NATURAL ANTIFILARIAL DRUGS: A REVIEW

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ABSTRACT

The filarial parasites were considered causing remarkable problems for the human beings and animals. Many modern synthetic medicines found to be very effective in curing diseases cause a lot of side effects. The natural drugs were proven to have less side effects inspite their relatively low activity. A large number of medicinal plants were claimed to possess antifilarial activity in traditional systems of medicine. Considering the folk claims, several medicinal plants have been evaluated for this activity using various invitro and invivo methods. The present review summarizes some important pharmacological and preliminary studies on antifilarial medicinal plants, products and isolated principles from them, which can be investigated further to achieve lead molecules in the search of novel herbal drugs to treat filariasis.

Key words: Antifilarial activity, Medicinal plants, Filariasis, Microfilaricidal activity, folklore antifilarial plants.

INTRODUCTION

Filariasis is "considered" endemic in tropical and sub-tropical regions of Asia, Africa, Central, South America and Pacific Island nations. World wide it effected a population over 120 million in tropics and over 17 million in sub tropics. Over one third of the population at risk lives on the Indian sub-continent with an estimated 45 million infected individuals [1].

Filariasis is divided into three groups as Lymphatic Filariasis, Subcutaneous Filariasis, and Serous Cavity Filariasis. Lymphatic Filariasis is caused by the worms Wuchereria bancrofti, Brugia malayi, and Brugia timori. These worms occupy the lymphatic system, including the lymph nodes, and in chronic cases these worms lead to the disease Elephantiasis. Subcutaneous Filariasis is caused by Loa loa (the African eye worm), Mansonella streptocerca, Onchocerca volvulus, and Dracunculus medinensis (the guinea worm). These worms occupy the subcutaneous layer of the skin, the fat layer. Serous Cavity Filariasis is caused by the worms Mansonella perstans and Mansonella ozzardi, which occupy the serous cavity of the abdomen. In all cases, the transmitting vectors are either blood sucking insects (fly or mosquito) or Copepod crustaceans in the case of Dracunculus medinensis. The recent developments in the diagnosis of lymphatic filariasis are Membrane filtration method [2], Ultrasonography [3], Lymphoscintigraphy [4], Immunochromatographic test (ICT) [5].

An ideal anti filarial agent should have high cure with even a low dose of the drug, free from any toxicity, effective against adult worms and should be cost effective. Unfortunately no available synthetic drug meets these requirements. Even the most used Albendazole [6],
Diethyl carbamazine (DEC) have proven to cause nausea, vomiting, gastric disturbances and giddiness [7] and also the unwanted tolerance of the parasite to the drug. DEC does not act directly on the parasite but its action is mediated through the host immune system. When the parasites are not sensitive even repeated doses do not have any effect on the adult parasite [8]. Ivermectin has no proven action against the adult parasite or in tropical eosinophilia [9].

Thus there is an urgent need for an agent that kills and/or sterilizes the adult worms, since adult parasites not only produce millions of microfilaria that are picked up by mosquito vector and transmitted, but are also responsible for the debilitating pathological lesions and to limit the side effects reported above.

Because of the limited affordability and adverse effects of synthetic drugs, most proportion of the world’s population depend on the traditional plant drugs for the treatment. As the plant drugs ensure the availability and cost affectivity, plant derived products stand as the source to cure filariasis. India has rich sources of the herbal drugs and was supported by the complimentary alternative medicinal systems like Ayurveda, Siddha, Unani, Homeopathy and folklore. Many researchers had given the experimental evidences for the folklore claims of the plant drugs to be used effectively for the treatment of filariasis [10]. In the present article, the researches to prove various plant drugs showing antifilarial activity along with their other uses have been reviewed.

PLANT DRUGS
1. Zingiber officinale (Zingiberaceae): Dried Z. officinale rhizome is a main ingredient in many Ayurvedic formulations, and so it is called Mahawushadh, the ‘great medicament’ [11]. Z. officinale has a long history of treating ailments such as nausea, respiratory disorders, cardiovascular health, sedative, analgesic, anti-inflammatory, antibacterial also includes filariasis, rheumatic disorders [12] and also used as hepatoprotective [13]. It also has immunomodulatory properties and is reported to inhibit various inflammatory mediators such as prostaglandins and pro-inflammatory cytokines [14,15].

