

## Review Article

### Antiparasitic, antiprotozoal, molluscicidal and insecticidal activity of medicinal plants (part 2) – plant based review

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**Abstract:** In our previous paper, we reviewed the medicinal plants possessed antiparasitic, antiprotozoal, molluscicidal and insecticidal activity. These included *Achillea santolina*, *Ailanthus altissima*, *Allium species*, *Ammi majus*, *Antirrhinum majus*, *Apium graveolens*, *Arachis hypogaea*, *Artemisia campestris*, *Arundo donax*, *Asclepias curassavica*, *Ballota nigra*, *Bauhinia variegata*, *Betula alba*, *Bidens tripartite*, *Brassica nigra*, *Bryophyllum calycinum*, *Caccinia crassifolia*, *Caesalpinia crista*, *Calendula officinalis*, *Calotropis procera*, *Canna indica*, *Capparis spinosa*, *Carum carvi*, *Cassia occidentalis*, *Celosia cristata* and *Chenopodium album*. This review was designed as a second part of medicinal plants exerted antiparasitic, antiprotozoal, molluscicidal and insecticidal activity.

**Keywords:** antiparasitic, antiprotozoal, molluscicidal, insecticidal, medicinal plants, herbs.

#### Introduction:

Helminths, protozoa and ectoparasites could resist many types of drugs by different mechanisms [1-11]. In our previous paper [12], we reviewed the medicinal plants possessed antiparasitic, antiprotozoal, molluscicidal and insecticidal activity as an alternatives. These included *Achillea santolina* [13], *Ailanthus altissima* [14], *Allium species* [15], *Ammi majus* [16], *Antirrhinum majus* [17], *Apium graveolens* [18], *Arachis hypogaea* [19], *Artemisia campestris* [20], *Arundo donax* [21], *Asclepias curassavica* [22], *Ballota nigra* [23], *Bauhinia variegata* [24], *Betula alba* [25], *Bidens tripartite* [26], *Brassica nigra* [27], *Bryophyllum calycinum* [28], *Caccinia crassifolia* [29], *Caesalpinia crista* [30], *Calendula officinalis* [31], *Calotropis procera* [32], *Canna indica* [33], *Capparis spinosa* [34], *Carum carvi* [35], *Cassia occidentalis* [36], *Celosia cristata* [37] and *Chenopodium album* [38]. This review was designed as a second part of medicinal plants exerted antiparasitic, antiprotozoal, molluscicidal and insecticidal activity.

#### *Chrysanthemum cinerariaefolium*

Pyrethrum is first insecticide recorded in history at the time of China's Chou Dynasty, some 2000 years ago. The flower was traded along the Silk Route into Europe where it was widely grown. The Dalmatian region was the predominant pyrethrum-producing region from the late 19<sup>th</sup> century through to the advent of World War I, when the predominant product was referred to as "Dalmatian Flea Powder". Japan became the major supplier after 1918 and remained so until

1940. Kenya began production after the introduction of *Chrysanthemum cinerariaefolium* in 1928 and, by 1940, had replaced Japan as the dominant world supplier of pyrethrum extract. Neighbouring East African countries, particularly Tanzania, Rwanda, and Uganda also developed infrastructure to support pyrethrum cultivation and have produced significant amounts of pyrethrum from time to time. Small commercial plantings for production of pyrethrum extract were made in Albania, Algeria, Angola, Argentina, Australia (Canberra and NSW prior to Tasmania), Bermuda, Bolivia, Brazil, Bulgaria, Canada, Chile, China, Congo, Cyprus, Ecuador, Egypt, Republic of Ireland, England, Ethiopia, Fiji, France, Greece, Guatemala, India, Italy, Jamaica, Madagascar, Mexico, Morocco, New Zealand, Nigeria, Palestine, Persia, Peru, Philippines, Puerto Rico, United States, St. Helena, Spain, Sudan, Sweden, Switzerland, Trinidad, Turkey, Russia, South Africa and Zimbabwe [39-40].

The plant products were available for use even though the chemistry of active ingredients was unknown. In 1924, German chemist Herman Staudinger (1881-1965) and a Croatian scientist, Lavoslav Ružička (1887- 1976), winner of the 1939 Nobel Prize in Chemistry, identified chemical structure of the active pyrethrin ingredients, pyrethrin I and pyrethrin II [41].

Pyrethrin is mainly concentrated in the flower heads, 93.7 % of pyrethrin is accumulated in achenes, and minor quantities in disc florets (2.0 %), ray florets (2.6 %), and receptacles (2.6 %). The term pyrethrin is

referred to the six insecticide active ingredients: pyrethrin I, cinerin I, jasmolin I, pyrethrin II, cinerin II and jasmolin II. Pyrethrin I, cinerin I and jasmolin I are closely related insecticidal esters of chrysanthemic acid, while pyrethrin II, cinerin II and jasmolin II are insecticidal esters of pyrethric acid. The three chrysanthemic acid esters are commonly referred as pyrethrins I, and pyrethric acid esters as pyrethrins II. Among these compounds pyrethrin I and pyrethrin II are the most predominant and active [42-45].

