Continental Veterinary Journal
ISSN: 3079-0212 (ONLINE)
www.cvetj.com; editor@cvetj.com

REVIEW ARTICLE

DOI: 10.71081/cvj/2026.068

Unveiling the Antiparasitic Potential of Plant Extracts to Mitigate Leishmaniasis of Zoonotic Importance

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ARTICLE INFO

ARTICLE HISTORY: CVJ-26-228

Received: 25 September 2025
Revised: 18 December 2025
Accepted: 03 February 2026
Published online: 04 March 2026

Key words:
Alternatives
Chemotherapy
Leishmaniasis
Parasites
Plant extracts
Resistance
Vector control

ABSTRACT

Leishmaniasis is a zoonotic disease caused by the intracellular protozoa belonging to the genus *Leishmania*, which is transmitted to humans by the bite of a vector sandfly, primarily *Phlebotomus* and *Lutzomyia*. Current chemotherapy depends on pentavalent antimonials, miltefosine, amphotericin B deoxycholate, liposomal amphotericin B, amphotericin B lipid complex, amphotericin B cholesterol dispersion, paromomycin, pentamidine, sitamaquine, and azoles. However, these drugs are characterized by many limitations, including triggering resistance mechanisms in parasites, severe adverse effects, limited potency, extreme toxicity, duration of treatment, and high cost. Medicinal plant extracts and their metabolites can combat leishmaniasis due to their unlimited chemical diversity. They can be used to develop new medications due to their affordability, low risk of adverse reactions, and high efficacy. In the present review, the special focus is on the phytochemicals, including flavonoids, terpenes, phenolic compounds, and alkaloids, and their mode of action against *Leishmania* by disruption of biological membranes, cell cycle arrest, induction of apoptosis, and diminishing the enzyme activity. This review highlights the current status of chemical control strategies, their limitations, and the potential of plant-based alternatives as novel therapeutic agents against leishmaniasis. In the future, they may offer a sustainable and effective approach for future leishmaniasis management.

To Cite This Article: Shahzad M, Rehman RA, Abeer K, Iqbal J, Nisa ZU, Baryar FH, Khan AMA, Zahra I, Shahzad T, 2025. Unveiling the antiparasitic potential of plant extracts to mitigate leishmaniasis of zoonotic importance. Continental Vet J, x(x): xxx http://dx.doi.org/10.71081/cvj/2026.068

INTRODUCTION

Leishmaniasis (cutaneous, visceral, and mucocutaneous) is a zoonotic disease caused by the intracellular protozoan *Leishmania* and is transmitted to human beings by the bite of vector sandflies, primarily *Phlebotomus* and *Lutzomyia* (Cecílio et al. 2022). It occurs in tropical and subtropical regions, including Europe, Asia, the Middle East, North America, and part of South America (Scarpini et al. 2022). This disease inhabits all continents except Oceania, and it is endemic in regions of Central and South America, the Middle East, Southeastern Mexico, Northeastern Africa, and Southern Europe (Kyari 2024). The World Health Organization marked leishmaniasis as one of the seven most prevalent tropical diseases. It is documented that there are 350 million people globally at risk of getting the disease, and between 12 and 15 million people have already been infected (Li et al. 2025).

Almost 90 species of sandflies are responsible for transmitting *Leishmania* protozoa to humans while taking a blood meal that aids in laying eggs (World Health Organization 2023). Dipterans of the genus *Lutzomyia* in North America, South America, and Caribbean islands, and *Phlebotomus* in Asia, Africa, and Europe are the potential carriers of the various species and subspecies of

protozoa of the *Leishmania* genus (Valigurová and Kolářová 2023). The *Leishmania* species responsible for human infection include 3 species of *L. donovani* complex (*L. infantum, L. donovani*, and *L. chagasi),* 3 main species of *L. mexicana* complex (*L. venezuelensi, L. mexicana,* and *L. amazonensis), L. tropica*, *L. aethiopica, L. major*, and 4 main species of subgenus *Viannia (L. (V.) braziliensis*, *L. (V.) peruviana, L. (V.) guyanensis*, *L. (V.) panamensis) (*Azami-Conesa et al. 2021).

Leishmaniasis has become a potentially dangerous global health problem that exhibits an extensive spectrum of clinical manifestations (Pal et al. 2022). The clinical signs and symptoms of leishmaniasis can range from inflammatory skin lesions at the sandfly bite site in the cutaneous leishmaniasis to the more severe forms of mucocutaneous and visceral leishmaniasis (Talukder et al. 2024). Its severity depends on host-parasite interaction, the emergence of coinfection, the species of parasite, and the host's immunity (Yasmin et al. 2022).

