***Review article:***

MEDICINAL PLANTS WITH ANTIFILARIAL ACTIVITY: A REVIEW

**ABSTRACT**

Aim: *Lymphatic filariasis* is a significant global health issue. Their endemicity affects present-day subtropical regions, particularly those in Asia, Latin America, and Africa. Currently, the primary antifilarial medications used to control human filariasis are diethylcarbamazine (DEC), ivermectin, and albendazole. Diethylcarbamazine and ivermectin are microfilaricidal drugs, causing adverse reactions and resistance, prompting the search for safer and effective alternatives.. The objective of this study is to review plants and isolated compounds with filaricidal activity.

Methodology: Several electronic databases, such as PubMed, Google Scholar, and Science Direct, were used to gather pertinent data on Lymphatic filariasis, medicinal plants, plant constituents, traditional uses of chosen medicinal plants, and some pure compound isolates of many chosen medicinal plants that have been shown to have filaricidal potencies using *in vitro* and *in vivo* models. Several plants, notably: *Pongamia pinnata*, *Sphaeranthus indicus*, *Quisqualis indica* and *Terminalia bellerica* showed activity against filarial infections at dose/ %inhibition of  250µg/mL, 1mg/ml, 34.50µg/mL and 27mg/ml respectively against adult parasitic stages.

Conclusion: The results suggest plants as a promising source for antifilarial agents. Further research is needed to establish their mechanisms of action, toxicities and clinical potentials. The leaves were primarily used for extraction due to easy accessibility. The Fabaceae family contains the most plants with anti-filarial activity.

***Keywords:*** Filaricidal, antifilirial, medicinal plants, herbal medicine, filariasis, *in vivo*, *in vitro*

**1.0 INTRODUCTION**

*Lymphatic filariasis* (L.F.) is a neglected vector-borne infection, caused by three filarial worms: *Wuchereria bancrofti*, *Brugia timori* and *Brugia malayi* through the bites of infected Anopheles, Aedes or Culex mosquitoes (1). Common clinical symptoms of *Lymphatic filariasis* are acute filarial fever, hydrocele, lymphedema and elephantiasis. These symptoms result in disability, mental stress, social stigma and the inability of the affected individuals to work (2). Lymphatic filariasis is ranked as one of the major disease burdens, even though the clinical manifestations are not fatal (3). It is debilitating and has been one of the predominant diseases in Africa, Asia, parts of America and the Western Pacific (4). Currently, an estimated 67.88 million people are infected with microfilaria, 16.68 million and 19.43 million are suffering from lymphedema and hydrocele respectively (1).

The elimination of lymphatic filariasis can be achieved by halting the spread of the infection through preventive chemotherapy. The World Health Organization (WHO) recommends a preventive chemotherapy strategy known as mass drug administration (MDA) for this purpose (5). MDA entails the distribution of an annual dose of medications to the entire at-risk population. Although these medications have a limited effect on adult parasites, they are effective in reducing the density of microfilariae in the bloodstream, thereby preventing the transmission of parasites to mosquitoes.

Potential herbal plants for treating parasitic diseases have attained greater significance in the manufacture of novel drugs. Several plants have been reported to have antiparasitic effects (6, 7) with various chemical constituents. Plants are ostensibly one of the main sources of compounds against infectious agents. This review highlights various plant species from different families that have been documented for their potential in treating filariasis.

**1.1** **Life cycle of worms that cause** *Lymphatic filariasis*

The life cycle is divided into two main stages which are the mosquito and human stages. The early stage begins with the mosquito. Usually, the mosquito ingests the microfilariae during a bite. After ingestion, the microfilariae develop into first-stage larvae and subsequently into third-stage larvae (fig 1).

During the human stages of infection, a bite from an infected mosquito typically from the *Mansonia* or *Aedes* species during a blood meal transfers third-stage filarial larvae onto the skin of the human host, allowing them to penetrate the wound. Once inside, the larvae develop into adult worms that primarily reside in the lymphatic system (8).



Fig 1. Life cycle of filarial; the figure was designed using Adobe illustrator (Version 27.7.0.421) based on (9).

**2.0 METHODOLOGY**

2.1 Search Database

Electronic databases such as Google Scholar, PubMed, Science direct, Booksc.org and emerald were used to search for publications on medicinal plants with anti-filarial activity. A total of 80 publications were included in the dataset for analysis after two rounds of selection. Keywords and phrases used for the search were “*Lymphatic filariasis*”, “Medicinal plants with anti-filarial”, “Elephantiasis”, “Geographical distribution of the plants”, “Overview of Lymphatic filariasis”, “Overview of the plants with anti-filarial”.

2.2 Inclusion and exclusion criteria

Information obtained excluded articles written in languages other than English and articles published before the year 2000. The articles used were appraised to determine if they contained validated *in vivo* and/ or *in vitro* anti-filarial models.

Articles were reviewed with respect to the plant botanical names, parts of plants used, solvent used for extraction, traditional and documented medicinal uses of the plants, anti-filarial and models used (*in vivo* or *in vitro*), active pharmacological constituent used and pure plant isolates with anti-filarial activity.

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow chart was used to conduct a thorough review as described by (10).

This chart is divided into four main stages, as illustrated in fig 2. These stages include identifying relevant literature, screening the reports, reading the full text to determine eligibility, and applying exclusion and inclusion criteria.

2.3 Data Analysis

The initial search strategy identified around One hundred and eighteen (118) articles. In this study, ninety (90) studies were accepted for further screening and met all of the inclusion criteria (article in English, have full text, related to anti-filarial properties of plants and dated mainly from the year 2009 to 2024). Different parts of each article, including the title, abstract, introduction, methods, results, discussion, and conclusion, were assessed. The inclusion and exclusion criteria, sampling method, existence of valid instruments was also checked. Based on the search results, eighty (80) studies were identified; however, fourteen (14) articles were excluded from the review and sixty-six (66) articles were left for more analysis.