It is used for the control of a wide range of insects and mites in public health and on domestic and farm animals and for the control of chewing and sucking insects and spider mite on fruit, vegetables, field crops, ornamentals, glasshouse crops, and house plants. Pyrethrin also acts as a repellent. It has a quick knock-down effect on a wide range of insect species, causing paralysis within a few minutes. It acts as contact poison and affects the central nervous system of insects. The commonly accepted mechanism of action of pyrethroids is the prolongation of the open state of voltage-dependent sodium channels in nervous tissue. These altered sodium channels result in repetitive firing or depolarizing block of the neuron, depending on how long the channel open state is prolonged. Other channel and receptor systems in neuronal tissues have been proposed to play a role in the generation of compound-specific clinical symptoms in mammals, including calcium channels and GABA<sub>A</sub> receptors [43, 46].

In studying the mechanism of biosynthesis of pyrethrins, the results of experiments using <sup>13</sup>C-labeled glucose as the biosynthesis precursor indicated that the acid and alcohol moieties are biosynthesized via the 2-C-methyl-D: -erythritol 4-phosphate (MEP) and oxylipin pathways, respectively. Further study on the effects of wound-induced signals in leaves showed that biosynthesis is enhanced in response to both volatile and nonvolatile signals [47]. In other study the acid was found produced by the same route, but the authors mentioned that the alcohol moiety was possibly biosynthesized from linolenic acid [48].

Tissue cultures of *Chrysanthemum cinerariaefolium* were used to study the production of pyrethrin insecticides, and their precursor chrysanthemic acid. Callus cultures and root-differentiated cultures did not contain pyrethrins whereas shoot differentiated callus was found to produce the pyrethrins. Chrysanthemic acid was isolated by extraction from callus cultures, and feeding <sup>14</sup>C-labelled chrysanthemic acid to a cell suspension of *Chrysanthemum cinerariaefolium* established that the acid accumulates largely as a glucoside ester [49].

The main use of pyrethrum at present is in household formulations to kill houseflies, cockroaches and mosquitoes. Insects react very quickly when dosed with pyrethrum, and this quick knock-down effect is a

very valuable property for household insecticides as the user sees the onset of paralysis within 2–3 minutes. Pyrethrum acts on a very wide spectrum of insect species – more so than with most individual synthetic insecticides. It is also a very powerful repellent to mosquitoes. The process of piercing the skin using saliva injected as a lubricant, finding and piercing a blood capillary followed by sucking of blood into the insect is a very precise and complicated process and coordination is lost when even a few molecules of pyrethrum are present. Synergised pyrethrum formulations are particularly effective against the mosquitoes and midges, which bite humans, and to date there have been no reports of resistance developing in these species to this biopesticide. Pyrethrins are very quickly degraded in sunlight leaving no toxic residues and are ideal for use as pre-harvest sprays to remove insect pests on edible crops – up to 24 hours before harvest [50-51].

The efficacies of pyrethrum and albendazole against experimental sheep gastrointestinal nematode infection were compared. Sheep were infected orally with 10,000 larvae (*Haemonchus* spp. (60.1%), *Oesophagostomum* spp. (13.9%), *Trichostrongylus* spp. (13.2%), *Cooperia* spp. (8.3%), *Nematodirus* spp. (3.5%), *Strongyloides* spp. (0.8%) and *Ostertagia* spp. (0.2%). Faecal egg count reduction in albendazole-treated sheep was 100% by day 4 following treatment, compared to 37.03%, 31.3%, 38.9% and 51.8% on days 4, 6, 8 and 10 in pyrethrum treated sheep. These effects were statistically significant on days 8 and 10 post-treatment ( $p < 0.05$ ) [52].

### **Cichorium intybus**

It appeared that the animals grazing on chicory have a lower incidence of gastrointestinal nematode infestations, the total number of abomasal helminths was found to be lesser in the lambs grazing on this plant. The anthelmintic activity of the plant attributed to the condensed tannins and sesquiterpene lactones [53-54]. The effects of condensed tannins (CT) and an extract containing crude sesquiterpene lactones (CSL) from chicory (*Cichorium intybus*) on the motility of the first-(L1) and third-stage (L3) larvae of deer lung worm *Dictyocaulus viviparus* and the L3 larvae of gastrointestinal nematodes was studied *in vitro*, using the larval migration inhibition (LMI) assay. The CT and CSL had a profound effect on the motility of the larvae displayed by their ability to inhibit larval passage through nylon mesh sieves. Incubation of lungworm L1 larvae in rumen fluid (collected from deer fed pasture) containing 100, 400 and 1000 microg CT/ml, inhibited 12, 28 and 41% of the larvae from passing through the sieves, respectively, while the incubation of L3 larvae with rumen fluid (pH 6.6) containing the same concentrations inhibited 26, 37 and 67% of L3 larvae from passing through the sieves, respectively. Gastrointestinal larvae seem more susceptible to CT than lungworm larvae especially at

