) 0.125 mg/kg</td>
<td>146.06±0.11</td>
<td>3.5±0.11</td>
<td>135.7±0.07</td>
<td>2.9±0.03</td>
<td>2.0±0.09</td>
<td>4.4±0.03</td>
<td>10.2±0.02</td>
<td>12.5±0.02</td>
<td></td>
</tr>
<tr>
<td>Group (4) 0.250 mg/kg</td>
<td>144.6±0.11</td>
<td>3.1±0.01</td>
<td>127.8±0.08</td>
<td>6.5±0.03</td>
<td>4.2±0.03</td>
<td>2.5±0.03</td>
<td>11.3±0.12</td>
<td>9.9±0.02</td>
<td></td>
</tr>
<tr>
<td>Group (5) 0.625 mg/kg</td>
<td>144.0±0.51</td>
<td>4.3±0.02</td>
<td>128.2±0.11</td>
<td>6.9±0.04</td>
<td>4.4±0.02</td>
<td>2.5±0.01</td>
<td>13.9±0.12</td>
<td>11.5±0.02</td>
<td></td>
</tr>
<tr>
<td>Group (6) 1.25 mg/kg</td>
<td>103±0.81</td>
<td>1.8±0.02</td>
<td>139.9±0.11</td>
<td>2.9±0.03</td>
<td>1.5±0.03</td>
<td>4.5±0.02</td>
<td>12.0±0.02</td>
<td>9.7±0.02</td>
<td></td>
</tr>
<tr>
<td>Group (7) 0.125 mg/kg twice/week for 2 weeks</td>
<td>149.7±0.03</td>
<td>5.9±0.02</td>
<td>133.5±0.08</td>
<td>7.8±0.23</td>
<td>4.4±0.02</td>
<td>2.8±0.01</td>
<td>13.0±0.20</td>
<td>10.1±0.02</td>
<td></td>
</tr>
<tr>
<td>Group (8) 0.125 mg/kg daily for 8 days</td>
<td>152.9±0.13</td>
<td>5.6±0.03</td>
<td>131.7±0.14</td>
<td>10.8±0.02</td>
<td>5.2±0.05</td>
<td>2.5±0.03</td>
<td>14.2±0.05</td>
<td>9.4±0.03</td>
<td></td>
</tr>
<tr>
<td>Group (9) 0.250 mg/kg twice/week for 2 weeks</td>
<td>153.3±0.24</td>
<td>4.6±0.04</td>
<td>138.1±0.07</td>
<td>5.2±0.03</td>
<td>3.4±0.02</td>
<td>2.4±0.01</td>
<td>11.9±0.02</td>
<td>10.9±0.01</td>
<td></td>
</tr>
<tr>
<td>Group (10) 0.250 mg/kg daily for 8 days</td>
<td>134.3±0.04</td>
<td>4.3±0.07</td>
<td>136.5±0.159</td>
<td>5.7±0.08</td>
<td>3.7±0.07</td>
<td>3.2±0.02</td>
<td>14.5±0.10</td>
<td>10.8±0.02</td>
<td></td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes p<0.05.
Table (8) The Bilirubin, Direct bilirubin, Urea, Creatinine, Total protein, Albumin, Globulin, Cholesterol, Glucose, Phospholipids and Triglyceride in Nubian goats infected with T. evansi and given Cymelarsan (M±SE).

<table>
<thead>
<tr>
<th>ParameterGroups</th>
<th>Bilirubin (mg/dl)</th>
<th>Direct bilirubin (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Total protein (g/dl)</th>
<th>Albumin (g/dl)</th>
<th>Globulin (g/dl)</th>
<th>Cholesterol (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>0.56a±0.001</td>
<td>0.29a±0.002</td>
<td>18.7a±0.08</td>
<td>2.1a±0.08</td>
<td>8.5a±0.06</td>
<td>3.3a±0.03</td>
<td>5.2a±0.03</td>
<td>125a±0.06</td>
</tr>
<tr>
<td>Group (2)</td>
<td>0.85b±0.012</td>
<td>0.49b±0.01</td>
<td>13.0b±0.09</td>
<td>1.6b±0.05</td>
<td>12.0b±0.26</td>
<td>5.9b±0.18</td>
<td>7.1b±0.08</td>
<td>141.5b±0.14</td>
</tr>
<tr>
<td>Group (3)</td>
<td>0.125 mg/kg</td>
<td>1.05a±0.01</td>
<td>11.2a±0.05</td>
<td>1.6a±0.01</td>
<td>12.8a±0.04</td>
<td>4.5a±0.01</td>
<td>8.3a±0.03</td>
<td>129.3a±0.07</td>
</tr>
<tr>
<td>Group (4)</td>
<td>0.250 mg/kg</td>
<td>0.60a±0.01</td>
<td>18.0a±0.00</td>
<td>2.0a±0.01</td>
<td>9.0a±0.07</td>
<td>3.5a±0.07</td>
<td>5.5a±0.00</td>
<td>126.0a±0.01</td>
</tr>
<tr>
<td>Group (5)</td>
<td>0.625 mg/kg</td>
<td>0.58a±0.02</td>
<td>17.3a±0.01</td>
<td>1.9a±0.04</td>
<td>9.1a±0.04</td>
<td>3.9a±0.01</td>
<td>5.2a±0.03</td>
<td>138.1a±0.01</td>
</tr>
<tr>
<td>Group (6)</td>
<td>1.25 mg/kg</td>
<td>1.02b±1.20</td>
<td>8.2b±0.01</td>
<td>0.5b±0.04</td>
<td>14.9b±0.06</td>
<td>8.4b±0.05</td>
<td>6.5b±0.01</td>
<td>128.4b±0.09</td>
</tr>
<tr>
<td>Group (7)</td>
<td>0.125 mg/kg</td>
<td>0.99b±0.003</td>
<td>15.0b±0.07</td>
<td>2.3b±0.08</td>
<td>10.8b±0.07</td>
<td>6.9b±0.05</td>
<td>3.9b±0.02</td>
<td>141.3b±0.17</td>
</tr>
<tr>
<td>Group (8)</td>
<td>0.125 mg/kg daily</td>
<td>0.12c±0.013</td>
<td>11.0b±0.04</td>
<td>1.5b±0.04</td>
<td>10.9b±0.13</td>
<td>9.9b±0.04</td>
<td>1.1b±0.08</td>
<td>143.7b±0.14</td>
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<tr>
<td>Group (9)</td>
<td>0.250 mg/kg</td>
<td>1.04b±0.005</td>
<td>14.0b±0.08</td>
<td>1.8b±0.09</td>
<td>10.3b±0.06</td>
<td>7.9b±0.01</td>
<td>2.4b±0.005</td>
<td>144.0b±0.19</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Parameter Groups</th>
<th>LDH (U/L)</th>
<th>CK (U/L)</th>
<th>PK (U/L)</th>
<th>GOT (U/L)</th>
<th>GPT (U/L)</th>
<th>ALP (U/L)</th>
<th>SDH (U/L)</th>
<th>Amylase (U/L)</th>
<th>Lipase (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>326.6 ±0.38</td>
<td>33.4 ±0.13</td>
<td>31.6 ±0.08</td>
<td>35.5 ±0.14</td>
<td>14.0 ±0.09</td>
<td>87.0 ±0.37</td>
<td>27.2 ±0.14</td>
<td>102.80 ±0.11</td>
<td>315.6 ±0.621</td>
</tr>
<tr>
<td>Group (2)</td>
<td>37.0 ±0.49</td>
<td>35.0 ±0.124</td>
<td>40.4 ±0.44</td>
<td>40.3 ±0.14</td>
<td>15.5 ±0.07</td>
<td>76.3 ±0.49</td>
<td>33.1 ±0.25</td>
<td>95.39 ±0.09</td>
<td>242.4 ±0.6</td>
</tr>
<tr>
<td>Group (3)</td>
<td>315.7 ±0.13</td>
<td>40.8 ±0.03</td>
<td>39.4 ±0.63</td>
<td>42.6 ±0.07</td>
<td>17.3 ±0.07</td>
<td>63.0 ±0.01</td>
<td>36.1 ±0.03</td>
<td>81.4 ±0.06</td>
<td>266.3 ±0.47</td>
</tr>
<tr>
<td>Group (4) 0.25mg/kg</td>
<td>321.3 ±0.23</td>
<td>40.7 ±0.11</td>
<td>36.6 ±0.12</td>
<td>40.6 ±0.08</td>
<td>15.9 ±0.26</td>
<td>63.0 ±0.35</td>
<td>32.2 ±0.16</td>
<td>48.8 ±0.27</td>
<td>279.0 ±0.73</td>
</tr>
<tr>
<td>Group (5) 0.625mg/kg</td>
<td>318.3 ±0.13</td>
<td>38.5 ±0.02</td>
<td>36.9 ±0.09</td>
<td>40.8 ±0.04</td>
<td>13.6 ±0.05</td>
<td>69.0 ±0.36</td>
<td>36.2 ±0.09</td>
<td>101.5 ±0.03</td>
<td>267.2 ±0.37</td>
</tr>
<tr>
<td>Group (6) 1.25mg/kg</td>
<td>321.2 ±0.252</td>
<td>39.9 ±0.05</td>
<td>36.7 ±0.11</td>
<td>40.1 ±0.11</td>
<td>15.5 ±0.02</td>
<td>66.7 ±0.23</td>
<td>39.1 ±0.18</td>
<td>96.9 ±0.07</td>
<td>246.4 ±0.27</td>
</tr>
<tr>
<td>Group (7) 0.125mg/kg</td>
<td>318.0 ±0.11</td>
<td>36.8 ±0.02</td>
<td>35.0 ±0.09</td>
<td>36.2 ±0.03</td>
<td>14.1 ±0.03</td>
<td>66.9 ±0.35</td>
<td>32.4 ±0.07</td>
<td>98.5 ±0.08</td>
<td>343.7 ±0.46</td>
</tr>
<tr>
<td>Group (8) 0.125mg/kg</td>
<td>315.9 ±0.11</td>
<td>35.2 ±0.19</td>
<td>37.7 ±0.09</td>
<td>43.6 ±0.14</td>
<td>14.4 ±0.03</td>
<td>60.7 ±0.27</td>
<td>32.5 ±0.52</td>
<td>98.0 ±0.03</td>
<td>349.9 ±0.47</td>
</tr>
<tr>
<td>Group (9) 0.25mg/kg</td>
<td>369.4 ±0.00</td>
<td>39.3 ±0.06</td>
<td>36.8 ±0.12</td>
<td>35.4 ±0.23</td>
<td>14.3 ±0.35</td>
<td>59.5 ±0.21</td>
<td>35.1 ±0.52</td>
<td>97.2 ±0.09</td>
<td>330.4 ±0.51</td>
</tr>
<tr>
<td>Group (10) 0.5mg/kg</td>
<td>315.9 ±0.19</td>
<td>34.2 ±0.08</td>
<td>36.0 ±0.11</td>
<td>36.3 ±0.26</td>
<td>17.1 ±0.11</td>
<td>63.0 ±0.36</td>
<td>38.2 ±0.18</td>
<td>104.3 ±0.23</td>
<td>491.6 ±0.87</td>
</tr>
</tbody>
</table>

Table (9) The Lactate dehydrogenase (LDH) Creatinine Kinase (CK), Pyrovate Kinase (PK), (GOT), (GPT), Alkaline phosphatase (ALP), Succinate Dehydrogenase(SDH), Amylase and Lipase in Nubian goats infected with T. evansi and given Cymelarsan (M±SE).

Same letters in one column showed no significant changes p<0.05.
Table (5) The Hemoglobin concentration, Packed Cell volume, the count of Red blood Cell, Reticulocyte, White Blood Cell, Platelet, Eosinophils, Basophiles, Monocytes, lymphocyte and Neutrophils in Nubian goats infected with *T. evansi* and given Cymelarsan (M±SE).

<table>
<thead>
<tr>
<th>Parameter Groups</th>
<th>Hb (g/dl)</th>
<th>PCV (%)</th>
<th>RBC (x10⁶/m³)</th>
<th>Reticulocytes (10⁶/m³)</th>
<th>WBC (x10⁶/m³)</th>
<th>Platelet (x10³/m³)</th>
<th>Eosinophils (%)</th>
<th>Basophils (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>9.0 ±0.24</td>
<td>32.3 ±0.02</td>
<td>14.5 ±0.21</td>
<td>5.7 ±0.02</td>
<td>11.7 ±0.32</td>
<td>410.7 ±0.73</td>
<td>2.0 ±0.00</td>
<td>0.00 ±0.00</td>
</tr>
<tr>
<td>Group (2)</td>
<td>5.7 ±0.02</td>
<td>24.8 ±0.21</td>
<td>10.7 ±0.31</td>
<td>7.8 ±0.02</td>
<td>13.8 ±0.31</td>
<td>489.5 ±0.71</td>
<td>3.6 ±0.00</td>
<td>2.8 ±0.01</td>
</tr>
<tr>
<td>Group (3)</td>
<td>3.4 ±0.01</td>
<td>16.7 ±0.22</td>
<td>11.4 ±0.13</td>
<td>11.4 ±0.13</td>
<td>13.2 ±0.18</td>
<td>520.3 ±0.74</td>
<td>2.1 ±0.05</td>
<td>1.5 ±0.05</td>
</tr>
<tr>
<td>Group (4)</td>
<td>9.2 ±0.01</td>
<td>33.1 ±0.21</td>
<td>13.4 ±0.20</td>
<td>6.1 ±0.01</td>
<td>12.5 ±0.17</td>
<td>415.1 ±0.74</td>
<td>2.5 ±0.04</td>
<td>1.0 ±0.04</td>
</tr>
<tr>
<td>Group (5)</td>
<td>8.5 ±0.01</td>
<td>31.7 ±0.21</td>
<td>13.8 ±0.19</td>
<td>5.5 ±0.1</td>
<td>13.9 ±0.18</td>
<td>419.9 ±0.82</td>
<td>2.0 ±0.04</td>
<td>2.5 ±0.02</td>
</tr>
<tr>
<td>Group (6)</td>
<td>4.4 ±0.12</td>
<td>15.4 ±0.01</td>
<td>9.5 ±0.20</td>
<td>5.7 ±0.02</td>
<td>15.3a ±0.14</td>
<td>530.1 ±0.79</td>
<td>7.5 ±0.01</td>
<td>1.0 ±0.01</td>
</tr>
<tr>
<td>Group (7)</td>
<td>6.1 ±0.02</td>
<td>15.0 ±0.01</td>
<td>10.0 ±0.21</td>
<td>13.7 ±0.12</td>
<td>15.5a ±0.72</td>
<td>490.7 ±0.40</td>
<td>3.5 ±0.00</td>
<td>1.5 ±0.00</td>
</tr>
<tr>
<td>Group (8)</td>
<td>5.0 ±0.01</td>
<td>14.1 ±0.09</td>
<td>9.5 ±0.22</td>
<td>13.0 ±0.31</td>
<td>12.2a ±0.52</td>
<td>520.4 ±0.50</td>
<td>6.5 ±0.02</td>
<td>1.5 ±0.00</td>
</tr>
<tr>
<td>Group (9)</td>
<td>5.5 ±0.01</td>
<td>13.1 ±0.00</td>
<td>8.4 ±0.09</td>
<td>12.8 ±0.09</td>
<td>13.4a</td>
<td>495.7 ±0.50</td>
<td>5.5 ±0.00</td>
<td>2.5 ±0.00</td>
</tr>
</tbody>
</table>
### Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (10)</th>
<th>Body temperature (°C)</th>
<th>Respiratory rate (1/min)</th>
<th>Pulse rate (1/min)</th>
<th>Body weight (Kg)</th>
<th>Blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>39.5a ±0.01</td>
<td>26.1a ±0.00</td>
<td>75.5a ±0.02</td>
<td>9.5a ±0.05</td>
<td>125/75a ±1.12/1.5</td>
</tr>
<tr>
<td>Group (2)</td>
<td>34.3b ±0.02</td>
<td>38.5b ±0.01</td>
<td>60.5b ±0.01</td>
<td>7.8b ±0.04</td>
<td>90/44b ±1.11/1.3</td>
</tr>
<tr>
<td>Group (3)</td>
<td>36.5c ±0.03</td>
<td>25.8c ±0.05</td>
<td>68.0c ±0.02</td>
<td>7.0c ±0.01</td>
<td>87/42c ±0.9/1.4</td>
</tr>
<tr>
<td>Group (4)</td>
<td>39.5c ±0.01</td>
<td>26.5c ±0.01</td>
<td>80.3c ±0.02</td>
<td>11.2c ±0.05</td>
<td>117/58c ±0.8/1.2</td>
</tr>
<tr>
<td>Group (5)</td>
<td>38.7d ±0.01</td>
<td>26.5d ±0.02</td>
<td>81.3d ±0.03</td>
<td>12.5d ±0.04</td>
<td>125/65d ±0.5/1.3</td>
</tr>
<tr>
<td>Group (6)</td>
<td>38.4e ±0.05</td>
<td>32.0e ±0.25</td>
<td>85.3e ±0.05</td>
<td>6.2e ±0.01</td>
<td>75/40e ±0.4/0.1</td>
</tr>
<tr>
<td>Group (7)</td>
<td>39.5e ±0.03</td>
<td>20.0e ±0.04</td>
<td>75.5e ±0.01</td>
<td>7.5e ±0.05</td>
<td>80/50f ±0.8/0.5</td>
</tr>
<tr>
<td>Group (8)</td>
<td>41.3f ±0.03</td>
<td>15.5f ±0.04</td>
<td>70.5f ±0.01</td>
<td>9.4f ±0.05</td>
<td>70/40f ±0.05</td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes p≤0.05.

Table (3) The body weight and temperature, respiratory rate, blood pressure and fate of the animals in Nubian goats infected with *T. evansi* and given Cymarslan (M±SE).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Table 6: The mean ± Standard Error (M±SE) of (MCV), (MCH), and (MCHC) in Nubian goats infected with *T. evansi* and given Cymelarsan.

<table>
<thead>
<tr>
<th>Parameter Groups</th>
<th>MCV (fl)</th>
<th>MCH (pg)</th>
<th>MCHC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>22.2 ± 0.03</td>
<td>62.06 ± 0.04</td>
<td>27.8 ± 0.01</td>
</tr>
<tr>
<td>Group (2)</td>
<td>23.17 ± 0.00</td>
<td>53.2 ± 0.05</td>
<td>22.9 ± 0.03</td>
</tr>
<tr>
<td>Group (3) 0.125 mg/kg</td>
<td>14.6 ± 0.05</td>
<td>29.9 ± 0.1</td>
<td>20.35 ± 0.01</td>
</tr>
<tr>
<td>Group (4) 0.250 mg/kg</td>
<td>24.7 ± 0.02</td>
<td>68.6 ± 0.08</td>
<td>27.8 ± 0.02</td>
</tr>
<tr>
<td>Group (5) 0.625 mg/kg</td>
<td>22.9 ± 0.01</td>
<td>61.5 ± 0.07</td>
<td>26.8 ± 0.04</td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes p≤0.05.
Table (5) The calcium, phosphorus, urea, creatinine, total protein, albumin, globulin, cholesterol, glucose and triglycerides in camels naturally infected with *T. evansi* and given single and multiple dosages of Oxytetracycline (M±SE)

<table>
<thead>
<tr>
<th>Group</th>
<th>Calcium (mg/dl)</th>
<th>Phosphorus (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Total protein (g/dl)</th>
<th>Albumin (g/dl)</th>
<th>Globulin (g/dl)</th>
<th>Cholesterol (mg/dl)</th>
<th>Glucose (mg/dl)</th>
<th>Triglycerides (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(6)</td>
<td>16.2±0.01</td>
<td>46.31±0.03</td>
<td>28.5±0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(7)</td>
<td>40.6±0.07</td>
<td>61.0±0.07</td>
<td>40.6±0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>16.2±0.01</td>
<td>46.31±0.03</td>
<td>28.5±0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(8)</td>
<td>35.43±0.03</td>
<td>52.6±0.06</td>
<td>35.4±0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>35.43±0.03</td>
<td>52.6±0.06</td>
<td>35.4±0.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>(9)</td>
<td>41.9±0.02</td>
<td>65.7±0.03</td>
<td>41.9±0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>41.9±0.02</td>
<td>65.7±0.03</td>
<td>41.9±0.04</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(10)</td>
<td>35.8±0.04</td>
<td>69.8±0.02</td>
<td>35.8±0.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The different letters in one column showed the significant changes *p* ≤ 0.05.
Table (6) The glutamic oxalocetic transaminase (GOT), glutamic pyruvic transaminase (GPT), Alkaline phosphatase (ALP), T3, T4 and progesterone in camels naturally infected with *T. evansi* and given single and multiple dosages of Oxytetracycline (M±SE).

