

POTENTIAL MEDICINAL PLANTS FOR LYMPHATIC FILARIASIS: A REVIEW

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ABSTRACT

Lymphatic filariasis (LF) is deemed to be a major health problem in tropical and subtropical countries. Adult worms may live for several years in the infected individual, producing microfilariae (mf) and thereby facilitating transmission of the disease through the vector mosquitoes. Filarial nematodes are responsible for several diseases which include elephantiasis, river blindness and tropical pulmonary eosinophilia. The drug of choice for controlling filariasis exhibits numerous side effects. Current strategies to control filariasis are not thought to be completely safe and successful. This warrants an effective and safe drug targeted against the adult filarial worm. Some lead has been made by researchers to investigate the effect of several medicinal plants on filarial worm and many of them have been reported to have antifilarial activity. This review presents the profiles of the plants as antifilarial agents which not only affect the target but should have very low or no side effects.

Keywords: Lymphatic filariasis, Microfilariae, Antifilarial, Adult worms.

INTRODUCTION

Lymphatic filariasis (LF) is a vector-borne, long-standing chronic disease which is prevalent in many parts of the tropics and subtropics of the world affecting millions of people and is the second leading cause of long-term and permanent disability in the world [1]. LF is caused by the lymph-dwelling nematode parasites *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*. The filarial nematode *W. bancrofti*, accounts for 91% of LF infections while *B. malayi* and *B. timori* are responsible for the remaining 9% in South and South East Asia [2]. Quite often, poor people are infected from disease and suffer from physical, mental and socioeconomic hardships [3]. 1.4 billion people are at risk of infection in 72 countries where filaria is endemic [4]. Currently over 120 million people are affected by the infection with 40 million people showing chronic disease symptoms [1, 5]. This is approximately 40% of worldwide filariasis burdens and it is expected that there is an economic loss of about 720 corers per year in the management of the disease [6]. WHO has recognized this major health problem as one of the six important tropical diseases [7, 8]. Majority of the infections are asymptomatic and about 40 million peoples have clinically evident symptoms (mostly hydroceles and lymphedema), making LF a leading cause of long-term disability [9, 10].

The filarial worms need two types of host to conclude their development, i. e., human or other mammalian hosts such as primate or cat, and mosquito vector from numerous species of the genera *Culex*, *Aedes* and *Anopheles* in which the larval development takes place. Symptoms of LF range from sub-clinical lymphangiectasia with severe edema and elephantiasis. These lymphatic dwelling parasites cause damage/blockage to the lymphatic system [11] leading to the clinical symptoms such as lymphedema, elephantiasis and hydrocele. Hydrocele, scrotal elephantiasis and chyluria are only seen with bancroftian filariasis.

Due to its significant medical, social and economic impact, in 1997, the 50th World Health Assembly passed a resolution for the elimination of filariasis by 2020 [7, 12]. Now, under the leadership of WHO, the Global Programme to Eliminate Lymphatic Filariasis (GPELF) is being implemented in 1999 by means of mass drug administration (MDA) to disrupt parasite transmission [7, 13]. The treatment policy includes a single-dose of MDA yearly for 4 to 6 years for all people in the endemic region except pregnant women and children upto 2 years of age. A combination of diethylcarbamazine (DEC) and albendazole (ALB) is given in most endemic areas, except in some areas of Africa where bancroftian filariasis is also present with onchocerciasis, therefore a

combination of ivermectin and ALB is scheduled [5, 14]. However, unfortunately this disorder is continuing due to the technological limitations of MDA strategy [15]. In 8 years (2000–2007), 570 million individuals were treated in 48 of the 83 endemic countries [16]. China in 2007 and Korea in 2008 declared the elimination of filariasis, and additional 5 countries were reported to no longer have any active transmission foci [17]. By halftime in 2010, MDA had successfully reduced disease rates in many areas [1, 13]; however, confounding factors impede the fight for global elimination. Filariasis research has not adequately explored variability among the lymphatic dwelling parasite species.