higher concentrations. CT inhibited 27, 56 and 73% of gastrointestinal larvae from passing through the sieves when used at a concentration of 100, 400 and 1000 microg/ml, respectively. CT were more effective ( $P < 0.001$ ) at reducing the motility of lungworm L1 and L3 larvae when added to the rumen fluid than when added to the abomasal fluid (pH 3.0). Addition of 2 microg polyethylene glycol/microg CT eliminated the inhibitory effect of CT against L1 and L3 larvae especially during incubation in rumen fluid, confirming the effect as due to CT. The CSL extract also showed similar inhibitory activity against L1 and L3 lungworm and L3 gastrointestinal larvae in both fluids, indicating that this extract was not affected by the pH of the fluid, and was more effective against L3 than L1 lungworm larvae. Condensed tannins appeared to be more effective than CSL at inactivating L1 and L3 lungworm and L3 gastrointestinal larvae in rumen fluid, but CSL were particularly effective against L3 lungworm larvae in abomasal fluid [55-56].

To determine whether the individual sesquiterpene lactone compounds of *Cichorium intybus* [lactucin (LAC), 8-deoxylactucin (DOL), and lactucopicrin (LPIC)] differ in anthelmintic activity, their effects were studied on the hatching of a predominantly *Haemonchus contortus* egg population. The dominant constituents in the Puna and Forage Feast extracts were DOL and LAC, respectively; LPIC concentrations in the two extracts were similar. Extracts from both cultivars inhibited egg hatching at all concentrations tested ( $P < 0.001$ ), but there were significant differences in egg responses to the two extracts ( $P < 0.001$ ). With Puna, egg hatching decreased sharply in a linear fashion when the combined LAC, DOL, and LPIC concentrations ranged from 0 to 5.0 mg/ml. A biphasic effect on egg hatching occurred with the Forage Feast extract. The fraction of eggs that hatched decreased gradually to 65% as the sesquiterpene lactone concentrations increased from 0 to 6.7 mg/ml. Treatment with higher concentrations resulted in a sharp decline in egg hatchability. Concentrations of sesquiterpene lactones required for 50% lethality were determined by probit dose-effect analysis to be 2.6 mg/ml (95% confidence interval: 2.4-2.8 mg/ml) for the Puna extract and 6.4 mg/ml (95% confidence interval: 5.9-7.2mg/ml) for the Forage Feast extract ( $P < 0.0001$ ). These concentrations provided 1.3 and 1.5mg/ml of DOL and 0.8 and 3.9 mg/ml of LAC for Puna and Forage Feast extracts, respectively. However, the results showed that LAC has minimal effect on egg hatching [57].

The bitter compounds in the plant, namely, lactucin, lactucopicrin, and the guaianolide sesquiterpenes, isolated from aqueous root extracts of chicory were concluded to be the antimalarial components of the plant. Lactucin and lactucopicrin completely inhibited the HB3 clone of strain Honduras-

1 of *Plasmodium falciparum* at concentrations of 10 and 50  $\mu\text{g/ml}$ , respectively [58-59].

#### *Citrullus colocynthis*

Albino mice were intraperitoneally infected with  $100 \times 10^6$  promastigotes of *Leishmania donovani* (MHOM/ IQ/ 982/BRCI) strain. The inoculation of albino mice caused elevation of liver and spleen weight after 7-15 days. The mice treated with 20-100 mg/kg from *Citrullus colocynthis* showed decreased average liver and spleen weight in comparison to the positive control. The most important histopathological results in the positive control included scattered necrosis, lymphatic infiltration, proliferation of macrophages and a variable number of leishman bodies were observed. 80-100 mg/kg of *Citrullus colocynthis* return liver section to normal histology [60-61].

Larvicidal activity of crude hexane, ethyl acetate, petroleum ether, acetone, and methanol extracts of the leaf of five species of cucurbitaceous plants, *Citrullus colocynthis*, *Coccinia indica*, *Cucumis sativus*, *Momordica charantia*, and *Trichosanthes anguina*, were tested against the early fourth instar larvae of *Aedes aegypti* L. and *Culex quinquefasciatus* (Say) (Diptera: Culicidae). The larval mortality was observed after 24 h of exposure. All extracts showed moderate larvicidal effects; however, a high larval mortality was found in petroleum ether extract of *Citrullus colocynthis* against the larvae of *A. aegypti* ( $LC_{50} = 74.57$  ppm) and against lymphatic filariasis vector, *C. quinquefasciatus* ( $LC_{50} = 88.24$  ppm) [62].