<table>
<thead>
<tr>
<th>Parameter Dose</th>
<th>GOT (U/l)</th>
<th>GPT (U/l)</th>
<th>ALP (U/l)</th>
<th>Progesterone (nmol/l)</th>
<th>T3 (nmol/l)</th>
<th>T4 (nmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>47.7a</td>
<td>6.4a</td>
<td>31.0a</td>
<td>1.3a</td>
<td>75.4a</td>
<td>1.3a</td>
</tr>
<tr>
<td></td>
<td>±0.01</td>
<td>±0.05</td>
<td>±0.04</td>
<td>±0.05</td>
<td>±0.01</td>
<td>±0.09</td>
</tr>
<tr>
<td>Group (2)</td>
<td>46.1a</td>
<td>9.5a</td>
<td>24.06b</td>
<td>5.5b</td>
<td>56.6b</td>
<td>0.5b</td>
</tr>
<tr>
<td></td>
<td>±0.03</td>
<td>±0.04</td>
<td>±0.06</td>
<td>±0.02</td>
<td>±0.03</td>
<td>±0.07</td>
</tr>
<tr>
<td>Group (3) 20 mg/kg</td>
<td>41.8b</td>
<td>11.5b</td>
<td>25.6b</td>
<td>3.8c</td>
<td>65.2c</td>
<td>0.5c</td>
</tr>
<tr>
<td></td>
<td>±0.03</td>
<td>±0.08</td>
<td>±0.01</td>
<td>±0.05</td>
<td>±0.02</td>
<td>±0.03</td>
</tr>
<tr>
<td>Group (4)</td>
<td>38.9b</td>
<td>8.5b</td>
<td>21.6b</td>
<td>2.1a</td>
<td>65.1a</td>
<td>0.7a</td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes \( p \leq 0.05 \).
### Table (4) The Haemoglobin (Hb), Packed Cell volume (PCV), Red blood Cell count (RBC), White Blood Cell count (WBC), MCV, MCH and MCHC in camels naturally infected with *T. evansi* and given single and multiple dosages of Oxytetracycline (M±SE)

<table>
<thead>
<tr>
<th>Parameter Dose</th>
<th>Hb (g/dl)</th>
<th>PCV (%)</th>
<th>RBC (x10^6/m^3)</th>
<th>WBC (x10^3/m^3)</th>
<th>MCV (fl)</th>
<th>MCH (pg)</th>
<th>MCHC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1) 10mg/kg</td>
<td>10.3±0.08</td>
<td>25.5±0.01</td>
<td>8.3±0.05</td>
<td>11.4±0.03</td>
<td>30.7±0.01</td>
<td>12.4±0.03</td>
<td>40.3±0.05</td>
</tr>
<tr>
<td>Group (2) 20mg/kg</td>
<td>4.9±0.03</td>
<td>21.7±0.07</td>
<td>6.4±0.04</td>
<td>14.1±0.07</td>
<td>34.4±0.02</td>
<td>7.7±0.01</td>
<td>22.5±0.02</td>
</tr>
<tr>
<td>Group (3) 40mg/kg</td>
<td>7.3±0.04</td>
<td>20.6±0.03</td>
<td>6.3±0.01</td>
<td>10.2±0.07</td>
<td>32.6±0.03</td>
<td>11.5±0.01</td>
<td>35.4±0.01</td>
</tr>
<tr>
<td>Group (4) 50mg/kg</td>
<td>10.1±0.02</td>
<td>23.7±0.01</td>
<td>7.5±0.03</td>
<td>12.3±0.06</td>
<td>31.6±0.05</td>
<td>13.4±0.03</td>
<td>42.6±0.02</td>
</tr>
<tr>
<td>Group (5) 100mg/kg</td>
<td>7.7±0.08</td>
<td>25.1±0.06</td>
<td>8.9±0.06</td>
<td>10.3±0.08</td>
<td>28.2±0.02</td>
<td>8.6±0.01</td>
<td>30.6±0.02</td>
</tr>
<tr>
<td>Group (6)</td>
<td>8.5a</td>
<td>25.6a</td>
<td>6.6b</td>
<td>12.3a</td>
<td>35.0a</td>
<td>15.5a</td>
<td>33.4a</td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes p≤0.05.
**Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)**

<table>
<thead>
<tr>
<th>Group (7)</th>
<th>20mg/kg daily for 8 days</th>
<th>20mg/kg twice/week for 2 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>±0.02</td>
<td>±0.02</td>
</tr>
<tr>
<td></td>
<td>±0.05</td>
<td>±0.05</td>
</tr>
<tr>
<td></td>
<td>±0.00</td>
<td>±0.02</td>
</tr>
<tr>
<td></td>
<td>±0.01</td>
<td>±0.01</td>
</tr>
<tr>
<td></td>
<td>±0.05</td>
<td>±0.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Calcium (mg/dl)</th>
<th>Phosphorus (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Total protein (g/dl)</th>
<th>Albumin (g/dl)</th>
<th>Globulin (g/dl)</th>
<th>Cholesterol (mg/dl)</th>
<th>Glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1)</td>
<td>9.4±a ±0.02</td>
<td>6.5±a ±0.01</td>
<td>35.5±a ±0.02</td>
<td>2.3±a ±0.00</td>
<td>6.4±a ±0.02</td>
<td>2.5±a ±0.02</td>
<td>4.1±a ±0.01</td>
<td>36.5±a ±0.05</td>
<td>91.0±a ±0.02</td>
</tr>
<tr>
<td>2)</td>
<td>6.8±b ±0.02</td>
<td>4.3±b ±0.02</td>
<td>24.9±b ±0.02</td>
<td>1.1±b ±0.01</td>
<td>8.2±b ±0.02</td>
<td>4.1±b ±0.04</td>
<td>4.1±b ±0.04</td>
<td>31.3±b ±0.08</td>
<td>93.3±b ±0.02</td>
</tr>
<tr>
<td>3)</td>
<td>9.8±a ±0.02</td>
<td>7.6±a ±0.03</td>
<td>32.2±a ±0.02</td>
<td>1.6±a ±0.07</td>
<td>5.7±a ±0.02</td>
<td>3.0±a ±0.01</td>
<td>2.6±a ±0.05</td>
<td>40.5±a ±0.02</td>
<td>85.2±b ±0.01</td>
</tr>
<tr>
<td>4)</td>
<td>10.8±b ±0.03</td>
<td>7.0±b ±0.01</td>
<td>34.0±b ±0.02</td>
<td>2.5±b ±0.03</td>
<td>5.3±b ±0.04</td>
<td>2.2±b ±0.03</td>
<td>3.1±b ±0.06</td>
<td>39.4±b ±0.00</td>
<td>86.8±b ±0.00</td>
</tr>
<tr>
<td>5)</td>
<td>10.7±b ±0.03</td>
<td>7.9±b ±0.02</td>
<td>36.8±b ±0.03</td>
<td>2.3±b ±0.01</td>
<td>4.3±b ±0.02</td>
<td>3.0±b ±0.03</td>
<td>1.2±b ±0.01</td>
<td>39.4±b ±0.02</td>
<td>87.4±b ±0.01</td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes p≤0.05.

**Table (5)** The calcium, phosphorus, urea, creatinine, total protein, albumin, globulin, cholesterol, glucose and triglycerides in camels naturally infected with *T. evansi* and given single dosages of Cymelarsan (M±SE)
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Same letters in one column showed no significant changes p≤0.05.

Table (6) The glutamic oxalocetic transaminase (GOT), glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), T3, T4 and progesterone in camels naturally infected with *T. evansi* and given single dosages of Cymelarsan (M±SE)

<table>
<thead>
<tr>
<th>Parameter Dose</th>
<th>GOT (U/l)</th>
<th>GPT (U/l)</th>
<th>ALP (U/l)</th>
<th>Progesterone (nmol/l)</th>
<th>T3 (nmol/l)</th>
<th>T4 (nmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>47.7a ±0.01</td>
<td>6.4a ±0.05</td>
<td>31.0a ±0.04</td>
<td>1.3a ±0.05</td>
<td>75.4a ±0.01</td>
<td>1.3a ±0.09</td>
</tr>
<tr>
<td>Group (2)</td>
<td>46.1a ±0.03</td>
<td>9.5b ±0.04</td>
<td>24.06b ±0.06</td>
<td>5.5b ±0.02</td>
<td>56.6b ±0.03</td>
<td>0.5b ±0.07</td>
</tr>
<tr>
<td>Group (3) 0.250mg/kg</td>
<td>44.4a ±0.02</td>
<td>5.7a ±0.02</td>
<td>33.06a ±0.07</td>
<td>4.0a ±0.03</td>
<td>80.3a ±0.07</td>
<td>0.8a ±0.06</td>
</tr>
<tr>
<td>Group (4) 0.625mg/kg</td>
<td>35.12b ±0.01</td>
<td>5.18b ±0.06</td>
<td>28.4b ±0.03</td>
<td>2.0b ±0.08</td>
<td>81.3b ±0.04</td>
<td>1.4b ±0.05</td>
</tr>
<tr>
<td>Group (5) 0.125 mg/kg</td>
<td>33.7b ±0.04</td>
<td>6.2b ±0.01</td>
<td>31.3b ±0.02</td>
<td>1.5b ±0.08</td>
<td>77.9b ±0.02</td>
<td>1.4b ±0.01</td>
</tr>
</tbody>
</table>
Table (4) The Haemoglobin (Hb), Packed Cell volume (PCV), Red blood Cell (RBC), White Blood Cell (WBC), MCV, MCH and MCHC in camels naturally infected with *T. evansi* and given single dosages of Cymelarsan (M±SE)

<table>
<thead>
<tr>
<th>Parameter Dose</th>
<th>Hb (g/dl)</th>
<th>PCV (%)</th>
<th>RBC (x10^6/m³)</th>
<th>WBC (x10^3/m³)</th>
<th>MCV (fl)</th>
<th>MCH (pg)</th>
<th>MCHC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>10.3±0.08</td>
<td>25.5±0.01</td>
<td>8.3±0.05</td>
<td>11.4±0.03</td>
<td>30.7±0.01</td>
<td>12.4±0.03</td>
<td>40.3±0.05</td>
</tr>
<tr>
<td>Group (2)</td>
<td>4.9±0.03</td>
<td>21.7±0.07</td>
<td>3.5±0.04</td>
<td>14.1±0.07</td>
<td>34.4±0.02</td>
<td>7.7±0.01</td>
<td>22.5±0.02</td>
</tr>
<tr>
<td>Group (3), 0.250mg/kg</td>
<td>9.9±0.08</td>
<td>27.4±0.01</td>
<td>8.03±0.08</td>
<td>11.5±0.04</td>
<td>21.03±0.01</td>
<td>10.9±0.09</td>
<td>51.1±0.01</td>
</tr>
<tr>
<td>Group (4), 0.625mg/kg</td>
<td>10.7±0.07</td>
<td>27.9±0.01</td>
<td>8.7±0.01</td>
<td>12.1±0.06</td>
<td>25.3±0.05</td>
<td>11.27±0.01</td>
<td>44.5±0.09</td>
</tr>
<tr>
<td>Group (5), 0.125 mg/kg weekly/3weeks</td>
<td>10.4±0.04</td>
<td>27.5±0.03</td>
<td>8.3±0.01</td>
<td>12.1±0.01</td>
<td>28.3±0.09</td>
<td>11.5±0.04</td>
<td>41.1±0.02</td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes p≤0.05.
Table (5) The calcium, phosphorus, urea, creatinine, total protein, albumin, globulin, cholesterol, glucose and triglycerides in camels (*Camelus dromedarius*) naturally infected with *T. evansi* and given single dosages of Cymelars and Oxytetracycline combination (M±SE)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Calcium (mg/dl)</th>
<th>Phosphorus (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>Total protein (g/dl)</th>
<th>Albumin (g/dl)</th>
<th>Globulin (g/dl)</th>
<th>Cholesterol (mg/dl)</th>
<th>Glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.75 g MelCy</td>
<td>9.4±0.02</td>
<td>6.5±0.01</td>
<td>35.5±0.02</td>
<td>2.3±0.00</td>
<td>6.4±0.02</td>
<td>2.5±0.02</td>
<td>4.1±0.01</td>
<td>36.5±0.05</td>
<td>91.0±0.02</td>
</tr>
<tr>
<td>1.5 g MelCy</td>
<td>6.8±0.02</td>
<td>4.3±0.02</td>
<td>24.9±0.02</td>
<td>1.1±0.01</td>
<td>8.2±0.02</td>
<td>4.1±0.04</td>
<td>4.1±0.04</td>
<td>31.3±0.08</td>
<td>93.3±0.02</td>
</tr>
<tr>
<td>2.5 g MelCy</td>
<td>7.9±0.03</td>
<td>6.2±0.06</td>
<td>39.4±0.04</td>
<td>1.0±0.05</td>
<td>7.0±0.03</td>
<td>3.0±0.04</td>
<td>4.0±0.06</td>
<td>40.3±0.03</td>
<td>90.7±0.01</td>
</tr>
<tr>
<td>0.75 g OTC</td>
<td>6.6±0.05</td>
<td>6.5±0.06</td>
<td>33.9±0.06</td>
<td>0.7±0.06</td>
<td>6.2±0.01</td>
<td>2.0±0.04</td>
<td>4.0±0.03</td>
<td>40.3±0.01</td>
<td>87.0±0.06</td>
</tr>
<tr>
<td>1.5 g OTC</td>
<td>9.1±0.03</td>
<td>6.9±0.05</td>
<td>35.6±0.01</td>
<td>0.7±0.03</td>
<td>6.5±0.02</td>
<td>6.0±0.08</td>
<td>1.5±0.02</td>
<td>34.8±0.03</td>
<td>88.3±0.01</td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes p≤0.05. MelCy = Cymelarsan OTC = Oxytetracycline
Table (6) The glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), T3, T4 and progesterone in camels (Camelus dromedarius) naturally infected with *T. evansi* and given single dosages of Cymelarsand Oxytetracycline combination (M±SE)

<table>
<thead>
<tr>
<th>Parameter Dose</th>
<th>GOT (U/l)</th>
<th>GPT (U/l)</th>
<th>ALP (U/l)</th>
<th>Progesterone (nmol/l)</th>
<th>T3 (nmol/l)</th>
<th>T4 (nmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group(1)</td>
<td>47.7±0.01</td>
<td>6.4±0.05</td>
<td>31.0±0.04</td>
<td>1.3±0.05</td>
<td>75.4±0.01</td>
<td>1.3±0.09</td>
</tr>
<tr>
<td>Group(2)</td>
<td>46.1±0.03</td>
<td>9.5±0.04</td>
<td>24.06±0.06</td>
<td>5.5±0.02</td>
<td>56.6±0.03</td>
<td>0.5±0.07</td>
</tr>
<tr>
<td>Group(3) 0.250mg/kg of MelCY+20mg/kg of OTC</td>
<td>39.5±0.04</td>
<td>8.8±0.02</td>
<td>28.6±0.07</td>
<td>1.4±0.02</td>
<td>80.2±0.06</td>
<td>0.9±0.04</td>
</tr>
<tr>
<td>Group(4) 0.125mg/kg of MelCY+50mg/kg of OTC</td>
<td>40.1±0.03</td>
<td>9.5±0.03</td>
<td>29.8±0.05</td>
<td>1.3±0.04</td>
<td>80.2±0.04</td>
<td>1.5±0.08</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>g/kg of OTC</th>
<th>Group(5)</th>
<th>0.125mg/kg of MelCY+100 mg/kg of OTC</th>
<th>Hb (g/dl)</th>
<th>PCV (%)</th>
<th>RBC (x10^6/m^3)</th>
<th>WBC (x10^3/m^3)</th>
<th>MCV (fl)</th>
<th>MCH (pg)</th>
<th>MCHC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35.4\textsuperscript{a} ±0.04</td>
<td>28.7\textsuperscript{a} ±0.03</td>
<td>13\textsuperscript{a} ±0.02</td>
<td>77.7\textsuperscript{a} ±0.03</td>
<td>1.3\textsuperscript{a} ±0.05</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.0\textsuperscript{a} ±0.06</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Same letters in one column showed no significant changes p\leq0.05. MelCy = Cymelarsan, OTC = Oxytetracycline

Table (4) The Haemoglobin (Hb), Packed Cell volume (PCV), Red blood Cell (RBC), White Blood Cell (WBC), MCV, MCH and MCHC in camels (Camelus dromedarius) naturally infected with T. evansi and given single dosages of Cymelars and Oxytetracycline combination (M±SE)

<table>
<thead>
<tr>
<th>Parameter Dose</th>
<th>Hb (g/dl)</th>
<th>PCV (%)</th>
<th>RBC (x10^6/m^3)</th>
<th>WBC (x10^3/m^3)</th>
<th>MCV (fl)</th>
<th>MCH (pg)</th>
<th>MCHC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group(1)</td>
<td>10.3\textsuperscript{a} ±0.08</td>
<td>25.5\textsuperscript{a} ±0.01</td>
<td>8.3\textsuperscript{a} ±0.05</td>
<td>11.4\textsuperscript{a} ±0.03</td>
<td>30.7\textsuperscript{a} ±0.01</td>
<td>12.4\textsuperscript{a} ±0.03</td>
<td>40.3\textsuperscript{a} ±0.05</td>
</tr>
<tr>
<td>Group(2)</td>
<td>4.9\textsuperscript{b} ±0.03</td>
<td>18.3\textsuperscript{b} ±0.04</td>
<td>6.3\textsuperscript{b} ±0.04</td>
<td>14.1\textsuperscript{b} ±0.07</td>
<td>29.0\textsuperscript{a} ±0.02</td>
<td>7.7\textsuperscript{a} ±0.01</td>
<td>26.7\textsuperscript{b} ±0.02</td>
</tr>
<tr>
<td>Group(3) 0.250mg/kg of MelCY+20mg/kg of OTC</td>
<td>9.5\textsuperscript{a} ±0.03</td>
<td>21.7\textsuperscript{a} ±0.07</td>
<td>8.7\textsuperscript{a} ±0.06</td>
<td>10.5\textsuperscript{a} ±0.04</td>
<td>24.9\textsuperscript{a} ±0.08</td>
<td>10.9\textsuperscript{b} ±0.07</td>
<td>43.7\textsuperscript{a} ±0.07</td>
</tr>
<tr>
<td>Group(4) 0.125mg/kg of MelCY+50mg/kg of OTC</td>
<td>10.6\textsuperscript{a} ±0.08</td>
<td>23.8\textsuperscript{a} ±0.05</td>
<td>9.4\textsuperscript{a} ±0.08</td>
<td>12.4\textsuperscript{a} ±0.06</td>
<td>25.3\textsuperscript{a} ±0.02</td>
<td>11.1\textsuperscript{a} ±0.07</td>
<td>44.5\textsuperscript{a} ±0.07</td>
</tr>
<tr>
<td>Group(5) 0.125mg/kg of MelCY+100mg/kg of OTC</td>
<td>8.05\textsuperscript{a} ±0.04</td>
<td>22.5\textsuperscript{a} ±0.06</td>
<td>6.9\textsuperscript{a} ±0.06</td>
<td>11.9\textsuperscript{a} ±0.02</td>
<td>32.6\textsuperscript{a} ±0.04</td>
<td>11.9\textsuperscript{a} ±0.01</td>
<td>35.8\textsuperscript{b} ±0.08</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Same letters in one column showed no significant changes p≤0.05.  MelCy = Cymelarsan      OTC = Oxytetracycline

Table (4) The Mean ±Standard Error of MCV, MCH and MCHC in camels (Camelus dromedarius)
naturally infected with *T. evansi* and given multiple doses of Cymelars and Oxytetracycline (M±SE)

<table>
<thead>
<tr>
<th>Parameter Dose</th>
<th>MCV (fl)</th>
<th>MCH (pg)</th>
<th>MCHC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group(1)</td>
<td>30.7±0.01</td>
<td>12.4±0.03</td>
<td>40.3±0.05</td>
</tr>
<tr>
<td>Group (2)</td>
<td>34.4±0.02</td>
<td>7.7±0.01</td>
<td>22.5±0.02</td>
</tr>
<tr>
<td>Group(3) 0.250mg/kg of MelCY+20mg/kg of OTC</td>
<td>21.4±0.08</td>
<td>10.9±0.07</td>
<td>51.9±0.07</td>
</tr>
<tr>
<td>Group(4) 0.125mg/kg of MelCY+50mg/kg of OTC</td>
<td>34.7±0.02</td>
<td>13.3±0.07</td>
<td>38.4±0.07</td>
</tr>
<tr>
<td>Group(5) 0.125mg/kg of MelCY+100mg/kg of OTC</td>
<td>31.6±0.04</td>
<td>11.9±0.01</td>
<td>37.8±0.08</td>
</tr>
</tbody>
</table>
**Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)**

Same letters in one column showed no significant changes $p \leq 0.05$.

$\text{Mel Cy} = \text{Cymelarsan} \quad \text{OTC} = \text{Oxytetracycline}$

**Table (11)** The concentration of Oxytetracycline in organs, bile and urine (µg/g) in Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan and oxytetracycline combination (M+SE).