Records identified through database searching (PubMed, Google Scholar) (n= 118)

Identification

Records after duplicates removed

(n=90)

Screening

Records excluded

(n=10)

Records screened

(n=90)

Full-text articles assessed for eligibility

(n=80)

Full-text articles excluded

(n=14)

Eligibility

Studies included in the review analysis

(n=66)

Included

Fig 2. PRISMA-adapted flow diagram of included and excluded studies.

**3.0 RESULTS**

Table 1 describes the Scientific name, Family Name, plant secondary metabolites, location, method of extraction, screening method (in vitro or in vivo), mechanism of action, parts used and other traditional uses. Approximately thirty (30) plants were found to possess anti-filarial properties, with most of these plants located in Southern Asia, Africa, and South America.

Figure 3 is a detailed graph showcasing the distribution of various plant parts, prominently featuring the vital components such as leaves roots, flowers, and fruits. Meanwhile, Figure 4 offers an intriguing depiction of plant family distribution, providing insights into the diversity and relationships among different plant groups.

**3.1 Literature on plants reported to have filaricidal activity**

Numerous plant-based medicines have been reported to be filaricidal which include the following:

*Aegle marmelos* (L.) Correa also called golden apple, leaves at **100 mg/mL** dose revealed complete loss of movement after 48h of incubation of *B. malayi* microfilariae (11). Also, a half maximal inhibitory concentration $(IC\_{50})$ of 70 µg/ml was obtained by methanolic extract of *Aegle marmelos* leaves.

*Alnus nepalensis* D. Don also called Nepalese alder, crude methanolic extract of *Alnus nepalensis* leaves have been analyzed for antifilarial activity in a study undertaken by (12). The results revealed that crude methanolic extract exerted superior microfilaricidal with 100% lethal dose $(LC\_{100})$ of 15.63µg/ml and $IC\_{50}$ of 6.00µg/ml than macrofilaricidal activity. Chloroform with $LC\_{100}$ of 125 µg/ml and $IC\_{50}$ of 13.14 µg/ml, and n-butanol fractions with $LC\_{100}$ of 11.84 µg/ml, $IC\_{50}$ of 31.25 µg/ml, showed greater macrofilaricidal than microfilaricidal effect. Alnus dimer, and (5S)-5-hydroxy-1-(4-hydroxyphenyl)-7-(3,4-dihydroxyphenyl)-3-heptanone possessed excellent in vitro macrofilaricidal ($IC\_{100}$: 15.63µg/ml, $IC\_{50}$: 6.57–10.31µg/ml) and microfilaricidal ($IC\_{100}$: 31.25–62.5µg/ml, $IC\_{50}$: 11.05–22.10µg/ml) activity (12).

*Andrographis paniculata* Burm.is commonly known as King of Bitters. The aqueous extract of the dried leaves of *Andrographis paniculata* Burm. evaluated by *in vitro* studies against adult worms of sub periodic *Brugia malayi* hasbeen reported to have anti-filarial activity. At concentrations of 1.0, 5.0 and 10.0 mg/ml, the relative mobility values of 32, 0 and 0 respectively were observed after 24-hour incubation period, exhibiting anti-filarial effect in a dose-dependent manner (13).

*Azadirachta indica* A. Juss commonly known as neem, (14) evaluated the potential effect of Alcohol and aqueous extracts of flowers of *A. indica* on lymphatic filariasis *in vitro* against microfilariae, nerve muscle preparation and whole worm of *Setaria cervi*. An initial rise in amplitude, tone and rate of contractions characterized the response on the whole worm. Nerve muscle preparation responded with an absent of initial stimulation phase and dose dependent inhibition of spontaneous motility followed by reversible loss of motion. $LC\_{50 }$of alcohol extract was 15µg/ml and that of the aqueous extract was 18ng/ml.

*Bauhinia racemosa* Lam., commonly called Burmese silk orchid, is a small deciduous tree that grows in poor and very harsh environment. Galactolipid and catechin were obtained from the n-butanol fraction of ethanolic extract of the leaves of *B. racemosa,* in an experiment conducted to investigate galactolipids as a new class of antifilarial compound against *Brugia malayi* (15).

*Botryocladia leptopoda* (J. Agardh) Kylin., popularly called sea grapes or red grape alga, is thallus like, broadened and about 10-30 cm tall. An experiment undertaken by (16) to affirm the use of *Botryocladia leptopoda* in lymphatic filariasis was done using *Litomosoides* *sigmodontis* and *Acanthocheilonema* *viteae* and a subperiodic strain of the human lymphatic ﬁlarial parasite *Brugia malayi*. From the results obtained, the crude ethanol extract was active in all three parasites; the $LC\_{100}$ was 62.5µg/ml for *Acanthocheilonema viteae*, 31.25µg/ml for *Litomosoides sigmodontis* and 125µg/ml for *Brugia malayi*.

*Butea monosperma* Lam. popularly known as Flame of the forest, is a medicinal legume tree widely distributed in India and Himalaya (17).The leaves of *B. monosperma* L. tested against *S. cervi* showed an incredible antifilarial activity with $IC\_{50}$ of 1.25mg/ml for methanol and 3.6 mg/ml for hexane-ethanol extract (18). (19) also reported that aqueous extract of *B. monosperma* leaves exhibited a complete loss of microfilariae movement at 100 µg/mL concentration as compared to controls. However, the roots extracts showed dose dependent inhibition of movement of microfilariae. Another study revealed a high degree of correlation between the antifilarial effect of *Butea monosperma* and the level of lipid peroxidation and protein carbonylation in a dose dependent manner (20).