The larvicidal activity of crude acetone, hexane, ethyl acetate, methanol, and petroleum ether extracts of the leaf of *Citrullus colocynthis* (Linn.) Schrad were assayed for their toxicity against the early fourth instar larvae of *Culex quinquefasciatus* (Diptera: Culicidae). The larval mortality was observed after 24 h exposure. The highest larval mortality was found in whole plant petroleum ether extract of *Citrullus colocynthis*. Bioassay-guided fractionation of petroleum ether extract led to the separation and identification of fatty acids; oleic acid and linoleic acid were isolated and identified as mosquito larvicidal compounds. Oleic and linoleic acids were quite potent against fourth instar larvae of *Aedes aegypti* L. (their  $LC_{50}$  were 8.80, 18.20 and  $LC_{90}$  35.39, 96.33 ppm respectively), *Anopheles stephensi* Liston ( $LC_{50}$  9.79, 11.49 and  $LC_{90}$  37.42, 47.35 ppm respectively), and *Culex quinquefasciatus* Say ( $LC_{50}$  7.66, 27.24 and  $LC_{90}$  30.71, 70.38 ppm respectively) [63].

Methylene chloride, n-hexane, chloroform and ethanol extracts of *Citrullus colocynthis* fruits were tested against *Aphis craccivora*. The highest insecticidal effect ( $LC_{50}$ : 11003 ppm) was obtained from the ethanol extract. The residue remaining after evaporation of ethanol extract was re-extracted by

different solvents with increasing polarity. Each fraction was tested against *Aphis craccivora*. The butanol extract showed the maximum insecticidal effect. The effective compound was identified as 2-O- $\beta$ -D-glucopyranosylucurbitacin E [64].

*Citrullus colocynthis* was evaluated as new therapeutic approach for scorpion envenomation mainly *Androctonus australis* hector venom (Aah). Local action (paw edema) and systemic effects (inflammatory, metabolic parameters, oxidative stress and hyperglycemia) were studied in pretreated mice with *Citrullus colocynthis* (50 mg/kg), 30 min before injection of sublethal dose of *Androctonus australis* hector venom (10  $\mu$ g/20 g). Results showed that injected *Citrullus colocynthis* extract before envenomation is able to protect animals against the toxicity of the venom. It significantly reduced paw edema, cell migration, exudation, hyperglycemia, and MDA. *Citrullus colocynthis* decreased also some inflammatory markers (MPO and EPO activities, CRP and C3) and maintain the level of CPK, ASAT and ALAT. *Citrullus colocynthis* appeared to be a potential tool that can reduce pathophysiological effects induced after envenomation (inflammation and oxidative stress) [65].

#### Citrus species

Methanolic extract of *Citrus medica* was evaluated for anthelmintic activity against Indian adult earthworm *Pheretima posthuma*. Various concentrations of extract were tested and results were expressed in terms of time for paralysis and time for death of worms. Piperazine citrate (10 mg/ml) was used as a reference standard and distilled water as a control group. Dose dependent anthelmintic activity was possessed by the methanolic extract of *Citrus medica* [66].

Petroleum ether extracts of *Citrus medica* leaves also possessed dose dependant anthelmintic activity against the Indian adult earthworms (*Pheretima posthuma*). The effect which could be attributed to inhibition of glucose uptake in the parasites and depletion of its glycogen synthesis. It also activated nicotinic cholinergic receptor in the worms resulting in either persistent depolarization or hyperpolarization [67].

The anthelmintic activity of petroleum ether extract of the peels of *Citrus sinensis* was studied against Indian adult earthworms, *Pheretima posthuma*, it exhibited a dose dependent inhibition of spontaneous motility (paralysis), and evoked responses to pin-prick, and the effects were comparable with that of piperazine citrate [68].

The effect of aqueous extract of this *Citrus medica* on viability of the protoscolices of *Echinococcus granulosus* *in vitro*, in a concentration of

90 mg/ml, the aqueous extract was effective in killing all protoscolices after four days of incubation [69].

Alcoholic extracts of the rind of *Citrus medica* showed *in vitro* anthelmintic activity against human *Ascaris lumbricoides* [70].

The larvicidal potential of hexane and petroleum ether extracts of *Citrus limetta* peels was assessed against dengue fever vector, *Aedes aegypti*, and malarial vector, *Anopheles stephensi*, by evaluating the toxicity effects on early fourth instars. Both the extracts were found effective against both the species. The bioassay with hexane extracts resulted in LC<sub>50</sub> values of 132.45 and 96.15 ppm against *A. stephensi* and *A. aegypti*, respectively; while the petroleum ether extracts from the *C. limetta* peels showed LC<sub>50</sub> values of 244.59 and 145.50 ppm, respectively. It revealed that the hexane extracts possessed 1.9-fold more larvicidal potential against *A. stephensi* and 1.5-fold more efficacy against *A. aegypti* as compared to the extracts obtained using petroleum ether as solvent. The data further revealed that the extracts were 1.4-1.7 times more effective against *A. aegypti* as compared to *A. stephensi* [71].