<table>
<thead>
<tr>
<th>Site of injection</th>
<th>Leg Muscle</th>
<th>Uterus</th>
<th>Ovary</th>
<th>Testis</th>
<th>Bile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>0.5±0.0/1.0±0.03/1.0/0.0±0.01</td>
<td>0.4±0.0/1.0/0.3±0.01</td>
<td>0.5±0.5/0.4±0.00</td>
<td>0.3±0.00/0.02±0.01</td>
<td>0.4±0.0/1.0/0.3±0.02</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.04±0.001/0.01±0.001</td>
<td>0.03±0.00/0.01±0.001</td>
<td>1±0.3/0.05±0.2</td>
<td>0.5±0.4/0.05±0.5</td>
<td>0.2±0.1/0.01±0.00</td>
</tr>
<tr>
<td>Heart</td>
<td>0.01±0.01±0.001</td>
<td>0.001±0.001/0.001</td>
<td>0.001±0.001/0.001</td>
<td>0.01±0.00/1/0.01±0.00</td>
<td>0.02±0.0/1/0.05±0.02</td>
</tr>
<tr>
<td>Lung</td>
<td>5±0.5/1.0±0.000</td>
<td>5±0.1/1.0±0.000</td>
<td>2.5±0.00/0.5±0.01</td>
<td>0.5±0.1±0.5±0.01</td>
<td>0.5±0.0/1.0/0.3±0.02</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.5±0.01/0.3±0.02</td>
<td>0.5±0.01/0.3±0.02</td>
<td>10±1.5/7±1.0</td>
<td>5±0.5/5.5±0.3</td>
<td>5±0.2/5±0.1</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0.5±0.01/0.3±0.02</td>
<td>0.5±0.01/0.3±0.02</td>
<td>10±1.5/7±1.0</td>
<td>5±0.5/5.5±0.3</td>
<td>5±0.2/5±0.1</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>0.5±0.01/0.3±0.02</td>
<td>0.5±0.01/0.3±0.02</td>
<td>10±1.5/7±1.0</td>
<td>5±0.5/5.5±0.3</td>
<td>5±0.2/5±0.1</td>
</tr>
<tr>
<td>Fat</td>
<td>0.5±0.01/0.3±0.02</td>
<td>0.5±0.01/0.3±0.02</td>
<td>10±1.5/7±1.0</td>
<td>5±0.5/5.5±0.3</td>
<td>5±0.2/5±0.1</td>
</tr>
<tr>
<td>Site of injection</td>
<td>Leg Muscle</td>
<td>Uterus</td>
<td>Ovary</td>
<td>Testis</td>
<td>Bile</td>
</tr>
<tr>
<td>Leg Muscle</td>
<td>10.5±1.0/15.0±1.1</td>
<td>5±0.1/3±0.2</td>
<td>5±0.1/5±0.5</td>
<td>0.5±0.0/1.0/0.3±0.02</td>
<td>0.3±0.01/0.2±0.01</td>
</tr>
<tr>
<td>Uterus</td>
<td>5±0.1/1.0±0.02</td>
<td>10.5±1.0/15.0±1.1</td>
<td>5±0.1/3±0.2</td>
<td>5±0.1/5±0.5</td>
<td>0.5±0.0/1.0/0.3±0.02</td>
</tr>
<tr>
<td>Ovary</td>
<td>5±0.1/1.0±0.02</td>
<td>10.5±1.0/15.0±1.1</td>
<td>5±0.1/3±0.2</td>
<td>5±0.1/5±0.5</td>
<td>0.5±0.0/1.0/0.3±0.02</td>
</tr>
<tr>
<td>Testis</td>
<td>5±0.1/1.0±0.02</td>
<td>10.5±1.0/15.0±1.1</td>
<td>5±0.1/3±0.2</td>
<td>5±0.1/5±0.5</td>
<td>0.5±0.0/1.0/0.3±0.02</td>
</tr>
<tr>
<td>Bile</td>
<td>5±0.1/1.0±0.02</td>
<td>10.5±1.0/15.0±1.1</td>
<td>5±0.1/3±0.2</td>
<td>5±0.1/5±0.5</td>
<td>0.5±0.0/1.0/0.3±0.02</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Site of injection</th>
<th>Leg Muscle</th>
<th>Uterus</th>
<th>Ovary</th>
<th>Testis</th>
<th>Bi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>5 ±0.001/ 2.5 ±0.00</td>
<td>0.1 ±0.02/ ≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Kidney</td>
<td>20±0.1</td>
<td>0± 0.2</td>
<td>1/5.5± 0.02</td>
<td>0±0.1</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Heart</td>
<td>20.5±0.5</td>
<td>5±0.2</td>
<td>1/5.5± 0.02</td>
<td>0±0.1</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Lung</td>
<td>0±0.2</td>
<td>1/5.5± 0.02</td>
<td>0±0.1</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Spleen</td>
<td>5.2±0.3</td>
<td>1/20± 1.2</td>
<td>30.5±0.8</td>
<td>7.5±0.3</td>
<td>3.0±0.00</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>3.0±0.00</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>3.0±0.00</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Fat</td>
<td>3.0±0.00</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Site of injection</td>
<td>5 ±0.2</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Leg Muscle</td>
<td>2.2±0.01</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.5±0.02</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Ovary</td>
<td>0.2±0.01</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Testis</td>
<td>0.12±0.03</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Bi</td>
<td>0.2±0.01</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
</tbody>
</table>

Table(7) Mean±standard error (SE) of the concentration of Cymelarsan in different organs(µg/100g) and serum, urine, bile(µg/ml) in camels (Camelus dromedarius) infected with T. evansi and given single and multiple dosages of Cymelarsan (M+SE).

MelCy = Cymelarsan® OTC = Ox tetracycline (Remacyclin®), Week1 (w1)=14day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4= 35d.p.t and w5=42d.p.t.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

Week1 (w1)=14day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4= 35d.p.t and w5=42d.p.t.

Table (10) The concentration of Cymelarsan (Arsenic) in Different organs (µg/g) and serum, bile and urine µg/ml Nubian goats infected with *T. evansi* and given single or multiple dosages of Cymelarsan (M±SE).

<table>
<thead>
<tr>
<th>Serum</th>
<th>Liver</th>
<th>Kidney</th>
<th>Heart</th>
<th>Lung</th>
<th>Spleen</th>
<th>Cerebellum</th>
<th>Cerebrum</th>
<th>Fat Site of injection</th>
<th>Leg Muscle</th>
<th>Uterus</th>
<th>Ovary</th>
<th>Testis</th>
<th>Bi</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
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<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td></td>
</tr>
<tr>
<td>0.10±0.14</td>
<td>3±0.2/0.0/</td>
<td>5±0.2/0.2/</td>
<td>0.1±0.0</td>
<td>0.1±0.0</td>
<td>0.2±0.0/</td>
<td>0.5±0.1/</td>
<td>0.7±0.0/</td>
<td>0.1±0.0/</td>
<td>0.2±0.0/</td>
<td>0.2±0.0/</td>
<td>1.5±0.1/</td>
<td>1.5±0.1/</td>
<td></td>
</tr>
<tr>
<td>≥0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td></td>
</tr>
<tr>
<td>0.12±0.14</td>
<td>3±0.0/3.5±0.0/</td>
<td>5±0.2/0.2/</td>
<td>0.1±0.0</td>
<td>0.1±0.0</td>
<td>0.2±0.0/</td>
<td>0.5±0.1/</td>
<td>0.7±0.0/</td>
<td>0.1±0.0/</td>
<td>0.2±0.0/</td>
<td>0.2±0.0/</td>
<td>1.5±0.1/</td>
<td>1.5±0.1/</td>
<td></td>
</tr>
<tr>
<td>≥0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td></td>
</tr>
<tr>
<td>0.15±0.19</td>
<td>3±0.0/3.5±0.0/</td>
<td>5±0.2/0.2/</td>
<td>0.1±0.0</td>
<td>0.1±0.0</td>
<td>0.2±0.0/</td>
<td>0.5±0.1/</td>
<td>0.7±0.0/</td>
<td>0.1±0.0/</td>
<td>0.2±0.0/</td>
<td>0.2±0.0/</td>
<td>1.5±0.1/</td>
<td>1.5±0.1/</td>
<td></td>
</tr>
<tr>
<td>≥0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td></td>
</tr>
<tr>
<td>2.7±0.09</td>
<td>30±1.1/25±1.0</td>
<td>35±0.2/30±0.4</td>
<td>40±0.1/23±0.9</td>
<td>20±1.0/25±1.2</td>
<td>20±0.2/15±0.1</td>
<td>10±0.4/15±0.1</td>
<td>15±0.1/10±0.3</td>
<td>3±0.1/20±0.3</td>
<td>5±0.01/5.5±0.2</td>
<td>25±0.2/20±0.5</td>
<td>10±1.0/8±0.7</td>
<td>5±0.1/5±0.0</td>
<td>15±0.2/20±0.3</td>
</tr>
<tr>
<td>2.5±0.02</td>
<td>50±1.5/60.5±1.3</td>
<td>70±0.5/85±0.2</td>
<td>30±1.5/35±1.2</td>
<td>15±0.9/20±0.3</td>
<td>40±0.3/35±0.5</td>
<td>5±0.4/15±0.1</td>
<td>50±0.4/45±0.5</td>
<td>80±0.2/15±0.1</td>
<td>5±0.01/20±0.3</td>
<td>30±0.4/25±0.4</td>
<td>10±1.0/15±1.2</td>
<td>30±0.5/25±0.4</td>
<td>20±0.4/40±0.4</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

The different letter in one columns showed significant changes $p<0.05$. Week 1 ($w_1$)=14 day post treatment (d.p.t), $w_2=21$ d.p.t, $w_3=28$ d.p.t, $w_4=35$ d.p.t and $w_5=42$ d.p.t.

Table (7) Mean±standard error (SE) of the concentration of Oxytetracycline in Different organs(µg/g) and serum, bile, urine µg/ml in camels *Camelus dromedarius* infected with *T. evansi* and given single and multiple dosages of oxytetracycline (M+SE).

<table>
<thead>
<tr>
<th>Organs</th>
<th>Dose</th>
<th>Liver</th>
<th>Kidney</th>
<th>Heart</th>
<th>Lung</th>
<th>Spleen</th>
<th>Cerebellum</th>
<th>Cerebrum</th>
<th>Fat</th>
<th>Site of injection</th>
<th>Leg Muscle</th>
<th>Uterus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.5°</td>
<td>±0.01</td>
<td>105±2.2/140±2.2</td>
<td>130±0.3/110±0.2</td>
<td>90±1.1/95±1.4</td>
<td>30±0.5/40±0.7</td>
<td>80±0.2/85±0.5</td>
<td>75±0.2/70±2.5</td>
<td>45±0.8/40±0.3</td>
<td>105±0.1/120±0.2</td>
<td>100±2.1/105±2.3</td>
<td>50±0.3/55±0.3</td>
</tr>
<tr>
<td></td>
<td>3.0°</td>
<td>±0.001</td>
<td>100±2.4/105±2.3</td>
<td>140±0.5/155±0.6</td>
<td>160±0/1/140±0.7</td>
<td>85±1.2/801.9</td>
<td>120±0/0.1/120±0.2</td>
<td>115±3.4/180±3.5</td>
<td>160±0.8/150±0.4</td>
<td>200±3.0/3/300±1.5</td>
<td>180±0.4/200±0.5</td>
<td>250±2.3/2.3</td>
</tr>
<tr>
<td></td>
<td>5.9°</td>
<td>±0.03</td>
<td>250±1.9/300±2.5</td>
<td>300±1.7/305±1.8</td>
<td>250±2/4/300±2.0</td>
<td>120±1.1/130±2.0</td>
<td>350±2/3/360±2.7</td>
<td>350±3.1/250±3.2</td>
<td>150±0.1/60±0.1</td>
<td>305±1.1/250±0.2</td>
<td>450±0.1/250±0.2</td>
<td>300±2.5/250±2.2</td>
</tr>
</tbody>
</table>

Note: The different letter in one columns showed significant changes $p<0.05$. Week 1 ($w_1$)=14 day post treatment (d.p.t), $w_2=21$ d.p.t, $w_3=28$ d.p.t, $w_4=35$ d.p.t and $w_5=42$ d.p.t.
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (4) 50mg/kg</th>
<th>20±0.1/15±0.5</th>
<th>15±0.00/10±0.001</th>
<th>1.5±0.01/0.5±0.4</th>
<th>5±0.1/6±0.2</th>
<th>1.5±0.0/1/1.5</th>
<th>5.5±0.05/3±0.07</th>
<th>3.5±0.05/3±0.07</th>
<th>25±1.2/20±1.3</th>
<th>10±0.5/5±0.01</th>
<th>5.5±1.0/5±1.1</th>
<th>25±1.2/20±1.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (5) 100mg/kg</td>
<td>35±1.1/30±1.2</td>
<td>15±1/1.7/10±1.1</td>
<td>2.5±0.1/3.5±0.2</td>
<td>4±0.1/3±0.2</td>
<td>2±0.01/0.5±0.0</td>
<td>10±0.01/15±0.04</td>
<td>4.5±0.01/5±0.01</td>
<td>2.5±0.00/2.5±0.00</td>
<td>30±1.0/30±1.1</td>
<td>20±0.0/25±0.00</td>
<td>10±1.1/8±1.2</td>
</tr>
<tr>
<td>Group (6) 20mg/kg/week for 2weeks</td>
<td>15±0.1/15±0.5</td>
<td>5±0.04/5±0.07</td>
<td>3.5±0.1/5±0.2</td>
<td>1.5±0.0/0.1/1±0.01</td>
<td>2.5±0.01/2±0.07</td>
<td>10±0.1/15±0.3</td>
<td>5.5±0.02/7.5±0.01</td>
<td>5±0.04/7/0.05</td>
<td>25±1.7/25±1.3</td>
<td>15±1.1/20±0.5</td>
<td>15±1.4/20±0.5</td>
</tr>
<tr>
<td>Group (7) 20mg/kg daily for 8days</td>
<td>40±1.3/50±1.5</td>
<td>60±1.1/70±1.3</td>
<td>10±0.1/15±0.1</td>
<td>2.5±0.1/2±0.01</td>
<td>5±0.01/5±0.02</td>
<td>15±0.1/20±0.2</td>
<td>10±0.01/15±0.02</td>
<td>8±0.02/10±0.01</td>
<td>30±1.5/25±1.4</td>
<td>15±1.5/20±0.5</td>
<td>25±1.2/30±1.1</td>
</tr>
</tbody>
</table>

Week1 (w1)=14d.p.t, w2=21d.p.t, w3=28d.p.t, w4=35d.p.t and w5=42d.p.t.

Table 10: The concentration of Cymelarsan (Arsenic) in Different organs (µg/g) and serum, bile and urine (µg/ml) in Nubian goats infected with *T. evansi* and given single or multiple dosages of Cymelarsan and Oxytetracycline combination (M±SE).

<table>
<thead>
<tr>
<th>Organs</th>
<th>Dose</th>
<th>Serum</th>
<th>Liver</th>
<th>Kidney</th>
<th>Heart</th>
<th>Lung</th>
<th>Spleen</th>
<th>Cerebellum</th>
<th>Cerebrum</th>
<th>Fat</th>
<th>Site of injection</th>
<th>Leg</th>
<th>Muscle</th>
<th>Uterus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>≤0.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group (2)</td>
<td>≤0.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group (3) 0.125 mg/kg of MelCy+10mg/kg of OTC</td>
<td>0.42±0.04</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.4±0.05</td>
<td>0.1±0.0</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td></td>
</tr>
<tr>
<td>Group (4) 0.125 mg/kg of MelCy+50 mg/kg of OTC</td>
<td>0.55±0.01</td>
<td>0.5±1.22/≤0.07</td>
<td>0.1±0.00/≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.1±0.0/0/≤0.07</td>
<td>0.2±0.01/≤0.07</td>
<td>≤0.07</td>
<td>0.1±0.0/1≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group (5) 0.125 mg/kg of MelCy+20 mg/kg of OTC twice/week for 2weeks</td>
<td>1.89±0.14</td>
<td>70±0.00/90±0.00</td>
<td>40±1.5/45±1.6</td>
<td>30±1.2/35±1.6</td>
<td>40±1.1/35±1.3</td>
<td>15±1.4/18±1.5</td>
<td>7±1.01/10±1.03</td>
<td>60±1.1/50±1.3</td>
<td>70±1.4/80±1.5</td>
<td>45±1.1/55±1.5</td>
<td>30±1.0/35±1.9</td>
<td>15±1/20±1.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group (6) 0.125 mg/kg</td>
<td>3.1±0.02</td>
<td>110±1.5/120±1.9</td>
<td>120±1.1/100±1.4</td>
<td>85±1.7/85±1.8</td>
<td>75±2.5/70±1.5</td>
<td>80±1.9/80±1.5</td>
<td>75±1.7/70±1.8</td>
<td>45±1.1/45±1.2</td>
<td>100±1.4/110±1.3</td>
<td>120±1.1/110±1.3</td>
<td>105±2.0/100±1.1</td>
<td>60±1.1/65±1.1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)**

The same letters in one column showed no significant changes $p \leq 0.05$. OTC = Ox tetracycline (Remacycline®) MelCy = Cymelarsan® Week1 ($w_1$) = 14 day post treatment (d.p.t), $w_2$ = 21 d.p.t, $w_3$ = 28 d.p.t, $w_4$ = 35 d.p.t and $w_5$ = 42 d.p.t.

Table (10) the concentration of Quinapyramine (%) in Different organs in Nubian goats in Nubian goats infected with *T. evansi* and given single or multiple doses of Quinapyramine (M±SE).

<table>
<thead>
<tr>
<th>Organs Dose</th>
<th>Liver</th>
<th>Kidney</th>
<th>Heart</th>
<th>Lung</th>
<th>Spleen</th>
<th>Cerebellum</th>
<th>Cerebrum</th>
<th>Fat</th>
<th>Site of injection</th>
<th>Leg Muscle</th>
<th>Uterus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Group (2)</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Group (3) 5mg/kg</td>
<td>10±0.05/2 ±0.02/0.5 ±0.01/nil</td>
<td>13±1.5/10±1.8±5±1.4/2 .5±0.1±0.5±0.1</td>
<td>0.5±0.5±0.1 ±0.3±0.01±0.2/0.05±0.01/nil</td>
<td>nil</td>
<td>2±0.1/1.5±0.2/0.5±0.1 /nil</td>
<td>0.1±0.00/0.2±0.5/0.0</td>
<td>0.1±0.00/0.2±0.5/0.0</td>
<td>nil</td>
<td>0.05±0.01/0.01±0.02/nil</td>
<td>0.01±0.01/l/nil</td>
<td>0.05±0.05/nil</td>
</tr>
<tr>
<td>Group (4) 12.5 mg/kg</td>
<td>10±1.5±5±0.2/0.1±0.5±0.0/0.1±0.01</td>
<td>10±1.5±1±1.5±0±0.5/0.2±0.3/0.1±0.2</td>
<td>1.5±0.00/1.2±1/0.5±0.5±0.0</td>
<td>0.1±0.1±0.5±0.1</td>
<td>1.0±0.00/0.2±0.00/0.5±0.00/0.1±0.00/nil</td>
<td>0.5±0.02/0.2±0.00/0.1±0.1±0.00/nil</td>
<td>5±1.5±2/5±0.1±2/0.2/5±0.5±0.2</td>
<td>nil</td>
<td>0.5±0.00/nil</td>
<td>nil</td>
<td>0.5±0.01/0.1±0.00/nil</td>
</tr>
<tr>
<td>Group (5) 25mg/kg</td>
<td>10±1.5/7.5±1.1/5.5±1.3/5±0.4±2.5±0.5</td>
<td>15±0.5/10±0.02/8±5±0.05/8±0.03</td>
<td>2.5±0.00/2 ±0.00/1.5/0.00/1.0±0.00/5±0.0</td>
<td>nil</td>
<td>2±0.00/1±0.01/1.5±0.0</td>
<td>2.5±0.00/2±0.00/1.5±0.0</td>
<td>8±0.3±5±0.4/0±0.3/2.5±0.2/2.5±0.2</td>
<td>nil</td>
<td>1±0±0.01/0.5±0±0.02/0.0±0.01/0.1±0.00/0.2±0.01</td>
<td>1±0±0.01/0.5±0±0.02/0.0±0.01/0.1±0.00/0.2±0.01</td>
<td></td>
</tr>
<tr>
<td>Group (6) 50mg/kg</td>
<td>15±0.5/10±0.6</td>
<td>5±0.00/5.5±0.0</td>
<td>7.5±0.00/4.5±0.01</td>
<td>nil</td>
<td>5±1±2.3±5±1±0</td>
<td>2.5±0.01/2±0.02</td>
<td>5±0.5/3±0.2</td>
<td>2.5±0.00/2±0.00/1.0±0.0</td>
<td>1.5±0±0.04/1±0.3</td>
<td>nil</td>
<td></td>
</tr>
<tr>
<td>Group (7) 5 mg/kg weekly for</td>
<td>10±0.5±5±0.3</td>
<td>5.5±10.0±5.5±1±0</td>
<td>3.5±0.1±2±0.0</td>
<td>nil</td>
<td>5±0.1±3.5±0.2</td>
<td>2±1.5±1.5±0.1</td>
<td>nil</td>
<td>10±1.5±8.5±1±0</td>
<td>4.5±1.2±2.5±0.1</td>
<td>1.5±0±0.5±2±0.1</td>
<td>2.5±0.02/2±0.23</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>3weeks</th>
<th>Group(8) 5mg/kg days for 8 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>30±1.5/35±1.7</td>
<td>25±1.5/20.5±1.1</td>
</tr>
</tbody>
</table>

Week1 (w1)=14day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4= 35d.p.t and w5=42d.p.t.

