Bioorganic & Medicinal Chemistry xxx (2013) xxx–xxx

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry

journal homepage: www.elsevier.com/locate/bmc

Review

Natural product based leads to fight against leishmaniasis

Nisha Singh [a,†], Bhuwan B. Mishra [b,†], Surabhi Bajpai [a], Rakesh K. Singh [a,*], Vinod K. Tiwari [b,*]

[a] Molecular Immunology Laboratory, Department of Biochemistry, Faculty of Science, Banaras Hindu University, Varanasi 221005, India
[b] Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi 221005, India

ARTICLE INFO

Article history:
Received 19 October 2013
Revised 18 November 2013
Accepted 23 November 2013
Available online xxxx

Keywords:
Leishmaniasis
Drug targets
Natural compounds
Alkaloids
MDR

ABSTRACT

The growing incidence of parasitic resistance against generic pentavalent antimonials, specifically for visceral disease in Indian subcontinent, is a serious issue in *Leishmania* control. Notwithstanding the two treatment alternatives, that is amphotericin B and miltefosine are being effectively used but their high cost and therapeutic complications limit their use in endemic areas. In the absence of a vaccine candidate, identification, and characterization of novel drugs and targets is a major requirement of leishmanial research. This review describes current drug regimens, putative drug targets, numerous natural products that have shown promising antileishmanial activity alongwith some key issues and strategies for future research to control leishmaniasis worldwide.

Contents

* Corresponding authors. Tel.: +91 542 2570215; fax: +91 542 2368174 (R.K.S.); tel.: +91 542 6702477; fax: +91 542 2368174 (V.K.T.).
E-mail addresses: rakesh_bc@bhu.ac.in (R.K. Singh), tiwari_chem@yahoo.co.in (V.K. Tiwari).
† Equal contribution.

0968-0896/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.bmc.2013.11.048

1. Introduction

Leishmaniasis is a poverty-associated disease caused by more than 20 species of protozoan parasites that belong to family kinetoplastida and genus *Leishmania*. It is a wide spectrum of vector born disease with great epidemiological and clinical diversity. The disease is spreaded by more than 30 species of sand fly of the genus *Phlebotomus* in the old world and *Leutzomia* in the new world.[1] The *Leishmania* species are generally zoonotic in nature and carried by rodents and canids that are main reservoir hosts. Only two *Leishmania* species can maintain anthroponotic human–human cycle. They are *Leishmania donovani*, responsible for visceral leishmaniasis (VL) in Indian subcontinent & East Africa, and *Leishmania tropica*, responsible for cutaneous leishmaniasis (CL) in the old world.[2,3] Three major clinical forms of the disease are visceral (VL), cutaneous (CL), and mucocutaneous leishmaniasis (MCL), which differ in immunopathologies and degree of morbidity and mortality. Most VL caused by *L. donovani* is fatal if untreated, whereas CL caused by *Leishmania major, Leishmania mexicana, Leishmania braziliensis,* and *Leishmania panamensis* is significantly associated with morbidity.[4,5]

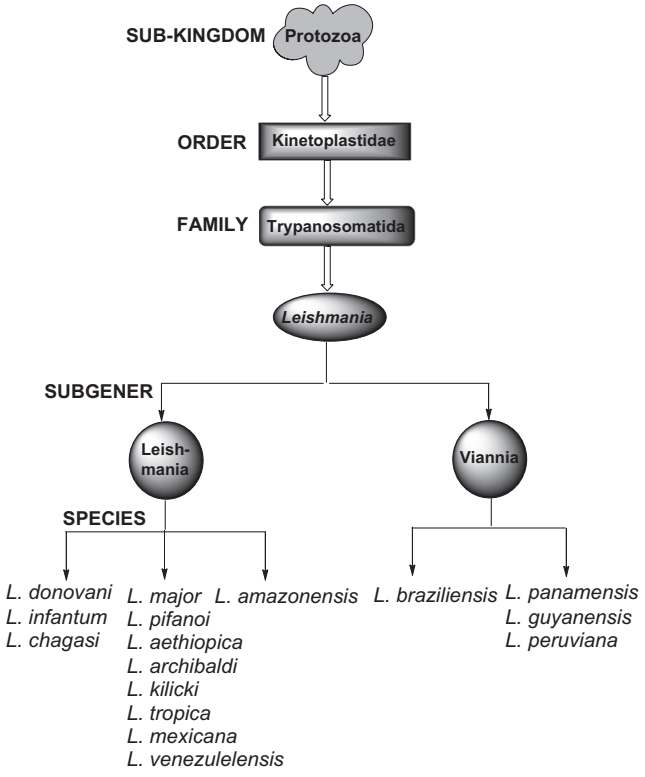

Figure 1. Taxonomic classification of *Leishmania* spp.

Leishmanial infections are prevalent in more than 98 countries most of which are either poorly developed or developing. The global annual burden of all forms of leishmaniasis is approximately 12 million per year in which about 350 million people are at risk however, exact statistical data are lacking.[6] In a recent report, it has been observed that approximately 0.2 to 0.4 VL cases and 0.7 to 1.2 million CL cases occur each year however, there is gross under reporting of cases in endemic areas.[7] More than 90% cases of VL ensue in five countries: India, Bangladesh, Nepal, Sudan, Brazil, and 90% of CL cases occur in seven countries: Afghanistan, Algeria, Brazil, Iran, Peru, Saudi Arabia, and Syria.[8] Although, spread of disease in endemic and non-endemic regions is multi-factorial but lack of effective control measures for both, parasite and its vector are main factors.[9]

The poor knowledge about the disease and lack of effective health policies are the primary hurdles in the elimination of leishmaniasis from every corner of the world is far from reality. Sodium stibogluconate, a drug belongs to class of pentavalent antimonials, is the cornerstone of leishmanial chemotherapy in disease endemic countries especially in Indian subcontinent.[10] However, the growing incidence of resistance has raised serious concern for its use in disease endemic area. The other second line drugs like amphotericin B, its liposomal formulations, and miltefosine have become prevalent as first line treatments. These drugs are being used in the treatment with more efficacies and dramatic potential for