The mosquito repellent activity of extracts from Peels of five citrus fruit species, *Citrus sinensis*, *Citrus limonum*, *Citrus aurantifolia*, *Citrus reticulata* and *Citrus vitis*, were studied using five different concentrations, 5%, 10%, 15%, 20% and 25% (volume by volume). Topical application of the extract concentrations on human volunteers revealed that 20% and 25% repelled mosquitoes 2 hours and 5 hours, respectively. Short-lived and mild skin itching and sneezing reactions were observed as side effects [72].

#### Clerodendrum inerme

Leaf extracts were evaluated for their nematicidal efficacy against root-knot nematodes. In the juvenile mortality assay against egg masses, leaf extracts of *C. inerme* significantly inhibited the development [73-74].

The aqueous extract of *Clerodendron inerme* (*C. inerme*) plant leaves was evaluated against laboratory strain *Aedes aegypti* larvae. The extract elucidated 100% inhibition of adult emergence at 2% concentration of extract, and concentrations above 4% led to prolongation of larval developmental period without moulting leading to death during larval stage. Mortality during larval stage was found to be dose-dependent elucidating 100% mortality at 16% concentration. It is apparent that the extract interferes in the developmental process affecting larval developmental period and disruption of larval-pupal moult [75].

Laboratory and field investigations have been made to evaluate the combined effect of *Clerodendron*

*inerme* and *Acanthus ilicifolius* on three species of mosquito vectors, *Anopheles stephensi*, *Aedes aegypti* and *Culex quinquefasciatus*. Different concentrations of *Clerodendron inerme* and *Acanthus ilicifolius* have been tested on the various stages of species of mosquito vectors. They were active against different larval stages of mosquitoes. The lethal effect on mosquito larvae may be due to the active plant compounds on the gut lining of the mosquito larvae. The larval density was decreased after the treatment with the *Clerodendron inerme* extracts at the breeding sites (drinking water and ditches water) [76].

The dry powder of *Clerodendron inerme* leaves was tested (10 to 60 mg) against freshly moulted fourth instar larvae of dengue mosquito vector *Aedes aegypti*. The results revealed that there was no larval mortality in the treated larvae and they moulted to pupae after 60h from the start of the experiment and the process was completed by 72h. Control larvae also required 60–72h to pupate. There were no visible behavioural changes in the treated larvae, except for the fact that they were not as active as those of control ones after 24h of treatment. During pupal stage also, the pupae in treated flasks were not as active as control groups. Flasks containing 40, 50 and 60 mg powder showed pupal mortality after about 18-20h. At the end of 72h, the percent pupal mortality in the same treated groups was 48, 74 and 96 respectively. Flasks containing 20 and 30 mg of powder exhibited less than 10% pupal mortality. In order to determine the quantity of powder required to cause larval mortality, the quantity of powder was increased from 100 to 200 mg with 20 mg increment between the treatments. The results showed dose-dependent larval mortality. As much as 85% larval mortality was seen when the powder quantity was increased to 160 mg. It was further noted that the fourth instar larvae that moulted to pupae died during the early pupal stage. The final analysis of results revealed 100% mortality in all the experimental flasks, which included larval as well as pupal mortality. Microscopic examination of dead larvae revealed that the larval cuticle had started sclerotization, which appeared to be a characteristic feature of the pupal cuticle. The dead pupae on the other hand, showed less sclerotization of the cuticle compared to untreated ones, and in majority of the pupae, the head capsule remained attached to the pupal head [77]. It was stated that petroleum ether extract of *Clerodendron inerme* gave 3h protection against mosquitoes at 9% concentration [78].

The Petroleum ether, Chloroform, Ethyl acetate, Ethanol and water fractions of the powdered leaves of *Clerodendron inerme* were tested for their efficacy against the stored grain insect pest *Corcyra cephalonica* (Stainton) (Lepidoptera Pyralidae). Seven different doses (0.05, 0.1, 0.15, 0.5, 1.0, 1.5, and 2.0 g) per 20.0 g of rice were tested against this common insect pest of rice to evaluate their effect on its life

cycle and mortality. Three higher doses were further tested for their effect on physiological parameters like total haemocyte count (THC), total protein content and glycogen level along with starved insects. *C. inerme* exhibited biopesticidal activity as evidenced by the high mortality rate in treated insects. There was also a significant reduction in the THC (39-53%), protein (30-38%) and glycogen (40-61%) content in *C. inerme* treated larvae with respect to their controls [79].