Table(10) The concentration of Oxytetracycline in organs, bile and urine(µg/g or/ml) in Nubian goats infected with T. evansi and given single and multiple dosages

<table>
<thead>
<tr>
<th>Organs</th>
<th>Dose</th>
<th>Liver</th>
<th>Kidney</th>
<th>Heart</th>
<th>Lung</th>
<th>Spleen</th>
<th>Cerebellum</th>
<th>Cerebrum</th>
<th>Fat</th>
<th>Site of injection</th>
<th>Leg Muscle</th>
<th>Uterus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>0.3±0.00/0.05±0.00</td>
<td>0.4±0.01/0.3±0.01</td>
<td>0.1±0.01/0.2±0.02</td>
<td>0.5±0.001/0.01±0.00</td>
<td>0.5±0.01/0.00±0.00</td>
<td>0.05±0.00/0.01±0.00</td>
<td>0.01±0.00/0.00±0.00</td>
<td>1±0.05/1±0.00</td>
<td>0.3±0.04±0.05±0.00</td>
<td>0.01±0.02±0.00</td>
<td>0.01±0.04±0.01±0.05</td>
<td>nil</td>
</tr>
<tr>
<td>Group (2)</td>
<td>5±0.001/2±0.1/0.5±0.1±0.1/0.01±0.00</td>
<td>5±0.1/1±0.1/0.8±0.1/0.7/0.01±0.1±0.00</td>
<td>1±0.1/0.5/0.0/0.1±0.5±0.0/0.00</td>
<td>0.1±0.01/0.00 /0.05±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.5±0.001/0.3±0.00</td>
<td>0.1±0.01/0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.5±0.001/0.2±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>nil</td>
</tr>
<tr>
<td>Group (3) 20mg/kg</td>
<td>5±0.001/2±0.1/0.5±0.1±0.1/0.01±0.00</td>
<td>5±0.1/1±0.1/0.8±0.1/0.7/0.01±0.1±0.00</td>
<td>1±0.1/0.5/0.0/0.1±0.5±0.0/0.00</td>
<td>0.1±0.01/0.00 /0.05±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.5±0.001/0.3±0.00</td>
<td>0.1±0.01/0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.5±0.001/0.2±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>nil</td>
</tr>
<tr>
<td>Group (4) 50mg/kg</td>
<td>5±0.001/2±0.1/0.5±0.1±0.1/0.01±0.00</td>
<td>5±0.1/1±0.1/0.8±0.1/0.7/0.01±0.1±0.00</td>
<td>1±0.1/0.5/0.0/0.1±0.5±0.0/0.00</td>
<td>0.1±0.01/0.00 /0.05±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.5±0.001/0.3±0.00</td>
<td>0.1±0.01/0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.5±0.001/0.2±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>nil</td>
</tr>
<tr>
<td>Group (5) 100mg/kg</td>
<td>5±0.001/2±0.1/0.5±0.1±0.1/0.01±0.00</td>
<td>5±0.1/1±0.1/0.8±0.1/0.7/0.01±0.1±0.00</td>
<td>1±0.1/0.5/0.0/0.1±0.5±0.0/0.00</td>
<td>0.1±0.01/0.00 /0.05±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.5±0.001/0.3±0.00</td>
<td>0.1±0.01/0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>0.5±0.001/0.2±0.00</td>
<td>0.0±0.001/0.05±0.00</td>
<td>nil</td>
</tr>
</tbody>
</table>
**Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)**

**Group (6)**

- 20 mg/kg weekly for 3 weeks
- Data: 7 ± 0.25/5 ± 0.2/5 ± 0.1
- 7 ± 0.1/5 ± 0.2/5 ± 0.01
- 7 ± 0.1/5 ± 0.2/5 ± 0.001
- 5.5 ± 0.1/5 ± 0.2/5 ± 0.000
- 5.5 ± 0.1/5 ± 0.2/5 ± 0.000
- 10 ± 0.1/5 ± 0.2/5 ± 0.001

**Group (7)**

- 20 mg/kg twice/week for 2 weeks
- Data: 15 ± 1.3/20 ± 1.5 ± 0.5
- 1.6 ± 0.1/2.8 ± 0.1
- 1.3 ± 0.1/1.0 ± 0.05
- 5.6 ± 0.2/3.3 ± 0.2
- 1.6 ± 0.0 ± 0.000
- 24.8 ± 2.2/20 ± 2.1
- 30 ± 1.5/25.5 ± 1.5
- 5 ± 0.0/8.5 ± 0.3

**Group (8)**

- 20 mg/kg daily for 8 days
- Data: 10 ± 1.3/5 ± 1.2 ± 1.1
- 1.6 ± 0.1/0.5 ± 0.01
- 0.5 ± 0.2/0.2 ± 0.1
- 2 ± 0.0/1.0 ± 0.01
- 0.2 ± 0.0/0.3 ± 0.02
- 0.0 ± 0.0/0.0 ± 0.01
- 10 ± 1.8/5 ± 1.5
- 7 ± 0.1/25 ± 1.5
- 2 ± 0.0/1.0 ± 0.01

Week 1 (w1) = 14 day post treatment (d.p.t), w2 = 21 d.p.t, w3 = 28 d.p.t, w4 = 35 d.p.t and w5 = 42 d.p.t.

---

**Table (11) The concentration of Quinapyramine (%) in serum of Nubian goats infected with T. evansi and given single and multiple dosages of Quinapyramine (M±SE).**

<table>
<thead>
<tr>
<th>Dose Days</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) treated with 5 mg/kg</th>
<th>Group (4) 12.5 mg/kg</th>
<th>Group (5) 25 mg/kg</th>
<th>Group (6) 50 mg/kg weekly for 3 weeks</th>
<th>Group (7) 5 mg/kg weekly for 8 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hours</td>
<td>nil</td>
<td>nil</td>
<td>5 ± 0.01</td>
<td>12 ± 0.1</td>
<td>13 ± 0.0</td>
<td>15 ± 0.7</td>
<td>9 ± 1.5</td>
</tr>
<tr>
<td>3 hours</td>
<td>nil</td>
<td>nil</td>
<td>8 ± 0.02</td>
<td>11 ± 1.1</td>
<td>14 ± 0.2</td>
<td>20 ± 0.5</td>
<td>9 ± 1.3</td>
</tr>
<tr>
<td>24 hours</td>
<td>nil</td>
<td>nil</td>
<td>5 ± 0.04</td>
<td>13 ± 1.2</td>
<td>16 ± 0.1</td>
<td>21 ± 1.2</td>
<td>10 ± 1.2</td>
</tr>
<tr>
<td>3 days</td>
<td>nil</td>
<td>nil</td>
<td>5 ± 0.01</td>
<td>15 ± 1.0</td>
<td>18 ± 0.3</td>
<td>24 ± 1.0</td>
<td>10 ± 0.5</td>
</tr>
<tr>
<td>7 days</td>
<td>nil</td>
<td>nil</td>
<td>5 ± 0.01</td>
<td>10 ± 1.3</td>
<td>22 ± 0.1</td>
<td>15 ± 0.5</td>
<td>13 ± 0.4</td>
</tr>
<tr>
<td>10</td>
<td>nil</td>
<td>Nil</td>
<td>2 ± 0.00</td>
<td>14 ± 0.1</td>
<td>18 ± 0.3</td>
<td>15 ± 0.3</td>
<td>32 ± 2.1</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Days</th>
<th>14 days</th>
<th>21 days</th>
<th>28 days</th>
<th>35 days</th>
<th>42 days</th>
<th>49 days</th>
<th>56 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>nil</td>
<td>Nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td></td>
<td>5±0.5</td>
<td>5±0.2</td>
<td>3±0.00</td>
<td>1</td>
<td>8±0.01</td>
<td>10±0.5</td>
<td>10±0.1</td>
</tr>
<tr>
<td></td>
<td>21 days</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td></td>
<td>5±0.2</td>
<td>3±0.00</td>
<td>2±0.00</td>
<td>7±0.03</td>
<td>40.02</td>
<td>8±0.5</td>
<td>15±0.0</td>
</tr>
<tr>
<td></td>
<td>28 days</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td></td>
<td>12.5±0.3</td>
<td>12±0.2</td>
<td>10±0.5</td>
<td>10±0.1</td>
<td>20±1.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>35 days</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td></td>
<td>5±0.02</td>
<td>30.01</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>42 days</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td></td>
<td>49 days</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
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<tr>
<td></td>
<td>56 days</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td></td>
<td>5±0.03</td>
<td>3.5±0.02</td>
<td>5±0.02</td>
<td>5±0.02</td>
<td>10±1.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Week1 (w1)=14day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4=35d.p.t and w5=42d.p.t.

Table(11) The concentration of Quinapyramine(%) in serum of Nubian goats infected with *T. evansi* and given single and multiple dosages of Quinapyramine and ethidium combination(M±SE).

<table>
<thead>
<tr>
<th>Groups Days</th>
<th>Group(1)</th>
<th>Group(2)</th>
<th>*Group(3) 5mg/kg of quina.+25mg/kg of eth.</th>
<th>*Group(4) 12.5mg/kg of quina.+1mg/kg of eth.</th>
<th>**Group(5) 5mg/kg of quina.+1mg/kg of eth.</th>
<th>**Group(6) 5mg/kg of quina.+2.5mg/kg of eth.</th>
</tr>
</thead>
<tbody>
<tr>
<td>hours</td>
<td>nil</td>
<td>nil</td>
<td>5±0.01</td>
<td>5±0.03</td>
<td>7±0.05</td>
<td>10±1.5</td>
</tr>
<tr>
<td>hours</td>
<td>nil</td>
<td>nil</td>
<td>5±0.02</td>
<td>3±0.01</td>
<td>6±0.01</td>
<td>8±1.1</td>
</tr>
<tr>
<td>4 hours</td>
<td>nil</td>
<td>nil</td>
<td>6±0.03</td>
<td>3±0.00</td>
<td>7±0.02</td>
<td>9±0.5</td>
</tr>
<tr>
<td>days</td>
<td>nil</td>
<td>nil</td>
<td>8±0.04</td>
<td>4±0.00</td>
<td>5±0.01</td>
<td>10±1.0</td>
</tr>
<tr>
<td>days</td>
<td>nil</td>
<td>nil</td>
<td>5±0.03</td>
<td>3.5±0.02</td>
<td>5±0.02</td>
<td>10±1.0</td>
</tr>
</tbody>
</table>
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3)</th>
<th>Group (4)</th>
<th>Group (5)</th>
<th>Group (6)</th>
<th>Group (7)</th>
<th>Group (8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 mg/kg</td>
<td>20 mg/kg</td>
<td>100 mg/kg</td>
<td>20 mg/kg</td>
<td>20 mg/kg</td>
<td>20 mg/kg</td>
<td>20 mg/kg</td>
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<tr>
<td>50 mg/kg</td>
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<td>50 mg/kg</td>
<td>50 mg/kg</td>
<td>50 mg/kg</td>
<td>50 mg/kg</td>
<td>50 mg/kg</td>
</tr>
<tr>
<td>100 mg/kg</td>
<td>100 mg/kg</td>
<td>100 mg/kg</td>
<td>100 mg/kg</td>
<td>100 mg/kg</td>
<td>100 mg/kg</td>
<td>100 mg/kg</td>
<td>100 mg/kg</td>
</tr>
</tbody>
</table>

Table (11) The concentration of Oxytetracycline in serum (µg/ml) in Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan and oxytetracycline combination(M+SE).

*RDS* = Resistance to doxycycline.

** = Infection was done by *T. vivax*. quina.= quinapyramine. hom. = homidium bromide. Week1 (w1)=14day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4= 35d.p.t and w5=42d.p.t.
# Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) 1.25 mg/kg of MelCy+10 mg/kg of OTC</th>
<th>Group (4) 1.25 mg/kg of MelCy+50 mg/kg of OTC</th>
<th>Group (5) 1.25 mg/kg of MelCy+20 mg/kg of OTC twice /week for</th>
<th>Group (6) 1.25 mg/kg of MelCy+20 mg/kg of OTC daily for 8days</th>
</tr>
</thead>
<tbody>
<tr>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>6±0.08</td>
<td>5±0.03</td>
<td>9±0.05</td>
<td>6±0.01</td>
</tr>
<tr>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>2.5±0.01</td>
<td>4±0.01</td>
<td>8±0.07</td>
<td>5±0.01</td>
</tr>
<tr>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>5±0.001</td>
<td>10±0.1</td>
<td>4±0.01</td>
</tr>
<tr>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>6±0.02</td>
<td>6±0.001</td>
<td>5±0.02</td>
<td>8±0.2</td>
</tr>
<tr>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>5±0.02</td>
<td>5±0.002</td>
<td>5±0.00</td>
<td>12±0.3</td>
</tr>
<tr>
<td>nil</td>
<td>nil</td>
<td>Died</td>
<td>4±0.001</td>
<td>6±0.003</td>
<td>5±0.00</td>
<td>8±1.0</td>
</tr>
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<td>nil</td>
<td>3±0.01</td>
<td>5±0.004</td>
<td>3±0.01</td>
<td>5±0.00</td>
</tr>
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<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>6±0.005</td>
<td>nil</td>
<td>4±0.02</td>
</tr>
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</tr>
<tr>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Week1 (w1)=14day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4=35d.p.t and w5=42d.p.t.

Table (12) The concentration of Oxytetracycline in serum (µg/ml) in Nubian goats infected with *T. evansi* and given single and multiple dosages of Cymelarsan followed by oxytetracycline combination (M±SE).
<table>
<thead>
<tr>
<th></th>
<th>MelCy</th>
<th>OTC</th>
<th>2weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1 hours</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>5±0.1</td>
</tr>
<tr>
<td><strong>3 hours</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>6±0.5</td>
</tr>
<tr>
<td><strong>24 hours</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>6±0.4</td>
</tr>
<tr>
<td><strong>3 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>8±0.3</td>
</tr>
<tr>
<td><strong>7 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>7±0.2</td>
</tr>
<tr>
<td><strong>10 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>5±0.1</td>
</tr>
<tr>
<td><strong>14 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>5±1.1</td>
</tr>
<tr>
<td><strong>21 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>Died</td>
</tr>
<tr>
<td><strong>28 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td><strong>35 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td><strong>42 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td><strong>49 days</strong></td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
</tbody>
</table>

MelCy = Cymelarsan®  
OTC = Ox tetracycline (Remacycline®), Week1 (w1)=14 day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4= 35d.p.t and w5=42d.p.t.
Table (10) The concentration of Cymelarsan (Arsenic) in Different organs (µg/g) and serum, bile and urine µg/ml. Nubian goats infected with *T. evansi* and given single or multiple doses of Cymelarsan supplemented with zinc (Zn) and copper (Cu) (M±SE).

<table>
<thead>
<tr>
<th>Organ</th>
<th>Serum</th>
<th>Liver</th>
<th>Kidney</th>
<th>Heart</th>
<th>Lung</th>
<th>Spleen</th>
<th>Cerebellum</th>
<th>Cerebrum</th>
<th>Fat</th>
<th>Site of injection</th>
<th>Leg Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group (1)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>≤0.07</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group (2)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>≤0.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group (3)</strong></td>
<td>0.41b</td>
<td>0.2±0.05</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.5±0.02/ ≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>0.25mg/kg+ Zn+ Cu</td>
<td>±0.05</td>
<td>≤0.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Group (4)</strong></td>
<td>3.2c</td>
<td>25.4020.07</td>
<td>25±0.01</td>
<td>30±0.21</td>
<td>10.0±0.05</td>
<td>1.505</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>55.2±0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>0.25mg/dkg+Zn + Cu daily for 8 days</td>
<td>±0.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The same letters in one column showed no significant changes p ≤ 0.05. Week 1 (w1)=14day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4=35d.p.t and w5=42d.p.t.
Table (11) the concentration of Oxytetracycline (µg/g) in Different organs in Nubian goats infected with *T. evansi* and given single or multiple doses of Cymelarsan and Oxytetracycline combination (M±SE).

<table>
<thead>
<tr>
<th>Organs</th>
<th>Liver</th>
<th>Kidney</th>
<th>Heart</th>
<th>Lung</th>
<th>Spleen</th>
<th>Cerebellum</th>
<th>Cerebrum</th>
<th>Fat</th>
<th>Site of injection</th>
<th>Leg Muscle</th>
<th>Uterus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1)</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Group (2)</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Group (3)</td>
<td>0.5±0.01</td>
<td>0.3±0.02</td>
<td>0.4±0.01</td>
<td>0.3±0.00</td>
<td>0.4±0.01</td>
<td>0.04±0.00</td>
<td>0.03±0.00</td>
<td>1±0.3</td>
<td>nil</td>
<td>0.5±0.4</td>
<td>0.2±0.1</td>
</tr>
<tr>
<td>0.125 mg/kg of MelCy+10mg/kg of OTC</td>
<td>0.2±0.00</td>
<td>0.2±0.02</td>
<td>0.2±0.01</td>
<td>0.01±0.0</td>
<td>0.01±0.00</td>
<td>0.01±0.00</td>
<td>0.05±0.2</td>
<td>0.01±0.00</td>
<td>nil</td>
<td>0.05±0.5</td>
<td>0.01±0.00</td>
</tr>
<tr>
<td>Group (4)</td>
<td>3.5±0.01</td>
<td>1.5±0.00</td>
<td>5±0.1/</td>
<td>5±0.01</td>
<td>2.5±0.00</td>
<td>0.5±0.01</td>
<td>0.5±0.01</td>
<td>10±1.5</td>
<td>nil</td>
<td>5±0.5/</td>
<td>5±0.2/</td>
</tr>
<tr>
<td>0.125 mg/kg of MelCy+50mg/kg of OTC</td>
<td>1.2±0.01</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>7±1.00</td>
<td>5±0.01</td>
<td>5±0.01</td>
<td>5±0.2/</td>
</tr>
<tr>
<td>Group (5)</td>
<td>5±0.1/</td>
<td>10±0.2/</td>
<td>15±0.1/</td>
<td>15±0.00</td>
<td>5±0.1/</td>
<td>3±0.01</td>
<td>5±0.01</td>
<td>10±1.0</td>
<td>5±0.1/</td>
<td>5±0.01</td>
<td>5±0.2/</td>
</tr>
<tr>
<td>0.125 mg/kg of MelCy+20 mg/kg of OTC twice/week</td>
<td>0.5±0.00</td>
<td>0.5±0.00</td>
<td>8.5±0.01</td>
<td>2±0.03/</td>
<td>5±0.00</td>
<td>2±0.04/</td>
<td>5±0.00</td>
<td>7.5±0.5/</td>
<td>3±0.01/</td>
<td>3±0.01/</td>
<td>5±0.4/</td>
</tr>
<tr>
<td>Group (6)</td>
<td>5±0.01</td>
<td>10±0.00</td>
<td>15±0.00</td>
<td>15±0.00</td>
<td>5±0.01</td>
<td>3±0.01</td>
<td>5±0.01</td>
<td>10±1.0</td>
<td>5±0.01</td>
<td>5±0.01</td>
<td>5±0.4/</td>
</tr>
<tr>
<td>0.125 mg/kg of MelCy+20mg/kg of OTC daily for 8 days</td>
<td>0.3±0.01</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>7±1.00</td>
<td>5±0.01</td>
<td>5±0.01</td>
<td>5±0.4/</td>
</tr>
</tbody>
</table>

MelCy = Cymelarsan, OTC = Ox tetracycline (Remacyclin), Week 1 (w1)=14 days post treatment (d.p.t), w2=21 d.p.t, w3=28 d.p.t, w4=35 d.p.t and w5=42 d.p.t.
Table (10) The concentration of Quinapyramine (%) in organs, bile and urine of Nubian goats infected with *T. evansi* and given single and multiple dosages of Quinapyramine and ethidium combination (M±SE).