Various chemical drugs have been utilized over the years to control this hazardous disease. For example, sodium stibogluconate (SSG) and meglumine antimoniate (MA) have been considered the first-line treatment for leishmaniasis (Solomon et al. 2024). Similarly, Amphotericin B is an antifungal drug extracted from the *Streptomyces nodosus*, considered a second-line treatment for leishmaniasis and administered at a standard dose of 0.75-1 mg/kg for 15 days to target amastigotes and promastigotes (Zulfiqar et al. 2022). Another drug, miltefosine, an alkyl phospholipid oral antileishmanial agent, has been reported to achieve a 94% long-term cure rate at a standard concentration of 50-100 mg/day for 28 days (Majoor et al. 2025). The drugs currently utilized for treating leishmaniasis also have several limitations, such as resistance, severe toxicities, and multiple adverse reactions, which discourage patients from treatment and encourage the appearance of resistant strains (Wijnant et al. 2022). In addition to these complications, the expensive nature of the drugs makes the treatment unsuitable, and unfortunately, the cost has been increasing progressively throughout the year (Abbasi and Saeedi 2022). These limitations have led scientists and researchers to explore new, safe, cost-effective, and sustainable alternative therapeutic strategies.

Botanicals and their chemical constituents have garnered significant attention due to their antioxidant, antibacterial, antiviral, and antiparasitic properties (Štrbac et al. 2023). Among botanicals, plant extracts and their phytochemicals represent a promising natural alternative to zoonotic leishmaniasis in terms of safety, accessibility, and decreased resistance risk (Shang et al. 2025). Therefore, this review article describes the therapeutic potential of plant extracts to overcome zoonotic leishmaniasis, particularly their mechanism of action, current challenges, and future prospects for developing novel plant-based products of human and veterinary importance. Furthermore, it also highlights the resistance mechanism of chemically synthesized antiprotozoal drugs.

Chemical resistance: Drug resistance to leishmaniasis in medical and veterinary treatments, along with the expensive medication, intravenous route of administration, and high toxic level, are considered serious problems, especially in developing countries where the disease is endemic (Wijnant et al. 2022). The frequent, continuous, overuse, and misuse of chemical drugs have led to the development of resistance. Furthermore, genetic mutations and genetic recombination in the parasite can develop drug resistance (Tenorio et al. 2025). In vitro investigations demonstrated that isolates of resistant strains of *L. donovani* from unresponsive patients require three to five times as much Pentavalent Antimony to be as effective against the parasite as those from Pentavalent Antimony responders (Nery et al. 2024). Table 1 summarizes the important chemotherapeutic agents used against leishmaniasis, their mode of action, and associated limitations, including drug resistance and toxicity.

Life cycle of *Leishmenia*

The bite of an infected female phlebotomine sandfly transmits leishmaniasis. While taking the blood meal, the sandfly injects the parasitic stage (promastigotes) from its proboscis. Macrophages and other kinds of mononuclear phagocytic cells phagocytize promastigotes that arrive at the puncture site. Inside these cells, promastigotes transform into the tissue stage of the protozoa known as amastigotes, which proliferate until the cell ruptures and invades other mononuclear phagocytic cells to carry on the cycle (Cecílio et al. 2022; Laroche 2022).

The occurrence of signs and symptoms and the emergence of cutaneous or visceral leishmaniasis depend on the parasite, host, and other circumstances (Costa et al. 2023). Consumption of contaminated cells during blood meals causes infection in the sandfly. There is the transformation of amastigotes into promastigotes in the gut of the sandfly and then moves to the proboscis (Bursali and Touray 2024). A sand fly species must accomplish the following five conditions to pass on zoonotic *Leishmania*: (1) exhibit the complete growth of the protozoa until it becomes pathogenic; (2) take blood supply from the human reservoir in zoonotic propagation cycles; (3) be infected naturally with the same species of Leishmania that inhabits humans; (4) be able to transmit the parasite during sucking of blood; and (5) be anthropophilic (Cecílio et al. 2022).

Plant extracts and their secondary metabolites

Secondary metabolites of medicinal plants exhibited several pharmacological characteristics, such as antifungal (Khan et al. 2023), antioxidant (Nwozo et al. 2023), antibacterial (Elshafie et al. 2023), antitumor (Khan et al. 2022), anti-litholitic (El Menyiy et al. 2021), and antileishmanial activities (Amang et al. 2023). These phytochemicals are complicated molecules with various cellular mechanisms, including polyphenols, lignans, quinones, stilbenoids, xanthones, miscellaneous, aurones, cannabinoids, chalcones, chromenes, terpenoids, flavonoids, isoflavonoids, and coumarins (Mohammadi-Cheraghabadi and Hazrati 2023). Herbal medicines' primary benefits are their affordability, low probability of adverse reactions, and high efficacy (Ahmed et al. 2023). Thus, new investigations on the antileishmanial properties of therapeutic plant products proved the effectiveness of these products in suppressing the growth and development of various *Leishmania*

species, including *L. major* and *L. infantum*, *L. amazonensis, L. tropica*, *L. aethiopica*, *L. braziliensis*, *L. mexicana*, *L. chagasi*, and *L. donovani* (Hassan et al. 2022; Lozano et al. 2023; Worku et al. 2024). Therefore, therapeutic plants should be a primary objective of the present research investigation in controlling and managing leishmaniasis. Fig. 2 illustrates important species that have an anti-leishmanial effect.