The efficacy of *Clerodendron inerme* leaf extract was evaluated against *Pieris brassicae*. Larva, pupa and adult of *P. brassicae* have been treated with the aqueous extract of *C. inerme* leaf of different concentration. The results show that extract was quite effective against all the three stages in general, and pupa in particular. A typical extract with 12.5% concentration showed a mortality rate of 20% for larvae which rises to 55% for pupa. The mortality rate generally increases with increase in the concentration, reached to its maximum at 10% to 17.5% of concentration and then decreased or became constant for different developmental stages [80].

#### *Clitoria ternatea*

The ethanolic extract of *Clitoria ternatea* (100mg/ml) bring paralysis within 15-20 min and bring death within 28-30 min to the Indian earthworm *Pheritima posthuma* [81-82]. However, the anthelmintic activity of ethanolic extracts of flowers, leaves, stems and roots of *Clitoria ternatea* were also evaluated on adult Indian earthworms *Pheritima posthuma*. Results showed that roots of the *Clitoria ternatea* took less time to paralyze and death of the earthworms. Roots were further extracted successively with petroleum ether, chloroform, ethyl acetate and methanol and these extracts were screened for anthelmintic activity. Results showed that methanol extract of *Clitoria ternatea* root is the more potent [83].

The *in vitro* comparative study of anthelmintic activity of aqueous and ethanolic extracts of leaves of *Clitoria ternatea* was carried out against *Eisenia foetida* at three different concentrations (100, 50, 25 mg/ml). The study involved the determination of time of paralysis and time of death of the worms. At the concentration of 100 mg/ml both the ethanolic and the aqueous extracts showed very significant anthelmintic activities as compared to the standard drug, levamisole (0.55 mg/ml). In case of aqueous extract the time of paralysis and death time was observed as  $18 \pm 1.57$  min and  $53.33 \pm 0.33$  min, and in case of ethanolic extracts  $12.33 \pm 0.80$  min and  $32.33 \pm 0.71$ min respectively [84].

The mosquito larvicidal activity of *Clitoria ternatea* was investigated against three major mosquito vectors *Aedes aegypti*, *Culex quinquefasciatus*, and *Anopheles stephensi*. Among the methanol extracts of *Clitoria ternatea* leaves, roots,

flowers, and seeds, the seed extract was effective against the larvae of all the three species with LC<sub>50</sub> values 65.2, 154.5, and 54.4 ppm, for *A. stephensi*, *A. aegypti*, and *C. quinquefasciatus*, respectively. Among three tested plant species, *Clitoria ternatea* was showing the most promising mosquito larvicidal activity [85].

#### *Corchorus capsularis*

The mosquitocidal activities of *Corchorus capsularis* against a common malarial vector, *Anopheles stephensi* and a dengue vector *Aedes aegypti* was studied. The larvicidal activity exerted by ethyl acetate was more prominent than acetone and methanol extracts in all concentrations tested against *Ae. aegypti* larvae. Evaluation of the lethal concentration values (LC<sub>50</sub> and LC<sub>90</sub>) of acetone, ethyl acetate and methanol extract of the plant against *An. stephensi* and *Ae. aegypti* revealed that LC<sub>50</sub> of 197.34ppm and LC<sub>90</sub> of 358.59ppm was recorded for acetone extract against the *An. stephensi*; furthermore, the larvae of *Ae. aegypti* showed the LC<sub>50</sub> and LC<sub>90</sub> values of 222.45 and 383.06ppm respectively, with the treatment with the acetone extract of *Corchorus capsularis*. Minimum LC<sub>50</sub> values were observed among the experimental larval groups treated with methanol extract of *Corchorus capsularis* were 176.19ppm and 182.06ppm against *An. stephensi* and *Ae. Aegypti* respectively. With regard to the ovicidal activity of acetone, ethyl acetate and methanol extract, it was apparent that 300 -450 ppm concentrations resulted with no hatchability on *An. stephensi* and 375-450pp concentrations in *Ae. aegypti*. The authors referred to the possible utilization of *Corchorus capsularis* to control mosquito menace to a greater extent [86].

The efficacy of emulsified petroleum ether extract of *Corchorus capsularis* seed was studied against three stored product pests (*Callosobruchus chinensis*, *Sitophilus oryzae* L and *Tribolium castaneum* Herbst) in adult phase. The residual film technique method was conducted to determine the LC<sub>50</sub> value of the mentioned plant extract against three stored product pests. LD<sub>50</sub> (µg /cm) of *Corchorus capsularis* against *C. chinensis* was 74.26 (50.26 - 109.74) after 24 hrs and 6.67 (0.49 - 90.07) after 48hrs. LD<sub>50</sub> against *S. oryzae* was 84.61 (61.98-115.50) after 24 hrs and 32.87 (16.03-67.39) after 48hrs. While, LD<sub>50</sub> against *T. castaneum* was 547.08 (477.38 - 626.97) after 24 hrs and 452.51 (380.30 - 538.42) after 48hrs [87].