<table>
<thead>
<tr>
<th>Dose Days</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>*Group(3) 5mg/kg of quina.+25mg/kg of eth.</th>
<th>*Group(4) 12.5mg/kg of quina.+1mg/kg of eth.</th>
<th>**Group(5) 5mg/kg of quina.+1mg/kg of eth.</th>
<th>**Group(6) 5mg/kg of quina.+2.5mg/kg of eth.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>Nil</td>
<td>Nil</td>
<td>10±0.01/2±0.02/0.5±0.03/mil</td>
<td>10±1.5/5±0.5/2±0.1/0.5±0.01/1±0.01/0.1±0.01</td>
<td>6.5±0.02/2.3±0.02/1±0.02/0.5±0.01</td>
<td>10±0.01/5±0.02/4±0.03/2.5±0.04</td>
</tr>
<tr>
<td>Kidney</td>
<td>Nil</td>
<td>Nil</td>
<td>15±1.5/10±1.8±1.4/2.5±0.1/0.5±1</td>
<td>10±1.5/5±1.1/5.5±0.2±0.3/1±0.2</td>
<td>10.2±0.01/7.3±0.02/mil</td>
<td>5.5±0.02/7.5±0.01/3.5±0.02/2±0.00/1±0.05</td>
</tr>
<tr>
<td>Heart</td>
<td>Nil</td>
<td>Nil</td>
<td>1±0.5/0.3±0.3±0.01/0.2/0.00±0.01/mil</td>
<td>1.5±0.01/1±0.1/0.5±0.1/0.5±0.00/0.1±0.00</td>
<td>10±0.00/6.5±0.02/7±0.00/5±0.02/3±0.01</td>
<td>10.2±0.01/8±0.01/5±0.02/2.5±0.01/1±0.03</td>
</tr>
<tr>
<td>Lung</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>7±0.01/5±0.02/3.5±0.02/1.2±0.02/mil</td>
<td>10.5±0.01/8.5±0.01/3.5±0.02/nil</td>
</tr>
<tr>
<td>Spleen</td>
<td>Nil</td>
<td>Nil</td>
<td>3±0.1/2.5±0.2/0.5±0.1/mil</td>
<td>1.5±0.00/4±0.00/0.5±0.00/1±0.00/0.01/nil</td>
<td>0.5±0.02/1±0.03/mil</td>
<td>0.5±0.00/1±0.00/1±0.05/nil</td>
</tr>
<tr>
<td>cerebellum</td>
<td>Nil</td>
<td>Nil</td>
<td>0.1±0.00/2.0±0.5/0.05±0.3-nil</td>
<td>0.5±0.02/0.2±0.001/0.1±0.00/nil</td>
<td>2±0.03/3±0.00/1.5±0.01-nil</td>
<td>3±0.02/4.5±0.02/5.5±0.04/4±0.02/5.0±0.02</td>
</tr>
<tr>
<td>cerebrum</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>1.5±0.02/1±0.02/nil</td>
<td>2±0.02/nil</td>
</tr>
<tr>
<td>Fat</td>
<td>Nil</td>
<td>Nil</td>
<td>3±0.5/0.5±0.2±0.02±0.4/0.05±0.5-nil</td>
<td>5±1.5/2±1±0.2±0.2±1.5±0.5±0.2</td>
<td>2.5±0.02/2±0.01/1±0.5±0.02</td>
<td>3.5±0.02/2.5±0.04/2±0.05/1±0.05/nil</td>
</tr>
<tr>
<td>Site of injection</td>
<td>Nil</td>
<td>Nil</td>
<td>0.05±0.01/0.01/0.02-nil</td>
<td>0.5±0.00-nil</td>
<td>1±0.03/1.5±0.02/0.5±0.03/1±0.05-nil</td>
<td>15±0.00/10±0.02/7.5±0.02/5.5±0.02/3.5±0.02-nil</td>
</tr>
<tr>
<td>Uterus</td>
<td>Nil</td>
<td>Nil</td>
<td>3±0.5/0.5±0.2±0.02±0.4/0.05±0.5-nil</td>
<td>0.5±0.01/0±0.00/nil</td>
<td>1.5±0.02/1±0.02/0.5±0.001/0.5±0.01-nil</td>
<td>2.5±0.03/2±0.03/1.5±0.00/1±0.02-nil</td>
</tr>
<tr>
<td>Ovary</td>
<td>Nil</td>
<td>Nil</td>
<td>0.05±0.03-nil</td>
<td>0.5±0.00-nil</td>
<td>1±0.03/0.5±0.03/0.5±0.01-nil</td>
<td>12±0.03/10±0.05/8±0.02/5.5±0.01-nil</td>
</tr>
<tr>
<td>Testis</td>
<td>Nil</td>
<td>Nil</td>
<td>0.05±0.05-nil</td>
<td>1.5±0.00/0.5±0.00/nil</td>
<td>2±0.03/1±0.05/1.5±0.03/1±0.02-nil</td>
<td>0.5±0.05/0.2±0.01/2±0.2±0.00/0.00/2±0.02</td>
</tr>
<tr>
<td>Bile</td>
<td>Nil</td>
<td>Nil</td>
<td>2.5±0.01/2±0.02/1.5±0.00/0.2±0.02/mil</td>
<td>30.0±0.00/10.0±0.03</td>
<td>7±0.00/3.5±0.01/2.0±0.00/2±0.00/nil</td>
<td></td>
</tr>
<tr>
<td>Urine</td>
<td>Nil</td>
<td>Nil</td>
<td>0.5±0.03/0.1±0.00-nil</td>
<td>9±0.5/5±1/0±1±0.0±0.05/0.3±0.02</td>
<td>1.5±0.00/0.5±0.00-nil</td>
<td>2±1.5±0.01/0.5±0.00/nil</td>
</tr>
</tbody>
</table>

* = Infection was done by *T. evansi*, ** = Infection was done by *T. vivax*, quina. = quinapyramine, hom. = homidium bromid

Week1 (w1)=14day post treatment (d.p.t), w2=21d.p.t, w3=28d.p.t, w4= 35d.p.t and w5=42d.p.t.
Table 7: The concentration of Cymelarsan in different organs (µg/100g) and serum and urine (µg/ml) in camels infected naturally with *T. evansi* infected and given single and multiple dosages of Cymelarsan within the withdrawal period (M±SE).

<table>
<thead>
<tr>
<th>Groups Organs</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) 0.25mg/kg</th>
<th>Group (4) 0.625mg/kg</th>
<th>Group (5) 0.125 mg/kg weekly/3weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>2.3±0.01</td>
<td>8.3±0.02</td>
<td>5.6±0.00</td>
</tr>
<tr>
<td>Liver</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Lung</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Kidney</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>10 ±0.05 /3 ±0.01</td>
<td>10 ±0.01 /5 ±0.02</td>
<td>10 ±0.02 /4 ±0.00</td>
</tr>
<tr>
<td>Heart</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.5 ±0.01 /0.6±0.00 /≤0.07</td>
<td>0.5±0.01 /0.5±0.00 /≤0.07</td>
<td>0.8±0.00 /0.3±0.00 /≤0.07</td>
</tr>
<tr>
<td>Spleen</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.1 ±0.02 /≤0.07</td>
<td>0.5 ±0.00 /≤0.07</td>
<td>0.5 ±0.01 /≤0.07</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Fat</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.5 ±0.05 /≤0.07</td>
<td>0.5 ±0.00 /≤0.07</td>
<td>0.5 ±0.00 /≤0.07</td>
</tr>
<tr>
<td>Site of injection</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>5 ±0.2 /≤0.07</td>
<td>5 ±0.02 /≤0.07</td>
<td>5 ±0.02 /≤0.07</td>
</tr>
<tr>
<td>Leg muscle</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Uterus</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>2.2 ±0.01 /≤0.07</td>
<td>2.5 ±0.02 /≤0.07</td>
<td>2.02 ±0.01 /≤0.07</td>
</tr>
<tr>
<td>Ovary</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.5 ±0.02 /≤0.07</td>
<td>0.7 ±0.00 /≤0.07</td>
<td>0.8 ±0.00 /≤0.07</td>
</tr>
<tr>
<td>Testis</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.2 ±0.01 /≤0.07</td>
<td>0.5 ±0.01 /≤0.07</td>
<td>0.9 ±0.01 /≤0.07</td>
</tr>
<tr>
<td>Urine</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
</tbody>
</table>
Table (7) the concentration of Oxytetracycline in Different organs (μg/g) and serum and urine (μg/ml) in camels infected naturally with *T. evansi* and given single and multiple dosages of Oxytetracycline within the withdrawal period (M±SE).

<table>
<thead>
<tr>
<th>Groups (Organs)</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) 20 mg/kg</th>
<th>Group (4) 50mg/kg</th>
<th>Group (5) 100 mg/kg</th>
<th>Group (6) 20mg/kg twice/week for 2 weeks</th>
<th>Group (7) 20mg/kg daily for 8 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>Nil</td>
<td>Nil</td>
<td>20±0.1/15 ±0.2</td>
<td>20±0.1/15 ±0.2/5.5±0.02/nil</td>
<td>35±1.1/30±0.02/20±0.1/5±0.5/10±0.1/nil</td>
<td>35±1.1/30±0.02/20±0.1/5±0.5/10±0.1/nil</td>
<td>35±1.1/30±1/2/20±0.03/15±0.01/5±0.02/nil</td>
</tr>
<tr>
<td>Kidney</td>
<td>Nil</td>
<td>Nil</td>
<td>15±0.01/10 ±0.02</td>
<td>15±0.00/10 ±0.01/3±5±0.02/nil</td>
<td>15±1.7/10 ±0.01/3±5±0.02/nil</td>
<td>5±0.04/5 ±0.02/5±0.01/1.5±0.02/1/nil</td>
<td>60±1.1/70±1.3/35±0.02/40±0.03/25±0.02/</td>
</tr>
<tr>
<td>Heart</td>
<td>Nil</td>
<td>Nil</td>
<td>3.5±0.1/4.5±0.2</td>
<td>3.5±0.1/0.5±0.4/2.5±0.02/0.1/nil</td>
<td>2.5±0.1/3±5±0.02/1/5±0.02/nil</td>
<td>3.5±0.1/5 ±0.2/2.5±0.01/2±0.03/1.5±0.01/nil</td>
<td>10±0.1/15±0.1/10±0.02/8±0.01/5±0.02</td>
</tr>
<tr>
<td>Lung</td>
<td>Nil</td>
<td>Nil</td>
<td>3±0.01/2 /0.1</td>
<td>5±0.1/6±0.2/4±0.02/2.5±0.02/nil</td>
<td>4±0.1/3±0.2/1/5±0.01/0.5±0.02/nil</td>
<td>1.5±0.00/1.1±0.01/0.5±0.02/1/nil</td>
<td>2.5±0.1/2/0.1±0.02/1.5±0.01/0.5±0.02/nil</td>
</tr>
<tr>
<td>Spleen</td>
<td>Nil</td>
<td>Nil</td>
<td>3.5±0.01/1.5 /2.5±0.02</td>
<td>1.5±0.01/1.5 ±0.02/10.02/0.5±0.3±0/nil</td>
<td>2±0.01/0.5±0.01/3±0.02/0.01/nil</td>
<td>2.5±0.01/2±0.01/0.7±1.8±0.01±3/1.4±0.01±0.5±0.02</td>
<td>5±0.01/5±0.02/3.5±0.02/2.5±0.02/1.5±0.02</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>Nil</td>
<td>Nil</td>
<td>5±0.01 /2±0.04</td>
<td>5.5±0.05/7 ±0.03/5.5±0.02/30±1.5±0.02/nil</td>
<td>10±0.01/15 ±0.04/10±0.05/5±0.03/0.5±0.02/nil</td>
<td>10±0.1/15 ±0.3±0/10±0.03/5±0.02/2.5±0.06/nil</td>
<td>15±0.1/20±0.2/15±0.02/10±0.02/5.5±0.00/nil</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>Nil</td>
<td>Nil</td>
<td>3±0.01 /2.5±0.02</td>
<td>3.5±0.05/3 ±0.07/1.5±0.02/1/5±0.03/nil</td>
<td>4.5±0.01/5 ±0.01/3±5±0.01/2±0.01/1±nil</td>
<td>5.5±0.02/2±0.3±5±0.01/5±0.01/3±0.03±2±0.02</td>
<td>10±0.01/15±0.02/10±0.00/5.5±0.05/3.5±0.02/nil</td>
</tr>
<tr>
<td>Fat</td>
<td>Nil</td>
<td>Nil</td>
<td>5±0.01 /2.5±0.02</td>
<td>3.5±0.05/3 ±0.07/1.5±0.02/1/5±0.03/nil</td>
<td>2.5±0.00 /2.5±0.00/5±0.04/2.5±0.00/nil</td>
<td>5±0.04/7±0.05/3.5±0.04/5±0.00/5±0.02</td>
<td>8±0.02/10±0.01/5.5±0.00/3.5±0.02/3±0.01/nil</td>
</tr>
<tr>
<td>Site of injection</td>
<td>Nil</td>
<td>Nil</td>
<td>15±1.1/20 ±0.00</td>
<td>25±1.2/20 ±1.3/10±0.5±2.5±0.2 /1±0.01/nil</td>
<td>30±1.0/30 ±1.1/25±0.02/20±0.03/nil</td>
<td>25±1.7/25 ±1.3/5±0.06/2/12±0.05/8±0.02/nil</td>
<td>30±1.5/25±1.4/2/20±0.00/15±0.02/10±0.02/nil</td>
</tr>
<tr>
<td>Leg muscle</td>
<td>Nil</td>
<td>Nil</td>
<td>15±0.7 /5±0.7</td>
<td>10±0.5/5 ±0.01/2±1/0.01/nil</td>
<td>20±0.0/25 ±0.01/15±0.02/10±0.01/nil</td>
<td>15±1.1/20 ±0.5/15±0.02/10±0.03±8±0.02/nil</td>
<td>15±1.5/20±5/15±0.02/10±0.02/5.5±0.00/nil</td>
</tr>
<tr>
<td>Uterus</td>
<td>Nil</td>
<td>Nil</td>
<td>7±1.2/7.5 ±1.3</td>
<td>5.5±1.0/5 ±1.1/2.5±0.2/1±0.05/nil</td>
<td>10±1.1/8 ±0.02/7±0.02/7.5±0.03/nil</td>
<td>15±1.4/20 ±0.5/18.0/20±0.03/10±0.5±0.02/10±0.03±5±0.02</td>
<td>25±1.2/30±1.1/20±0.00/15±0.02/5/5±0.02</td>
</tr>
<tr>
<td>Ovary</td>
<td>Nil</td>
<td>Nil</td>
<td>0.5±0.1 /0.2</td>
<td>2.5±0.2/1 ±0.02/5±0.02/0.2±0.01/nil</td>
<td>2.5±0.01/1±0.02/5±0.02/0.2±0.01/nil</td>
<td>3±0.1/3±5±0.4/2.5±0.06/1.5±0.03±5±0.04/nil</td>
<td>5±0.1/6.5±0.3/2.5±0.00/1.5±0.01/5±0.00</td>
</tr>
<tr>
<td>Testis</td>
<td>Nil</td>
<td>Nil</td>
<td>7.5±0.07 /8.5±0.08</td>
<td>5±0.01/1.1 /0.10 ±0.5/8.5±0.02/1.5±0.06/nil</td>
<td>5±0.01/2.5 ±0.02/0.03/1±0.02/nil</td>
<td>8.5±0.1/10.5 ±0.2/5±0.06/2±0.5±0.01/2±0.01</td>
<td>8±0.1/10.5 ±0.03/5.5±0.00/2.5±0.00/1.01/0.02</td>
</tr>
<tr>
<td>Urine</td>
<td>Nil</td>
<td>Nil</td>
<td>3.5±0.01 /4±0.02</td>
<td>5±0.1/5.5 ±0.2/3.8±0.08/2.5±0.01/nil</td>
<td>5.5±0.1/4.5 ±0.01/2.3±5±0.01/2/0.02/1±0.01/nil</td>
<td>4.5±0.1/4.5 ±0.01/3.5±0.01/2±0.02/1±0.01/nil</td>
<td>5±0.01/5/±0.02/2.5±0.02/1.5±0.03/1±0.00/nil</td>
</tr>
</tbody>
</table>
Table (7) the concentration of Cymelarsan in different organs(µg/100g), serum and urine (µg /ml )in camels infected naturally with *T. evansi* and given single dosages of Cymelarsan and Oxytetracycline within the withdrawal period (M±SE).

<table>
<thead>
<tr>
<th>Groups Organs</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) 0.25mg/kg of MelCY+20mg/kg of OTC</th>
<th>Group (4) 0.125mg/kg of OTC MelCY+50mg/kg of OTC</th>
<th>Group (5) 0.125mg/kg of OTC MelCY+100mg/kg of OTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>1±0.02</td>
<td>2.5±0.02</td>
<td>0.5±0.03</td>
</tr>
<tr>
<td>Liver</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>2.5 ±0.02 /≤0.07</td>
<td>2.5 ±0.01 /≤0.07</td>
<td>1.5±0.02 /≤0.07</td>
</tr>
<tr>
<td>Lung</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Kidney</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>2 ±0.001 /≤0.07</td>
<td>5 ±0.02 /2.5 ±0.03 /0.5 ±0.00 /≤0.07</td>
<td>0.3±0.01 /≤0.07</td>
</tr>
<tr>
<td>Heart</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>1.5 ±0.01 /≤0.07</td>
<td>0.2 ±0.02 /0.5 ±0.02 /0.7 ±0.001 /≤0.07</td>
<td>0.1±0.03 /≤0.07</td>
</tr>
<tr>
<td>Spleen</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.1 ±0.001 /≤0.07</td>
<td>0.2±0.01 /≤0.07</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.1 ±0.02 /≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Fat</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.6±0.01 /≤0.07</td>
</tr>
<tr>
<td>Site of injection</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.5 ±0.02 /≤0.07</td>
<td>0.5 ±0.03 /≤0.07</td>
<td>0.3±0.00 /≤0.07</td>
</tr>
<tr>
<td>Leg muscle</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.2 ±0.001 /≤0.07</td>
<td>0.5±0.01 /≤0.07</td>
</tr>
<tr>
<td>Uterus</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.2 ±0.05 /≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Ovary</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>≤0.07</td>
<td>0.1 ±0.02 /0.1 ±0.03 /≤0.07</td>
<td>≤0.07</td>
</tr>
<tr>
<td>Testis</td>
<td>Nil</td>
<td>Nil</td>
<td>≤0.07</td>
<td>0.2 ±0.001 /≤0.07</td>
<td>/≤0.07</td>
</tr>
<tr>
<td>Urine</td>
<td>Nil</td>
<td>Nil</td>
<td>0.5 ±0.001 /≤0.07</td>
<td>0.5 ±0.02 /≤0.07</td>
<td>≤0.07</td>
</tr>
</tbody>
</table>

MelCy = Cymelarsan®    OTC = Oxytetracycline (Remacycline®)
**Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)**

Table (8) the concentration of Oxytetracycline in different organs (µg/g) and serum and urine (µg/ml) in camels infected naturally with *T. evansi* and given Cymelarsan followed by Oxytetracycline within the withdrawal period (M±SE).