Treatment strategy

Current drugs used for MDA implementation by national programmes such as ivermectin, ALB and DEC, which have been the drugs of choice for filariasis control [18]. These drugs are effective in reducing microfilariae counts but not effective in killing adult worms [19–21]. Hence, these drugs provide only partial benefit to infected patients, and very often are associated with adverse reactions. DEC has been reported to cause side effects such as fever, gastrointestinal disturbance, headache, malaise and a skin rash that reduce patient compliance [22, 23].

Unavailability of vaccines as well as the pressure of increased risk of development of drug resistant worms urge for an urgent need of a cheap, non-toxic and novel antifilarial drug with long term antimicrofilarial or macrofilaricidal activity [24, 25]. Several medicinal agents have been derived and based on plants and utilized in traditional therapeutics. India has a rich tradition of using medicinal plants or their products in treating different disease conditions through Ayurveda, Unani and Siddha systems of medicine. Natural products of plant origin with insecticidal properties have been tried in the recent past for control of a variety of insect pests and vectors [26]. Many medicinal plants containing pentacyclic triterpene and oleanolic acid have antifilarial activity [27]. Several anti-filarial agents have been also discovered through research on medicinal plants used by local healers. This review focuses on isolated compounds, medicinal plants and folklore plants having antifilarial activity.

Plants effective against filarial parasite

Acacia auriculiformis A. Cunn. ex Benth. (Fam: Fabaceae)

Triterpenoid saponins acaciaside-A and acaciaside-B isolated from the funicles of *A. auriculiformis* are effective against both microfilaria and adult worm of *Setaria cervi* [28]. Except cestocidal effect, these

saponins at a concentration of 4 mg/mL killed 97% of microfilaria of *S. cervi* and 100% of adults within 100 min [29]. Ethanolic extract obtained from the funicles of the plant, when administered orally to pariah dogs (at 150mg/Kg/day for 45 days) naturally infected with *Dirofilaria immitis*, proved to be effective against both microfilaria and adult worm [30]. Drug probably causes a very high physiological stress on adult worms, resulting in their death and expulsion. It has been reported that these saponins enhance the cell membrane lipid peroxidation [31]. Also it has been reported that the conjugated unsaturated system of these saponins is involved in the formations of free radicals, which induce membrane damage through peroxidation of membranes in helminthes [32].

Aegle marmelos Corr. (Fam: Rutaceae)

It is famous for its ethanobotanical use for the treatment of Filariasis [33]. Methanolic extract of leaves at a concentration of 100ng/mL showed complete loss of motility of *B. malayi* microfilariae after 48 h, indicating the inhibition of the essential physiological process in larvae [34]. In another study inhibitory concentrations (IC₅₀) of methanolic extract of leaves was found to be 70 ng/mL [35]. Leaves were reported to have polyphenolic and coumarins compounds which shows dose dependent increase in the levels of lipid peroxidation and protein carbonylation. High degree of correlation coefficients was observed between the increase in the different oxidative parameters and the resultant loss of microfilarial motility [36].

Alnus nepalensis D. Don (Fam: Betulaceae)

A. nepalensis is a deciduous or semi-deciduous tree native to Pakistan, south-western China, hilly regions of Eastern and Northeastern India [37]. Crude extract of leaves of this plant have antifilarial activity *in vitro* on adult worm. *In vivo* results revealed that chloroform fraction produced >50% macrofilaricidal activity whereas methanolic fraction and n-butanol fraction caused 38–40% macrofilaricidal activity against *B. malayi* along with some female sterilizing effect. The isolated compound diarylheptanoid was also reported for antifilarial activity [38, 39].

Andrographis paniculata Burm. f. (Fam: Acanthaceae)

It is an annual herb, native to India. Water based decoction of the leaves of *A. paniculata* is reported for antifilarial activity against *Dipetalonema reconditum* microfilariae in dogs [40] and adult worms of subperiodic *B. malayi* [41, 42].

Asparagus adscendens Roxb. (Fam: Liliaceae)

Plant extracts showed strong antifilarial activity against *S. cervi*. Both alcoholic as well as aqueous extracts caused death of microfilariae *in vitro*. LC₅₀ and LC₉₀ being 8 and 16 ng/mL for aqueous extract, 3 and 12 ng/mL for alcoholic extract was observed respectively [43].