Table 1: Concentrations, treatment time, efficacy, molecular targets, and limitations of different chemical drugs against leishmaniasis.

Chemical Drug	Concentration	Treatment Time	Efficacy	Molecular Targets	Limitations	References
Sodium Stibogluconate (SSG)	20 mg/kg/day	28-30 days (standard), 30-40 days (Bihar, India)	For resistant strains, 3-5x higher doses are required	Thiol-containing enzymes (via reduction to trivalent antimonials)	Toxicity (includes QT prolongation, myalgia, pancreatitis, cardiac arrhythmias, arthralgia, hepatotoxicity), ineffective for HIV-VL-coinfection	(Kumari et al. 2021)
Meglumine Antimoniate (MA)	20 mg/kg/day	20 days (CL), 28-30 days (ML), 30-40 days (NWCL)	First-line chemotherapy, high efficacy	Thiol-containing enzymes (via reduction to trivalent antimonials)	The toxicity profile is similar to SSG. Relapse in diffuse cutaneous leishmaniasis (DCL)	(Kumari et al. 2021; Singh et al. 2023)
Amphotericin B deoxycholate	0.75-1.0 mg/kg per infusion	15-20 intravenous infusions	High efficacy	Binding to the ergosterol and creates pores, leading to ion leakage.	Myocarditis, hypokalemia, nephrotoxicity, and infusion reactions.	(Sundar et al. 2024)
Liposomal amphotericin B (L-AmB)	30 mg/kg (East Africa); 18-21 mg/kg (Mediterranean/South America); 10 mg/kg (India)	Varies by Region; Upto 10 days (East Africa); 4-10 days (India); Single dose (India)	High efficacy	Target amastigotes-containing macrophages in the liver, spleen, and bone marrow.	Expensive medication and cold chains are required.	(Berman et al. 2019; Shirzadi 2019)
Amphotericin B cholesterol dispersion (ABCD)	7.5 mg/kg	9-14 days, depending on the patient's conditions	High efficacy	Elevates the absorption by amastigote-bearing macrophages.	Infusion-related reactions include fever and chills. High treatment Cost	(Mansur-Alves et al. 2022)
Miltefosine	50-100 mg/day	28 days (monotherapy)	High efficacy	Targets signal transduction pathways, phospholipid, and mitochondrial membranes in *Leishmania*	Mild gastrointestinal side effects, teratogenicity, long residence time in the body, and limited participation in national elimination programs	(Berman 2015; Pinto-Martinez et al. 2018)
Paromomycin	15-20 mg/kg/day (systemic)	20-28 days (systemic)	Moderate efficacy	Decrease in mitochondrial membrane potential, Inhibition of mitochondrial and cytoplasmic protein synthesis, and binding of the drug to the leishmanial glycocalyx.	Reversible ototoxicity, pain at the injection site, hepatotoxicity, need for parenteral administration, and potential for resistance in monotherapy.	(Shaw 2016; Foulkes 2020; Pokharel et al. 2021).
Pentamidine	4 mg/kg/day (alternate days)	1 week (*L. braziliensis*)	No clinical implications due to its low efficacy	Influences nuclear mechanism, mitochondrial damage, and inhibits the synthesis of RNA and DNA	Serious toxicities include insulin-dependent diabetes mellitus, pain, declining efficacy, Hypotension, nausea, vomiting, headache, dizziness, myalgia, transient hyperglycemia, hypoglycemia, and syncope.	(Sundar and Chakravarty 2015; Chanda 2021)
Sitamaquine	2 mg/kg/day (standard dose)	21 days	No clinical implications due to its low efficacy	Molecular targets remain to be identified	Methemoglobinemia, nephrotoxic with doses of more than 2mg/kg	(de Menezes et al. 2015)
Azoles (Fluconazole, Itraconazole, Ketoconazole)	Fluconazole: 400 mg/day; Itraconazole: 4 mg/kg/day Ketoconazole: 600 mg/day	6 weeks (Fluconazole); 6 weeks (Itraconazole); 4-6 weeks (Ketoconazole)	Moderate efficacy	Inhibition of ergosterol synthesis of Leishmania parasites	Hepatotoxicity, Gastrointestinal symptoms, low efficacy in some cases	(Sundar and Chakravarty 2015)

