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Promising mosquito repellent and mosquito larvicidal plants from the genus *Coleus*: A review

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Abstract
Mosquitoes are important group of arthropods in terms of public health. Most of the life-threatening diseases like Malaria, Filaria, Yellow Fever, Vest Nile Virus infection, Japanese Encephalitis, Dengue Fever, Chikungunya and Zika fever are transmitted by the mosquitoes that lead to millions of deaths every year. The continuous application of synthetic insecticides has disrupted the natural biological control systems and led to development of resistance in the mosquito population. This has also resulted in the development of resurgence of mosquito population, biological manifestation of toxic substances through food chain, undesirable effects on non-target organisms including human beings. Bio-pesticides are an alternate mosquito control strategy as it is long lasting, eco-friendly, less expensive, and harmless. The family Lamiaceae is specially noted for plants having abundance in the volatile constituents, ease of propagation, wide distribution and therapeutic implications. In addition to all the family is preferably known to contain genera like *Ocimum*, *mentha*, *lavendula* having potentiality for controlling mosquito population. The present review focusses only on the genus Coleus, one of the largest genera of the family Lamiaceae.The genus contain so many plants found to have detrimental effect on mosquitos and other insect pests but only few studies are conducted to prove their activities and also have a need to isolate and identify the phytoconstituents responsible for the same. The objective of the review also extends to the adaptation of modern techniques such as nanoparticle technology to improve the biological activities of the phytoconstituents attributed to be responsible for toxic effect on mosquitos.

Keywords: coleus amboinicus, coleus vettiveroides, coleus malabaricus

Introduction

Phytochemicals derived from various botanical sources have provided numerous beneficial effects, ranging from pharmaceuticals to insecticides. Synthetic pesticides although notably efficacious against target species such as mosquitoes, can be damaging to nontarget organisms including man. In addition to the negative environmental impacts of conventional pesticides, the majority of major mosquito disease vectors and pest species have developed physiological resistance to several of these chemicals. These issues have resulted in the demand for environmentally friendly, biodegradable, and mosquito-specific pesticides. The quest for such chemicals has been focused on the plant kingdom [1].

According to WHO report, vector borne diseases account for more than seven million deaths annually among which mosquito borne diseases are the most threatening due to their wide spread occurrence and higher frequency of disease transmission. Mosquitoes have been designated as the world's "public enemy number one" by the World Health Organization (WHO). Among the different mosquito families, Culicidae is a large family (3,300 Service species-41 genera) of which *Anopheles*, *Culex*, and *Aedes* are the most detrimental. *Anopheles* species are carriers of major life-threatening diseases like malaria, filariasis transmitting agents, such as *Wuchereria bancrofti*, *Brugia malayi, and Brugia timori* and also of a few *Arbo* viruses [2, 3].

Mosquito borne diseases are found in more than 100 countries throughout the world, affecting over 700 million people each year, including 40 million Indians. In practically all tropical and subtropical nations, as well as many other regions of the world, they operate as a vector for most life threatening diseases such as malaria, yellow fever, dengue fever, chikungunya fever, filariasis, encephalitis, west nile virus infection and so on. Among these infectious diseases, Japanese encephalitis is endemic in about 21 countries. It is the leading cause of viral encephalitis in Asia, with 3 billion cases annually. In India the state Uttar Pradesh, which is at a risk of developing Japanese encephalitis, causing 52.40% of all deaths from Japanese encephalitis. Lymphatic filariasis, commonly known as elephantiasis, is considered another major public health problem because of its prevalence and social stigma caused by the symptoms of the disease. It is the second most common vector parasite disease after malaria and occurs in 81 tropical and subtropical countries. Lymphocytic filariasis affects at least 120 million people in 73 countries in Africa, India, Southeast Asia and the Pacific Islands. India alone accounts for about 40% of the world's filaria load. *Wuchereria bancrofti* infection by the mosquito, *Culex quinqueasciatus* say accounts for 95% of all cases of lymphatic filariasis in India. *Anopheles gambiae* is the major vector of malaria and *Aedes aegypti* is the principal transmitter of yellow fever, dengue fever, dengue haemorrhagic fever and Chikungunya fever [3].