Ginger contains up to three percent of an essential oil which constitutes sesquiterpenoids, (–)-zingiberene as the main component. Smaller amounts of other sesquiterpenoids (β-sesquiphellandrene, Bisabolene and Farnesene) and a small monoterpenoid fraction (β-phellandrene, Cineol, and Citral) have also been identified. The characteristic odour, flavor of ginger and gastric emptying is caused by a mixture of Zingerone, 6-shogaols and 6, 8, 10-gingerols [16,17], volatile oils that compose one to three percent of the weight of fresh ginger.

The alcoholic extract of the rhizomes were administered subcutaneously at 100 mg/kg body weight to Dirofilaria immitis infected dogs. It reduced the microfilaria in the blood to about 98%. Fifty days after last injection, it showed 83% reduction in microfilarial concentration proving the antifilarial activity of the plant [18].

2. Solanum khasianum C. B. Clarke (Solanaceae): The Solasodine glycosides, Solamargine, Khasianine and Solakhasoside (1) [19] have been isolated from berries of Solanum khasianum, the structure of Khasianine, Tomatine and Solasonine has been elucidated [20].

A steroidal alkaloidal glycoside, Solamargine, isolated from the ripe berries of the plant killed in vitro 100% adults and microfilaria (mf) of Setaria cervi at a 4 mg/ml concentration in 60 and 88 min, respectively. The drug, when administered orally at 100 mg/ kg to S. cervi intra peritoneal implanted rats, reduced the blood mf count by more than 30% after the first phase, 72% after the second phase, followed by the third and the fourth phases of treatments, the mf density was reduced by more than 90%. One hundred percent reduction of mf count was obtained 15 days after the fourth and final phase of treatment which was of 5 days duration. At a dose (100 mg/kg x 4 phases), Solamargine killed 100% adult worms without incident toxicity [21].

3. Sencio nudicaulis Buch. Ham. (Senecioneae): Both aqueous and alcoholic extracts exhibited microfiliaricidal action on Setaria cervi in vitro. LC50 and LC90 being 10 and 15 mg/ml for aqueous extract, 5 and 12 mg/ml for alcoholic extract. The concentration of aqueous and alcoholic extracts were 1/3 rd and 1/20 th respectively. The anti motility effect of the plant was similar to that of the DEC unlike Nifidipine which block the stimulant effect of Acetylcholine response [22].

4. Centella asiatica L. urban (Umbelliferae): The leaves of the plant have a prominence in Ayurveda where in they are used a nervine tonic. Researches prove the cardio protective effect of Centella asiatica on antioxidant tissue defense system during Adriamycin induced cardiac damage in rats. The plant possess anti-inflammatory, memory improvement, anti-lipid peroxidative, anticancer activities and free radical scavenging activities and also used to treat venous hypertension and atherosclerosis [23]. The active constituents present in the Centella asiatica
extracts are Asiatic acid, Asiaticoside and also contain high phenolic contents (3.23–11.7 g/100 g dry sample). Phenolic compounds, particularly flavonoids, exhibit a wide range of biological effects, including antibacterial, antiviral, and anti-inflammatory, anti-allergic, anti-thrombotic and vasodilatory actions [24].

Ethanol extract obtained from the leaves of C. asiatica was administered orally at 30 mg/kg/day for 30 days on two stray dogs naturally infected with Dirofilaria immitis [25]. There was a gradual raise in the microfilarial density in blood till 90 days then it reduced to 98% by the day 240. It did not produce any notable side effects in the treated dogs. The prolonged maintenance of the reduced level of microfilarial density may be due to the sizeable reduction of adult worm loads.

5. Mallotus philippensis Lam. Muell. Arg (Euphorbiaceae): Many flavonoids have been reported from this plant. Two chalcone dimers namely Kamalachalcones A (1) and B (2) were isolated from the plant. The relatives of the plant in the genus Mallotus have been reported to have cytotoxic activity [26].

The concentration required to inhibit the movements of nerve-muscle (n.m.) preparation was 1/5th for aqueous and 1/11th for alcoholic extract, which is due to the cuticular permeability barrier. On the microfilariae the LC50 and LC90 were 18 and 20 mg/ml for aqueous and 12 and 15 mg/ml for alcoholic extracts respectively. Aqueous extract at higher concentration showed immediate reduction in the spontaneous movements of the whole worm and n.m. preparation of Setaria cervi and on the survival of microfilariae in vitro. The stimulatory response of acetylcholine was blocked by aqueous extract on whole worm movements [27].

