ECRONICON OPEN ACCESS

EC PHARMACOLOGY AND TOXICOLOGY
Editorial

Leishmaniasis: Healthcare Burden and Opportunities for Drug Discovery from Natural Products

Ibrahim Sulaiman Al Nasr[1]* and Faiyaz Ahmed[2]

[1]*College of Arts and Science in Onaizah, Qassim University, Saudi Arabia*

[2]*College of Applied Health Sciences in Ar Rass, Qassim University, Ar Rass, Saudi Arabia*

***Corresponding Author:** Ibrahim Sulaiman Al Nasr, College of Arts and Science in Onaizah, Onaizah, Qassim, Saudi Arabia.

Received: January 23, 2017; **Published:** April 11, 2017

Leishmaniasis is a serious disease caused by a flagellated protozoan parasite of genus *Leishmania* (Trypanosomatidae family). Visceral leishmaniasis (VL) and cutaneous leishmaniasis(CL) are the most wild spread clinical forms prevalent in many part of the tropical and subtropical world, causing significant morbidity and mortality. The parasite is transmitted through the bites of infected female sand flies *Phlebotomus* and *Lutzomyia* [1,2]. According to WHO, leishmaniasis is one of the most neglected diseases in the world, which is prevalent in 88 countries of the world mainly in rural areas, and about 350 million people are at risk. More than 1.6 million new cases occur annually worldwide but only about 600,000 are reported. Of these 1.6 million estimated cases about 500,000 are VL mostly in Bangladesh, Brazil, Ethiopia, India, Nepal and Sudan and 1.1 million cases are CL mainly in Afghanistan, Algeria, Brazil, the Islamic Republic of Iran, Peru, Saudi Arabia, Sudan and the Syrian Arab Republic. In addition to infecting approximately 1.6 million people every year, leishmaniasis is associated with about 2.4 million disability-adjusted life years (caused by enduring physical impairments and/or scarring that alter the lifestyles of the affected individuals) and approximately 70,000 deaths annually. Due to the high incidence of infection and the potential to be fatal, leishmaniasis has proven to be a pressing international health threat [3].

The basic treatment for all leishmaniasis forms consists of the administration of pentavalent antimonials that were developed more than 60 years ago. Two organic salt preparations, sodium stibogluconate (Pentostam®) and meglumine antimoniate (Glucantime®) are commonly used. These drugs are generally considered to be equivalent in terms of efficacy and toxicity. They are administered intravenously or intra-muscular, and side effects like chemical pancreatitis, elevations in serum aminotransferases and electro-cardiographic abnormalities are usually reversible [4,5]. Antimonials have been abandoned in the Indian subcontinent after decades of use. Antimonials drug resistance studies show the experimental resistance is predictive of what has been observed in clinical situations. The knowledge on antimonials drug resistance could be used to counter resistance, by guiding the choice of combination therapy or liposoml formulation [6].

Moreover, reports of unresponsiveness and the emergence of drastic resistance to antimony treatment have become frequent [2,7]. Amphotericin B is the second-line drug in the therapy of VL. Two preparations are currently used for treatment are amphotericin B desoxycholate (Fungizone®) and liposomal formulations (e.g. AmBisome®) [8]. High cure rates are obtained in treatment of antimonial-unresponsive patients, though severe side effects including fever, bone pain, renal toxicity and high costs limit the general use of amphotericin B in therapy. New clinical formulations of amphotericin B in lipid complexes have proven to be less toxic but are expensive; a major problem in treating VL in developing countries. Also, amphotericin B and amphotericin B-lipid complexes do not appear to be suitable for treatment of non-visceral disease. There is a clear and urgent need for the development of improved treatments for leishmaniasis that are safe, inexpensive, and consumable orally available. Miltefosine has replaced antimonials in the Indian subcontinent. After a decade of use, efficacy dropped significantly, but so far, this was not associated with Miltefosine drug resistance. In parallel, mechanisms of experimental

Miltefosine drug resistance has been unravelled. It may be a matter of time before Miltefosine drug resistance emerges and spreads in the Indian subcontinent. Robust chemotherapy I a major element among strategies of disease control. Thus, treatment failure and drug resistance are one of the major risk factors from emergence and spreading of leishmaniasis worldwide. It is essential to protect the few existing drugs as well as the new coming ones against drug resistance [9].