*Caesalpinia bonducella* L. Fleming is a tropical shrub widely distributed in Asia, South America and Eastern and Southern Africa. It is commonly known as Fever nuts and nicker nut (21). Alcoholic extract of the seed kernel of *C. bonducella* decreased microfilariae count in *L. sigmodontis* from day 8 post-treatment and by 95% fall, killed 96% adult worms and sterilized female adult worm completely. Butanol fraction reduced microfilariae count by 73.7%, killed 82.5% of adult worms and caused absolute female worm sterilization. The aqueous fraction exhibited more than 90% microfilaricidal activity and sterilized the worms completely. Two chromatographic fractions of hexane soluble fraction exhibited 64% and 95% macrofilaricidal activity, respectively, reduced microfilariae count and sterilized the worm totally (22).

*Cardiospermum halicacabum* Linn. is an herbaceous plant which grows in Africa, America, Bangladesh, India and Pakistan. It is also known as balloon vine, heart vine or love-in-a-puff (23). (24) investigated the *in vitro* antifilarial effect of *Cardiospermum halicacabum* and reported that its aqueous extract reduced movement of the adult female after 24h of exposure, adult males after 3 days and the release of microfilariae beginning from the second day at a concentration greater than 500µg/ml. At 2µg/ml, ethanol extract caused inhibition of movement of adult worm and release of microfilariae from the female worm. However, at 500µg/ml, ethanol extract rapidly decreased the movement of the microfilariae on the second day.

*Eucalyptus globulus* Labill., commonly known as blue gum, is an evergreen tree, 40-70m tall with straight trunk 0.6-2m in diameter with narrow and irregular branches. A study by (25) evaluated *Eucalyptus globulus* Labill. against *Brugia malayi* using the jird model *Meriones unguiculatus* and *Mastomys coucha*. The $IC\_{50}$ of 62.5μg/ml and 31.2μg/ml obtained for adult and microfilariae respectively showed that ethanolic extract had *in vitro* activity. It also revealed 66.7% macrofilaricidal and microfilaricidal effect on *B. malayi* in *Mastomys* at 5 × 100 mg/kg dose when administered orally.

*Excoecaria agallocha* L. is an evergreen mangrove species that occurs in India, Pichavaram mangrove forest and Australia (26). Methanol extract of the leaves of *E. agallocha* demonstrated a dose dependent positive response as evident from stimulation of mortality in the developmental stages of *Setaria digitata* (27).

*Ficus racemosa* Linn., is a large deciduous tree which grows in moist localities, banks of streams, evergreen forests and deciduous forest. Aqueous and alcoholic extracts of the fruits of *F. racemosa* impeded the spontaneous movement of whole worm at 150 µg/mL and 50 µg/mL respectively and nerve muscle preparation of *Setaria cervi* at 350 µg/mL and 250 µg/mL, respectively. The extracts killed microfilariae in vitro with $LC\_{50}$ of 21 µg/mL and 27 µg/mL for aqueous and alcohol respectively and $LC\_{90}$ of 35 ng/mL and 42 ng/mL, respectively (14).

*Glycyrrhiza glabra* Linn. is a small perennial herb originated from Mediterranean region, central and southwest Asia and otherwise called sweet wood or Liquorice. It grows in the Mediterranean basin of Africa, Southern Europe and India (28). A study by (29) chemically analyzed the roots of *G. glabra*. In the study, they isolated and characterized an antifilarial agent, glycyrrhetinic acid, as effective against adult worms. Glycyrrhetinic acid was converted into six analogs and investigated for antifilarial activity by *in vitro* motility study and MTT reduction assays using microfilariae and adult worms of *Brugia malayi*. Of the six analogs, benzyl amide analog caused mortality to adults at 25µM and microfilariae at 50µM concentration and inhibited 49% MTT reduction of the adult worms. $IC\_{50}$ values were obtained as 8.8 µM for adult and 2.2µM for microfilariae.

*Gymnema sylvestre* R. Br., commonly known as “gurmar”, is an indigenous perennial herb that grows in tropical Africa, Australia, China, India, Malaysia, and Sri Lanka. Studies by (16, 30) reported $IC\_{50}$ of 65.0 μg/ml and 32.5 μg/ml against adult worm and microfilariae respectively. This shows that ethanolic extract of *Gymnema sylvestre* R. Br. was active *in vitro* by killing 65.0% of adult worm and embryo of *B. malayi* in *Mastomys*. These were obtained at a dose of 5 × 100mg/kg by oral route. In an *in vivo* test carried out at 5×100mg/kg by subcutaneous route, a significant macrofilaricidal efficacy by death of 65.0% transplanted adult *B. malayi* and powerful microfilaricidal effect on the day of autopsy.

*Haliclona oculata* C. also known as mermaid’s glove, is a species of marine sponges. It is a rich source of nitrogen containing metabolites with various biological activities (31). In a study, to assess the *in vitro* and *in vivo* antifilarial effect of *Haliclona oculata* against *Brugia malayi*, the methanol extract (15.61µg/ml), chloroform fraction (7.81µg/ml) and chromatographic fractions (7.81µg/ml) of the whole plant of *H. oculata* eradicated *B. malayi* microfilariae and adult worm effectively. $IC\_{50}$ was obtained as 1.80 µg/ml in the presence of methanol extract, 5.00 µg/ml in the presence of chloroform and 1.62µg/ml in the presence of chromatographic fractions. The $IC\_{50}$ for microfilariae were 1.72, 1.881 and 1. 19lµg/ml, respectively under the same exposure conditions. In the primary jird model, 51.3%, 64.0% and 70.7% macrofilaricidal activity were demonstrated by methanol extract, chloroform and chromatographic fractions respectively at a dose of 100 mg/kg. They also caused 45–50% mortality of adult worms with less effect on microfilariae in secondary model. Mimosamycin, Xestospongin-C, Xestospongin-D and Araguspongin-C in the chromatographic fraction were responsible for its highest antifilarial activity (31).