6. Acacia auriculiformis A. Cunn (Mimosaceae): The stems were reported to have antioxidant, anti-inflammatory, anti-mutagenic and anti-carcinogenic activity due to the presence of phenols and polyphenols. Methyl glucuronic acid, Glucuronic acid, Galactose, Arabinose was found to be the richest constituents in the plant. The presence of tannins and triterpenoid saponins gave the plant filaricidal, spermicidal and CNS depressant properties [28].

Two triterpenoid saponins, Acaciaside A and B, isolated from the funicles of the Acacia auriculiformis were combined with the leaf ethanol extract from Centella asiatica (1:1) and administered orally at 0.04 mg/kg body weight/d for 45 days on Dirofilaria immitis microfilarial infected dogs. The microfilarial (mf.) density blood reduced to 99% and activity remained for 120 days when treated with mixture of crude extracts [29].

7. Cardiospermum halicacabum Linn. ( Sapindaceae): Experiments have shown the analgesic, anti-inflammatory and vaso-depressant activities of this plant. Tannins, saponins and traces of alkaloids have been isolated from the leaf of the plant. The ethanolic extract of the plant, in a concentration dependant administration (200–600 mg/kg) inhibited gastric ulcers induced by oral administration of ethanol and antipyretic activity [30].

The aqueous extract of Cardiospermum halicacabum, at less than 500 µg/ml concentration significantly reduced motility of Brugia pahangi adult females after 24 h of exposure and adult males after 3 days. This also significantly reduced microfilarial release from female worms from day 2. The reduction in the motility of adult worms and the pattern of microfilarial release from female worms were identified concentration and time dependent. However, the aqueous extract did not affect the motility of microfilariae with the exception of those in higher concentration extracts but the ethanol extract, at 500 µg/ml rapidly reduced the motility of microfilariae on day 2. Higher concentrations of ethanol extracts (2 mg/ml) inhibited both the motility of adult worms and the release of microfilariae from females. Little effect of ethanol extracts on the worms was detected by the MTT assay [31].

8. Xylocarpus granatum (Meliaceae): Xylocarpus granatum has been used traditionally to treat cholera and fever, as an astringent and emollient. A number of limonoids, lignins, tannins, alkaloids and sterols have been reported from Xylocarpus granatum. The bark of this plant was used for tanning and for the preparation of an amber dye and has a significant anti-diarrheal activity [32]. A fungicidal lactone was isolated from the plant [33].

Aqueous extracts of dried husks, dried seeds and dried leaves of the plant were compared for the antifilarial activity. The aqueous extract of the stems showed the maximum activity relative to the extracts of leaves and husks [34]. Aqueous extracts of different parts of this plant are also reported to have significant antifilarial activity [35].

9. Tinospora crispa (Menispermaceae): Literature revealed the anticholera and antidiabetic effects of the plant. The raw plants were taken to control high blood pressure, diabetes and to relieve abdominal pains. The dried stems were proven to show the antifilarial activity and were compared to the efficacy of the Xylocarpus.
The relative motility of the aqueous extracts of the stems was measured for an observation period of 24 hours on the in vitro culture of the organism *Brugia malayi*. Results showed the plant comparatively less active [34].

10. *Andrographis paniculata* (Acanthaceae): The plant demonstrated high antimalarial effect in vitro and in vivo [36] and as a remedy for snakebite [37]. The decoctions of leaves or roots were used against stomachache, dysentery, thypus, cholera, influenza and bronchitis, as a vermifuge and also considered as diuretic. The decoction of the plant leaves was used to treat diabetes and reduce high blood pressure and also relieve itchy skin and insect bites [34].

The aqueous extract of the leaves of the plant were studied for the antifilarial activity on the in vitro culture of the adult worms of *Brugia malayi*. The results showed that *A. paniculata* has less activity compared to *X. granatum* and more effective than the aqueous extracts of the stems of *T. crispa* [34].