<table>
<thead>
<tr>
<th>Groups Organs</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) 0.25mg/kg of MelCY+20mg/kg of OTC</th>
<th>Group (4) 0.125mg/kgoft MelCY+50mg/kg of OTC</th>
<th>Group (5) 0.125mg/kgoft MelCY+100mg/kg of OTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>Nil</td>
<td>Nil</td>
<td>10 ±0.5/5 ±0.2/3.5±0.02 2±0.01/1±0.02</td>
<td>60 ±1.7/55 ±1.8/40±0.01 33±0.02/20±0.05</td>
<td>70±0.03/35±0.02/20 ±0.08 /15 ±0.02/5±0.02</td>
</tr>
<tr>
<td>Lung</td>
<td>Nil</td>
<td>Nil</td>
<td>1.5±0.1/1.2±0.1/nil</td>
<td>2±0.1/2.5±1.5/1±0.05/0.5±0.2/0.2±0.04</td>
<td>40±0.03/20±0.04/15 ±0.02 /15 ±0.07/10±0.02</td>
</tr>
<tr>
<td>Kidney</td>
<td>Nil</td>
<td>Nil</td>
<td>10 ±0.2/15 ±0.3/10±0.01/3.5±0.02/1.5±0.03</td>
<td>80 ±1.8 /60 ±1.4/45±0.02/30±0.03/25±0.02</td>
<td>100±0.03/90±0.02/70±0.02 /55±0.01/40±0.02</td>
</tr>
<tr>
<td>Heart</td>
<td>Nil</td>
<td>Nil</td>
<td>2 ±0.2 /0.5±0.02/nil</td>
<td>5 ±0.1/3.5=0.02/1.5±0.03/nil</td>
<td>15±0.08/20±0.03/15 ±0.03 /10±0.02/4.6±0.02</td>
</tr>
<tr>
<td>Spleen</td>
<td>Nil</td>
<td>Nil</td>
<td>0.5±0.01/1±0.1/nil</td>
<td>3±0.01/3.5±0.02/2.5±0.01/1.5±0.01/0.5±0.07</td>
<td>10±0.00/5±0.05/1.5±0.02 /0.5±0.02/0.5±0.01</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>Nil</td>
<td>Nil</td>
<td>5 ±0.3/5 ±0.5/3±0.01/1.5±0.2/0.2±0.01</td>
<td>15 ±1.1/15 ±1.0/10±0.03/5.5±0.04/4.5±0.02</td>
<td>30±0.01/15±0.04/5±0.03 /1.5±0.05/nil</td>
</tr>
<tr>
<td>Cerebrum</td>
<td>Nil</td>
<td>Nil</td>
<td>3.5 ±0.01 /3±0.02/1.5±0.04/nil</td>
<td>20 ±0.01/15 ±0.02/10.4±0.01/nil</td>
<td>50±0.02/15±0.02/11±0.05/5.5±0.02/0.5±0.02</td>
</tr>
<tr>
<td>Fat</td>
<td>Nil</td>
<td>Nil</td>
<td>2.5 ±0.00 /2.5 ±0.00/1.5±0.01/0.5±0.01/2±0.01</td>
<td>3.5 ±0.02 /2.5 ±0.05/1.5±0.02/0.6±0.02/0.3±0.01</td>
<td>50±0.00/40±0.02/35 ±0.02/25 ±0.01/20±0.01</td>
</tr>
<tr>
<td>Site of injection</td>
<td>Nil</td>
<td>Nil</td>
<td>15 ±0.0 /15 ±0.0/10.3±0.02/5.8±0.01/2.5±0.03</td>
<td>25 ±1.02/25±1.01/20±0.03/15±0.08/5.5±0.07</td>
<td>15±0.02/10±0.00/10 ±0.02 /10.01/5±0.02/1.5±0.05</td>
</tr>
<tr>
<td>Leg muscle</td>
<td>Nil</td>
<td>Nil</td>
<td>10 ±0.5 /8 ±0.3/5±0.02/1.5±0.03/0.5±0.06</td>
<td>30±1.1/25±1.2/15±0.03/10.5±0.03/5±0.03</td>
<td>50±0.01/45±0.07/30±0.01/25±0.02/15±0.03</td>
</tr>
<tr>
<td>Uterus</td>
<td>Nil</td>
<td>Nil</td>
<td>5.5 ±0.5 /5 ±0.3/2.5±0.07/1±0.03/nil</td>
<td>10±0.2/10±0.1/5.5±0.02/3.5±0.02/2±0.04</td>
<td>7±0.00/5±0.01/3±0.03 /2±0.01/1±0.02</td>
</tr>
<tr>
<td>Ovary</td>
<td>Nil</td>
<td>Nil</td>
<td>0.5±0.01 /0.5±0.01/nil</td>
<td>3±0.1/2.5±0.2/100.05/0.5±0.02/0.2±0.03</td>
<td>10±0.03/5±0.01/5.5±0.07 /3.5±0.04/2±0.01</td>
</tr>
<tr>
<td>Testis</td>
<td>Nil</td>
<td>Nil</td>
<td>4 ±0.05 /3 ±0.07/2±0.03/nil</td>
<td>5.5 ±0.01/3±0.02/1.5±0.02/0.5±0.02/0.5±0.02</td>
<td>10±0.02/6±0.02/5.5±0.09 /3 ±0.05/1.1±0.02</td>
</tr>
<tr>
<td>Urine</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>0.5±0.02/0.5±0.02/0.2±0.03/nil</td>
<td></td>
</tr>
</tbody>
</table>

MelCy = Cymelarsan®  OTC = Oxtetracycline (Remacycline®)
### Table (9) The concentration of Oxytetracycline in serum (µg/ml) in camels infected naturally with *T. evansi* and given single dosages Cymelarsan by Oxytetracycline within the withdrawal period (M±SE).

<table>
<thead>
<tr>
<th>Dose Days</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) 0.25mg/kg of MelCY+20mg/kg of OTC</th>
<th>Group (4) 0.125mg/kg of MelCY+50mg/kg of OTC</th>
<th>Group (5) 0.125mg/kg of MelCY+100mg/kg of OTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hours</td>
<td>Nil</td>
<td>Nil</td>
<td>15±0.01</td>
<td>30±0.01</td>
<td>40±0.00</td>
</tr>
<tr>
<td>3 hours</td>
<td>Nil</td>
<td>Nil</td>
<td>25±0.02</td>
<td>3±0.025</td>
<td>55±0.01</td>
</tr>
<tr>
<td>24 hours</td>
<td>Nil</td>
<td>Nil</td>
<td>20±0.01</td>
<td>5±0.05</td>
<td>25±0.01</td>
</tr>
<tr>
<td>3 days</td>
<td>Nil</td>
<td>Nil</td>
<td>6±0.00</td>
<td>3±0.00</td>
<td>15±0.01</td>
</tr>
<tr>
<td>7 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>15±0.06</td>
</tr>
<tr>
<td>10 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>14 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>21 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>28 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>35 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>42 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>49 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
</tbody>
</table>

*MelCy = Cymelarsan®  OTC = Oxtetracycline (Remacycline®)*

### Table (8) The concentration of Oxytetracycline in serum (µg/ml) in camels infected naturally with *T. evansi* and given single and multiple dosages of Oxytetracycline within the withdrawal period (M±SE).

*Table (8)* The concentration of Oxytetracycline in serum (µg/ml) in camels infected naturally with *T. evansi* and given single and multiple dosages of Oxytetracycline within the withdrawal period (M±SE).
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels)

<table>
<thead>
<tr>
<th>Dose Days</th>
<th>Group (1)</th>
<th>Group (2)</th>
<th>Group (3) 20mg/kg</th>
<th>Group (4) 50 mg/kg</th>
<th>Group (5) 100 mg/kg</th>
<th>Group (6) 20 mg/kg twice/week for weeks</th>
<th>Group (7) 20mg/kg daily for 8 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hours</td>
<td>Nil</td>
<td>Nil</td>
<td>20±0.05</td>
<td>35±0.02</td>
<td>40±0.02</td>
<td>20±0.05</td>
<td>20±0.01</td>
</tr>
<tr>
<td>3 hours</td>
<td>Nil</td>
<td>Nil</td>
<td>25±0.02</td>
<td>3±0.020</td>
<td>50±0.02</td>
<td>25±0.02</td>
<td>25±0.02</td>
</tr>
<tr>
<td>24 hours</td>
<td>Nil</td>
<td>Nil</td>
<td>15±0.01</td>
<td>5±0.02</td>
<td>20.5±0.01</td>
<td>15±0.00</td>
<td>30±0.02</td>
</tr>
<tr>
<td>3 days</td>
<td>Nil</td>
<td>Nil</td>
<td>6±0.00</td>
<td>2.5±0.00</td>
<td>15±0.001</td>
<td>6.00±0.00</td>
<td>35±0.02</td>
</tr>
<tr>
<td>7 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>10±0.02</td>
<td>20.3±0.02</td>
<td>45±0.01</td>
</tr>
<tr>
<td>10 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>15±0.01</td>
<td>30±0.04</td>
</tr>
<tr>
<td>14 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>15±0.02</td>
<td>5±0.01</td>
</tr>
<tr>
<td>21 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>10±0.02</td>
<td>Nil</td>
</tr>
<tr>
<td>28 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>10±0.03</td>
<td>Nil</td>
</tr>
<tr>
<td>35 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>12±0.00</td>
<td>Nil</td>
</tr>
<tr>
<td>42 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>10±0.02</td>
<td>Nil</td>
</tr>
<tr>
<td>49 days</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>10±0.01</td>
<td>Nil</td>
</tr>
</tbody>
</table>
Chapter four

Discussion

The study of the toxicity and efficacy of Cymelarsan in goats and camels infected with *T. evansi* experimentally or naturally respectively showed that the infection of *T. evansi* in Nubian goats needs more 3 days for parasitaemia to develop, reaching maximum at 7 days and as the disease progresses, the parasitaemia continues very severe for 3 days, the goats dying on day 11 and the camels dying on day 17. Mutayoba *et al.* (1980) found in infected goats the parasitaemia would appear on day 5-9, reach the maximum on day 8-12, the death occurring 17 weeks post-infection. Also Naylor, (1971b) and Fairouz, (2000) studied the parasitaemia in infected *T. evansi* goats, and found that the parasitaemia appeared on day 3, in Fairouz study it reached maximum on day 7, death occurring on day 5. However, death occurred after 33-49 days in Arowlo *et al.*, (1988) study when they studied the parasitaemia in goats infected with *T. evansi*. Goats seem to be more susceptible than camels to *T. evansi* infection although, the end result was same as all animals died. This variation might be due to the difference in strains or method of storing the strains (activation), (Solusby, 1982), or to the age of the animals as from this study the younger animals were more susceptible than older. This is in agreement with Elmalik, (1983) who found that Nubian goats infected with *T. evansi*, the parasitaemia appeared 2-30 day post-infection, the death was 10%, the variation might be due to the difference in species of the animals, agrees with the suggestion of (Elamin, 1980 and Elmalik, 1983). However, no effects were observed ascribable to sex of the animals in this study.

It is well known that Cymelarsan inhibits the metabolism of the cells by an enzyme which is central to the regulation of the thiol/disulfide redox balance in
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the parasite and absent from the host. Also the drug has a rapid trypanocidal activity where, trypanosomes are destroyed within a few hours (Bujon, 1990). All camels were parasite free post treatment. In the goats which received a single half therapeutic recommended dose 0.125 mg/kg, the parasitaemia is slight (+ or ++), and the animals were dead, which may be attributed to the clinicopathological effects of the parasite. The therapeutic dose cleared the parasite from the peripheral blood within 4 days post-treatment and the animals survived. When the drug is administered at two and a half the recommended therapeutic dose the blood was cleared immediately post dosing and the animals survived but, the animals died 15 days post-treatment with five times the therapeutic recommended dose, in groups (7-10) the peripheral blood is cleared from the parasite and animals died, this might be due to the stress of the vital organs by the parasite and to the effect of the drug which contained arsenical molecules. The present study also showed that parasites detected by the liver impression smear completely disappeared in all camels, in goats (4-10) which agree with the results obtained in the peripheral blood or whole blood. Furthermore, results obtained by liver impression smears in group (3) agree with that of peripheral blood or whole blood indicating the existence of the parasite and support our belief that, the cause of death is due to the parasite, while the death in the other treated groups may be due to the clinicopathological effects of the drug on the stressed vital organs. The present study indicates therapeutic activity of Cymelarsan at doses of 0.25-0.625 mg/kg. Also, the half and the recommended therapeutic dose at twice/week for two weeks or at daily administered for 8 days is toxic and fatal which believe that the drug has accumulative effect. This supported by Bujon, (1990) mentioned that the maximum tolerated dose is 3-5 mg/kg in camels, but in this study the goats appear to be more sensitive to the drug toxicity that the maximum tolerated dose appeared to be >0.625 mg/kg.

The clinical signs observed in camels infected naturally with T. evansi are similar to those observed by Musa et al., (1991). The clinical signs manifested by all infected groups reflected the intensity of parasites and were similar to those
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) described by Elamin, (1980) and Olaho et al., (1996). The swollen testes were also mentioned by Elamin, (1980) and the keratitis was observed by De-Villa et al., (1991).

In the present study the signs of acute form of the disease had also been observed. Bujon, (1990) mentioned that Cymelarsan is a trivalent arsenical compound formed by conjugation of one equivalent of melarsenoxide and two equivalent of cystamine. Radositis et al., (2000) mentioned that the trivalent arsenical compounds cause severe syndrome and arsenic is a general tissue poison combining with and inactivating sulfahydryl groups in tissue enzymes. Although all tissues are affected, deposition and toxic effect are greatest in those tissues which are rich in oxidative enzymes system such as alimentary tract, liver, kidney, spleen and lungs leading to general depression of metabolic activity. The same author also mentioned that nervous signs caused by organic arsenic as a result of inhibition of dehydrogenase enzyme system, e.g. pyruvate, α keto glucourate system) causing degenerative changes while poisoning with arsenilic acid compounds the lesion are mostly in optical nerve causing blindness. In the poisoning with phenyl arsonic group, the nerves of the limbs appear to be affected most. Radositis et al., (2000) mentioned that local skin lesions include initial hyperaemia followed by necrosis and sloughing, leaving indolent lesions, which are extremely slow to heal, increase in the respiratory rate, heart rate, and the pulse small in amplitude. Also Blood and Henderson, (1974), Bentram and Anthony, (1993), and Joseph, (2001) mentioned that the trivalent As absorbed from gastrointestinal tract, skin, respiratory system, all mucous surfaces and the acute form causes gastroenteritis, nausea, vomiting, pain, colic, diarrhoea (rice water), capillary damage, dehydration, shock. Chronic form causes skin damage, loss of hair, bone marrow depression, anaemia, weak pulse, ruminal atony, prostration and high morbidity and mortality rate, while in the subacute form watery bloody diarrhea, depression, dehydration and anuria are prevalent.
The present study showed that following treatment signs become less severe and some disappeared mainly in goats in groups (3-5) but it is clear that the effect of the high dose of the drug was apparent especially in goats of groups (6-10). Additionally the parasitaemia in blood and liver supports our belief that the clinical signs appearing in groups (6-10), and the fatalities, are due to the toxic effect of the drug which contained arsenical molecule specially for the skin lesion, blindness, bloody urine, gastroenteritis manifested by colic, bloody diarrhoea, nervous signs, paralysis, in addition to the presence of fever, changes in respiratory and cardiovascular signs which have also been mentioned by Rubaiul et al, (2004).

It is well known that cardiac muscle is rich in mitochondria (Bloom and Fawcett, 1986 and Banks, 1992). Curtis and John (2003) mentioned that arsenic inhibits the energy-linked functions of mitochondria in two ways: competition with phosphate during oxidative phosphorylation and inhibition of energy-linked reduction of NAD, leading to inhibition of mitochondria respiration resulting in decreased cellular production of ATP, increased production of hydrogen peroxide, which might cause oxidative stress through the production of reactive oxygen species. In the light of this information and our results showing blood pressure decrease in groups (6-10) indicate weakness cardiac muscle of which terminally lead to cardiovascular failure. This belief is in agreement with the findings of Smith, (2001) and Rubaiul et al., (2004). These a single dose at 0.25-0.625mg/kg is toleratable, safe and can therefore be used with safety and efficacy in this animal species.

In the present study most of the goats in group (2) showed moderate to severe congestion in vital organs such as brain, heart, liver, spleen and intestine. In addition, the carcass appeared pale, emaciated, body fat stores are depleted, severe swollen mucopurulent conjunctivitis, scattered foci of alopecia 3-7cm diameter of irregular shape mostly at the abdomen and back of the animals. The buttock region was soiled by offensive watery faecal material, the testes were swollen, the lymph nodes were swollen and congested specially the prescapular, the heart is soft,
flabby and dilated, and the pericardial sac contains straw coulor fluids, the haemorrhagic lesion in the lungs were seen as petechial haemorrhage. These lesions resemble those observed by Elamin, (1980 and 1992), Damayanti et al.(1994), Olaho et al.,(1996), Dam et al.(1998) and Fairouz, (2000). These signs did not change clearly in goats of group (3) but dramatic changes were observed in goats of group (4and 5) where they either disappeared or became slight.

Also the present study showed that in goats of groups (6-10) lesions were moderate to severe and the cardiac lesions became more severe, site of injection swollen, inflamed, orchitis, the liver was significantly enlarged, abomasums approximately empty but, contained slight mucopurlent material, the intestines flatulent and appeared swollen and the blood vessels were congested and the alopica progressed towards normal.

Our present results in trypanosome infected animals which showing diffuse vaculation round the neurons and glial cells proliferation, widening in prevascular spaces in both the brain and the spinal cord in addition to vaculation and irregular axon sheets, degeneration of neurons in spinal cord are in accord with clinical signs exhibited by the animals such as hypothermia (Agag et al., 1993), constricted pupils, shivering, convulsion, muscle tremor in the limb and the neck. Radositis et al., (2000), Moulton et al.,(1976) and Elamin, (1980) mentioned that under similar circumstances severe non suppurative menengioencephalitis or myocarditis may result, degenerative lesions in different organs may also be present. Thomas, et al., (1996/2003) mentioned that T. brucei, T. vivax, T. congolense, caused mononuclear inflammatory reaction in the brain, spinal cord and meningeal. The same author added that T. cruzi caused in the brain, oedema, congestion particularly in the meningeal and some prevascular lymphocytic infiltration and nodules of mononuclear and glial cells may occur throughout the brain in addition destruction of neuron may lead to chronic neurologic sequalae.
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The pathological gross findings are similar to that described by Agag et al., (1993) and Charles, (2003) but, it is noticed that they are more oriented towards the lungs, heart, kidneys, spleen and intestines. The present study showed clear neural pathological changes in the nervous system especially in the cerebellum, cerebrum and spinal cord, where there are vacculation and glial cells proliferation in addition to congestion and haemorrhage. Also the haemorrhage found in the lungs and bronchioles, congestion and haemorrhage in the heart, kidney and liver in addition to lymphocytic infiltration all were indicative of neurocardiopathy, hepatitis and nephritis. The enteritis leads to diarrhoea and decrease of appetite, loss of appetite, emaciation, which all might expose the animals to secondary infections.

Goats of groups (6-10) showed similar lesions as those of group (2) but, these groups were aparasitaemic which means that lesions are attributed to action of the drug containing arsenical molecules. Fever, depression, apathy, constriction of the pupil, muscle tremor and fasciculation, pressing the head and lips against objects, tonic paralysis of the forelimb, shivering, blindness might be due to degenerative changes in the peripheral nerves, cerebellum and spinal cord. Lorgue et al.,(1996), and Radositis et al.,(2000) mentioned that toxicity of arsenic results in lesions in the optic nerves, optic tract, peripheral nerves (sciatic nerve and brachial plexus), kidney, spleen (lymphoid hyperplasia), sensory loss of peripheral nervous system can appear one or two weeks after great exposures, consisting of wallerian degeneration of axons, fragmentation of myelin sheaths and axonal degeneration, in addition to enlargement in liver, bronchopneumonia, flabby heart, cachexia and generalized oedema.

The pneumonic, cardiomyopathy observed in the present study is not surprising in infected goats and it has been mentioned before by Moulton et al., (1976) and Elamin, (1980) these two organs are also affected seriously by Cymelarsan containing arsenical molecule especially in goats of groups (6-10) where the heart becomes enlarged, myocardium yellow, myocardial sac containing fluids where
the right ventricle becomes extended, the ventricle wall is thin with an eventual cardiovascular failure. Curtis and Johon, (2003) mentioned that injection of large doses of arsenic may be fatal, result in cardiac arrhythmia are upper respiratory tract symptoms.

The livers and kidneys in parasitaemic goats showed congestion, sinusoidal dilatation, degenerative and /or necrosis of hepatocyte, while the renal tubules were dilated with increase of glomerular cellularity. These signs are in agreement with what was observed by Elamin, (1992), while the lesion observed in goats of groups (6-10) were more acute and in accord with that observed by Thomas et al.,(1996) and Radositis et al., (2000).

The micro and macroscopic lesions, as well as the colic and the bloody diarrhoea indicate gastroenteritis where the mucous membrane of alimentary tract appeared swollen, epithelium readily coming away when gently rubbed. The inflammatory changes are probably due to the dilatation of the capillaries combined by increase in capillary permeability with passage of fluids in the tissues. In addition, there is direct action in the epithelial cells by arsenic while produce local effect on the alimentary tract mucosa identical to that caused by ingestion or when given through other routes. (Clarcke et al., 1981). The gut contents are very fluid, contain mucous and shreds of mucosa and subendocardial haemorrhages, severe degeneration in liver, kidney, myocardium, optic and peripheral nerves such manifestation are mentioned also in Blood and Henderson (1974).

Horst et al., (1996) mentioned that the immunosuppressive action of trypanosome exceed the actual course of trypanosomosis, secondary infection from other pathogen are activated. Fore example Mwangi et al.,(1990) mentioned that cattle infected with T. congolense produce a decrease in immunosuppressive after the application of B. ancerasis spores suspension than non infected animals. This information supports our belief that gastroenteritis in the trypanosome parasitic disease is due to immunosuppressive effect activating secondary infection. Curtis
and John (2003) mentioned that arsenic is one of the xenobiotics which are capable of immunosuppression.

The RBC might have been destroyed by the parasite or its toxins. (Horst et al., 1996). Spleenomegaly, observed in the spleen of parasitaemic or treated animals, may be attributed to anaemia resulting from excessive destruction of the RBC by the parasite or toxins produced by the trypanosomes. (Horst et al., 1996). But spleenomegaly, observed in the treated goats might have been due to the mode of the action of the arsenical group such that the sulphahydryl groups in tissue enzymes are rich in oxidative enzyme system would promote production of hydrogen peroxide which in turn might produce reactive oxygen radicals (Radositis et al., 2000).

High doses of inorganic arsenical compound given to pregnant experimental animals produced various malformations in fetus and offspring. However, such effects have not been noted in humans with excessive occupation exposure to arsenic compounds (Curtis and John, 2003). Radositis et al., (2000) mentioned that trypanosome caused regenerative changes in infected animals; also he mentioned that the mononuclear inflammation may occur in the uterus. Thomas and Rebecca, 2003) mentioned that the testis lesions caused by T. curzi may be severely elevated where the germinal cells become laden with the organism, intense lymphocytic infiltration occur in the interstitial stroma. Josef, 2001 mentioned that arsenic produce pathological effect on the reproductive system, which is confirmed by our findings that the testis were inflamed and underwent pathological changes which might be attributed to the tendency of As to accumulate in large quantities in this tissues.

