The preclinical discovery and development of oral miltefosine for the treatment of visceral leishmaniasis: a case history

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ABSTRACT

Introduction

Visceral leishmaniasis (VL) is a vector-borne disease caused by *Leishmania donovani* or *Leishmania infantum*. Closely related to poverty, VL is fatal and represents one of the main burdens on public health in developing countries. Treatment of VL relies exclusively on chemotherapy, a strategy still experiencing numerous limitations. Miltefosine (MF) has been used in the chemotherapy of VL in some endemic areas, and has been expanded to other regions, being considered crucial in eradication programs.

Areas covered

This article reviews the most relevant preclinical and clinical aspects of MF, its mechanism of action and resistance to *Leishmania* parasites, as well as its limitations. The authors also give their perspectives on the treatment of VL.

Expert opinion

The discovery of MF represented an enormous advance in the chemotherapy of VL, since it was the first oral drug for this neglected disease. Beyond selection of resistant parasites due to drug pressure, several other factors can lead to treatment failure such as, for example, factors intrinsic to the host, parasite and the drug itself. Although its efficacy as a monotherapy has reduced over recent years, MF is still an important alternative in VL chemotherapy, especially when used in combination with other drugs.

Keywords:

Alkyl-phosphocholine, clinical pharmacology, *Leishmania donovani, Leishmania infantum,* mechanism of action, miltefosine, pharmacodynamics, pharmacokinetics, preclinical pharmacology, visceral leishmaniasis