HIV=human immunodeficiency virus, VL= visceral leishmaniasis, CL=cutaneous leishmaniasis, ML=mucocutaneous leishmaniasis, NWCL=New world cutaneous leishmaniasis

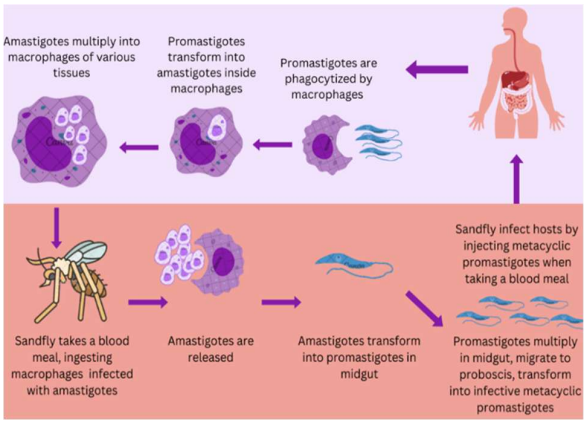

Fig.1: Diagrammatic representation of the life cycle of *Leishmania.*

Antiparasitic mode of action of plant extract

Natural products combat *Leishmania* through various antiparasitic mechanisms such as deterioration of biological membranes, suppression of enzyme action, disruption of electron transport, energy-dependent transport of vital substances, coagulation of intracellular material, impairment of protein motive force, cell cycle arrest, and induction of apoptosis (Gervazoni et al. 2020).

Disruption of biological membranes

Different plant extracts are known for their antileishmanial activity against the cell membranes of *Leishmania* (de Oliveira Lemos et al. 2025). The Antileishmanial activity of α-bisabolol, extracted from the stem of *V. arborea* (Asteraceae), inhibited the growth of promastigotes of *L. amazonensis* (Perin et al. 2025). The extract changed the morphology and structure of the parasite by interfering with the ergosterol biosynthetic pathway via the accumulation of lipid precursors within the cell membrane, with enlarged flagellar pockets and mitochondrial Kinetoplast, irregular chromatin condensation in the nucleus, and abnormalities of the nuclear membrane (Eddin et al. 2022; Bhattacharya 2025). Antileishmanial activity of essential oil, extracted from the aerial parts of *Cymbopogon citratus* (Poaceae), was considered among the strongest cytotoxic agents against *L. donovani* promastigotes proliferation with IC50 values ranging from 640-442 µg/mL (Abdullah et al. 2022). Derivative of coumarin isolated from *Calophyllum brasiliense* affected the ultrastructure and morphology of *L. amazonensis* promastigotes by targeting the exogenous and endogenous sterols of mitochondrial membrane, altered the lipid composition by downregulating the essential lipids of the plasma membrane and nuclear membrane, hence causing destabilization of mitochondrial membrane potential (Shaha 2025). Similarly, berberine chloride is a plant-originated isoquinoline alkaloid that inhibits the growth of promastigotes of *Leishmania* by triggering the proton pumps in the inner membrane of mitochondria that disturb the transmembrane proton gradient and membrane potential. It results in the accumulation of reactive oxygen species (ROS) and ultimately apoptosis (De Sarkar et al. 2019). The growth and proliferation of *L. amazonensis* promastigotes and amastigotes were diminished by aqueous extract of *Physalis angulata* with IC50 values of 39.5 and 43.4 µg/mL, respectively. It modified the ultrastructure of the parasite by the emergence of vacuoles and myelin-like structures in the membrane of flagellar pockets and changes in the flagellar membrane, leading to the deterioration of the plasma membrane (Novitasari et al. 2024).

Inhibition of Enzyme Actions

Plant extracts can suppress the activity of several important enzymes of *Leishmania,* leading to deteriorating impacts such as the generation of oxidative stress, inhibition of cell growth and proliferation, and effect the *Lesihmania*'s ability to penetrate macrophages (Ali et al. 2021). Apigenin, vitexin, quercitrin, isovitexin, galangin, iso quercitrin, orientin, iso orientin, fisetin, 7, 8-dihydroxyflavone, and quercetin, a group of dietary flavonoids, retarded the growth of *L. amazonensis.* It targeted the activity of the arginase enzyme. The hydroxyl group at position 3 rendered fisetin a highly potent inhibitory agent (87%) by downregulating the activity of arginase enzymes, resulting in blockage of the polyamine biosynthetic pathway and generation of oxidative stress, leading to cell damage (Carter et al. 2021). Rutin (IC_{50}; 91.2 µg/mL) exhibited a higher inhibitory effect on the promastigotes of *L. tropica* than quercetin (IC_{50}; 182.3 µg/mL), gallic acid (IC_{50}; 198.00 µg/mL), and lupeol (IC_{50}; 200.77 µg/mL) due to high hydrophobic interactions (Goyzueta-Mamani et al. 2024). Epigallocatechin-3-gallate (EGCG), a phytochemical extracted from the *Camellia sinensis,* downregulated the activity of trypanothione reductase in *Leishmania infantum* (Inacio et al. 2021). *Arrabidaea chica* hexanic extract exhibited leishmanicidal activity against *L. amazonensis and L. infantum* promastigotes with IC50 values of 37.2 and 18.6 µg/mL respectively by inhibiting the activity of peptidase enzyme (Do Nascimento et al. 2022).