In the present study in goats the Hb concentration, PCV% and the RBC count were within the reference interval in goats of groups (4 and 5), but they are decreased in goats of groups (2, 3 and 6-10). It is well known that trypanosomosis causes anaemia attributed to erythrophagocytosis as a result of stimulation and
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expansion of the mononuclear phagocytic system throughout the reticuloendothelium system and to the mechanical cell and tissue damage caused by the active mechanical invasion of the extraordinary strong and mobile pathogens; resulting in spleenomegaly (Horst et al., 1996). This is in agreement with our result where the monocytes increased in the infected untreated group spleenomegaly were manifest.

In the present study anaemia accompanied by reticulocytosis in parasitaemic goats was even more prominent in goats received high dosages of Cymelarsan. The slight increase in the MCV and the decrease in the MCHC indicate that the anaemia is macrocytic and hypochromic. These findings confirmed that the anaemia is regenerative and supported by (Kenneth et al., 2003) who mentioned that in regenerative anaemia the bone marrow is actively responding to anaemia by increased production of erythrocytes, reticulocytosis in addition to monocytosis and hypochromasia. In goats of group (3) anaemia changed to microcytic hypochromic and changes in the MCV values indicate defective erythrocytes maturation. The observation in group (3and 6) where the content of serum iron is decreased indicates also iron deficiency anaemia.

In camels the decrease in the Hb concentration, PCV%, RBC count is indicative of anaemia, which is macrocytic, and hypochromic as the MCV increased while MCH and MCHC decreased, Anosa, (1988a) and Kenneth et al., (2003) mentioned that T. evansi caused regenerative haemolytic anaemia.

In the present study dosages of Cymelarsan in goats of groups (4and 5) caused dramatic response and results were shifted towards normal values. In goats, which received multiple dosages of the drug, the reticulocytosis and the increased MCV, is more prominent indicating regenerative anaemia. However the hyperchromasia is surprising. Steven et al., (2002) mentioned that if there is an increase in MCHC value, the value is usually an erroneous value and the true value may be within reference interval or even decreased and the pathologic conditions that can cause
true increase in MCHC value are rare. Steven et al.,(2002) and Kenneth et al.(2003) mentioned that trypanosome spp. causes haemolytic anaemia of unknown pathogenesis and caused splenomegaly, monocytosis, thrombocytosis (platelet), hyperproteinaemia suggesting that the anaemia is of an extravascular type. But in goats which received the drug in high doses (five times the recommended dose or multiple dosages), the anaemia may be haemolytic and of intravascular type though it is mild to moderate. Where there is slight increase in the total bilirubin and the unconjugated bilirubin, this might mean that the liver is still capable of removing the bilirubin from plasma. In addition the increase of the MCV and MCHC indicate cell membrane deformity as glutathione reductase, one of the enzymes which contain thiol group, was possibly inactivated by the arsenic molecules present in the drug. Further toxic substances released when the parasite is destroyed within the circulatory system have been reported to damage the lining of the blood vessels.

Platelets, also referred to as thrombocytes, increased mildly in the present study in parasitaemic groups. The present study showed that experimental animals express cellular defense mechanisms (through neutrophilia except group (4 and 5) where they are within reference interval). Goats receiving high dosages of the drug showed immunosuppressive effects of humoral nature as the globulins were decreased significantly with concurrent decrease in the lymphocytes and monocytes.

The present study showed that there are no changes in serum sodium, potassium and chloride concentrations and the slight decrease or increase in the experimental animals is within reference intervals. Also in the present study decrease in the PCV, high total proteinaemia and albuminaemia, and the loss of body weight are indicative of dehydration especially in parasitaemic group and those receiving high doses of Cymelarsan. Itazi and Inyaru, (1975) discussed the urinary change in rabbits chronically infected with *T. brucei brucei* they found that in the observed proteinurea, relatively were globulins than albumins were excreted and suggested
that renal malfunction might be one of the cause of death in rabbits infected with this trypanosomes species.

The dehydration might be attributed to loss of appetite or inability of the animals to move towards water points as a result of recumbency and/or weakness of the hind limbs. Kenneth et al., (2003) mentioned that normonatraemia can occur when there is decreased extra cellular fluids (ECF) H2O (isotonic dehydration) in cases of diarrhoea, exudation, gut fluid sequestration, haemorrhage and renal diseases. He mentioned that hypernatraemia can occur when there is decreased ECF H2O (hypotonic dehydration) in cases of diarrhoea, loss of Na-rich fluids and renal diseases. Also Kenneth et al., (2003) mentioned that hyperkalaemia results from changes in internal balance (shifts of K ions from intra cellular fluids (ICF) to ECF) in cases of diarrohea, marked muscle exertion (mild K⁺ increase) and massive tissue necrosis in the one hand, and on the other, hand hypokalaemia can result due to changes in external balance(decreased K⁺ intake or increased K⁺ loss to environment) where there are anorexia (specially herbivores), loss of gastrointestinal fluids, abomasal stasis and diarrhoea or through increased renal loss (kaliuresis).

The present study in goats showed that the serum Cl⁻ concentration is increased in the experimental groups compared to control group but the slight increase observed in serum Cl⁻ concentration is still within the reference intervals. Steven et al., (2002) mentioned that hyperchloraemia typically occurs when there is hypernatraemia or when there is a decreased (HCO₃⁻). Generally changes in Cl⁻ are related to attempts to main electrical neutrality and it is well seen in cases of water deficit, metabolic acidosis (alimentary loss of HCO₃- diarrhoea- and renal loss of HCO₃ and the respiratory alkalosis.)

The present study showed that serum calcium and phosphorus follow a declining trend, though within the reference interval. But goats of group (6) which received a single five times the recommended dose showed severe decline in the value of
Pharmacotoxicity of some trypanocidal drugs in food animals (Nubian goats and camels) serum calcium and phosphorus and an increase in the serum magnesium. The serum calcium and phosphorus is decreased significantly in goats of groups (3and 6), and we believe that this decrease can be attributed to the prolonged anorexia and recumbency in addition to the gastroenteritis which might hinder mineral absorption, or might be due to renal excretion. Respiratory alkalosis and metabolic acidosis might have played a role in the calcium- phosphorus picture.

Also the present study showed no significant changes in the serum concentration of urea and creatinine, GPT activity while there are slight increases in the activities of serum GOT and SDH in most of experimental groups. The gross and histopathological findings indicate that the parasite and the high drug dosing levels have an effect in the liver (hepatocytic degeneration and/or necrosis) and in the kidneys (disappearance, lobulation and hypercellularity of some glomerular, renal tubules might be dilated and some of the epithelial cells have undergone degeneration and/or necrosis). Kenneth et al., (2003) mentioned that significant renal disease may be present in the absence of clinical signs or laboratory abnormalities due to the extensive reserve capacity of the kidney, and urea excretion in ruminants is governed by nitrogen intake where animals that are on a nitrogen –deficient diet or that have severe anorexia excrete almost all blood urea via the gastrointestinal tract and very little via the kidneys. Therefore urea can be within the reference intervals in some ruminants with severe renal disease. Decreased urea production via decrease hepatic urea cycle function occurs in cases of hepatic insufficiency. The same author mentioned that creatinine is freely filtered by glomerular and tubular reabsorption. Thus serum creatinine is a more accurate measurement of GFR and the creatinine concentration is a more sensitive indicator of renal diseases in cows and horses than BUN because in these species the potential for gastrointestinal excretion of creatinine is limited in contrast to urea.

Steven et al, (2002) mentioned that hepatocyte of horses and cattle have so little ALT that ALT is not a useful marker of hypatocyte damage in these species. The
same author also mentioned that AST is a common marker of hepatocytes damage, but muscle damage, haemolysis and other processes also increase serum AST activity. Far away the SDH indicates hepatocytic damage and used primary in horses and cattle because other common hepatocytic cytosolic enzymes (AST and ALD) are not liver-specific. The slight increase in the serum activity of LDH and CK is attributed mostly to muscle damage (mostly skeletal, occasionally cardiac, rarely smooth). Also it is noticed that the fluctuation in the serum activity of AMS (amylase) and LBS (lipase) is within reference intervals and might be due to the dehydration.

Generally we belief that trypanosome has a clear pathologic role on the kidney and the liver, which is indicative of the rise in the activities of serum GOT and SDH, in addition to the electrolytes imbalances. This phenomenon is more prominent in groups, receiving high doses of the drug and where the parasitaemia is treated. It is obvious that the drug also has a serious fatal role in the parasite-precipitated lesions.

Post treatment with Cymelarsan and oxytetracycline alone or combined, camels were healthy full, regain their appetite, all the clinical signs pathological findings disappeared and blood chemistry, haematological parameters within reference interval. But serum concentration of total protein, albumin, globulin, cholesterol, glucose and triglyceride, are also improved but slowly.

The present study showed that the thyroid gland in goats is exposed to pathological changes such as loss of thyroid tissue, although we did not measure the gland activity but we belief there is hypothyroidism (Mutayoba et al, 1992 and Abeb et al., 1996). The hypercholesterolaemia, hypercortisonaemia, hypertriglyceridaemia and hyperlipoaemia although mild, can be attributed to the hypothyroidism. Mutayoba et al, (1992) mentioned that trypanosome-induced hypothyroid status may play a role in the impairment of mitochondrial ATPase activity, a key enzyme in energy metabolism. Also the present study showed that
Slight hypoglycemia is observed in parasitaemic group and groups receiving high dosages of the drug. It is well known that trypanosomes consume glucose and essential nutrient, in addition the prolonged anorexia and starvation also leads to hypoglycemia.

Ralph and Hung (1944) mentioned that the toxicity of arsenical compounds is primarily a function of the degree to which they are bound by tissues, and that the red blood cells form a valid model for the body tissues constitutes a reliable index of systemic toxicity, as the sequence of events in the blood stream reflect what occurs in body tissues. After leaving the blood, toxic compounds were firmly bound by the organs and relatively high levels were found in the liver and kidney 48hrs. after the injection. This supports our findings that tissues such as liver, spleen, kidney, heart and lung, can accumulate considerable amounts of arsenic as these organs contain large quantities of the enzymes containing thiol groups. Bujon, (1990) mentioned that the general maximum tolerated dose at the range of 3-5 mg/kg (12-20 times the recommended therapeutic dose) gives a large safety margin when therapeutic doses are used in camels.

The nervous system contains large amounts of fats and repeated administration of the drug revealed a tendency of the drug to accumulate in the fat and nervous tissues which support our clinical and pathological findings in the nervous system agree with this phenomenon.

Zweygarth et al., (1992) mentioned that Cymelarsan is partially effective at doses of 0.625 mg/kg, but the present study shows that doses higher than 0.625mg/kg can be effective in treatment of trypanosomes of the CNS but unfortunately such doses proved to be fatal. Drug accumulation might have taken place due to the fact that large and repeated doses are over the capacity of the vital organs responsible for the arsenic detoxification and excretion. The accumulation of arsenic at high levels in the muscles and site of injection in parallel to our results where myositis at the site of injection took place due to the irritating effect of arsenic to tissues.
Many studies report that injection of the drug I/M caused swelling and inflammation but it disappeared gradually (Bujon, 1990 and Lun et al., 1991). Also Kenneth et al., (2003) mentioned that arsenic caused degeneration at various levels to muscular tissue thereby accounting for the weakness of the animals and their inability to move ending in a state of recumbency. Tager-Kagan et al., (1989) reported that at a dose of 3.7mg/kg of the drug induced significant necrosis of tissue at a point of injection.

It is noticed that in camels the serum, kidneys, site of injection recorded the highest values compared to the other organs. The minimum effect concentration of Cymelarsan to killed trypanosomes is 0.005-0.04 µg/ml this is supported by Zhang et al., (1992) who studied the sensitivity of *trypanosoma evansi* in vivo and *in vitro*. While Sones, (1991) mentioned that residues of total arsenic were noted in fat, liver and kidney all result of assay for total As were less than 2mg/kg, no residues were observed in plasma, no residues in one camel seven days after treatment when he studied the residues in seven infected camels in Kenya were treated with 0.25 mg/kg of Cymelarsan I/M and slaughter either 7days, 14 or 21. Toutain, (1989) mentioned that RM 110 was rapidly and completely absorbed after S/C injection 24h. when 0.1, 0.15, 0.2 or 0.3 mg/kg injected in Morocco dromedaries.

In goats which received half recommended therapeutic dose twice a week for two weeks or once weekly for three weeks in camels the picture is surprising as goats recorded higher values of As than that recorded in camels. This may be due to species difference. Cymelarsan which has arsenical molecules, has a high affinity to pound to RBC compared to that of the camels this supported by the increase level of arsenic in goats especially goats that received the recommended dose twice a week for two weeks and also by the high concentration of As in kidney and urine in goats compare to that of camel. This might be attributed to that camel having other route of excretion of arsenic. It could be through saliva or faeces or it might be deposited in bones. Or the camels might have a high capacity to excrete arsenic throw the kidneys rapidly in less than 28days post treatment. The
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Accumulative effect in goats is more evident than in camels which might explain why camels can tolerate five times the recommended therapeutic dose and also supports what was reported by Bujon, (1990) who mentioned that camels can tolerate 12-20 times the recommended therapeutic dose.

The presence of trypanosomosis relapse after treatment is not a surprising as, Losos and Ikede et al., (1972), Baltz et al., (1989) and Payne et al., (1994) mentioned that infection with brucei group of trypanosomes is usually associated with the presence of extravascular parasites sequestered in sites where the drug cannot penetrate. Trypanosomes in sites such as the brain and cerebrospinal fluids are protected from certain drugs by the blood brain barrier. Yet Cymelarsan was effective in the treatment of trypanosome infections involving the central nervous system suggesting that the drug can cross the blood-brain barrier.

Treatment with OTC-LA at 100mg/kg, 20 mg/kg twice a week for two weeks and 20mg/kg daily for 8 days showed period of free parasitism in the peripheral blood followed by a relapse of mild parasitaemia. Dosages of daily 20mg/kg for 8 days have fatal end 16 days post treatment. This result is supported by liver impression smear where the livers were cleared 21 days post treatment and after cessation of the drug. Fairouz, (2000) found that the oxytetracycline decreased parasitaemia in Nubian goats by 75%, death occurring by 7 days later. The relapse in trypanosomosis it might be attributed to maturation of immature stages of the trypanosome (Solusby, 1983). Relapse also depends upon the concentration of the drug or its metabolism in the blood circulation acting on certain stages of the parasite. The present study also indicates that the animals can tolerate single dosages up to 100mg/kg and also can tolerate multiple dosages of 20mg/kg weekly for 3 weeks or twice a week for two weeks, but dosages of daily 20mg/kg for 8 days result in fatal ends.

When OTC-LA is given to camels in recommended therapeutic dose it failed to clear peripheral blood or liver tissues from the parasite and the animals died 20 day post treatment. However, when the drug is given at two and half and five fold
curative dose or the curative dose twice weekly for two weeks it was capable of freeing the parasite only from the peripheral blood approximately 21 days, mild relapse occurring.

The clinical signs observed in *T. evansi* infection in goats or camels were generally similar.

Goats which received the daily therapeutic dose for 8 days didn't tolerate the drug, and the animals dying on day 18 this may be due to species-oriented phenomena. Sharp decrease in pulse rate, blood pressure and respiratory rate in goats which receiving the drug with fatal end may be attributed to the pneumocardiopathy which end with circulatory insufficiency.

Macroscopic and microscopic changes observed in infected treated or untreated goats are indefinite. However, changes as observed in goats are dramatically reversed in camels infected with *T. evansi* and treated with OTC-LA this may be attributed to a species difference.

Increase in WBC counts might be due to the irritant effect of the drug at site of injection (Bywater et al., 1991). Decrease in the lymphocytes may be accounted for by the fact that trypanosomes have immunosuppressant (Hamnies et al., (1991) and Sellon et al., (1997)). But, the increase in platelet and reticulocyte counts may indicate of haematocrisis stimulation (Schalm et al., (1985)).

The slight increase in serum of potassium, chloride in addition to decrease of calcium, phosphorus as well as the decrease in the T3, T4 in addition to the pathological changes in some groups infected with *T. evansi* and treated with either single or repeated dosages indicate renal and/or metabolic disorders and acid-base imbalances.

Similarly, serum potassium level was decreased in camels in infected with *T. evansi* (Anosa, 1988b) and also in infected *T. evansi* goats (Fairouz, 2000), serum calcium and serum phosphorus decrease in *T. evansi* infected goats (Elamin, 1980 and Fairouz, 2000) while no changes were recorded in serum sodium level was seen post infection (Anosa, 1988b, Otsile et al., 1991 and Fairouz, 2000).
Both oxytetracycline and tetracycline are eliminated unchanged primarily via glomerular filtration. Patients with impaired renal function can have prolonged elimination half-lives and may accumulate the drug with repeated dosing. These drugs apparently are not metabolized, but are excreted into the GI tract via both biliary and nonbiliary routes and may become inactive after chelation with fecal material. (Pfizer, 2005).

It is noticed that goats which received the daily program recorded least phosphorus value and recorded high manganese serum level and Melvin and Swenson, (1995) reported that higher level of manganese interfere with the retention, also Myra et al., (1981) mentioned that manganese ions antagonism has been observed in baby pigs and a level of 50-150ppm of manganese with a diet interfere with haemoglobin formation.

Also it is noticed that slight decreases were observed in iron in repeating dosing program this may cause iron deficiency anaemia. The death may be due to anaemia or vital organs. Curtis and John, (2003) mentioned that tetracycline and chlortetracycline is a drug associated with the development of a plastic anaemia, also the same author mentioned that tetracyclines is one of cyanobiotic that developed specific coagulation factors inhibitor (Von willebrand) factor. Also the same author mentioned that OTC-LA has cardiotoxicity manifested by negative entropic effect through decreasing Ca-ions.

Amodu and Ige, (1975) elucidated the mechanism of development of anaemia in rabbits experimentally infected with T. brucei and concluded that the anaemia is possibly a result of an auto reaction together with anaemia and specific organ damage, a wider range of immunological abnormalities appear to characterise the pathology of the disease.

Slight increase were observed in GOT, which might be attributed to the degeneration in muscle, liver because it is not a liver specific enzyme, muscle, kidneys, heart….etc(Varley, 1965).
Also the present study indicates that camels which are *T. evansi* infected are responding and tolerating OTC-LA at total doses ranged of 50-160 mg/kg where the serobiochemical improved when there is increase of dosages. The drug at single I/M 50-100mg/kg or 20mg/kg twice a week for two weeks reduced trypanosomosis in the blood, liver tissues 75% and kept the animals alive survived with mild parasitaemia for 49 days post treatment. This might justify the use of OTC by the Vets in the Sudan with a view to overcoming the immunosuppressant effect of trypanosomes concomitant with conventional trypanocides.

The present study show for the first time that OTC-LA at 20mg/kg daily for 8 days is curative tolarable and not toxic in camels infected with *T. evansi*. This is remarkable as animals survived even after 49 days post treatment.

It is noticed that in all groups, infected or infected treated, the body weight is not retain to that of group (1) until the end of experiment and its also noticed that most of these groups showed triglycerideaemia, phospholipidaemia and also an slight increase in cholesterol and glucose levels. In addition, liver and kidneys showed slight fatty changes.

Like the findings of Benzo, (1987) OTC-LA increased hepatic lipids and depressed body weight. Soback *et al.*., (1987) studied the pharmacokinetic changes of several antibiotics in children inducing fatty liver and found positive.

The amount of the drug which absorbed from the site of injection was higher in camels than in goats approximately 5 folds. It is clear that the drug is cleared rapidly in camels than in goats which might be due to factors associated with the species differences in excretion and metabolism. (Bloom and Fawcett, (1982) and Banks, (1989)).

The present study showed that the concentration of the drug in urine and bile is higher in camels than in goats and it released up to 5.5 µg/ml which is the therapeutic figure (Xia *et al*.1983). Oorgans such as testis, ovary, uterus, leg muscle, site of injection in camels recorded higher values than that of goats but the tendency of drug to accumulate in fat of goats was higher by 4 folds than that of
camels while, the drug accumulation in the cerebellum and was more in camels than in goats although the nervous tissues contained large amount of fat and this might be attributed to physiological barriers of the body.

Similarly the residual concentration of the drug in the liver and kidneys was camels than in goats of these results generally indicate that the drug attains higher concentration in the body fluids and tissues of camels more than in those of goats. This might be due to the kidneys as this is a major route of excretion of OTC-LA after paraenteral administration.

There is good correlation between the levels of OTC-LA in the serum and in the liver, kidneys in camels while this correlation is not observed in goats.

Luthman and Jacobson, (1982) mentioned that the plasma concentration of OTC-LA exceed 0.5 µg/ml therapeutically active concentration for about 60hr. in calves. Bertzlaff, et al., (1982) mentioned that the concentration of OTC in plasma is 4.86+0.45 µg/ml, 5 µg/ml in uterine tissues when single I/V dose 22mg/kg of OTC was given to cows. a serum level of 12µg/ml cleared the parasites from the blood and liver tissues and terminated fatal.