Azadirachta indica A. Juss. (Fam: Meliaceae)

It is also claimed for antifilarial activity [44]. Alcohol and aqueous extracts of flowers of *A. indica* were evaluated *in vitro* for its antifilarial activity against whole worm, nerve muscle preparation and microfilariae of *S. cervi*. The response on the whole worm was characterized by an initial increase in rate, tone and amplitude of contractions along with reversible paralysis. The primary stimulant effect is due to an irritant effect on the cuticle. There is an inhibition of spontaneous movements followed by reversible paralysis in nerve muscle preparation. The inhibition was concentration related. Alcohol and aqueous extracts had more or less analogous lethal effect on the *S. cervi* microfilariae; the LC₅₀ was reported to be 15 and 18 ng/mL, respectively. Flower extract was also effective against filarial worm *Setaria digitata* [45]. Antifilarial effect of polyphenol rich ethanolic extract obtained from the leaves of *A. indica* was demonstrated against adults and microfilariae of *S. cervi*. A dose-dependent reduction in microfilariae as well as adult worm viability was observed. The extract causes morphological alteration like thickening of epithelium, cuticle and muscle layers of the treated adult worms. Major apoptotic signs such as a higher amount of chromatin condensation, presence of fragmented chromatin and brighter fluorescence were observed in both adult and microfilariae of *S. cervi*. Reactive oxygen species (ROS) up regulation also contribute in antifilarial efficacy [46].

Bauhinia racemosa Lam. (Fam: Caesalpinaeae)

It is a small deciduous tree commonly distributed throughout the tropics including India, Ceylon, China and Timor. Galactolipid and catechin class of the phytochemicals were isolated from the n-butanol fraction of ethanolic extract of the leaves of *B. racemosa*. Among the active galactolipids, one (characterized as (2S)-1, 2-di-O-linolenoyl-3-O-α-galactopyranosyl-(1/6)-O-β-galactopyranosyl glycerol) emerged as the lead molecule which was active on the lymphatic filarial parasite, *B. malayi* [19].

Butea monosperma L. (Fam: Fabaceae)

It is a traditionally used medicinal plant in many Ayurvedic formulations in India which revealed promising adulticidal activity against intestinal worms [47]. Its leaves showed significant antifilarial activity against adult of *S. cervi* with inhibitory concentrations (IC₅₀) 1.25 and 3.6 mg/mL methanol, hexane-ethanol extracts respectively [48]. In another study against *B. malayi*, aqueous extracts of leaves and roots showed significant activity [35]. In comparison to leaf extract the roots extracts exhibit dose dependent inhibition of motility of microfilariae [49]. Polyphenolic compounds present in leaves increase the levels of lipid peroxidation and protein carbonylation which is responsible for their mortality [36].

Caesalpinia bonducella L. (Fam: Caesalpiniaceae)

It is a perennial climbing shrub, which is distributed worldwide in tropical and subtropical regions such as southern and western Africa and the Indo-Pakistan subcontinent, and is native in tropical Asia. Leaves juice and seed powder is used for the worm infestations. The leaves have antifilarial effect [50]. *C. bonducella* seed kernel extract (2g/kg) demonstrate microfilaricidal, macrofilaricidal and female-sterilizing efficacy against *L. sigmodontis* and *B. malayi* in animal models [51].

Cardiospermum halicacabum Linn. (Fam: Sapindaceae)

Antifilarial activity of the plant ethanolic and aqueous extracts has been reported against *B. pahangi*. There was a concentration and time dependent reduction in motility of adult worms and the pattern of release of microfilariae from the female worms [52].

Cassia alata Linn (Fam: Caesalpiniaceae)

The plant extracts was claimed to possess activity against the model bovine filarial parasite *S. digitata* [44].

Cedrus deodara Roxb. (Fam: Pinaceae)

It is abundantly found all over the western Himalayas at altitudes of 1200–3000m. Plant wood extracts was claimed to possess 47.97 and 86.56% inhibition in formazan formation at 1 mg/mL at an exposure period of 1 and 4 h, respectively and showed a significant macrofilaricidal activity against *S. digitata* [53].

