

Bioactive Treasures

Unlocking Nature's Pharmacy

Volume-2

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ISBN:978-93-48683-03-8

2025

LPU Publication House

Lovely Professional University, Phagwara, Punjab - 144411

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Chapter 6: Leishmanial Herbal Bioactives

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Abstract

Leishmaniasis, a neglected tropical disease caused by protozoan parasites of the genus *Leishmania*, affects millions globally, especially in tropical and subtropical regions. Chemotherapy remains the primary treatment, but its limitations include drug toxicity, resistance, high cost, and prolonged administration. In recent years, natural products from medicinal plants have garnered considerable attention as potential antileishmanial agents. These herbal bioactives, including alkaloids, terpenoids, flavonoids, and essential oils, offer novel therapeutic avenues due to their structural diversity and bioactivity profiles. This chapter explores the current knowledge on leishmanial herbal bioactives, their mechanisms of action, advantages, and potential for future drug development.

Keywords: Leishmaniasis, Herbal bioactives, Antileishmanial agents, Plant-derived compounds, Traditional medicine, Natural products

6.1 Introduction

Leishmaniasis is a vector-borne disease transmitted through the bite of infected female phlebotomine sandflies. It is endemic in over 90 countries, with an estimated 1.3 million new cases and 20,000–30,000 deaths annually. The clinical manifestations range from cutaneous to mucocutaneous and visceral forms, with *Leishmania donovani*, *L. tropica*, *L. major*, and *L. braziliensis* being the most prevalent pathogenic species (Alvar *et al.*, 2012).

Despite advances in parasitology and immunology, treatment options remain unsatisfactory due to the emergence of resistance, treatment failures, toxicity, and cost. The search for novel, safe, and effective therapies has redirected attention toward natural products. Herbal bioactives, derived from centuries-old traditional medicine systems, provide a rich reservoir of chemical diversity. Numerous *in vitro* and *in vivo* studies have documented their antileishmanial properties, making them strong candidates for drug discovery (Sundar and Chakravarty 2015).

6.2 Overview of *Leishmania* Biology

The *Leishmania* parasite undergoes a digenetic life cycle involving two morphological stages: promastigotes (flagellated form in sandflies) and amastigotes (non-flagellated intracellular form in mammalian macrophages). Infection begins when the sandfly injects promastigotes into the host's skin. These are phagocytosed by macrophages, where they differentiate into amastigotes and multiply, leading to clinical symptoms (Lamotte *et al.*, 2017).

The parasite's survival inside host macrophages is facilitated by its ability to subvert the host's immune response and oxidative stress mechanisms. Understanding this biology is vital in identifying molecular targets for drug development, especially for herbal compounds (Mishra and Towari 2011; Ghosh *et al.*, 2012).

6.3 Limitations of Conventional Antileishmanial Therapies

Drugs such as pentavalent antimonials (sodium stibogluconate), amphotericin B, miltefosine, and paromomycin are used for treatment (Ghosh *et al.*, 2012). However, these agents are often associated with the following limitations:

- **Toxicity:** Severe nephrotoxicity and cardiotoxicity, particularly with amphotericin B.
- **Resistance:** Increasing reports of resistance to antimonials and miltefosine.
- **Cost and Accessibility:** High-cost limits usage in endemic, low-income countries.
- **Parenteral Administration:** Most require hospitalization and intravenous infusion.

Given these challenges, phytomedicine has emerged as a complementary or alternative strategy to combat