# Identification and In vitro Evaluation of New Antileishmanial Drugs using Bioinformatics

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## Introduction

Leishmaniasis is a major public health problem in several parts of the world. It is caused by the obligate intracellular protozoan parasite of the genus leishmania and is transmitted by the female sand fly of the genera phlebotomus and lutzomyia. It presents in different clinical forms: cutaneous (CL) diffuse cutaneous (DCL), visceral (VL), mucocutaneous (MCL), mucosal (ML) or post kalazar dermal leishmaniasis (PKDL). Leishmaniasis is difficult to treat and there is increasing resistance developing against the currently available drugs which are toxic, expensive, given by injection and require hospitalization for long durations.

## Objectives

The aim of this study was to identify and evaluate selected drugs used for treatment of other diseases for anti-leishmanial activity using comparative bioinformatics and in vitro human macrophage (THP1) infection assay.

## Methods

Basic Local Alignment Search Tool (BLAST) was used to determine protein homology of the target sequence of isoniazid in Mycobacterium tuberculosis and Leishmania parasites. A similar search was done to determine protein homology of target sequence of sulfadoxine/pyrimehamine in Plasmodium and Leishmania parasites.

Based on the determined protein homology, anti-leishmanial activity of isoniazid, isoniazid plus sodium stibogluconate (SSG), isoniazid plus liposomal amphotericin B (AmBisome), sulfadoxine/ pyrimethamine combination was evaluated using in vitro human macrophage (THP1) infection assay. The data was statistically analyzed using paired sample t test.

## Results

Alignment of isoniazid target sequence in mycobacterium tuberculosis and leishmania major and donovani showed 50% maximum identities while alignment of Sulfadoxinepyrimethaminetarget sequence in plasmodium falciparum and Leishmania donovani and Leishmania major showed 53% maximum identities.

Significant anti-leishmanial activity of isoniazid against both Leishmania major and Leishmania donovani at 0.1, 0.2 and 0.4µg/ml concentrations was detected by decreasing the number of amastigotes compared to the negative control. A significant synergistic effect was detected when isonaizid was used in combination with sodium stibogluconate and with liposomal amphotericin B, by increasing the percentage of killing compared with that of each drug alone.

Sulfadoxinepyrimethamine combination showed minimum anti-leishmanial activity at 1.9 pyrimethamine and 38.1 sulfadoxine, 2.9 pyrimethamine and 57.1 sulfadoxine, 3.8 pyrimethamine and 76.2 sulfadoxine concentrations compared with SSG.

## Conclusion

Isoniazid showed significant anti-leishmanial activity and significantly enhanced the anti -leishmanial effect of SSG and amBisome, while Sulfadoxine/pyrimethamine combination had minimum anti-leishmanial activity.