Natural product research shows promise in finding new lead structures. Plants are valuable sources for the screening of bioactive secondary metabolites [10]. In countries where leishmaniasis is prevalent accessible treatments against malaria are mainly based on the use of folkloric medicines. Furthermore, these herbal remedies play a major role in the treatment of many diseases. However, scientific data on these herbal remedies is limited despite the fact that validation of traditional herbal medicines could lead to innovative strategies in control of malaria. Natural products from plants represent a virtually an inexhaustible reservoir of molecules with novel mechanisms of action against parasites. Most of these molecules are hardly explored and thus there is tremendous potential to improve the health status of human beings. The discovery of quinine which is the leading antimalarial compound from *Cinchona succiruba* represented a milestone in the history of antimalarial drugs from plants followed by the isolation of lactone artemisinin from *Artemisia annua* and hydroxynaphthoquinone have raised hope for the search for better molecules against malaria.

Traditionally a number of plants being used for the treatment of leishmanial infections have been found to be efficacious against the parasite [11-15]. These observations have initiated rigorous scientific investigations worldwide to explore phytochemicals as novel antileishmanial agents. However, these studies are limited to screening of the crude extracts for antileishmanial activity which just validates the traditional usage of these plants and does not provide information on their chemical composition and efficacy in real-time situations. For the effective utilization of bioactive natural products, the extracts need to be standardised in terms of their composition and bioactive marker compounds have to be identified. It is also essential to have toxicological profile for the individual extracts. In some cases, isolated compounds will be of great therapeutic and commercial value and thus efforts must be directed towards the identification and isolation of bioactive compounds.

In view of this, the author reiterate the views of (Hefnawy., *et al*.) that the drug resistance studies must be carried out at two different stages of drug development; 1- The efficiency of novel compounds should be confirmed on sets of strains including recent clinical isolates with drug resistance; 2- experimental drug resistance should be generated to promising compounds at an early stage of their development, to further optimize them and monitor clinical trials [6].

Bibliography

1. Hepburn NC. "Cutaneous leishmaniasis: an overview". *Journal of Postgraduate Medicine* 49.1 (2003): 50-54.

2. Croft SL and Coombs GH. "Leishmaniasis-current chemotherapy and recent advances in the search for novel drugs". *Trends in Parasitology* 19.11 (2003): 502-508.

3. World Health Organization. "Leishmaniasis: worldwide epidemiological and drug access update" (2012).

4. Sundar S and Olliaro P. "Miltefosne in the treatment of leishmaniasis: clinlcal evidence for informed clinical risk management". *Therapeutics and Clinical Risk Management* 3.5 (2007): 733-740.

5. Chappuis F., *et al* "Visceral leishmaniasis: what are the needs for diagnosis, treatment and control?" *Nature Reviews Microbiology* 5.11 (2007):873-882.

6. Hefnawy *et al*., "Exploiting knowledge on Leishmania drug resistance to support the quest for new drugs". *Trends in Parasitology* 33.3 (2016): 162-174.

7. Sundar S., *et al*. "Failure of pentavalent antimony in visceral leishmaniasis in India: report from the centre of the Indian epidemic". *Clinical Infectious Diseases* 31.4 (2000): 1104-1107.

8. Adler-Moore J and Proffitt RT. "AmBisome: liposomal formulation, structure, mechanism of action and pre-clinical experience". *Journal of Antimicrobial Chemotherapy* 49.1 (2002): S21-S30.

9. Poloni T and Efferth T. "Leishmaniasis: Drug resistance and natural products (Review)". *International Journal of Molecular Medicine* 22.3 (2008): 277-286.

10. Al-Musayeib NM., *et al*. "Study of the in vitro antiplasmodial, antileishmanial and antitrypanosomal activities of medicinal plants from Saudi Arabia". *Molecules* 17.10 (2012): 11379-11390.

11. Manuel J., *et al*. "Variation of leishmanicidal activity in four populations of urechites andrieuxii". *Journal of Ethnopharmacology* 86.2-3 (2003): 243-247.

12. Peraza-Sanchez S., *et al*. "Leishmanicidal evaluation of extracts from native plants of the yucatan peninsula". *Fitoterapia* 78.4 (2007): 315-318.

13. Zhelmy M., *et al*. "In vitro activity of tridax procumbens against promastigotes of leishmania Mexicana". *Journal of Ethnopharmacology* 122.3 (2009): 463-467.

14. Iwu M., *et al*. "Evaluation of plant extracts for antileishmanial activity using a mechanism-based radio respirometric microtechnique (ram)". *Journal of Medicinal Plant and Natural Product Research* 58.5 (1992): 436-441.

15. Nasib S., *et al*. "Efficacy of desmodium gangeticum extract and its fractions against experimental visceral leishmaniasis". *Journal of Ethnopharmacology* 98.1-2 (2005): 83-88.

Volume 3 Issue 5 April 2017