However, On the other hand, in studying of the role of jute leaf (*Chorchorus capsularis*) phytochemicals on feeding, growth and reproduction of *Diacrisia casignetum* Kollar (Lepidoptera: Arctiidae), it appeared that the larval and post larval developmental duration was shorter on mature jute leaf fed insects whereas adult longevity was higher in it (P < 0.05) relative to young and senescent leaf fed insects. Fecundity of *D.*

*casignetum* was also highest on mature leaves followed by young and senescent leaves. The growth and development of *D. casignetum* were related to the nutrient content relative to the secondary metabolites of these three types of jute leaves. Higher levels of nutritional factors (total carbohydrates, proteins, lipids, nitrogen and amino acids including water content) and lower levels of anti-nutritional factors (secondary metabolites) in mature jute leaves have influenced lower developmental time along with higher growth rate, fecundity and accumulated survivability of *D. casignetum* than the young and senescent leaves [88-89].

#### *Cordia myxa*

The anti-leishmanial activity of the mucilage extract of *Cordia myxa* was examined against promastigotes of *L. infantum* (MCAN/IR/96/LON49) and *L. major* (MRHO/IR/75/ER) ( $1 \times 10^6$  cells/ ml). They were seeded in a 96-well microtiter plate, in the presence of the serial concentrations (0, 0.61, 1.22, 2.44, 4.88, 9.75, 19.5, 39, 78, and 156 mg/ ml w/v) of the extract and then incubated at 24°C, for 72 hours. Antileishmanial activity was assayed by light microscopy and (3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium bromide) MTT method. The concentration inhibiting parasite growth by 50% (IC<sub>50</sub> value) was calculated with a sigmoid dose-response curve. Mucilage extract of *Cordia myxa* was active against promastigotes form of *L. major* and *L. infantum*, with an IC<sub>50</sub> of  $26 \pm 2.2$  mg/ml and an IC<sub>50</sub> of  $35 \pm 2.2$  mg/ml, respectively. The survival percentage of *L. major* and *L. infantum* promastigotes after 72 hours treatment appeared concentration dependent. Percentage of survival *Leishmania major* after 72 hours reached 17.68% in a concentration of 156 mg/ml, while the percentage of survival of *L. infantum* promastigotes after 72 hours reached 16.68% in a concentration of 156 mg/ml [90-91].

*Cordia myxa* were tested for antiplasmodial activity. Antimalarial effects were quantified with respect to inhibition of parasite growth, as measured by the production of Plasmodium lactate dehydrogenase. Alkaloids extract of *Cordia myxa* showed good antiplasmodial activity, IC<sub>50</sub> was 6.2 µg/ml, while dichloromethane extract of *Cordia myxa* showed moderate antiplasmodial activity IC<sub>50</sub> was 4.2 µg/ml, followed by aqueous and methanol extracts [92].

The crude alkaloid compounds for *Cordia myxa* leaves was tested against *Culex pipines* at (10, 7.5, 5, 2.5, 0) mg /ml. It possessed significant effect on some biological aspects of *Culex pipines*. The results showed that of eggs and larval stages (1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>th</sup>, 4<sup>th</sup>) was (13.38, 0, 0, 0, 0) respectively in 10 mg /ml. At the same concentration, it also reduced productivity from 320 egg / female to 0 egg / female [93].

***Coriandrum sativum***

Commercial essential oils from 28 plant species were tested for their nematicidal activities against the pine wood nematode, *Bursaphelenchus xylophilus*. The best nematicidal activity against *B. xylophilus* was achieved with essential oils of coriander (*Coriandrum sativum*) [94].

*In vitro* anthelmintic activities of crude aqueous and hydro-alcoholic extracts of the seeds of *Coriandrum sativum* were investigated on the egg and adult nematode parasite *Haemonchus contortus*. The aqueous extract of *Coriandrum sativum* was also investigated for *in vivo* anthelmintic activity in sheep infected with *Haemonchus contortus*. Both extracts of *Coriandrum sativum* inhibited hatching of eggs completely at a concentration less than 0.5 mg/ml. ED<sub>50</sub> of aqueous extract of *Coriandrum sativum* was 0.12 mg/ml while that of hydroalcoholic extract was 0.18 mg/ml. There was no statistically significant difference between aqueous and hydroalcoholic extracts ( $p > 0.05$ ). The hydroalcoholic extract showed better *in vitro* activity against adult parasites than the aqueous one. For the *in vivo* study, sheep were artificially infected with *Haemonchus contortus*, crude aqueous extract of *Coriandrum sativum* was given at 0.45 and 0.9 g/kg dose levels. Efficacy was tested by faecal egg count reduction (FECR) and total worm count reduction (TWCR). On day 2 post treatment, significant FECR was detected in groups treated with higher dose of *Coriandrum sativum* ( $p < 0.05$ ) and albendazole ( $p < 0.001$ ). Significant ( $p < 0.05$ ) TWCR was detected only for higher dose of *Coriandrum sativum* compared to the untreated group. Reduction in male worms was higher than female worms. Treatment with both doses of *Coriandrum sativum* did not help the animals to improve or maintain their PCV, while those treated with albendazole showed significant increase in PCV ( $p < 0.05$ ) [95].