11. *Plumbago indica*rosea (Plumbaginaceae): The presence of Plumbagin in root, Leucodelphinidin in leaf has been reported. Plumbagin, Sitosterol, Stigmasterol and Campesterol from the aerial parts, Delphinidin, Cyanidin and Pelargonidin 3-rhamnoses, Kaempferol-3-rhamnose, Galloyl and Digalloyl glucose have been isolated from the petals of the plant [38].

Plumbagin was structurally elucidated as 5-hydroxy-2-methyl-1,4-naphthalenedione. Melting point determination, TLC and HPLC analysis and IR, 1H NMR, 13CNMR, and GC-MS analysis were done to elucidate the structure. Adult worms of Setaria digitata were incubated in a medium containing crude extract at concentrations 0.05, 0.04, 0.02, and 0.01 mg/ml for various incubation periods of 30 min, 1 hr, 2 hr, and 6 hr, respectively, at 37°C. Complete inhibition of motility was observed for concentrations ranging from 0.02 to 0.05 mg/ml. The activity of bioassay-guided fractionation of the crude extract by silica gel column chromatography fraction against adult worms was further confirmed by 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide-formazan colorimetric assay, which gave less than 50% inhibition for the active fraction at concentrations 0.05, 0.002, 0.005, and 0.0006 mg/ml at 30 min, 1 hr, 2 hr, and 6 hr incubation periods, respectively [39].

12. *Neurolaena lobata* L. (Asteraceae - Heliantheae): *N. lobata* has been used as a remedy against malaria, stomach pain, skin diseases, diabetes and cancer. The Germacranolide sesquiterpene lactones Neurolenin A and Neurolenin B, Germacranolide lobatin A (7) and Furanotheliangolides 9-11 were isolated from the plant. The Germacranolides 3-6 and the Furanotheliangolides 9-11 were isolated form aerial parts of the plant and structurally elucidated [40]. The occurrence of pyrrolizidine alkaloids [41] like Methyl ester alkaloids Tussilagine, Isotussilagine and their possible biosynthetic precursor 2-pyrrolidineacetic acid from methanolic leaf extract, 12 flavanoids and Thymol derivatives from the roots were also been reported from Neurolaena lobata. 6-hydroxykaempferol, 3-methyl ether 7-glucoside, 6-hydroxykaempferol 7-glucoside, Quercetaginin its 7-glucoside, Quercetagin 3, 6- and 3, 7- dimethyl ethers, Quercetagin 3-methyl ether 7-glucoside and 7-sulfate, 6-hydroxyluteolin 3'-methyl ether and 6- hydroxyluteolin 7-glucoside have been reported from the plant [42].

The ethanolic extracts of the leaves of the plant was tested for the activity along with eleven extracts of other plants in vitro for potential macrofilaricidal activity against *Brugia pahangi*. *N. lobata* showed best results in inhibiting the motility of the worms. The ethanolic extract of *N. lobata* was extensively examined in vitro for macro- and micro-filaricidal effects using a series of concentrations of 500, 250, 100, 50 and 10 µg/ml assessing the worm motility, microfilarial release by female worms and a MTT assay. The time required to stop motility of both sexes of adult worms was 6 h at 500 µg/ml, 24 h at 250 µg/ml, and 3 days for females and 4 days for males at 100 µg/ml. The movement of females was ceased at 4 days at a concentration of 50 µg/ml. Doses higher than 100 µg/ml even induced mortality of the microfilariae [43].

13. *Lantana camara* (Verbenaceae): Leaves of this plant were used as an antitumor, antibacterial, and antihypertensive agent [44], while the roots for the treatment of malaria, rheumatism, and skin rashes [45]. Various cytotoxic and anticancer chemical constituents like triterpenoids, naphthaquinones, flavonoids, glycosides, alkaloids, and lantanoids have been isolated from the plant. The leaf and flower oils were identified to contain a number of constituents like Sabinene (19.6–21.5%), 1, 8-Cineole (12.6–14.8%), α-Caryophyllene (12.7–13.4%) and α-Humulene (5.8–6.3%). Two rare sesquiterpenoids Humulene epoxide III and 8-Hydroxybicyclogermaene have been isolated from these oils. The ethanolic extract (860 g, 10.82%) was extracted to get n-hexane fraction (60 g, 0.75%), chloroform fraction (90 g, 1.125%), n-butanol fraction (180 g, 2.25%) and aqueous fraction (495 g, 6.18%). The Oleanonic acid as major triterpene from the n-hexane fraction, Oleanolic acid, α-Sitosterole, α-Sitosterole-D-glycoside and a mixture of fatty acids (Palmitic acid and Stearic acid) from the chloroform fraction, Ethyl-α-D-galactoside from the butanol fraction were isolated [46].
The antifilarial activity of the two compounds, Oleanonic acid and Oleanolic acid, isolated from n-hexane and chloroform extracts of the stem of the plant was reported. The crude extract at 1 g/kg for five days by oral route killed 43.05% of the adult *Brugia malayi* parasites and 76% of surviving female worms in the rodent model *Mastomys coucha*. The extract was also found effective against a subcutaneous rodent filarial, *Acanthocheilonema viteae* maintained in *Mastomys coucha*, where it exerted strong microfilaricidal (95.04%) and sterilization (60.66%) efficacy with mild macrofilaricidal action. The two compounds showed LC100 at 31.25 and 62.5 µg ml, respectively, on *B. malayi* in vitro [46].