The committee for veterinary medical products (CVMP) of the European agency for the evaluation of medicinal products (EAEMP, 1995) evaluated OTC-LA in the past, and established an acceptable daily intake (ADI) of 0-0.003 mg/kg bw based on the human gut flora. Based on this ADI and taking into account the typical residue distribution of OTC-LA in tissues, the following maximum residue limits (MRLs) established by 36th joint FAO/WHO expert committee on food additive (JECFA) were adopted: kidney 600 µg/kg, liver 300 µg/kg, eggs 200 µg/kg, muscle 100 µg/kg, milk µ100 g/kg. It was concluded that the antimicrobial potency of chlortetracycline and tetracycline is comparable to that of OTC-LA, the JECFA established a group ADI of 0-3 µg/kg b.w. for OTC-LA, tetracycline and chlortetracycline alone or in combination, the highest levels are in the kidney and liver, but they are not detectable in fat to any great extent. For the complete recovery compounds, the 4-epimers of OTC-LA, tetracycline and chlortetracycline, have to determine. The 4-empires of the compounds occur in
samples and are formed during sample preparation. The 4-empires are in equilibrium with the parent compound. Therefore, the marker residue is the sum of the parent drug and its 4-empires. (EAEMP, 1995).

The present study showed that when Cymelarsan and OTC-LA combination was given at half recommended therapeutic dose of both in goats which infected with *T. evansi*, the parasite is cleared from the peripheral blood by 50% and the animals were died at day 15 post treatment. The death is attributed to trypanosomosis. But when Cymelarsan administered at the half recommended therapeutic dose combined with OTC-LA either at two and half recommended therapeutic dose or at twice/week for two weeks or daily for 8 days, the blood was completely free from the parasite. It is also noticed that the liver is free from the parasite in the repeated dosages program. In single dosages the parasite was found in the liver at 25-50% after period of relapse for approximately two weeks post treatment, the combination cleared the blood and the liver from the parasite without death when given to camels naturally infected with *T. evansi* this seems to be in agreement with previous findings (Anosa, 1988a; Losos and Ikede *et al.*, 1972, Baltz *et al.*, 1989 and Fairouz, (2000)). The death in the daily treatment combination program is attributed to the toxic effects of these drugs although the blood and the liver are free of the parasites.

A good health improvement as judged by clinical signs, pathological findings and haematological and serum biochemical result, was observed in goats which received the combination of the half recommended therapeutic dose of Cymelarsan with single or two and half recommended therapeutic dose of OTC-LA. The same dose of Cymelarsan given with OTC-LA at the recommended therapeutic dose twice a week for two weeks or in treated camels, indicated that the combination was toleratable and successful to overcome the infection but when the combination was given at daily program the goats died although the blood and the liver were free of the parasite. Signs of Cymelarsan toxicity were noticed including hyperthermia, sharp decrease in the pulse rate, blood pressure with increase in the respiratory rate. All these indicate involvement of respiratory
and circulatory systems, in addition to the nervous system as indicated by the histopathological, lesions observed in the nervous tissue.

The measurement of the concentrations of Cymelarsan and OTC-LA residues in tissues, urine, bile and serum of camels and goats confirm the previous results obtained clinically, pathologically, haematological and on serum biochemistry where most tissues recorded normal values by the end of slaughter program and it is noticed that as OTC-LA increased the accumulation of arsenic is decreased specially in camels and this is explained the tolerating capacity in this species. In the present study when we compared the serum concentration of OTC-LA which was capable to eliminate the trypanosomes from the blood and tissues, and that of the in vitro study, it is found that both results were in agreement, where 4µg/ml and above of OTC-LA is needed to eliminate the parasite.

Combination preparation, may act by complementary mechanisms at different sites, or one of the drug may potentiate the clinical efficacy of the other by altering its distribution, biotransformation or excretion. (Baggot, 2001). Drugs are often given in combination with potentially beneficial or adverse effect results. When two drugs are given together, their effects may be additives, the final being the sum of the individual effects. Alternatively, the interaction may be synergistic, the effect then being greater when two drugs are given together than one would expect from their effect when given alone (Girdwood, (1978) and Bentram and Anthony, (1993).

This supported with Onyeyili et al., (1999) mentioned that the combined use of isometamidium chloride and difluromethylornithine in immunosuppressed rabbits, none of the treatments was effective in immunosuppressed rabbits at doses that were 100% effective in immunocompetent rabbits while, in Egwu et al., (1993) the combined use of isometamidium and difluoromethylornithine(DFMO) in rats infected with *T. brucei* in late stage was successful.

Mishra et al., (1983) mentioned that the treatment of infected cattle with *Theileria annulata* with three injection of Berenil with one injection of achrornycin for
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seven days with supportive administration of OTC, tetracycline, Belamyl, Novalgin, Mifex and Tonophosphan brought about the clinical recovery of the animals with marked reduction of parasitaemia and considerable rise of haemoglobin level. Treatment with Berenil- Oxysteclin combination for 6 days also gave comparable results. The administration of Berenil alone (3 injection) with supportive therapy some relief but there was recurrence of the clinical symptoms within 3-7 days. Dicrysticin administration was not found to be effective.

Also Baggot, (2001) mentioned that the synergistic antimicrobial effect produced by trimethoprim-sulphonamide combinations is due to the sequential blockade in bacterial biosynthetic pathway for folic acid. Also, pyrethrin- piperonyl butoxide is potentiated insecticidal efficacy of pyrethrin, penicillin-probenecid is increased the duration of effective penicillin concentration.

Also it is agree with Wooly et al., (1984) who found a synergistic inhibitory acquired was observed with combination of EDTA-tromethamine plus penicillin, nalidixic acid, OTC, chloramphenicol, polymyxin-B, sulfamethazine, sulfapyridine, and sulfathiazole and a synergistic effect was not recorded with combination of EDTA-tromethamine and streptomycin.

The efficacy of Cymelarsan when given at single I/M of 0.125mg/kg b.w. once or daily for 8 days resulted in complete clearance of the parasite from the peripheral blood and liver tissue and the animals survived until slaughter time or death. When the same dose was given to goats infected with *T. evansi* supported by the administration of 12 µmol/l zinc and copper once or daily for 8 days, the peripheral blood and liver tissue were completely free from the parasites and death occurred in repeated dose. This is in agreement with Baqui et al., (2002) who studied the effect of Zn supplementation on morbidity and mortality in Bangladeshi children with diarrhoea and found that Zn supplementation in children in a dose of 20mg/day for 14 days significantly decreased the incidence of diarrhoea and acute lower respiratory tract infection and attributed that to improved absorption of water and electrolyte by the intestine (Golden and Golden, 1985) and faster regeneration of gut epithelia (Bettger et al., 1981).

The present result are in accord with those of Mir Misbahuddin and Kamaluddin, (2002); that goats which received daily Cymelarsan which contain As molecules caused the same signs and lesions of arsenicosis although goats which received Zn and Cu supplemented Cymelarsan in a daily program, but it is worth to mention that Cu, Zn slightly improved the clinicopathological findings and most of the haematological and serobiochemical parameter which were measured compared to that which is given Cymelarsan alone or for 8 days program, that the
administration of Zn has a dramatic response in treatment of As when given for short period, this is clear in goats which received half therapeutic dose supplemented by the improvement of Cymelarsan in treating trypanosomes within 10 days without relapse or death until day 42 the end of the experiment also this in agree with Styblo and Thomas and Rebecca (2003) who observed that simultaneous administration of selenium and Zn may enhance the toxic effect of As, increasing its retention in tissues and suppressing its methylation, which may be a pathway of detoxification of arsenic. It is worth also to mention that this dose of Cymelarsan is weak for treating trypanosomosis and it is also worth to mention that clinical signs and pathological findings in addition to hematological and serobiochemical measurement were to worth the health goats. This is to enable the organs, tissues and the immunosystems to overcome the stress and damage cause by trypanosomosis.

The high content of urine with As in the group which supplemented with Zn and Cu compared to that which was given Cymelarsan alone in the 8 days program of the treatment, means that supplementation with Zn and Cu improved the metabolism and the excretion of Cymelarsan which contain arsenical molecules. In the group which received single half the curative dose, the concentration of As in the serum increased by 4 folds which mean that supplementation of Zn and Cu improved the absorption of As and this is in accord with (2). The same phenomena was observed in the site of injection. This is in agreement with Mir Misbahuddin and Kamaluddin, (2002) who found that oral administration of both zinc and arsenic when given for one month at a dose of 1mg/kg/day and 20 µg/kg respectively, is effective in the prevention of arsenic accumulation in different tissues such as spleen, lungs, kidneys, intestine and skin, but it is quite surprising that simultaneous administration of zinc and arsenic increase the accumulation of Zn in different tissues particularly kidneys and spleen. The mechanism by which Zn increases the accumulation of As is not known.

It is well known that copper is an integral part of the cytochrome system. Such enzyme as tyrosinase, laccase, ascorbic acid oxidase, cytochrome oxidase, plasma
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mono amine oxidase, erythrocuprin, urecase, superoxide dismutase contain Cu and their activity is dependant on this element. Zinc is a functional component of several enzymes systems such as carbonic anhydrase, carboxypeptidase, alkaline phosphatase, lactic dehydrogenase, glutamic dehydrogenase, also zinc is important in an enzymic system, necessary for synthesis of ribonucleic acid and is found in the pancreas, exhibit an active metabolic turnover and is important of maturation of spermatozoa (Melvin and William, 1993).

The study of the toxicity and efficacy of quinapyramine in goats infected with *T. evansi* showed that the drug at 5-25 mg/kg cleared the parasite from peripheral blood and liver tissues without fatalities. Also, the drug at 5 mg/kg b.w. weekly for 3 consecutive weeks cleared the peripheral blood and the liver tissue. But at 5 mg/kg daily for 8 days the drug cleared the parasite from the peripheral blood and the liver tissue, followed by death 12-20 days post treatment. The results indicate that the drug has fatal accumulative properties at 25 mg/kg as a total dose.

It is well known that trypanosomosis caused hypothermia, lacrimation, nasal discharges, depression, and diarrhoea, loss of appetite, loss of body weight, decrease of pulse and respiratory rates, emaciation then recumbency terminating in death (De-Villa *et al.*, 1991 and Fairouz, 2000). Other sings such as keratitis, alopicea, orchitis, and hypothyroidism were also reported (Mutayoba, *et al.*, 1992 and Abebe and Eley, 1992). These signs appear mild or absent in treated groups, but signs such as loss of appetite emaciation, loss of body weight, diarrhoea, decrease in blood pressure, pulse rate, increase in respiratory rate might be attributed to high dosages of the drug. Clarcke *et al.*, (1981), Alexander, (1985) and Girdwood, (1979) support our findings.

It is clear from the present study that an effect has been observed on CNS exemplified by cerebellum, cerebrum and spinal cord especially in trypanosome infected groups and more in cases which received the drug at 50mg/kg r.t.d. and 5 mg/kg r.t.d. repeated weekly for three weeks or daily for 8days. Also the later
groups showed an effect on thyroid gland, lungs, liver, kidneys, intestine and testis if compared to groups which received the drug at 5-25 mg/kg I/M.

Drug detoxification may be reduced and the drug becomes more toxic in animals with damaged liver or kidneys. Clarke et al., (1981) mentioned that post mortem findings include acute inflammation of gastro intestinal tract and nephrosis. Some toxins in drugs decrease the microsomal enzymes in the liver and so decrease serum enzymes activity (Ford et al, 1972).

Our results show that the parasite might have stressed the vital organs. Death might be attributed to histamine release and /or anticholinergic effect on stressed organs. Clinicopathological effects such as decreased blood pressure and pulse rate may be related to hydroperitoneum and hydropericardium, cardiomyopathy, hepatitis, nephritis, pneumonitis, orchitis and thyroid gland insufficiency.

The pathology of animal trypanosomosis was given in more details by Ikede, (1975) although the disease caused by the various species of trypanosomes has certain features in common, the types and mechanisms of injury done to the host may vary considerably with the species.

Haematological changes induced by trypanosomosis mostly returned to reference values although goats given 50 mg/kg b.w. needed more time to regain fully reference interval values. The increase in basophils and eosinophils in the infected group is well documented (Anosa, 1988b and De-Villa et al., 1991) but the presence of the eosonophils and basophiles in treated groups could be attributed to induced histamine release by the drug (Bentram ant Anthony, 1993).

The increase in serum sodium and chloride, in addition, to decrease in calcium, phosphorus, copper, and zinc is a sign of nephritis. The increased potassium, total bilirubin, direct bilirubin serum concentrations are indicative of haemolytic anaemia which might be attributed to toxins resulting from the dead parasites (Clarcke et al., 1981) or might be due to the effect of the drug on RBC membrane (Bywater et al.,1991).

The anaemia noticed in the eight days program is normochromic macrocytic, but there is evidence of iron, zinc and copper deficiency; these trace elements play a
role in the synthesis of haemoglobin and RBC (Varley, 1965). Or it might be attributed to loss of weight, loss of appetite and recumbency that the animals unable to reach the sources of food and water. Also increase in the creatinine in the eight day program is indicative of nephrosis. Non increase in urea in these groups (6and 8) is not surprising as nephritis occurred in these species without increase in urea. Consequently PCV decreased, hyperproteinaemia and albuminaemia thereby indicating haemoconcentration. The haemoconcentration can also be attributed to the drug inducing histamine release (hydroproteium and hydropericardium) (Bentram and Antohny, 1993).

The increase in serum SDH activity is an indication of liver necrosis and the decrease in serum activity of amylase and lipase indicate an effect of the drug on the pancreas. The increase in serum cholesterol concentration might be a consequence of hypothyroidism. Hypothyroidism and decrease of progesterone accompanying T. evansi infection is well known (Mutayoba et al., (1992) Osaer et al., (1998) and Fairouz, (2000)) but it is reverted to reference intervals when the is drug administered at a single dose of 5, 12.5 mg/kg, or at 5 mg/kg dose weekly for three weeks. The situation worsened in goats receiving single 50 mg/kg or 5 mg/kg daily for 8 days. This effect may be due to the action of the drug. The present study revealed increased globulin concentration at high doses the cellular defense mechanism might not have been affected seriously; Itazi and Inyaru, (1975) discussed the urinary change in rabbits chronically infected with T. brucei brucei they found that in the observed proteinurea, relatively were globulins than albumins were excreted and suggested that renal malfunction might be one of the causes of death in rabbits infected with this trypanosome species.

The study of showed of the toxicity and efficacy of ethidium in goats infected with T. vivax that T. vivax caused death within 13-17 days while T. evansi caused the death of goats within 7-11 days. These results indicate that T. evansi is more pathogenic and goats are more susceptible to T. evansi when the same counts of trypanosomes were used. Goats receiving single 1 mg/kg doses the peripheral blood was not cleared of the parasite completely and the animals died within 16-
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20 days post treatment. This is supported by Elmalik, (1983) who studied the efficacy of the same dose of *T. vivax* infected in goats, relapse and death occurred. Variation in the time of death might be due to the strain used.

Maxie, (1976) mentioned that in both goat and cattle infected with *T. vivax* parasitaemia was detected 6-7 days after inoculation with $1 \times 10^5$ but not in *T. congolense* infection. Mwambu, (1975) re-evaluated the value of ethidium for the treated of *T. brucei* subgroup infection in cattle and concluded that the use of this drug as a curative in *T. brucei* infection of cattle should be restricted. Kalu, 1983 observed complete disappearance of *trypanosoma vivax* from the blood 3 days after treatment with homidium bromide, berenil and samorin.

The clinical signs observed with *T. evansi* and *T. vivax* was not different, though they were more severe in *T. evansi* as observed by (Mubarak, 2002). Ethidium at single I/M 2.5 I/M mg/kg or at 1 mg/kg weekly for three weeks eliminate the parasite from the peripheral blood and liver tissue and the clinical signs are capable to the health status improved but doses such as single I/M 5 mg/kg or 1 mg/kg daily for 8 days worsen the health of the status of the animal although they are free from the parasite while, the single I/M 1 mg/kg partially eliminates the parasite, but death occurred after 16-20 day for 60% of the goats. The relapse of *T. vivax* is an ordinary phenomena where in our present study it occurred in 35 days.

The diarrhoea observed in infected or uninfected treated group may be a consequence of irritation of the intestine by the toxic metabolites of the parasite or toxic ingredients of the drug.

The hyperthermia and hypothermia is controversial, Elmalik, (1983) and Elamin, (1980) observed hyperthermia in trypanosomosis, but Fairouz, (2000) and Mubark, (2002) observed hypothermia; which may due to the different strains used.

Fever, increased in heart rate, anorexia, emaciation, and elevation of anaemia, body temperature were observed in *T. vivax* infected goat was also observed by Maxie *et al.*, (1979) and Ugochukwu, (1986). So acute and chronic forms of
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Anaemia in trypanosomosis has been attributed to inhibition of haemopoiesis (Losos and Ikede, 1970).

The pathological findings of Masake, (1980) in *T. vivax* in East African goats, Frisian cattle showed major changes in the lymph nodes, spleen, eyes, pituitary gland, testicles and heart, in infected Zebu cattle with *T. vivax* and *T. congolense* and treated 12th week post infection with Novidium and slaughtered for histological evidence of healing of the genital lesions in Sekoni, (1990) study, also in Isoun, (1975) observation *T. vivax* infected mice was generalized fibrin thrombus formation in the blood vessels of heart, lung, spleen and brain support our findings.

With ethidium the health of animals free of the parasite deteriorated to a fatal end sometimes. This might have been due to adverse effects of the drug on neural structures both centrally and peripherally, supporting the findings of Curtis and John, (2003) who observed cellular basis of neurotoxicity which included intramyelinic oedema, status spongiosis of white matter. And, those of Riet-Correa et al., (2002) who observed demyelination on the sciatic nerves in adult Wister-rats; schwann cells showed vacculated cytoplasm and separation of the sheath from the axon. With increase doses of ethidium collagen fibers also increased in number and progressively involved swollen number of remyelination axons composing new fascicles. In the present study neurocardiopathy is evident which might be attributed to cholinesterase inhibition.

Increase in blood plasma volumes and decrease in Hb, RBC, PCV, leukopenia and thrombocytopenia, indicate that the drug has an effect on erythroypiosis as suggested by Anosa and Isoun, (1976).

The slight increase in sodium, potassium, chloride, magnesium and creatinine decrease in phosphorus, calcium is indicative of renal insufficiency. In addition, the slight increase in serum GOT, SDH activity is indicative of hepatorenal effect. But the drug had no effect on the thyroid glands at doses used in this study.
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The study of the effect of quinapyramine and homidium in goats infected with *T. evansi* or *T. vivax* showed that *T. evansi* is more fatal than *T. vivax* death occurring after 11 days for *T. evansi* and after 17 days for *T. vivax*.

No apparent change was observed in the efficacy of quinapyramine and homidium bromide in goats infected with *T. evansi* at the level of dosages used compared to that of quinapyramine administered alone at the same dose level. Same was also observed in goats infected with *T. vivax*, where there are no changes observed in the efficacy of quinapyramine combined with ethidium at the two levels of combination when compared to that of ethidium administered alone and at the same dose level. In both infections (*T. evansi* and *T. vivax*) the presence of the parasite in the peripheral blood was more prevalent than when the drug was given alone. It is clear that combined effect of the drug is prominent. This is supported by Mubarak findings (2002).

In the present study there are no clear changes in the efficacy of a combination of quinapyramine and ethidium but the health condition of goats improved.

The present study with the combination revealed no prominent changes of efficacy at the peripheral blood level, but there appears to be is an unknown factor promoting the overall health of these animals.

**Recommendation:**

1/ In the light of the findings availed by the present study, we propose the following drug dosages regimen when treating trypanosomosis with Cymelarsan and/or oxytetracycline(OTC):

   a/in camels: 1/half of the conventionally recommended therapeutic dose of Cymelarsan plus two and half that of dose of OTC. 2/ half of the conventionally recommended therapeutic dose of Cymelarsan plus five times of OTC in camels. 3/half of the conventionally recommended therapeutic dose of Cymelarsan plus single recommended dose of OTC twice a week for 2 weeks. 4/a single dose of Cymelarsan plus a single dose of OTC or half the dose weekly for three weeks. 5/ single therapeutic dose. 6/ the two and half of therapeutic of Cymelarsan.
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b/ in goats: 1/a single dose of Cymelarsan plus a single dose of OTC. 2/ half dose of Cymelarsan plus two and half dose of OTC. 3/ half dose of Cymelarsan plus five times the dose of OTC. 4/ the single dose or two and half the dose of Cymelarsan.

c/ when OTC used goats: 1/ the five times therapeutically. 2/ the therapeutic dose weekly for three weeks. 3/ two and half of therapeutic. 4/ the single therapeutic dose twice a week for two weeks of OTC. in camels 1/ the two and half of therapeutic. 2/ five times and the single therapeutic dose of OTC.

d/ the half of the therapeutic dose of Cymelarsan plus zinc and copper.

e/ the therapeutic dose plus the two and half of therapeutic of quinapyramine and ethidium.

f/ the therapeutic dose weekly for three weeks, two and half of therapeutic dose of quinapyramine.

g/ the therapeutic dose weekly for three weeks, two and half of therapeutic dose of ethidium.

2/ the withdrawal periods of the drugs studied are more than mentioned by the manufacturers.
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