*Hibiscus mutabilis* Linn., also known as confederate rose, is a woody shrub which is native to China and cultivated throughout Southern Asia (32). Studies by (33, 34) analyzed methanolic extract of leaves of *Hibiscus mutabilis* against bovine *Setaria cervi* to investigate its activity in lymphatic filariasis treatment. Ferulic acid was isolated from ethyl acetate fraction of *Hibiscus mutabilis* as the bioactive compound responsible for its antifilarial effect. The crude methanolic extract and ferulic acid revealed excellent filaricidal efficacy against microfilariae and adult of *S. cervi*. It was also reported that antifilarial effect of ferulic acid was through initiation of programmed cell death, downregulation and changing the phases of some important antioxidants such as Glutathione (GSH), Glutathione S-transferases (GST) and Superoxide dismutases (SOD) of *Setaria cervi*.

*Hibiscus sabdariffa* Linn*.* commonly known as Roselle, is an annual herbaceous shrub. It is native to Asia and Tropical Africa and cultivated throughout Central America, Caribbean, Australia, Hawaii, Florida and Philippines. The crude methanolic extract of the leaves of *H. sabdariffa* revealed its antifilarial action when screened *in vitro* against *B. malayi*. N– butanol fraction isolated from the crude extract killed 100% microfilariae at a dose of 250 μg/ml. Leaf methanolic extract given at 500mg/kg concentration for 5 days yielded about 30% macrofilaricidal activity against *B. malayi* (35).

*Jatropha gossypiifolia* L. is a vegetal species often called “bellyache bush”. It is widely distributed in Africa, India, South America, West Indies, Central America, and the Caribbean. A study by (16) on the *in vitro* and *in vivo* antifilarial activity of *Jatropha gossypiifolia* L. against *Brugia malayi*. $IC\_{50}$ of 60.0 μg/ml and 30.0. μg/ml obtained for adult and microfilariae respectively showed that ethanol extract of the dried roots of *J. gossypiifolia* was active. It also revealed 60.0% adulticidal and embryostatic effect on *B.* *malayi* in Mastomys at a dose of 5 × 100 mg/kg by oral route. At 5×100 mg/kg by subcutaneous route, the ethanolic extract demonstrated an excellent adulticidal efﬁcacy with 60.0% mortality of transplanted adult *B. malayi* and a marked microﬁlaricidal action on the day of autopsy.

*Lantana camara* Linn. popularly known as Spanish flag or West Indian lantana, is a flowering ornamental plant which is widely distributed throughout Caribbean, Central America and Northern South America. A study by (36) analyzed the antifilarial activity of the stem of *L. camara* against *B. malayi* and sterilization of female worms using rodent model *Mastomys coucha*. The crude methanolic extract at 1g/kg administered for 5 days caused 43% mortality of the adult worms and sterilized 76% of the surviving female worms. After fractionation, chloroform fraction demonstrated a 34.5% adulticidal activity and 66% filaricidal of the female worms. Oleanonic acid and oleanolic acid, the two isolated compounds from hexane and chloroform fractions revealed $LC\_{100}$ at 31.25 and 62.5 µg/ml, respectively on *B. malayi* *in vitro*.

*Leucas cephalotes* Roth. Spreng commonly known as spider wort, is an annual herb mainly found in India. The genus Leucas has about 100 Asiatic and African species. A study by(37) assessed the aqueous and alcoholic extracts of the flower and stem of *Leucas cephalotes* as a potential antifilarial medicine. They observed that,alcoholic extracts inhibited the natural motility of whole worm and nerve muscle preparation and reduced the period for microfilariae survival. Aqueous extracts of the flower and stem caused permanent loss of movement in nerve muscle preparation, associated with a decrease in amplitude, sound and extent of contractions.

*Moringa oleifera* Lam. is commonly called horseradish tree, drumstick tree or ben oil tree. It is native to northern India and Pakistan.The gum extract of *M. oleifera* at 125 mg/ml concentration result in the inevitable loss of movement of microfilariae and inhibited about 56% MTT possible reduction of the adult female worms of *B. malayi.* *In vivo* study showed that the extract at 500 mg/kg dose given orally for five days led to 69% adulticidal and 83% female worm’s sterilization in primary screening and secondary model using *Mastomys coucha,*  44% of adult worm of *B. malayi* were eliminated (38).

*Neurolaena lobata* Linn. is an herbaceous plant grown throughout Central America and Northwestern regions of south America. Studies by (39, 40) assessed 12 extracts of 11 *Neurolaena lobata* plants for *in vitro* macrofilaricidal activity against *B. pahangi*. Of the 12 extracts used, ethanolic extract of leaves of *Neurolaena lobata* revealed the best prohibitory action against movement of adult worms. Also, *in vitro* test of the ethanol extract of *N. lobata* advocates promising microfilaricidal and macrofilaricidal effects.

*Piper betle* L. is an evergreen and perennial creeper also called betel vine and Paan in India. The herb is native to Malaysia and distributed throughout India (41). It has been reported by (42) that 100mg/kg of crude methanol extract and 30mg/kg of its n–hexane fraction caused adulticidal and female sterilizing effect. The crude methanol extract and n–hexane fraction raise the antibody producing cells count, hemagglutinating antibody and the cell–mediated immune responses in mice. The crude extract and its n–hexane and chloroform fractions stimulated significant release of nitric oxide (NO) from murine peritoneal macrophages. The initiation of variety of T–helper cell immune response prevailed over the immune suppression caused by *B. malayi* infection and the chloroform fraction induced type one cytokine response in the BALB/c in mice. The n–hexane fraction caused an increased interleukin 4 and decreased Interferon gamma production which are type two cytokine response.

*Plumbago indica* Linn. Commonly known as scarlet leadwort, is native to South Asia and widely distributed throughout India, Sri Lanka (43). The macroﬁlaricidal property of *Plumbago indica* was studied in vitro by (44) against *Setaria digitata*. Full hindrance of motility was seen for concentrations ranging from 0.02 to 0.05$mgmL^{-1}$, however, all the worms were active in the control. Bioassay-guided fractionation of the crude extract prompted the recognizable proof of a very active fraction. 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide–formazan colorimetric assay showed ˃50% inhibition for the active fraction at 0.05, 0.002, 0.005, and 0.0006$mgmL^{-1}$ concentrations at 30min, 1 h, 2 h, and 6 h incubation periods, respectively.