Despite a lot of research in vaccine development no effective and acceptable multivalent vaccines are currently available against mosquito borne diseases. Synthetic

pesticides such as organochlorine and organophosphate chemicals are used extensively in mosquito control operations. However due to human, technical, operational, ecological, and economic issues, this has not proven particularly effective. The use of several past synthetic insecticides in mosquito control programmes has been curtailed in recent years. It is because of a lack of new pesticides, the expense of synthetic insecticides, environmental concerns, adverse effects on human health, and other non-target groups. To alleviate these problems, major emphasis has been set on the use of natural plant-based products as Mosquito larvicidal, adulticides, oviposition deterrents, ovicides, pupicides and which can provide an alternate to synthetic insecticides [4].

Phytochemicals can be derived from whole plants or specific portions of plants, depending on the derivatives' activity. Phytochemicals are basically secondary metabolites that serve as a means of defense mechanism of the plants. Several groups of botanicals such as alkaloids, steroids, terpenoids, essential oils and phenolics from different plants and from different plant parts like fruits, leaves, stems, barks, roots *etc.* have been reported for their insecticidal activities. Insecticidal effects of plant extracts vary not only according to plant species, mosquito species, geographical varieties and parts used, but also due to extraction methodology adopted and the polarity of the solvents used during extraction. In all cases where the most toxic substances were concentrated upon, found and extracted for mosquito control [2]. Researchers have discovered that the efficacy of compounds generated from specific plant parts changes depending on the mosquito species. Some phytochemicals are poisonous at all phases of mosquito life, while others interfere with growth and reproduction, or act on the olfactory receptors, eliciting attractant or repellent reactions. The main strategy for mosquito control deals with the restriction of the vector population [1].

Several mechanisms are involved in the effectiveness of these phytochemicals on mosquitoes. Plant metabolites affect vital physiological functions of mosquitoes like inhibition of Acetyl choline as well as Gamma amino butyric acid (GABA) gated chloride channel, disruption of Na–K ion exchange etc. Consequently, the physiology is disrupted at numerous receptor sites, eventually causing an abnormality in the nervous system [2, 5]. Another strategy for mosquito control is focused on targeting breeding sites of mosquitoes for controlling their population density. If oviposition is inhibited, the mosquito's life cycle is disrupted and eggs are not laid. In addition, it has been proved that ovicides penetrate through the egg shell and act on the embryo inside [6].

From ancient time onwards so many plant products are used against insect pests such as the Neem (*Azadirachta indica*) belongs to the family Meliaceae, Pyrithrins from Pyrethrum plant, Nicotine from Tobacco etc [7]. Besides secondary metabolites, essential oils from plants were also recorded with effective mosquitocidal potentials. The essential oils from the plants belonging to different families like Lamiaceae, Zingiberaceae, Lauraceae, Rutaceae, Myrtaceae were also proved with bioactivity against various mosquito species. Aroma chemicals present in leaves and flowers have been widely used in aromatherapy since ancient times, suggesting that they have some beneficial health effects in addition to their pleasant odour. In addition to this, some herbs such as rosemary and sage are used to produce drugs classified as pharmaceuticals, representing a significant part of pharmaceutical market. The essential oils represent a highly complex class of natural product chemistry having well defined role in the economic development of a country. The oils affect the behaviour responses of pests, kill or repel the pests which are harmful to human, animals or crops. The sweet smelling terpenoids attract the insects on one hand and are ovicidal on the other [5]. The review focuses on plants coming under the genus Coleus of Lamiaceae having toxic effects or repellence on mosquitoes at any stage and development of the most dreadful vector. The review also pointed out that the plants under discussion should be exploited more to develop potential products to destroy the most dangerous enemy of human population without damaging the nature.