Centratherum anthelminticum (Willd.) Kuntz (Fam: Asteraceae)

It is a tall, robust annual herb with anthelmintic properties especially against threadworms. The principal constituent responsible for anthelmintic activity is primarily found in the fruits of the plant. The aqueous and methanolic extract of seed caused inhibition of spontaneous motility of the whole worm and the nerve-muscle preparation of *S. cervi*, characterised by reduced tone, amplitude and rate of contractions. Both the methanolic as well as the aqueous extracts causes death of microfilariae *in vitro*, LC₅₀ and LC₉₀ being 75 and 32.5 mg/mL, respectively [54]. The fruit extracts of *C. anthelminticum* showed 65.64% reduction in formazan formation at a concentration of 2 mg/mL at an incubation period of 4 h against *S. digitata* [53].

Excoecaria agallocha L. (Fam: Euphorbiaceae)

It is a mangrove species distributed throughout Bhitarkanika, Orissa. Antifilarial activity of the methanol extract of leaves at a very low dose of (10µg/mL) revealed a dose dependent relationship with induction of death of filarial parasite *S. digitata* in the developmental stages. Induction of death is due to reduction of motility of

microfilariae and loss of membrane integrity of both microfilariae and eggs. It is seen as a potential agent for blocking embryogenesis in filarial parasites as well as for reducing the oxidative stress generated during chronic manifestation of LF in human beings [55].

Ficus racemosa Linn. (Fam: Moraceae)

It is a large deciduous tree found all over India. Alcoholic and aqueous extracts of the fruits significantly inhibit the spontaneous movements of the worm. Both extracts causes death of microfilariae *in vitro* at LC₅₀ and LC₉₀ as 21 & 35 ng/mL for alcoholic extract and 27 & 42 ng/mL for aqueous extract respectively [56].

Glycyrrhiza glabra Linn. (Fam: Fabaceae)

Liquorice roots contain a unique triterpenic acid 'glycyrrhetic acid' as a major constituent in the form of saponin 'glycyrrhizic acid'. Glycyrrhetic acid is effective against microfilariae of *B. malayi* *in vitro* (LC₁₀₀: 12.5µM; LC₅₀: 1.20µM), but was inactive against adult worms. The synthetic amide analogs of Glycyrrhetic acid may exert antifilarial activity *in vitro* and *in vivo* by the elimination of *Wolbachia* [57], symbiont bacteria known to confer the survival value to the parasites [58].

Hibiscus mutabilis Linn. (Fam: Malvaceae)

Hibiscus extract and its isolated compounds have antibacterial [59] and antiparasitic [60] activities. Methanolic extract of leaves and ferulic acid isolated from ethyl acetate fraction of *H. mutabilis* showed significant antifilarial activity against both microfilariae and macrofilariae of *S. Cervi*. Ferulic acid exerts antifilarial effect through induction of apoptosis by generating oxidative stress and by down regulation and alteration of the level of some antioxidants like glutathione, glutathione-S-transferase and superoxide dismutase of the filarial nematode *S. cervi* [61].

Hibiscus sabdariffa Linn. (Fam: Malvaceae)

The antifilarial activity of crude extract of the leaves of *H. sabdariffa* was tested against human filarial parasite, *B. malayi* *in vitro*. The n-butanol fraction at 250 µg/mL killed 100% microfilariae. Leaf extract at 500 mg/kg (administered for 5 days) produced macrofilaricidal (about 30%) activity *in vivo* against *B. malayi* [60].

Lantana camara Linn. (Fam: Verbenaceae)

Crude extract prepared from the stem of *L. camara* exhibit considerable antifilarial activity against *B. malayi* and sterilization of female worms *in vivo*. *L. camara* stem extract administered at the dose of 1 g/kg for 5 days killed 43% of adults and sterilized 76% of the surviving female worms. Two isolated compounds, oleanonic acid and oleanolic acid might be responsible for this effect. All *B. malayi* worms were killed *in vitro* with extract at concentration of 0.031 mg/mL [27].

Leucas aspera (Willd.) Linn. (Fam: Lamiaceae)

It is distributed throughout India from the Himalayas down to Ceylon. The antiparasitic activity plant extract was tested against the model bovine filarial parasite *S. digitata* [44].