*Pongamia pinnata* (Linn.) Merr., regularly called Poonga oil tree or Indian beech, is an intermediate evergreen tree which is distributed throughout Australia, Florinda, India, Tropical Asia and South Eastern Asia (45). (46) conducted a study on the in vitro effect of aqueous and alcohol extracts of the fruits and leaves of *Pongamia pinnata* (Linn.) Merr. on the natural motility of the whole worm and the nerve– muscle preparation of *Setaria cervi* and on the lifespan of microﬁlariae. Significant antifilarial activity represented by hindrance to the natural motility of the whole worm and the nerve–muscle preparation of *S. cervi*. The introductory induction effect was not absent on the nerve-muscle preparation in the presence of aqueous extract of fruits. 250µg/mL concentration of aqueous, 120µg/mL of methanolic extract of fruits and 270µg/mL of alcohol extracts of the leaves were needed to impede motility of the whole worm preparation.

*Psoralea corylifolia* Linn., often named purple fleabane, is an annual herb which is distributed throughout India, China and Southern Africa. A study by (47) studied the *in vitro* effect of aqueous and alcohol extracts of the leaves and seeds of *Psoralea corylifolia* on natural motility of the whole worm nerve muscle preparation of *Setaria cervi* and on the lifespan of microfilariae. The inhibitory response of Alcohol extracts of the leaves and seeds on spontaneous motility of the whole adult worm and the nerve muscle preparation was identified by the introductory, brief minor rise in the sound of contractions followed by loss of movement. The concentration needed to impede motility of the whole worm and nerve muscle preparation were 160 and 30 µg/ml alcohol extracts of leaves and 150, 20 µg/ml, alcohol extracts of seeds, indicating a cuticular permeability hurdle. Alcohol extracts of leaves and seeds generated *in vitro* mortality of microfilariae. $LC\_{50}$ and $LC\_{90}$ for alcohol extract of leaves were 15 and 25 mg/ml and that of alcohol extract of seeds were 12 and 18 mg/ml, respectively.

*Quisqualis indica* L.is an evergreen plant which needs sturdy support for growth. It is cultivated across the world particularly in Africa, China, Philippines, Bangladesh, Myanmar, Malaysia and India. In vitro study of the hydroalcoholic extract of flowers of *Q. indica* on adult worms and microfilariae of *Brugia malayi* have been undertaken by (48) using motility and MTT reduction methods. It was observed that female adult worms with $LC\_{100}$ of 62.5 µg/mL and microfilariae with $LC\_{100}$ of 125 µg/mL died in the presence of hydroalcoholic extract. The extract caused more than 90% inhibition in MTT reduction potential of the adult worms.$ IC\_{50}$ values for female adult and microfilariae were obtained as 34.50 and 31.88 µg/ml respectively.

*Saxifraga stracheyi* Hook.f and Thorn., is an evergreen rhizomatous perennial plant commonly known as pigsqueak and elephant ears. A 140µg/ml aqueous and a 250µg/ml alcoholic extract of the roots inhibited the spontaneous motility of the whole worm of *S. cervi.* This was identified by an elevation in the amplitude and decreased rate of contractions but had no effect on the tone of the contractions. A 30µg/ml concentration of aqueous and a dose of 20µg/ml alcoholic extracts were needed to produce similar outcome on the nerve–muscle preparation suggesting a cuticular permeability barrier (49).

*Sphaeranthus indicus* Linn.is found as weed in rice field, dry waste places and cultivated lands. It is widely cultivated in Africa, India, Sri Lanka and Australia*.* Methanolic extract of the leaves of *Sphaeranthus indicus* exhibited 100% loss of worm motility and killed the worms at a dose of 1mg/ml. Results of MTT reduction test undertaken at 1mg/ml for 4 hours’ incubation period showed that *S. indicus* exerted 61.20% inhibition in formazan formation compared to the control (50).

*Terminalia bellerica* Roxb. popularly referred to as Baheda, is a large deciduous tree that is distributed throughout India, Sri Lanka, Southeast Asia and Bangladesh. The antifilarial activity of plant methanol extract has been assessed showing a macrofilaricidal activity. That is, 84.63 ± 1.11 at 10mg/ml in MTT reduction assay with $IC\_{50 }$value of 2.7mg/ml (51).

*Tinospora crispa* (L.) Hook.f. is a woody climber commonly called heartleaf moonseed. It is used for treating hypertension, diabetes and backache in Malaysia (52). (53) revealed that at 0.5,1.0, 5.0 and 10.0 mg/ml concentrations, the aqueous extract of the stem of *T. crispa* showed antifilarial activity against adult worms of *B. malayi* with a mean relative movability value of adult worms between 0-100, in a dose dependent manner after 24 hours of incubation compared to RPMI1640 culture medium as control. (54) in their studies reported that 10mg/ml aqueous extract of *T. crispa* exhibited the antifilarial activity against *Dirofilaria immitis* with a mean relative movability value of 30.15% and p< 0.05 after 24 hours of incubation compared to DMSO control.

*Trachyspermum ammi* L. is an annual herbaceous plant, indigenous to Egypt and widely distributed in India, Iran, Afghanistan, Pakistan and European regions (55). *In vitro* antifilarial effect of methanolic extract of fruits of *Trachyspermum ammi* has been studied against *Setaria digitata* worms. Motility test showed absolute movement at higher concentration. Methanolic extract of the fruits of *T. ammi* showed macrofilaricidal activity by MTT reduction assay with $IC\_{50}$values of 0.067 and 0.019 mg/mL at 24 and 48-hour incubation periods respectively (56).