14. *Piper betle* Linn. (Piperaceae): The betel leaves act as breath-freshener. There were also reports for its bioenhancer efficacy. The chief constituent of the leaves is a volatile oil which contains phenols, betel-phenol, Chavibetol, Chavicol, Cadinen and Hydroxychavicol which claims for their medicinal properties such as antitumor [47], anti-fertility [48], antiparasitic [49], digestive, antacid, decongestant, carminative, stimulant, antipyretic, anti-inflammatory, anti-allergic, anti-septic, hepatoprotective, radio-protective, anti-platelet, antifungal, nematocidal and anti-oxidant [50].

The n-hexane fraction (3 mg/kg) induced biased type 2 cytokine response as revealed by increased IL-4*+* and decreased IFN-γ*+* T-cell population, while the chloroform fraction (10 mg/kg) produced a predominant type 1 cytokines. Crude methanolic extract (100 mg/kg) gave a mixed type 1 and type 2 cytokine responses showing immunomodulatory property in this plant against filarial *Brugia malayi* infection [50].

15. *Psoralea corylifolia* Linn. (Fabaceae - Papilionaceae): It was mentioned in Ayurveda that the plant was used as stomachic, deobstruent, anthelmintic, diuretic, diaphoretic and aphrodisiac properties of the plant were reported. The tranquillo-sedative, anticonvulsant, and central muscle relaxant activities in rat, mice and rabbit were found due to the presence of Isopsoralen [51]. Bakuchiol, Neobavaisoflavone, Diadzein and Bakuchicin were isolated from the ethanolic extract of the plant [52]. The platelet inhibitory activity [53] was shown due to Isobavachalcone and Neobavaisoflavone. The anti-inflammatory activity was due to Bavachinine [54], a flavonoid and cytotoxicity against L929 cell culture was due to Psoralidin [55] and Bakuchiol isolated from ethanol extract of fruits. The aqueous, alcohol, petroleum ether extracts and essential oil obtained from the seeds of *P. corylifolia* has significant antibacterial activity and moderate antifungal activity. The oleoresins have been proved to have antimutagenicity on *Salmonella typhimurium* TA98 and can treat leucoderma. The seminal extract of *P. corylifolia* has shown an anti-cell adhesive activity at non-cytotoxic concentration [56].

The alcoholic extracts of the leaves and seeds of *Psoralea corylifolia* at concentrations of 160, 30, and 150, 20 mg/ ml, caused the inhibition of spontaneous movements of the whole worm and the nerve muscle preparation of *S. cervi*, characterized by initial, short lasting small increase in tone of contractions resulting in paralysis. LC50 and LC90 being 15 and 25 mg/ml, 12 and 18 mg/ml respectively for the alcoholic extracts of leaves and seeds [56].

16. *Caesalpinia bonducella* (Fabaceae): Reports are available that the leaves or seed kernel possess antipyretic, antiinflammatory, antibacterial, antiviral, anti-estrogenic and antidiabetic activities. Phytochemical analysis of the seeds indicated the presence of flavonoids, terpenoids, glycosides, saponins, tanins and alkaloids. Microfilaraemic cotton rats and *Mastomys coucha* harbouring *Litomosoides sigmodontis* and *Brugia malayi* respectively were treated with crude extract or fractions of the seed kernel *C. bonducella* through oral route for five days showed microfilaricidal, macrofilaricidal and female-sterilizing efficacy [57].