Induction of apoptosis

Apoptosis is a programmed cell death characterized by several morphological changes such as cellular shrinkage, fragmentation of apoptotic bodies, chromatin condensation and lack of inflammation (Sadr et al. 2025). Plant extracts primarily trigger leishmanicidal effects through the translocation of phosphatidylserine, generation of oxidative stress, cell cycle arrest, mitochondrial-dependent and caspase-independent apoptosis (Pyne et al. 2025). The Antileishmanial activity of *Q. velutina, C. procera,* and *N. tabacum* was demonstrated on promastigote and intra-macrophage amastigote stage of *L. tropica*. Q. velutina was most effective in triggering apoptosis in parasites by exposing the phosphatidylserine in the stationary phase from the inner membrane to the outer membrane, facilitating the recognition and phagocytosis by immune cells (Ilaghi et al., 2021). Artemisinin is an antileishmanial drug derived from the Chinese plant *Artemisia annua* L. have documented as an inhibitory agent for *L. donovani* promastigotes by inducing apoptosis through DNA fragmentation, destabilization of mitochondrial membrane potential, phosphatidylserine translocation, and cell cycle arrest in sub-G0/ G1 (Solano-Gálvez et al., 2024).

Similarly, *Aloe vera* leaf exudate exhibited a leishmanicidal effect against *L. donovani* promastigotes with IC50 values of 110 µg/mL by inducing caspase-independent cell death characterized by translocation of phosphatidylserine, followed by loss of mitochondrial membrane potential, cytosolic release of cytochrome C, and simultaneous nuclear alterations (Pyne et al. 2023).

Cell cycle arrest

Cell cycle arrest is the inability of the cell to progress into the next phase of the cell cycle, G1 phase, S phase, G2 phase, or M phase, triggered by DNA damage, cellular stress, activation of oncogene, and deprivation of nutrients (Huber et al. 2021; Matthews et al. 2022). Styrylpyrone, extracted from *Aniba panurensis*, exhibited antileishmanial activity against *L. amazonensis* promastigotes, with IC50 and IC90 values of 95.7 ± 0.2 µM and 187.5 ± 3.6 µM, respectively (Fernandes et al. 2021). Ethyl acetate fraction of Neem leaf extracts exhibited antileishmanial activity against *Leishmania donovani* promastigotes with an estimated IC50 value of 52.4 µg/mL by inducing growth arrest at sub G0/G1 phase of the cell cycle (Islas et al. 2020; Wylie and Merrell 2022). Artemisinin, a sesquiterpene lactone isolated from *Artemisia annua,* exhibited antileishmanial properties against *Leishmania donovani* promastigotes and amastigotes with IC_{50} values of 160 and 22 µM, respectively by inducing growth arrest at the sub-G_0/G_1 phase (Shaha 2025). *Embilica officinalis* L. showed leishmanicidal efficacy against *L. donovani* promastigotes and amastigotes with IC50 values 21.67 µg/mL and 34.82 µg/mL respectively by inducing cell cycle arrest in promastigotes at the G_0/G_1 phase and suppressing the proliferation of the parasite by blocking its progression into the S-phase (Ali et al. 2021).