*Vitex negundo* Linn. is an aromatic large shrub with quadrangular branches and also called five leaved chaste tree. It is dispersed throughout tropical Africa, Afghanistan, India, China, Madagascar and Philippines (57). An antifilarial study has been conducted by(11) on the Ethyl acetate extract of *Vitex negundo* leaves against *Setaria cervi*. They observed a complete loss of movement in the motility assay and the MTT reduction gave >50% at a dose dependent manner at 10-, 6- and 2-hours incubation period respectively for 0.20, 0.50 and 1.00mg/ml. $IC\_{50}$ for the plant was obtained as 0.16mg/ml. In 2008, (57) again investigated the *in vitro* activity of *Vitex negundo* on the movement of *B. malayi* microfilariae. They found out that at 100 µg/ml concentration, the ethanolic extracts revealed a 100% inhibition of movement of microfilariae as compared to controls.

*Withania somnifera*. commonly called “ashwagandha”, is distributed across India, South and east Africa, Southern Mediterranean region to the Canary Islands (58). Withaferin A, isolated from *Withania somnifera* has been reported for in vivo larvicidal effects at a lowest conc. of 7.8µg⁄mL against *B. malayi*. A decrease in 63.6% of microfilariae and 66.2% of defective embryogenesis in female worms have also been demonstrated with Withaferin A.

*Xylocarpus granatum* Koenigis an evergreen tree that grows up to 20m in height (59). It is widely distributed in East Africa, South and Southeast Asia. In an experiment conducted by (60) *X.* *granatum* crude aqueous ethanolic extract caused 52.8% death of the adult worms and 62.7% death of microfilariae of *B. malayi*. Only ethyl acetate fraction was after fractionation. Of the eight pure molecules isolated, only two compounds viz, Gedunin and Photogedunin induced death of 80% of adult worms and 70% death of the transplanted *B. malayi* at 5x100mg/kg concentration by subcutaneous route. Gedunin obtained an $IC\_{50}$= 0.239µg/ml and Photogedunin had $IC\_{50}$=0.213µg/ml. (54) reported earlier that the dried seed extract of *Xylocarpus granatum* Koenig has a strong antifilarial activity against adult worms of subperiodic *B.* *malayi.*

Table 1 A summary of the various plants reported to have anti- filarial activities