17. *Trachyspermum ammi* (Apiaceae): The plant has been investigated for antiviral, anti-inflammatory, antifungal, molluscicidal, antihelminthic, plant nematicidal, antipyretic, anti-aggregatory and antimicrobial activities. The *in vitro* activity of a methanolic extract of fruits of *Trachyspermum ammi* against adult bovine filarial *Setaria digitata* worms was proved. A phenolic monoterpene was isolated from the plant and was screened for *in vivo* antifilarial activity against the human filarial worm *B. malayi* in *Mastomys coucha*, which showed macrofilaricidal activity and female worm sterility *in vivo* against *B. malayi* [58].

18. Miscellaneous: The methanolic extracts of *Vitex negundo* L. (Verbenaceae), has been tested *in vitro* for the antifilarial activity along with the methanolic extracts of leaves and roots of *Butea monosperma* L. (Fabaceae) leaves of *Ricinus communis* L. (Ricinaceae)and leaves of *Aegle marmelos* corr. (Rutaceae)on the microfilaria of *Brugia malayi*. The results showed that *Ricinus communis* has no antifilarial activity and the others showed a good inhibition of the motility of the microfilaria. The inhibitory concentrations were found to be 82, 83 and 70 mg/ml respectively except *R. communis*. Reports that *V. negundo* and *A. marmelos* has good antifilarial activity at a concentration of 100 mg/ml were also reviewed [59].
Ethnomedical claims were reviewed. Powder of dried exocarp of *Adansonia digitata* (Bombaceae), decoction of fruits of *Citrus medica* (Rutaceae), powder of stem bark of the plant *Lannea microcarpa* (Anacardiaceae), oil extract of the seeds of *Khaya senegalensis* (Meliaceae) and the decoction of the leaves of the plant *Leonotis* (Lamiaceae) was used as the antifilarial [60].

Three biguanides and two dihydrotriazines were more potent against *B. malayi* microfilaria when compared to Trimethoprim and Pyrimethamine. The mechanism of action of the compounds was detected by the reversal of activity of active compounds by folic acid and folinic acid [61].

The methanolic extracts (100–0.09 µg/ml) of nine traditional plants, *Lophira alata* (Ochnaceae), *Greenwayodendron suaveolens* (Annonaceae), *Upacata togoensis* (Euphorbiaceae), *Zanthoxyllum heitzii* (Rutaceae), *Peperomia pellucid* (Piperaceae), *Piptadeniastrum africanaum* (Mimosaceae), *Petersianthus macrocarpus* (Lecythidaceae), *Vernonia conferta* (Compositae), and *Vernonia hymenolepis* (Asteraceae) were incubated with 20 *Loa loa* microfilariae isolated from patients at 37°C with 5% CO2 in modified Eagle’s medium supplemented with 10% fetal serum and antibiotics. The 50% lethal concentration and 50% inhibitory concentration for eukaryotic cells (IC50) ranged from 0.22 to 70.28µg/ml and from 8.52 to 119.52µg/ml respectively. Extracts of *P. macrocarpus*, *P. africana*um, *Z. heitzii* and *L. alata* were found highly selective for *L. loa* [62].

Flavonoids like Naringenin, Hesperetin, Flavone, Rutin, Chrysin and Naringin were evaluated against the human lymphatic filarial parasite, *Brugia malayi* using an *in vitro* motility assay with adult worms and microfilariae. Naringenin and Hesperetin killed the adult worms and inhibited (>60%) at 7.8 and 31.2 µg/ml concentration. Microfilariae (mf) were killed at 250–500 µg/ml. Flavone killed female adultworms at 31.2 µg/ml and microfilariae at 62.5 µg/ml. Rutin inhibited microfilariae at 125 µg/ml and inhibited MTT-reduction in female worms for >65% at 500 µg/ml. Chrysin killed microfilariae at 250 µg/ml. Naringin showed adulticidal effects at 125µg/ml The decreasing order of the activity is Naringenin > Flavone = Hesperetin > Rutin > Naringin > Chrysin [63].

Methanolic extracts of *Centratherum anhelminthicum*, *Cedrus deodara*, *Sphaeranthus indicus* and *Ricinus communis* were screened at 1–10 mg/ml for *in vitro* macrofilaricidal activity by worm motility assay against adult *Setaria digitata*. They exhibited 86.56, 72.39, 61.20 and 43.15% inhibition respectively [64].