Leucas cephalotes Spreng. (Fam: Labiatae)

It is an erect, scaberulous or pubescent, stout annual plant, 30–100 cm. height, found as a common weed in cultivated grounds and waste lands throughout India, ascending upto 1, 800 m. in the Himalayas. Alcohol and aqueous extracts of Flower as well as stem inhibit the spontaneous mobility of filarial parasite *S. cervi*. The alcohol extracts of flower and stem produced initial stimulation of the movements followed by paralysis of the whole worm. The alcohol extract of flower produced reversible while that of stem produced irreversible paralysis [62].

Mallotus philippensis (Lam.) Muell. Arg (Fam: Euphorbiaceae)

It commonly used in traditional medicine for the elimination of intestinal worms and also for skin irritation, ringworm as well as freckles. Aqueous and alcoholic extracts of the leaves have antifilarial effect against *S. cervi* probably due to alteration of membrane permeability [63].

Moringa oleifera Lam. (Fam: Moringaceae)

The gum extract (125 mg/ml) causes irreversible loss of motility of microfilariae and inhibited about 56% MTT reduction potential of the adult female worms of *B. malayi*. *In vivo* study revealed that the extract (500 mg/kg, p. o. for 5 days) causes 69% adulticidal and 83% female worm's sterilization in primary screening as well in a secondary model (*Mastomys coucha*) 44% of adult worm of *B. malayi* in were killed [64].

Neurolaena lobata Linn. (Fam: Asteraceae)

N. lobata extract has antifilarial effect on motility of adult worms of *B. pahangi* in a concentration and time-dependent manner. The concentrations of 10µg/mL prevent microfilarial release by females [65].

Piper betle Linn. (Fam: Piperaceae)

It is a widely distributed plant in the tropical and subtropical regions of the world and India and has been ascribed many medicinal properties. It is reported for antiparasitic activity [66]. Adulticidal and female sterilizing efficacy was observed for crude methanol extract (100 mg/kg) along with its n-hexane fraction (30 mg/kg). The crude methanol extract (100 mg/kg) along with its n-hexane fraction significantly raise the antibody producing cells count and hemagglutinating antibody as well as cell-mediated (lymphoproliferation, macrophage activation, delayed type hypersensitivity) immune responses in mice. The crude extract along with its n-hexane and chloroform fractions induced considerable release of NO from murine peritoneal macrophages. The initiation of variety of T-helper cell immune-response may overcome the immune-suppression caused by *B. malayi* infection. The n-hexane fraction shows type 2 cytokine response (increased IL-4 and decreased IFNγ production) while the chloroform fraction triggered type 1 cytokine response in BALB/c mice [67].

Plumbago indica Linn. (Fam: Plumbaginaceae)

It is a perennial shrub found throughout the India. The methanolic extract of the root of *P. indica/rosea* was screened for antifilarial activity against adults of the cattle filarial worm *S. digitata*. Lowest concentrations (0.01 mg/mL) of the crude extract causes 83.3% immobilization of the worms after 6 h. The isolated compound 5-hydroxy-2-methyl-1, 4-naphthalenedione, also known as 5-hydroxy-2-methyl-1, 4-naphthoquinone (plumbagin) from column chromatography with petroleum ether: chloroform solvent exhibited immobilization of worms at 0.0006 mg/mL. The isolated compound also shows >70% inhibition of formazan formation in MTT assay at 0.05 mg/mL [68].

Pongamia pinnata Linn. (Fam: Fabaceae)

The aqueous (250 µg/mL) and alcohol (120 µg/mL) extracts of fruits and the alcohol extract of leaves (270 µg/mL) causes inhibition of spontaneous movements of the whole worm *S. cervi*. The corresponding effect on the nerve-muscle preparation was also observed with aqueous extract (25 µg/mL), alcohol extract of fruits (5 µg/mL) and alcohol extract of leaves (20 µg/mL) [69].

Psoralea corylifolia Linn. (Fam: Fabaceae)

It is an erect, annual plant, and found throughout India. Antifilarial efficacy of alcohol extract of leaves and seeds was demonstrated on spontaneous movements of the whole worm and the nerve muscle preparation of *S. cervi*, which is characterized by initial, short lasting, small increase in tone of contractions followed by paralysis. The concentrations reported for inhibiting the movements of whole worm for alcohol extracts of leaves and seeds were 160, 30 µg/mL respectively and for and nerve muscle preparation, it was 150, 20 µg/mL. Alcohol extracts of both leaves and seeds caused death of microfilariae *in vitro*, LC₅₀ and LC₉₀ being 15 and 25 ng/mL for alcohol extract of leaves and 12 and 18 ng/mL for alcohol extract of seeds, respectively [70].