The Family Lamiaceae (Labiatae)

Lamiaceae, commonly known as "mint family" is one of the largest families among dicotyledons. The family includes most widely used culinary herbs such as mint, rosemary, basil, sage, thyme, Ocimum, Leucas, coleus, Lavendula etc. The plants are widely cultivated, owing to their ease of cultivation, ethnomedicinal importance, aromatic nature and most importantly pharmaceutical value as flavouring and perfuming agents [7]. In addition to the above-mentioned uses large number of plants are reported as effective insecticide or insect repellents. The essential oil constituents are primarily considered as the reason for this activity [8].

Important Lamiaceae plants which are proved as powerful mosquito repellence or mosquitocidal or mosquito larvicidal are leucas species such as *Leucas aspera*, *Leucas cephalotes* and *leucas martinicensis*. Among these first two *Leucas* species are used against wide range of insects but *Leucas martinicenses* is specifically used to repel mosquitoes in Africa. this is a strongly scented plant which is burned to get rid of mosquitoes. Another valuable category is the *Ocimum* species such as *Ocimum americanum*, *Ocimum basilicum*, *Ocimum suave* and *Ocimum viride*. Essential oil from the leaves of *Ocimum canum* is reported to exhibit insecticidal properties. These plants are either burned or emulsions prepared form these are used for getting mosquito or other insect repellent activity [9]. A study conducted by Gunarathna and Karunaratne showed that the plants belonging to the family like *Ocimum gratissimum, Coleus amboinicus, Ocimum tenuiflorum, Plectranthus zatarhendi* are effective as post-harvest grain protectants for the control of rice weevil *Sitophilus oryzae* [10]. Phyto constituents such as oleanolic acid and ursolic acid is found to be the insecticidal activity of *Leucas aspera*. The toxic effects on mosquitoes by various *Ocimum* species is proved to be methyl eugenol in case of *Ocimum sanctum*, Eugenol in the case of *O.gratissimum*, Eugenol methyl cinnamate in *O.americanum*, Carvacrol and Thymol in *O. syrianum* and all the plants are proved to be effective against *Aedes aegypti*.α-Terpenolein and thymol present in *Lavendula* species are studied to be effective against *Culex* species. Among the mentha species, Piperitone oxide in *Mentha longifolea*, Piperitone and Pulegone in the case of *M.microphylla* are proved to be effective against *Culex pipiens*. Pulegone and Carvone present in *Pulegium vulgare* is found to be toxic for *Culex pipens* [5].

The genus *Coleus*

Coleus is one of the largest genera of Lamiaceae and is found to be distributed through tropical and warm regions

like Africa, Australia, and India [11]. Like other genera the genus also consists of aromatic herbaceous plants with particular application as home remedies for various ailments. The genus name *Coleus* was derived from the Greek word 'Coleos', meaning sheath and the word was first described in 1790 by Loureiro. The Genus *Coleus* comes under the subfamily Nepetoideae of tribe Ocimeae and subtribe Plectranthinae. There existed numerous taxonomic problems in the naming of *Coleus* species, due to the lack of clear-cut morphological criteria for identification of different species within the genera, and species have often been placed in closely related genera like *Plectranthus*, *Solestemon*, *Englerastrum*. Paton *et al*., proposed a synopsis of the genera *Coleus* Lour, *Equilabium* A.J Paton & Mwany and *Plectranthus*L'Her and 212 names are changed to combinations in *Coleus* from *Plectranthus* based on the calyx and corolla morphology and treated *Coleus* as distinct from *Plectranthus* by having four stamens fused together rather than free to their base [12].