A study was performed on the ethyl acetate, acetone and methanol extracts of *Aegle marmelos* L., *Correa ex Roxb* (Rutaceae), *Andrographis lineata* Wallich ex Nees. (Acanthaceae), *Andrographis paniculata* (Burm.f.) Wall. ex Nees. (Acanthaceae), *Cocculus hirsutus* L. Diels (Menispermaceae), *Eclipta prostrata* L. (Asteraceae) and *Tagetes erecta* L. (Compositae) on ovicidal and oviposition-deterrant activities against filarial vector *Culex tritaeniorhynchus* Giles. The percentage of egg hatching in methanol extracts of *A. lineata*, *C. hirsutus* and *T. erecta* were 16, 12 and 16 exerted at 500 ppm respectively. The percentage of effective oviposition repellency was 97.77 at 500 ppm and the lowest repellency was 42.06 at 31.25 ppm in methanol and acetone extracts of *A. lineata* and *A. paniculata*, respectively [65].

The n-hexane and chloroform extracts of leaves of *Aegle marmelos*, *Andrographis lineata*, *Andrographis paniculata*, *Cocculus hirsutus*, *Eclipta prostrata*, and *Tagetes erecta* were tested for the repellent, ovicidal, and oviposition-deterrant activities against filarial vector *Culex tritaeniorhynchus* Giles. The percentage of effective oviposition repellency were 95.90, 94.75, 95.04, 90.58, 87.93 and 87.14 ppm in hexane, 94.82, 95.71, 92.26, 90.58, 83.35, and 78.16 in chloroform extracts at 500 ppm, and the lowest repellency was 69.93, 53.06, 64.81, 70.06, 51.82 and 54.54 ppm in hexane, 48.31, 66.71, 68.82, 61.85, 34.84, and 39.53 at 31.25 ppm in chloroform extracts respectively [66].

There are claims of antifilarial activity for *Azadirachta indica* [67] and *Pongamia pinnata* [68] against cattle filarial parasite *Setaria cervi*.

**Marine sources**

Zoanthids are marine animals related to sea anemones and corals. The chloroform methanol (1:1) extract of green zoanthus (*Phylum Coelenterata, Class Anthozoa*) showed promising in vitro adulticidal activity with a lethal concentration of 125 lg/ml on *Brugia malayi*. It showed a 52.2% reduction in circulating microfilariae of *B. malayi* at 250 mg/kg, oral dose [69].

1. **Botryocladia leptopoda** (J. Ag.) Kyln. Order (Rhodophyceae): Botryocladia, commonly known as sea grapes, red grape alga or bubble alga, is an abundant member of the red algae. Attempts were made...
to isolate the chemical constituents from these algae. The crude extract and its n-hexane Fraction showed reduction in the peripheral micro filarial level in both of the rodent filarial parasites L. sigmodontis and A. viteae [70].

2. Haliclona exigua: It is a sedentary marine sponge belonging to phylum Porifera, class Demospongia, order Haploscleridae, and family Halicloniidae. Haliclona sp. The crude methanol extract, n-butanol soluble fraction killed adult Brugia malayi at a concentration of 31.25µg/ml, the chloroform fraction was toxic at a lower concentration of 15.6µg/ml. Both these extracts also showed macrofilaricidal activity but were more significant in the chloroform fraction (50.2%). There was moderate adverse effect on the reproductive potential of female worms (crude extract 46.5%; chloroform 58.6%)[71].

CONCLUSION
Available literature, ancient literary works and Ethnomedical surveys described the traditional use of the plants as antifilarial agents assuring their clinical efficacy and safety. The present review is a survey of literature featuring the screening of plant extracts for the in vitro and in vivo antifilarial studies in support to the folklore claims. In future, the molecular mechanism of the plants drugs should be understood and lead molecules are to be isolated to meet the demand and requirement of the high potency and to develop best alternative herbal formulations to replace or compensate the currently available synthetic formulations as well as the standardization of the herbal extracts should be done to limit the quality and efficacy variations and to check the possible adulterants. The discovery of the novel lead molecules might hopefully bring advancement in the safe and effective treatment of filariasis.

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REFERENCES


