Journla of Molecular Pharmaceutics & Organic Process Research
Salerno and Bregni, J Mol Pharm Org Process Res 2014, 2:2
DOI: 10.4172/2329-9053.1000e114

Editorial Open Access

An Old Drug for the Modern Treatment of Leishmaniasis

Claudia Salerno and Carlos Bregni*

Department of Pharmaceutical Technology, Faculty of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires, Argentina

Leishmaniasis is a worldwide spread neglected disease caused by Leishmania parasites. Although it is an ancient disease, it has been recently classified as an emerging pathology with 2 million cases annually. It has become a public health problem since several factors favor its expansion such as migration, urbanization and deforestation, co-infection with human immunodeficiency virus and malnutrition, and inadequate vector o reservoir control, treatment failure and emerging drug resistance due to incomplete treatment. Moreover, diagnosis and treatment is not often possible in rural areas where the disease is more frequent. *Leishmania* parasites can cause four clinical forms: cutaneous (CL), diffuse cutaneous, mucocutaneous, and visceral pathology. Visceral leishmaniasis is the most severe form of the disease; however CL is the most prevalent. CL is caused mostly by *L. major* in the Old World and by *L. Mexicana, L. peruviana,* and *L. braziliensis* in the New World. The prognosis of the disease depends on the *Leishmania* specie and immunological condition of the patient. Although CL lesions may be self-limited, treatment helps to reduce scars and prevent disease dissemination. Main treatment with parenteral pentavalent antimonials produce serious side effects and patient compliance is difficult. The World Health Organization (WHO) also recommends intralesional treatment with antimonial drugs depending on clinical features. Oral alternatives such as miltefosine, allopurinol and azoles have been used. But, there is still lack of effective topical treatments for CL.

Azole antifungals inhibit a key enzyme for the production of ergosterol, the main sterol in membranes of fungi and parasites. Fluconazole (FLZ) is a bis-triazole antifungal with activity against *Candida spp., Blastomyces dermatitidis, Cryptococcus neoformans, Epidermophytom spp., Histoplasma, Microsporum spp.* and *Trichophyton spp.* It has been extensively used in the treatment of dermatophytoses; after oral administration FLZ concentration in the skin is high due to great affinity to the stratum corneum. However, the use of FLZ as topical treatment is not a general practice. Oral FLZ has been reported for the treatment of CL and has shown activity against *Leishmania spp.*; a six-week course of oral FLZ shortened healing time of *L. major* cutaneous lesions, but high doses (200 mg/day for 6 weeks) were needed and side effects are of concern. Nevertheless, results are controversial; a study reported that in vitro anti-leishmanial activity of FLZ was poor and a group of researchers compared FLZ topical cream (1, 2, or 10% w/w) and topical paromomycin gel, in BALB/c mice infected with *L. amazonensis* or *L. major*, and they concluded that FLZ was ineffective. In the latter case those formulations had propylene glycol and we found in previous works that the presence of this excipient may affect FLZ activity. Moreover, we reported that FLZ penetration and retention within the skin was greater when formulated in a microemulsion (ME) compared with other conventional topical dosage forms such as emulsion or emulgel.

In a preliminary assess of the in vitro activity of a FLZ-ME against *Leishmania* we found that a FLZ-ME showed similar activity against *L. Braziliensis* promastigotes than AmB Deoxycholate, a second line drug used for the treatment of CL. It is also important to mention that blank formulation inhibited the parasite growth, but FLZ-ME showed higher inhibition. The synergistic activity may be due to the high content of surfactants which alter membrane fluidity causing electrolyte or other vital substances depletion. This observation was also reported for a micellar formulation with Poloxamer 188. Furthermore, it was published that surfactants had strong lytic effect against *Trypanosoma cruzi,* a parasite of the same family as *Leishmania*, and enhanced antiparasitic drugs activity.

Considering these outcomes, we remark the importance of the vehicle on drug activity and also highlight the different drug susceptibility of *Leishmania* species. Further work is needed, but FLZ could be useful for the local treatment of CL in the New World. This fact is very important as topical alternatives are required to reduce oral and parenteral courses to help patient compliance. Topical treatment would be less expensive, with fewer adverse effects. Modern therapy challenge is to make drugs reach target sites with the minimal adverse effects, consequently treatment of CL needs rational selection of drugs and also an appropriate vehicle.

***Corresponding author:** Carlos Bregni, Department of Pharmaceutical Technology, Faculty of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires, Argentina, Tel: +541149648271; Fax: +541149648271; E-mail: cbregni@gmail.com

Received May 26, 2014; **Accepted** May 28, 2014; **Published** May 30, 2014

Citation: Salerno C, Bregni C (2014) An Old Drug for the Modern Treatment of Leishmaniasis. J Mol Pharm Org Process Res 2: e114. doi: 10.4172/2329-9053.1000e114