Owing to the tremendous application in the alternative systems of medicine and Pharmaceutical importance, more than 500 varieties of *Coleus* species are cultivating throughout the world nowadays. In spite of the worldwide distribution of the species, the chemistry and biological activities of so many species have to be studied more deeply. Lukohoba *et al.*, provided a comprehensive understanding of the global ethnobotany of the plants [13]. Rice *et al.*, presented an updated horticultural and ethnobotanical review of the South African species [14]. The genus *Coleus* has reported to contain monoterpenoids, sesquiterpenoids, diterpenoids, and phenols [15]. Major medicinal species of *Coleus* found in India are *Coleus amboinicus*, *Coleus forskohli*, *Coleus zeylanicus*, *Coleus vetiveroides.* Among these the most cited and well documented species is Coleus *amboinicus* [16].

Coleus amboinicus

Synonym: *Plectranthus amboinicus* (Lour.) Spreng. This is one of the plants among the genus *Coleus* with greater synonyms and local names. *Coleus amboinicus* is commonly known as Indian borage, Country borage (English) Indian Borage, Country borage, Spanish thyme, Mexican mint, French thyme, Indian mint (US), Cuban oregano, French thyme, Indian Mint, Soup Mint (South Africa &US), Mexican mint, Spanish thyme. Orégano: Orégano de Cartagena (Cuba), Da Shou Xiang (China), Latai, Suganda, Oregan, Toronjil de limón (Philippines), Orielle (France) and Jamaika thymian (Germany). Parna-Yavaani, Peterechur, Panikkurukka, Kap parillaku (India), Common names in Malayalam are Kannikkurkka, Panikkurkka, in Sanskrit are Karpuravalli, Sugandha Valakam and in Tamil are Karpuravalli, Omavalli [17]. It is a large succulent perennial, branched aromatic herb with approximately 30–90 cm in height and with thick fleshy stem and leaves. It is one of the most cited and well-documented species in the Lamiaceae family, which occurs naturally throughout the tropics and warm regions of Africa, Asia, and Australia, where it is used as traditional medicine, spice, and ornamental plant. Studies have revealed the occurrence of 76 volatile and 30 non-volatile compounds belonging to different classes of phytochemicals such as monoterpenoids, diterpenoids, diterpenoids, sesquiterpenoids, phenolics, flavonoids, esters, alcohols, and aldehydes. The major chemical compounds found in the essential oil of *Coleus amboinicus* are phenolic monoterpenes like carvacrol and thymol [18].

Govinda Rajan *et al*., studied the mosquito larvicidal activity of essential oil and thymol isolated from volatile oil against larvae of *Culex tritaeniorhynchus*, *Aedes albopictus* and *Anophelus subpictus*.The results revealed that thymol has more larvicidal potency against early third stage larvae than essential oil. The study concluded that the isolated constituents have more potential than oil and could be a suitable alternative for synthetic insecticides [19].

The essential oil of *C. amboinicus* and the isolated constituents such as β-caryophyllene, bergamontene and Carvacrol are found to be effective against different larval stages and adult population of mosquitoes and the plant and its volatile oil is used as natural larvicides to control larvae of *Culex tritaeniorhynchus*, *Anopheles subpictus* and *Aedes albopictus* [5]. The essential oil extracted from *C. aromaticus* revealed significant larvicidal property against *Anophelus gambiae* and can be used against the African malaria vector mosquito. Similarly, a study conducted using essential oil of *C. aromaticus* against white termites (*Odontotermes obesus* Rhamb.), resulting in 100% mortality. Essential oil of *C. aromaticus* was reported to be more effective than commonly used synthetic insecticides Primoban-20 and Thiodan [17].

Various literature reviews clearly showed that the plant has a potential larvicidal, ovicidal and repellent activity and the effect is dose related. Diethyl ether extract of *C. aromaticus* was an outstanding potential for controlling the dengue vector mosquito *Aedis aegypti* [20]. The green synthesized silver nanaoparticles from the leaf extracts showed prominent activity against *Culex quinquefasciatus* [21].

Ethanolic extracts of *Cynodon dactylon*, Aloe vera, *Hemidesmus indicus* and *Coleus amboinicus* were tested for their toxicity effect on the third-instar larvae of *Anopheles stephensi*, *Culex quinquefasciatus* and *Aedes aegypti*. The study proved that like other extracts *C. amboinicus* have both mosquitocidal and water sedimentation properties [22].