Current challenges and future perspectives

Some research studies have centered on how to prevent the adverse effects of the drugs effective against leishmaniasis for instance cisplatin with the simultaneous supplementation of a protective agent, including triggering antioxidant enzyme activity. Extracts of various medicinal plants are known for their protective abilities against toxicities induced by cisplatin (Abdelhiee et al. 2025). The presence of an infective form of *Leishmania*, amastigotes inside the macrophage, makes the treatment of the disease difficult. For example, (Lessa et al. 2025) investigations concluded that synthetic flavonoid dimers can enhance the accumulation of drug in the macrophage resulting in the prevention of resistance through the disruption of the ATPase pump. Some experimental studies concluded that the combination of traditional drugs with different natural components can control immunological control (de Almeida et al. 2024). For example, a combination of cisplatin and *W. somnifera* had demonstrated more leishmanicidal and immunological activity against *L. donovani* than cisplatin alone (Sachdeva and Sharma 2022). Macrophages are targeted actively and passively by microspheres, nanoparticles, liposomes and carbon nanotubes (Singh et al. 2022). Macrophages naturally phagocytosed the nanoparticles and liposomes, thus facilitating the drug delivery to the target site. Moreover, these components lessen the toxicity of the drug by facilitating the specific-site availability of the drug into the macrophages (Jamshaid et al. 2021; Singh et al. 2022). Gold nanoparticles conjugated with quercetin were used to dysfunction the oxygen protozoa in the macrophages (Bessa et al. 2024). Due to insufficient data generation from the *in vitro* investigation, it is challenging to fully utilize the above-mentioned plant extracts and plant-derived natural components in the development of new drugs.

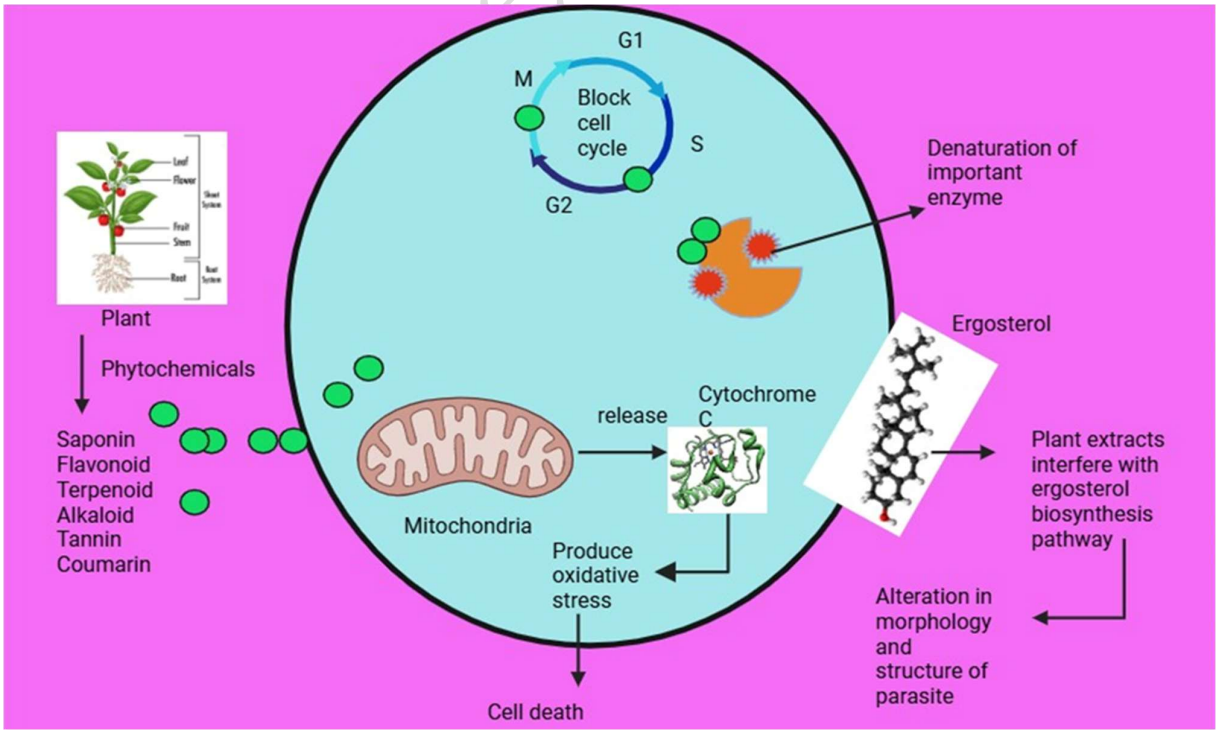

Fig. 2: Diagram demonstration of the mode of action of different phytochemicals against *Leishmania.*

Table 2: Plant extracts of various species control leishmaniasis by targeting different stages of *Leishmania in vitro*.