Ricinus communis Linn. (Fam: Euphorbiaceae)

It is claimed to possess activity against *S. digitata*. The seed extract causes 72.39% inhibition of formazan formation within 4 h of

exposure in MTT reduction assay and complete suppression of motility within 100 min at 1 mg/mL (lowest conc.) [55]. Methanolic extract revealed antifilarial activity in a dose dependent manner as evident from induction of death in the embryogenesis of filarial parasite *B. malayi*. The extract also shows dose dependent inhibition of microfilariae motility [71].

Saxifraga stracheyion Hook. f. & Thorns. (Fam: Saxifragaceae)

The root extract of *S. stracheyi* contain some constituents including b-sitosterol, (+) catechin-3-gallate and bergenin. Aqueous (140 µg/mL) and alcohol (250 µg/mL) extracts of the roots causes inhibition of spontaneous movements of the whole worm *S. cervi*, which is indicated by an increase in the amplitude and reduction in the rate of contractions, without effecting tone of the contractions. The concentration of *S. stracheyi* extracts required to produce an equivalent effect on the nerve-muscle preparation was 30 µg/mL for aqueous and 20 µg/mL for the alcohol extract, suggesting a cuticular permeability barrier [72].

Solanum khastanum Clarke. (Fam: Solanaceae)

Solamargine, a steroidal alkaloid glycoside from ripe berries of *Solanum khastanum* has Antifilarial effect. Solamargine at 4 mg/mL concentration killed 100% adults and microfilariae of *S. cervi* in 60 and 88 min, respectively [73].

Sphaeranthus indicus Linn. (Fam: Asteraceae)

It is well known as Gorakhmundi in Hindi. The external application of the herb paste has been reported to use treatment for pruritus, oedema, arthritis, filariasis, gout and cervical adenopathy [74]. The leaf extract of *S. indicus* showed 61.20 and 83.47% inhibition of formazan formation, respectively at 1 and 2 mg/mL at an exposure period of 4 h against *S. digitata* [55].

Streblus asper Lour. (Fam: Moraceae)

Aqueous and alcoholic extract of *S. asper* causes inhibition of spontaneous motility of the whole worm along with decreased tone, amplitude and rate of contractions in the nerve-muscle preparation of *S. cervi*. Both the extracts causes death of microfilariae *in vitro* with LC₅₀ and LC₉₀ being 90 and 33.5 ng/mL, respectively [75]. Aqueous extract of the bark of *S. asper* demonstrated considerable antifilarial activity against *S. digitata* [44]. The aqueous extract of the stem bark of *S. asper* has been reported to exhibit considerable macrofilaricidal activity against *Litomosoides carinii* and *Brugia malayi* in rodents. *In vitro* and *in vivo* activity of two cardiac glycosides asperoside and strebloside at the dose of 50 mg/kg against *B. malayi* has been reported [76].

An effective and safe filaricidal 'Filacid' has been reported from the stem bark of *S. asper*. Clinical efficacy of the same has also been reported [77]. Asperoside and strebloside have been reported for *in vitro* effects of on *S. cervi* females. Both causes death of the worms, inhibition of motility and glucose uptake of the parasites. These glycosides also inhibits the incorporation of [U-14] C-glucose into macromolecules of *S. cervi* females which results in lowered profiles of certain enzymes activities like glucokinase, malate dehydrogenase and succinate dehydrogenase, which suggests that the lethal effects were because of significant effects on glucose metabolism [78]. The interference of asperoside and strebloside with glutathione metabolism of the adult *S. cervi* was also reported which results in the interruption in various vital activities of the parasites that eventually result in the death of the parasites [79]. An ayurvedic preparation Shakhotaka Ghana Vati (aqueous extract in tablet form) was also found to be therapeutically effective [80].