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Scientific name**  | **Family Name** | **Chemical constituents present in plant** | **Preparation** | **PARTS USED**  | **OTHER TRADITIONAL USES** | **REFERENCE**  |
| *Aegle marmelos*  | Rutaceae | Coumarins Polyphenolic compounds  | Methanolic extraction by maceration | Dried leaves  | Asthma, fracture, hypertension, jaundice, wound healings, anemia, swollen joints  | (11, 20, 61) |
| *Alnus nepalensis*  | Betulaceae | Diarylheptanoids | Methanol and butanolic extraction by maceration  | Dried leaves | Recovery of wastelands, shifting cultivation, and coal mining  | (12, 62). |
| *Andrographis paniculata* | Acanthaceae | Labdane diterpenoid | Aqueous extraction by maceration | Dried leaves | Burns, common cold, diabetes, dysentery, fever, peptic ulcer, respiratory infections, skin infections, and snake bites  | (13, 63).  |
| *Azadirachta indica*  | Meliaceae | Azadirachtin | Alcohol and Aqueous extraction by maceration  | Leave Root Bark | Fever, chicken pox, foot fungi, neuromuscular pains, diabetes, cancer, heart diseases, herpes allergies, ulcer and hepatitis  | (64, 65) |
| *Bauhinia racemosa*  | Fabaceae | Galactolipid Catechin  | N-butanolic Ethanolic extraction by maceration  | Dried leaves  | Fever, headaches, dysentery, skin diseases, blood diseases, and diarrhea  | (15, 66) |
| *Botryocladia leptopoda*  | Rhizophoraceae | Palmitic acidCholesterol | Crude ethanol Hexane fraction by Soxhlet extraction  | All parts  | Antimicrobial, antiviral analgesics, antidiabetic, antipyretic, anti-inflammatory and antiprotozoal activities  | (16, 67) |
| *Butea monosperma*  | Fabaceae | Butrin | Ethanolic and Hexane-ethanolic extraction by maceration  | Dried Leaves  | Anti-diabetic, antifungal, anti-inflammatory, anti-diarrheal, dermal wound healing, anti-viral anthelmintic and anti-convulsive activities  | (19, 68) |
| *Caesalpinia bonducella*  | Fabaceae | BonducinCassane diterpenoids | Butanolic and Aqueous extraction by chromatography  | Seed  | Antidiabetic, antidiarrhea, anti-inflammatory, antitumor, and antimalarial activities | (21, 22) |
| *Cardiospermum halicacabum*  | Sapindaceae | Triterpenoid saponins | Aqueous and Ethanolic extraction by maceration  | Leave, stalk, root and whole plant | Diarrhea, dysentery, headache, diuretic, emetic, laxative, refrigerant rheumatism, snake bite and neck stiffness  | (24, 69) |
| *Eucalyptus globulus*  | Myrtaceae | Eucalyptol | Ethanolic extraction by maceration  | Leaves  | Asthma, tonsillitis, cold, hemorrhage, urinary disorders, bronchitis, malaria, rheumatism and wounds  | (25) |
| *Excoecaria agallocha*  | Euphorbiaceae | Excoecarianin | Methanolic extraction by maceration  | Leaves  | Sores, stings, leprosy and ulcer  | (26, 27) |
| *Ficus racemosa*  | Moraceae | Quercetin Kaempferol | Alcoholic and Aqueous extraction by maceration  | Fruit  | Diabetes, mumps, hydrophobia, hiccough, leprosy, wound washing, ulcer, menorrhagia and hemorrhoids  | (14, 70) |
| *Glycyrrhiza glabra*  | Fabaceae | Glycyrrhetinic acid Benzyl amide Octyl amide  | Aqueous extract by maceration  | Root  | Anemia, gout, sore throat, fever, cough, skin diseases, sexual debility, hiccough, jaundice, tonsillitis, and hyperdipsia  | (29, 71) |
| *Gymnema sylvestre*  | Asclepiadaceae | Gymnemic acids | Ethanolic extraction by maceration  | Leave  | Asthma, diabetes, complaint, inflammation, malaria and snake bite  | (16, 30) |
| *Haliclona oculata*  | Chalinidae | Mimosamycin, Xestospongin-C, Xestospongin-D Araguspongin-C  | Methanol and Chloroform fraction using chromatography  | Whole plant  | AntioxidantAnti-cancer | (31, 72) |
| *Hibiscus mutabilis*  | Malvaceae | Ferulic acid  | Methanol, ethyl acetate fraction, crude extraction by extraction  | Leave  | Mumps, persistent cough, menorrhagia, dysuria, burns, anodyne, and fistulae  | (33, 34) |
| *Hibiscus sabdariffa*  | Malvaceae | Delphinidin Cyanidin | N-butanolic extraction by maceration  | Leave  | Astringent, antiseptic, aphrodisiac, diuretic, demulcent, purgative, lever disease, hypertension, pyrexia  | (35, 73) |
| *Jatropha gossypiifolia*  | Euphorbiaceae | Jatrophone | Ethanolic extraction by maceration  | Root  | Hemorrhoids, eczema, itches, boils and carbuncles  | (16) |
| *Lantana camara*  | Verbenaceae | Oleanonic acid Oleanolic acid  | Chloroform extraction by maceration  | Stem Root Leave | Chicken pox, asthma, ulcer, swelling, cancer, malaria, antiseptic, bilious, fever and catarrhal infections  | (36, 74) |
| *Leucas cephalotes*  | Lamiaceae | Eugenol  | Aqueous and Alcoholic extraction by maceration  | Flower Stem  | Fever, asthma, paralysis, bronchitis, dyspepsia, swelling and leucoma  | (37, 75) |
| *Moringa oleifera*  | Moringaceae | Glucosinolates | Gum extraction by maceration  | Gum  | Fever, asthma, diabetes, wounds, hypertension, skin infections, cough, arthritis, body pains and weakness  | (38, 76).  |
| *Neurolaena lobata*  | Asteraceae | Neurolenin | Ethanolic extraction by maceration  | Leaves  | Cancer, ulcer, diabetes, inflammatory skin diseases, malaria, fungus infection, ringworm infections and pain  | (39, 40) |
| *Plumbago indica* | Plumbaginaceae | 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide–formazan  | Crude extraction by maceration  | Flower  | Anti-inflammatory, carminative, digestive anthelmintic, and nerve stimulatory  | (44, 77) |
| *Pongamia pinnata*  | Fabaceae | Pongamol | Alcoholic extraction by extraction  | Seed Fruit Leave | Bronchitis, chronic fever, whooping cough, and rheumatic joint pains, cold, dyspepsia, gonorrhea and leprosy  | (45, 46) |
| *Psoralea corylifolia*  | Fabaceae | PsoralenIsopsoralen | Aqueous and Alcoholic extraction by maceration  | Leaves Seeds  | Psoriasis, leukoderma, leprosy  | (47, 78) |
| *Quisqualis indica*  | Combretaceae | Quisqualic acid | Hydroalcoholic extraction by maceration  | Stem bark  | Parasitic worms, diarrhea gargling, nephritis, fever, rheumatism, headaches, flatulence, boils and ulcer  | (48, 79) |
|  | Saxifragaceae | Saxifragin | Aqueous and Alcoholic extraction by maceration  | Root  | Anti-arthritic, antidiabetic, anti-inflammatory and antimicrobial | (49) |
| *Sphaeranthus indicus*  | Asteraceae | Sphaeranthanol | Methanolic extraction by maceration  | Leaves  | Epilepsy, mental illness, headaches, jaundice, gastrointestinal disease, diabetes, leprosy, fever, chest discomfort, cough, hernia, hemorrhoids, worm infestation, dyspepsia, and skin diseases  | (50, 80) |
| *Terminalia bellerica*  | Combretaceae | Gallic acid | Methanolic extraction by maceration  | Fruit  | Hepatitis, asthma, eye diseases, diarrhea, cough and scorpion sting  | (51, 81) |
| *Tinospora crispa*  | Menispermaceae | Berberine | Aqueous extraction by maceration  | Stem | Hypertension, diabetes, backache  | (53, 54) |
| *Trachyspermum ammi*  | Apiaceae | Thymol | Methanolic extraction by extraction  | Fruits | Palsy, paralysis, tremor, cough, and gastrointestinal disorder  | (56) |
| *Vitex negundo*  | Lamiaceae | Vitexin | Ethyl acetate Ethanolic extraction by maceration  | Leaves  | Disease of the eye, asthma, biliousness, pain, and inflammation  | (11, 49) |
| *Withania somnifera*  | Solanaceae | Withanolides | Alcoholic extraction by maceration  | Leaves | Anthrax, arthritis, asthma, bronchitis, diarrhea, nausea, rheumatism, dropsy, tumors, typhoid, and wounds  | (38) |
| *Xylocarpus granatum*  | Meliaceae | Gedunin Photogedunin  | Aqueous extraction by maceration  | Leaves  | Hypertension, diabetes, backache  | (60) |

Figure 3. Bar graph showing plant parts distribution.

Figure 4: Bar graph Showing the plant family distribution

**DISCUSSION**

Numerous plants are traditionally employed for the treatment of various ailments. Among these, several have demonstrated anti-filarial activity that has been subject to investigation. This review consolidates various findings on plants exhibiting anti-filarial properties, with some having been studied through *in vivo*, *in vitro*, or a combination of both methods (12).