Scientific name (Plant)	Family	Plant Part used	Solvent used	Phytochemicals	Target organism	Target stage	IC50 (µg/ml)	Activity	References
Acanthospermum hispidum	Asteraceae	Whole plant	50% aqueous ethanol	Alkaloids	*L. donovani*	promastigotes	32.10	Moderate	Ohashi et al. 2018
Afzelia africana	Phyllosiphonaceae	Stem bark	50% aqueous ethanol	Alkaloids, saponins, tannins, flavonoids	*L. donovani*	promastigotes	77.10	weak	Ohashi et al. 2018
Argemone mexicana	Papaveraceae	Aerial part	Petroleum ether	-	*L. donovani*	Promastigotes	50.0	Moderate	Sultana 2021
Artemisia absinthium	Asteraceae	Leaves	Hydrodistillation	Essential oil	*L. major*	Promastigotes	1.49	High	Mathlouthi et al. 2018
Artemisia campestris	Asteraceae	Leaves	Hydrodistillation	Essential oil	*L. major*	Promastigotes	2.20	High	Mathlouthi et al. 2018
Artemisia herba-alba	Asteraceae	Leaves	hydrodistillation	Essential oil	*L. major*	Promastigotes	1.20	High	Mathlouthi et al. 2018
Baphia nitida	Fabaceae	Stem bark	50% aqueous ethanol	Tannins, flavonoids, saponins, glycosides	*L. donovani*	Promastigotes	34.40	Moderate	Ohashi et al. 2018
Bidens pilosa	Asteraceae	Whole plant	50% aqueous ethanol	Essential oil, flavonoids, alkaloids, saponins, triterpenes	*L. donovani*	Promastigotes	28.90	Moderate	Ohashi et al. 2018
Boswellia serrata	Burseraceae	Resin	Polar fractions of dichloromethane	Boswellic acids	*L. donovani*	Amastigotes	0.88	High	Greve et al. 2021
Bridelia ferruginea	Euphorbiaceae	Leaves	50% aqueous ethanol	Flavonoids, tannins, triterpenoids	*L. donovani*	Promastigotes	16.50	Moderate	Ohashi et al. 2018
Cassia alata	Leguminosae	Leaves	50% aqueous ethanol	Flavonoids, glycosides	*L. donovani*	Promastigotes	10.10	Moderate	Shah et al. 2016
Cassia glauca	Fabaceae	Leaves	Methanol	Flavonoids	*L. tropica*	Promastigotes	9.62	High	Shah et al. 2016
Cassia sieberiana	Fabaceae	Leaves	50% aqueous ethanol	Flavonoids, alkaloids	*L. donovani*	Promastigotes	62.90	Weak	Bouyahya et al. 2017
Ceiba pentandra	Malvaceae	Stem bark	50% aqueous ethanol	Isoflavones, sesquiterpenoids	*L. donovani*	Promastigotes	31.10	Moderate	Ohashi et al. 2018
Citrus sinensis	Rutaceae	Leaves	Methanol	Flavonoids	*L.tropica*	Promastigotes	12.27	Moderate	Shah et al. 2016
Cola acuminata	Sterculiaceae	Stem bark	50% aqueous ethanol	Purine alkaloids, catechins, (tannins)	*L. donovani*	Promastigotes	47.80	Moderate	Ohashi et al. 2018
Clausena anisata	Rutaceae	Roots	50% aqueous ethanol	Essential oil, indole alkaloids, coumarins	*L. donovani*	Promastigotes	12.10	Moderate	Ohashi et al. 2018
Cleistopholis patens	Annonaceae	Stem bark	50% aqueous ethanol	Flavonoids, saponins, alkaloids	*L. donovani*	Promastigotes	60.20	Weak	Ohashi et al. 2018
Cynara scolymus	Asteraceae	Stem leaf	Ethanol	-	*L.tropica*	Promastigotes	80.0	Weak	Yildirim et al. 2021
Eugenia uniflora	Myrtaceae	Seeds	50% aqueous ethanol	Essential oil, flavonoids, tannins	*L. donovani*	Promastigotes	26.60	Moderate	Santos et al., 2019
Glyphaea brevis	Malvaceae	Leaves	50% aqueous ethanol	Tannins, alkaloids, flavonoids	*L. donovani*	Promastigotes	43.40	Moderate	Ohashi et al., 2018
Guatteria latifolia	Annonaceae	Branch	n-hexane fraction of ethanol	Alkaloids	*L. amazonensis*	Promastigotes	51.7	Weak	Ferreira et al., 2017
Khaya grandifolia	Benin Mahogany	Stem bark	50% aqueous ethanol	Alkaloids, saponins, tannins	*L. donovani*	Promastigotes s	43.20	Moderate	Ohashi et al., 2018