Tinospora crispa (L.) Hook. f. & Thomson (Fam: Menispermaceae)

An infusion of *T. crispa* stem is used to treat fever, jaundice, malaria and worms in children [81]. Dried stem of *T. crispa* showed strong antifilarial activity against adult worms of subperiodic *B. malayi* [41].

Trachyspermum ammi Linn. (Fam: Apiaceae)

An *in vitro* study on motility as well as reduction in formazan formation in MTT reduction assay using adult *S. digitata* worms

shows that the crude extract and a phenolic monoterpene (2-isopropyl-5-methyl phenol with a position isomer 5-isopropyl-2-methyl phenol) isolated from hexane: ethyl acetate fraction have adulticidal property. Isolated active constituent was further investigated *in vivo* against the *B. malayi* in *M. coucha* rodent and shows significant macrofilaricidal and female sterility [82].

Vitex negundo Linn. (Fam: Verbenaceae)

Root extract of *V. negundo* L. at 100 ng/mL concentration showed complete loss of motility of *B. malayi* microfilariae *in vitro* after 48 h of incubation [83, 34]. Ethyl acetate extract of *V. negundo* leaves revealed promising adulticidal activity, against adult filarial worm *S. cervi* in the *in vitro* system. The treated worms were completely immobilized due to the lethal effect of the plant extract at lower concentrations in a dose dependent manner. MTT reduction assay of the worms treated with the drug confirmed its effect on the viability of the worms by acting at the cellular level, as indicated by the reduced level of mitochondrial enzyme that reduces the MTT to formazan [84].

Withania somnifera Dunal. (Fam: Solanaceae)

Withaferin A, isolated from *Withania somnifera* has been reported for its *in vivo* larvicidal effects at a lowest conc. of 7.8 µg/mL against *B. malayi*. It was also demonstrated that there was a reduction of 63.6% microfilariae and 66.2% defective embryogenesis in female worms [85].

Xylocarpus granatum Koenig (Fam: Meliaceae)

Dried seeds extract of *X. granatum*, showed strong antifilarial activity against adult worms of subperiodic *B. malayi* [41]. Gedunin and photogedunin, two very promising compounds isolated from *X. granatum* fruit exhibited *in vitro* and *in vivo* antifilarial activity against human lymphatic filarial parasite, *B. malayi*. Gedunin (IC₅₀ 0.239 µg/mL, CC₅₀ 212.5 µg/mL) and photogedunin (IC₅₀ 0.213 µg/mL, CC₅₀ 262.3 µg/mL) at five daily doses of 100 mg/kg subcutaneously revealed excellent adulticidal efficacy resulting in the death of 80 and 70% transplanted adult *B. malayi* in the peritoneal cavity of jirds [42].

Zingiber officinale Rosc. (Fam: Zingiberaceae)

This plant is commonly known as zinger. The rhizome contains about 2-3% essential oils, including the mono- and sesquiterpenes, borneol, geraniol, limonene, β-elemene, zingiberol and linalool. It has also been recommended for chronic skin diseases, obesity, abnormal bleeding after child birth and filariasis. Alcoholic extracts of *Z. officinale* rhizomes at 100 mg/kg reduced microfilarial concentration in blood by a maximum of 98% in dogs naturally infected with *D. immitis* [86].

CONCLUSION

The above review of literature demonstrates the importance of natural products especially plant derived test substances in treatment of various disease conditions. In spite of rich biodiversity in India and the traditional knowledge available through Ayurveda, Unani and Homeopathy, the pharmacological exploitation of these medicinal plants has still been limited. Though some of the plants have been extensively investigated, others await thorough investigation. Not only this, the scientific validation of the traditional value of the medicinal plants needs thorough study. The diverse bioactivity including anti-cancer, anti-inflammatory, anti-bacterial, anti-oxidant, health adjuvant and for treating skin disease, diabetes, arthritis, and epilepsy have been explored by researchers, however, there is a limited focus on the medicinal plant used for lymphatic filariasis. Limited data is available on important plants useful in filariasis. Our findings indicate the importance of in depth study of herbal drugs for fortification of the antifilarial therapeutic range. This traditional therapeutic alternative may actually prove better in terms of cost effectiveness and patient fulfillment in combating the filariasis.

CONFLICT OF INTEREST

None declared

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