From our studies, based on thorough screening of various peer reviewed published articles from aforementioned database, a total of 34 different plants are reported to exhibit remarkable anti-filarial properties. Various phytochemicals found in plants contribute to their anti-filarial properties. Notable examples include Azadirachtin, diarylheptanoids, saxifragin, eucalyptol and ferulic acid. Azadirachtin, a chemical constituent of *Azadirachta indica*, serves as a potent non-toxic anti-filarial agent against *Setaria cervi* in a study by (64). The diarylheptanoids present in *Alnus nepalensis* are also linked to its anti-filarial effects (62). Additionally, saxifragin, the 5-glucoside of the flavonoid quercetin, is found in plants and insects and is the primary chemical constituent in *Saxifraga stracheyi*. *Eucalyptus globulus* contains eucalyptol, which is rapidly absorbed from the gastrointestinal tract when taken orally; its lipid solubility is further enhanced in the presence of milk (25). Lastly, ferulic acid, which possesses antioxidant properties due to its phenolic hydroxyl group, is the main constituent in *Hibiscus mutabilis.* The leaves have been identified as the primary parts utilized, as illustrated in fig. 1. This finding or pattern dovetails with a study by our previous studies in (6), where plant leaves were reported to be the most used parts for their antimalarial activity.

 Additionally, other plant parts, including roots, stems, fruits, flowers, seeds, and the whole plant, are also utilized. In herbal medicine, leaves are predominantly used due to their high concentration of bioactive compounds, such as tannins, flavonoids, and essential oils. Furthermore, leaves are the most accessible part of the plant and contribute to the conservation of endangered species. This is attributed to their ability to regenerate quickly after harvesting, while harvesting roots can result in the destruction of the entire plant (82).

The Fabaceae family contains the highest number of plants with anti-filarial properties, followed by the Malvaceae family as reported in Figure 2.0. The Fabaceae family, commonly referred to as the legume family, is well-known for its extensive medicinal properties. Throughout various cultures, plants from this family have been traditionally utilized for their therapeutic benefits(83). Their notable efficacy against filaria, a type of parasitic disease, can be attributed to their rich phytochemical composition. These plants are abundant in a range of bioactive compounds, including flavonoids, alkaloids, and saponins, which have demonstrated anti-filarial properties (84).

The most prevalent method employed for extraction was maceration (85). This technique entails immersing plant materials in a liquid for an extended duration, allowing the liquid to draw out the desired compounds effectively (86). Its popularity stems from its straightforward nature, requiring no sophisticated equipment or intricate procedures. Additionally, the prolonged contact between the plant material and the liquid enhances the extraction process, ensuring that a rich array of beneficial substances is obtained (87). Recent research by (88) has revealed that cold maceration can effectively extract compounds with superior antimicrobial properties. This fascinating technique not only enhances the quality of the extracts but also showcases the potential for developing more potent natural remedies.

*Aegle marmelos, Alnus nepalensis, Andrographis paniculata,* and *Azadirachta indica* are traditional plants used for treating malaria and asthma, showing effectiveness against filarial infections. Crude extracts obtained with alcohol like methanol resulted in a loss of motility in the organisms. Research shows that *Bauhinia racemosa, Botryocladia leptopoda*, and *Butea monosperma* also have anti-filarial properties, with active compounds such as galactolipid and catechin in Bauhinia racemosa, palmitic acid and cholesterol in *Botryocladia leptopoda*, and butrin in *Butea monosperma* (12, 15, 20).

Research indicates that *Caesalpinia bonducella, Cardiospermum halicacabum, Eucalyptus globulus,* and *Excoecaria agallocha* have anti-filarial properties*,* with *Eucalyptus globulus* specifically showing macrofilaricidal effects against adult parasites, similar to metronidazole. The seeds and leaves are used for these properties, with alcohol as the extraction agent. Additionally*, Ficus racemosa, Glycyrrhiza glabra, Gymnema sylvestre, and Haliclona oculata* exhibit activityagainst *Setaria cervi and Brugia malayi, with Ficus racemosa* showing IC50 values of 21 ng/ml and 27 ng/ml from its aqueous and alcoholic extracts, respectively. *Glycyrrhiza glabra, Gymnema sylvestre, and Haliclona oculata* have IC50 values against *Brugia malayi* of 8.8 µg, 65.0 μg/ml, and 1.19 µg/ml, respectively (24, 25).

*Hibiscus mutabilis, Jatropha gossypiifolia*, and other medicinal plants have shown anti-filarial activity against *Brugia malayi* and *Strongyloides cervi*. *Hibiscus mutabilis* is effective against *Strongyloides cervi* due to ferulic acid, while *Jatropha gossypiifolia* shows significant effects against *Brugia malayi* at a dosage of 5 × 100 mg/kg in vivo. *Moringa oleifera* demonstrates a 69% adulticidal effect at 500 mg/kg over five days. Additionally, *Piper betle* stimulates nitric oxide release, enhancing immune responses against *B. malayi* infection (36, 38).

Several plants, including *Pongamia corylifolia, Quisqualis indica,* and *Terminalia bellerica,* exhibit anti-filarial activities with IC50 values of 25 to 40 mg/ml*.* Additionally*, Tinospora crispa, Trachyspermum ammi, Vitex negundo, Withania somnifera,* and *Xylocarpus granatum* have medicinal properties for treating asthma, malaria, and pain while also showing activity against filarial infections. Key constituents include thymol, vitexin, withanolides, gedunin, and photogedunin (54, 81).

**CONCLUSION**

The 34 medicinal plants discussed in this review demonstrate a significant filaricidal activity. This highlights their significance in finding effective treatment options for these diseases. Ongoing research into the phytochemicals responsible for these effects could result in the development of new anti-filarial agents and strategies for disease prevention, ultimately supporting public health initiatives worldwide. Overall, this study offers a thorough data repository for the scientific community engaged in drug development and design for tropical infections.

**Data Availability**

The data used to support the findings of this study are included in the article and also available from the corresponding author upon request.

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