Lantana camara	Verbenaceae	Leaves	Dichloromethane	Terpenoids	*L. amazonensis*	Amastigotes	21.8	Moderate	Delgado-Altamirano et al., 2017
Licania Salicifolia	Chrysobalanaceae	Leaves	Ethyl acetate	Flavonoids, Triterpenes	*L. panamensis*	Amastigotes	9.8	High	Wilson et al., 2020
Mondia whitei	Apocynaceae	Roots	50% aqueous ethanol	Glycosides	*L. donovani*	Promastigotes	31.0	Moderate	Ohashi et al. 2018
Murraya koenigii	Rutaceae	Stem	Petroleum ether	-	*L. donovani*	Promastigotes	98.0	Weak	Sultana 2021
Persea ferruginea	Lauraceae	Leaves	Ethyl acetate	Triterpenes, coumarins, leucoanthocyanidins	*L. panamensis*	Amastigotes	25.5	Moderate	Wilson et al., 2020
Phoenix dactylifera	Arecaceae	kernel	Methanol	Gallic acid	*L. major*	Promastigotes	23.0	Moderate	Albakhit et al., 2016
Prosopis juliflora	Fabaceae	Leaves	Methanol	Saponins, tannins, flavonoids, alkaloids	*L. donovani*	Promastigotes	3.12	High	Mutile et al. 2021
Prunus armeniaca	Rosaceae	Leaves	Ethanol	Alkaloids, terpenoids, coumarins, tannins, phenolics, flavonoids	*L. tropica*	Promastigotes	16.18	Moderate	Shaheen et al. 2020
Pyrus communis	Rosaceae	Leaves	Ethanol	Alkaloids, phenolics, tannins, flavonoids, terpenoids, quinones, saponins	*L. tropica*	Promastigotes	56.68	Weak	Shaheen et al. 2020
Pyrus pashia	Rosaceae	Leaves	Ethanol	Alkaloids, phenolics, tannins,	*L. tropica*	Promastigotes	60.95	Weak	Shaheen et al. 2020
Salvia clandestina	Lamiaceae	Aerial part	n- Hexane	-	*L. infantum*	Promastigotes	14.11	Moderate	Et-Touys et al., 2016
Schinus terebinthifolia	Anacardiaceae	Fruits	n- Hexane	Triterpenes	*L. amazonensis*	Promastigotes	13.90	Moderate	Wilson et al., 2020
Spondias mombin	Anacardiaceae	Leaves	50% aqueous ethanol	-	*L. donovani*	Promastigotes	81.50	Weak	Ohashi et al., 2018
Tamarindus indica	Fabaceae	Leaves	50% aqueous ethanol	Phenolics, flavonoids	*L. donovani*	Promastigotes	58.12	Weak	Ohashi et al., 2018
Terminalia ivorensis	Combretaceae	Leaves	50% aqueous ethanol	Terminolic acid, quercetin, β-glycyrrhetinic acid	*L. donovani*	Promastigotes	24.90	Moderate	Ohashi et al., 2018
Thonningia sanguinea	Balanophoraceae	Whole plant	50% aqueous ethanol	Alkaloids, tannins, flavonoids	*L. donovani*	Promastigotes	18.60	Moderate	Ohashi et al., 2018
Treculia africana	Moraceae	Stem bark	50% aqueous ethanol	Glycosides, catechin, cyanidin	*L. donovani*	Promastigotes	44.80	Moderate	Ohashi et al., 2018
Ximenia americana	Olacaceae	Stem and twigs	50% aqueous ethanol	Tannins, flavonoids, alkaloids	*L. donovani*	Promastigotes	36.10	Moderate	Ohashi et al., 2018
Ziziphus spina-christi	Rhamnaceae	Leaves	Methanol	Tannins, flavonoids, alkaloids, glycosides, terpenoids	*L. major*	Amastigotes	54.6	Moderate	Albalawi, 2021

Conclusion

Regardless of the extensive epidemiological studies of Leishmaniasis, this zoonotic disease is still unmanaged and uncontrolled. Considering Leishmaniasis is an overlooked parasitic disease with substantial healthcare ramifications, scientists from across the world should dedicate more efforts to it. Essentially, the most effective approaches to achieve satisfactory control concerning the full eradication of Leishmaniasis from certain developing nations include establishing the best possible monitoring system and control tactics to minimize the morbidity and mortality rate, an appropriate strategy to control vector population, recognizing and fighting potential hazards, and a secure, harmless, short and cost-effective treatment.

The current study demonstrates the important antileishmanial activities of a wide range of medicinal plant extracts *in vitro* experimental investigations. However, it is important to emphasize the necessity of incorporating the findings obtained from the *in vitro* investigations about the therapeutic value of plant extracts, their metabolic products, and compositions against multiple *Leishmania* species into healthcare practices.

DECLARATIONS

Funding: No.

Acknowledgement: None.

Conflict of interest: The authors declare no conflict of interest in this study.

Data Availability: Not Applicable

Ethics Statement: Not applicable

Author's Contribution: TS and ZUN: Idea and design; MS, RAR, JI, KA, and FHB: Wrote manuscript; AMAK and IZ: Reviewed and edited it.

Generative AI Statement: The authors confirm that no AI-contributed technologies were utilized when preparing this manuscript.

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