THERAPEUTIC MODALITIES TO COMBAT LEISHMANIASIS, A REVIEW

Hamid Iqbal[1*], Muhammad Ishfaq[1], Baharullah Khattak[1], Abdul Wahab[2], Muhammad Naseer Abbas[2], Najeeb Ullah[3], Ali Rehman[3]

[1]Department of Microbiology, Kohat University of Science &Technology, KPK, Pakistan

[2]Department of Pharmacy, Kohat University of Science & Technology, KPK, Pakistan

[3]Department of Chemistry, Kohat University of Science & Technology, KPK, Pakistan

Abstract

Leishmaniasis is an emerging major health problem that causes high morbidity and mortality levels with a wide spectrum of clinical complications. Current scenario of chemotherapeutic options with some attempts at immunotherapy has remained a dilemma for the treatment of leishmaniasis. Primary precautionary measure relies on the managed control of the host and sand fly bite prevention is difficult to establish, as the transmission of the disease is manifested by various *Leishmania* species. Secondary and tertiary prevention is dependent on the medical assistance using clinical guidelines and adequate therapy however long course of duration and resistant nature of drugs with pronounced side effects often lead to reduction or cessation of treatment. The aim of this article is to view advancements in the development of commercially available antileishmanial drugs; a review of natural plant extracts exhibiting antileishmanial activities *in vitro*, *in vivo* alone or in combination with recommended drugs seeming to validate their use in folk medicine and topical applications of ointments from clinical agents currently used to develop new compounds under trial, substantial efforts in vaccine development, insights about immunoregulation along with the recommendations and guidelines for future perspectives.

Keywords: Leishmaniasis, Medicinal plants, Chemotherapy, Antileishmanial activity.

Introduction

Leishmania is a tropical neglected disease caused by single cellular, heamoflagellate protozoan parasites of the genus *Leishmania* (family *Trypanosomatidae*) transmitted by the bite of an infected female sandfly *Lutzomyia* and/or *Phlebotomus* (Handman and Bullen, 2002). Sandflies are the vectors of *Leishmania* parasites that are distributed throughout intertropical and temperate regions of the world (Vannier *et al*., 2002). Only 60 of about 600 sand flies species are vectors for *Leishmania* around which 20 *Leishmania* species are described as human pathogens (Mehlhorn 2004). Leishmaniasis depends on the *Leishmania* spp. involved, site of bite, number of bites, type of sandfly, genus of parasite and genetic potential (Bari 2006; Markle and Makhoul 2004). Several major risk factors are involved in the emergence and spread of leishmaniasis worldwide; Treatment failure and drug resistance. Human-made environmental changes. Acute predisposition of host immune status (Desjeux, 2001). Other factors include; Human Immunodeficient Virus (HIV) epidemic, inadequate vector or reservoir control, lack of vaccines, international travels and international conflicts, urbanization and deforestation, movement of non-immune persons to endemic regions, massive migration from rural to urban areas, decline in social and economic circumstances (Sereno *et al.*, 2007). Consolidated data are frequently not available, only estimates have been provided (Croft and Coombs 2003). Worldwide prevalence is about 12 million, (Desjeux, 2001) endemic in 90 tropical and subtropical countries threatening approximately 350 million people each year approximately 90% of which occurs in the Sudan and Indian subcontinent (Davis *et al*., 2003). In most countries the incidence numbers are probably highly underestimated, since many cases are not recognized and there is no obligation to report the disease (Desjeux, 2004). Categorically, Leishmaniasis is classified into three different clinical forms: Cutaneous (CL), Mucocutaneous (ML) and Visceral (VL) leishmaniasis (Lianet, 2009); Cutaneous leishmaniasis is a dermal manifestation representing up to 75% of all the new cases with 1-1.5 million annual incidences commonly caused by *Leishmania major, L. tropica, L. aethiopica, L. mexicana, L. amazonensis,* and *L. braziliensis* (Hailu *et al*. 2006) in many parts of the world particularly in sub-continent and middle east (Donald 2003). CL is characterized by a small red papule which becomes darker and turn into ulcer with raised edges after several weeks. Ulcers can be moist and exude pus with a crusted scab; sores usually appear on exposed body parts of the skin, especially on the face and extremities (Markle and Makhoul, 2004). Although cutaneous leishmaniasis is not lethal, but can cause significant morbidity and course of the disease is often accompanied by psychological, social repercussion, stigmatization, painful disfiguration and severe secondary dermal manifestations neoplasms and sarcoidosis (Yanik *et al*., 2004; Davies *et al*., 2003). Localized cutaneous leishmaniasis is characterized by

lesions on face, nose, forehead, and lower limbs that usually heal naturally (Davies et al. 2003; Gilles 1999). Another type of CL is the diffuse cutaneous leishmaniasis (DCL) that produces symptoms like nodules, plates or lumps on the face, arms and legs never heal spontaneously and relapse after treatment (Davies *et al.*, 2003; Desjeux 1996). Mucocutaneous leishmaniasis (Espundia) is characterized by nasal obstruction and bleeding, disfiguration and generation of painful mucosal lesions and cartilage of the mouth, ear and pharynx (Vidyashankar and Agrawal 2007). Visceral Leishmaniasis (VL) or Kala-azaar is a kind of systemic disease caused by *L. donovani, L. infantum* and *L. chagasi* (Mehlhorn, 2004). Typical symptoms of the disease are irregular fever, weight loss, anemia, enlargement and invasion of spleen, lungs, bone-marrow and liver, skin pigmentation, leukopenia, liver, oral mucosa, larynx and sex cells (Gilles, 1999). The disease may be asymptomatic and self-resolving but usually becomes chronic and may be fatal if left untreated (Chan and Pena, 2001).