***Coleus vettivroides* K.C jacob**

Coleus vettiveroides K.C.Jacob, Synonym: *Plectranthus vettiveroides* (K.C.Jacob) is a small, richly branched juicy aromatic herb distributed mainly in south india. Commonly known as Hrivera (in Sanskrit) Valakor or Kuruver or Vilamichaiver or Vettiver (in Hindi). Iruveli (in Malayalam), Kuruveru or Vettiveru (in Telugu) and Muchivala or Lavanchi (in Kannada) [23]. The fresh scented roots of *Coleus vettiveroides* are used to decorate the idols of temples in Kollidam region of Tamil Nadu. The essential oil extracted from the roots of *Coleus vettiveroides* is orange-red in colour. The roots of *C. vettiveroides* plants are more valued in the market for their medicinal properties and are widely used in many Ayurvedic and Siddha formulations [24].

Traditionally the plant is used as an aromatic, bitter, cooling, febrifuge, diaphoretic, stimulant, diuretic, trichogenous and antipyretic and also for the treatment of hyperdipsia, vitiated conditions of pitta, burning sensation, strangury, leprosy, skin diseases, leucoderma, fever, vomiting etc [23].

Beesha *et al* evaluated the larvicidal activity of alcoholic extracts of the plant *Coleus vettiveroides* against human filariasis vector *Culex quinquifasciatus* and found that the percentage mortality of larval instars was found to be

increased with increased concentration of the extract and plant extract showed promising larvicidal activity at high concentrations. Decreased virulence, colour variation and sluggish movement was the other noticeable effects produced by all the larval stages [25].

Contact bioassay of alcoholic extract on *Anophelus subpictus* mosquito was studied by Beena Rani *et al*., The data clearly showed that contact bioassay dependent on concentration. As the concentration increased percentage mortality was also increased [26].

Coleus malabaricus

Synonyms: *Plectranthus malabaricus* (Benth.) R. H. Willemse, *Coleus macraei* Benth, *Coleus ovatus* Benth, *Coleus leptostachys* Benth, *Plectranthus malabaricus* var. *leptostachys* (Benth.), *Coleus walkeri* Benth [12].

The plant's local name in different languages is not included in any traditional manuscripts. Most of the names mentioned in the review are collected from the survey reports of tribal communities of different localities mentioned in various literature. Indian name: Ellambi, Tamil: Kurali, Periyathulasi, Malayalam: Parakkoorka, Kattuthulasi, Kattappa by the tribes of Wayanad region, Kerala [27].

The plant as a large erect herb reaching 3 feet, with often quadrangular purplish stem and leaves. Flowers pale lilac with dark blue upper lip. Leaves 15 × 13 cm, puberulous, ovate, obtuse or acute, leaf base is truncate or subcordate. Panicles terminal to 30 cm long. Calyx striate, upper lip broadly ovate, lower 3-lobed, lobes ovate- lanceolate. Corolla white with a purple tinge, 1 cm long, stamens exserted, filaments glabrous.

An ethnobotanical survey reports on tribal communities of south India the plant is used by the tribes for the treatment of asthma, orally for the smooth functioning of the heart and to prevent heart attack, for the treatment of cough and cold and the whole plant is made into a paste and applied knots for curing muscular pain and inflammations.

the tribal communities of Western Ghats area has been using the plant as mosquito repellent the underlying mechanism and the phytoconstituents involved in this need to be studied. Whole plant is kept indoors or crushed plant is placed indoors by tribal communities of various parts of south India for achieving mosquito repellent property [27].

***Coleus fruticosus* wight ex benth**

Synonym: *Plectranthus fruticosus* (Wight ex Benth.) or *Plectranthus deccanicus*, Distributed mainly in South west India [12]. Branched herbs upto 22 cm tall, stem creeping at the base with many stiff, erect branches and very short internodes. Leaves in whorls, 4-8 per node 8 × 2 mm, narrowly linear, apex acute, puberulous. Flowers pink in colour, minute in dense terminal spikes up to 5 cm long: bracts c. 2 mm long, persistent. Calyx 2 mm long, campanulate, pubescent: lobes triangular, erect, or slightly inflexed. Corolla 1.5-2 mm long: tube c.1mm long: lobes ovate-oblong, obtuse, hairy. Stamens 4, much exserted, bearded with purple hairs. Style flattened. Nutlets ellipsoid, smooth, yellowish-brown. The flowering and fruiting time December to June. *Coleus fruticosus* is a popular garden plant and is often grown as ornamental. The plant is endemic to Peninsular India, mainly seen in the Western Ghats, evergreen forests, and moist Localities. Often grown as live fences in the high ranges. In India, the plant is reported to form the states Kerala (Idukki-Kalvarimala) and Tamil Nadu (Coimbatore, Dindigul, Nilgiri). The plants are collected from the wild for local use as medicine. The plant is antimicrobial and is used to treat burns. The plant contains kaurane diterpenoids, which are partly responsible for the antimicrobial action. The plant is also used as an insect repellant. Bunches of the plants are hung up indoors, or the stems are rubbed on window sills to repel flies [27].

***Coleus laxiflorus* (Benth.) (*Plectranthus glandulosus* Hook) [12].**

Plectranthus glandulosus Hook is a plant whose leaves are often used to protect the grains stored in Cameroon from insect attack. The essential leaf oils extracted from plants have been shown to be effective against 4th instar larvae of *Aedis* and early pupae of *Aedes aegypti*, *Anophelus Gambiae* and *Culex quinquefaciatus*. Qualitative phytochemical analysis of plant leaves reveals the presence of alkaloids, terpenoids, steroids, saponins, lipids, fats, fatty oils, tannins and phenolic compounds. [8].

The essential oil of fresh and dried leaves of *Plectranthus glandulosus* Hook f. [syn. *Coleus laxiflorus* (Benth.) Roberty] from Cameroon were analysed by GC and GC/MS. The oils were characterized by a high percentage of oxygenated monoterpenes [28].

Methanol crude extracts of *Plectranthus glandulosus* and *Callistemon rigidus* leaves were sequentially fractionated in hexane, chloroform, ethyl acetate, and methanol to establish the most active fraction(s) against *Callosobruchus maculatus* in cowpea [29, 30].

***Coleus tenuicaulis* hook.**

Synonyms: *Plectranthus tenuicaulis* (Hook. f.) J. K. Morton, *Plectranthus minimus* Gürke [12] is one of the 14 species of the genus *Plectranthus* found in the flora of West Africa. The plant is mainly found in West tropical Cameroon, South west Tanzania to South tropical Africa. The plant is a small erect, branched, slender pubescent herb 2-36 in. high with lax panicles of small blue flowers and variegated leaves with purple dominant evergreen [31].

A study conducted by Deletre E pointed out that the leaf essential oil (Epoxy cymene) essential oil possess irritant and repellent effect on adults of the malaria vector *Anopheles gambiae* mosquito [32].

Conclusion

One of the most effective alternative approach for mosquito control is by exploring the floral diversity. Unlike the chemical pesticide plant derived insecticides are made up of botanical blends of chemical compounds that affect the physiological processes of mosquitoes without developing any resistance to activity. The review covers an outlook on the anti-vector potential of Coleus plants like *Coleus amboinicus* and *Coleus vettiveroides* and the plants like *Coleus malabaricus*, *Coleus laxiflorus*, *Coleus fruticosus*, *Coleus tenuicaulis* with known toxic potential but need further research to prove the anti-vector potential. In addition to the direct application of plant metabolite, the review also pointing towards the importance of newer technologies for the development of more effective and more specific agents.

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