The antiparasitic efficacy of *Coriandrum sativum* essential oils was studied by two *in vitro* assays on *Haemonchus contortus* using egg hatch test (EHT) and larval development test (LDT). *Coriandrum sativum* essential oils exhibited a dose-dependent effect in the EHT, inhibiting 81.2% of *H. contortus* larvae hatching, at a concentration of 2.5 mg/ml. The effective concentration to inhibit 50% (EC<sub>50</sub>) of egg hatching was 0.63 mg/ml. In LDT, *Coriandrum sativum* at concentration of 10 mg/ml inhibited 97.8% of *H. contortus* larval development [96].

The *in vitro* effect of fractions from *Coriandrum sativum* (coriander) on promastigotes and amastigotes of *L. infantum* was studied in addition to its toxicity against the murine monocytic cells RAW 264.7. All fractions were effective against *L. infantum* promastigotes and did not differ from the positive control pentamidine ( $p > 0.05$ ). However, the *Coriandrum sativum* methanol fraction, was the most

effective against amastigotes and did not differ from the positive control amphotericin B ( $p > 0.05$ ) [97].

The biological activity of essential oil of *Coriandrum sativum* seeds was tested against adult *Tribolium confusum* Duval (Coleoptera: Tenebrionidae) and *Callosobruchus maculatus* F. (Coleoptera: Bruchidae) in a series of laboratory experiments. The mortality of 1-7 day old adults of the insect pests increased with concentration from 43 to 357  $\mu\text{l/l}$  air and with exposure time from 3 to 24 h. In the probit analysis, LC<sub>50</sub> values showed that *C. maculatus* (LC<sub>50</sub> = 1.34  $\mu\text{l/l}$  air) was more susceptible than *T. confusum* (LC<sub>50</sub> = 318.02  $\mu\text{l/l}$  air) to seed essential oil of *Coriandrum sativum* [98].

The essential oil (EO) of the fruits of *Coriandrum sativum* was evaluated for its larvicidal and repellent activities against *Aedes albopictus* Skuse (Diptera: Culicidae). *Coriandrum sativum* EO exerted toxic activity against *A. albopictus* larvae: LC<sub>50</sub> was 421 ppm, while LC<sub>90</sub> was 531.7 ppm. Repellence trials highlighted that *Coriandrum sativum* EO was a good repellent against *A. albopictus*, RD<sub>50</sub> was 0.0001565  $\mu\text{l}/\text{cm}^2$  of skin, while RD<sub>90</sub> was 0.002004  $\mu\text{l}/\text{cm}^2$ . At the highest dosage (0.2  $\mu\text{l}/\text{cm}^2$  of skin), the protection time achieved with *Coriandrum sativum* essential oil was higher than 60 min [99].

The leaf oil had significant toxic effects against the larvae of *Aedes aegypti* with an LC<sub>50</sub> value of 26.93 ppm and an LC<sub>90</sub> value of 37.69 ppm, and the stem oil has toxic effects against the larvae of *A. aegypti* with an LC<sub>50</sub> value of 29.39 ppm and an LC<sub>90</sub> value of 39.95 ppm [100].

The seed oil had significant toxic effects against the larvae of *Aedes aegypti* with an LC<sub>50</sub> value of 21.55 ppm and LC<sub>90</sub> value of 38.79 ppm. The major components in the essential oil of coriander play an important role as immunotoxicity on the *A. aegypti* [101].

***Coronilla scorpioides***

Screening of *Ae. aegypti* larvicidal activity of 110 selected Egyptian plants proved that *Coronilla scorpioides* exhibited highest larvicidal activity, calculated as  $22.53 \pm 2.01$  mg% for aqueous extracts and  $18.53 \pm 1.95$  mg% for methanol extract [102].

***Coronilla varia***

A group of 3-nitropropanoyl-D-glucopyranoses was also isolated from active fractions of the crude extracts of the root. These compounds were toxic when administered orally to 3<sup>rd</sup> instar *Costelytra zealandica* larvae [103].

***Crocus sativus***

The effectiveness of *Crocus sativus* and its apoptotic activity against *Leishmania major*

(MRHO/IR/ 75/ER) promastigotes was studied using MTT assay to find viability of *L. major* promastigotes and the results were explicated as IC<sub>50</sub> (50% inhibitory concentration). ED<sub>50</sub> (50% effective doses) for *L. major* amastigotes were also analyzed. Annexin-V FLUOS staining was performed to study the cell death properties of saffron by using FACS analysis. Qualitative analysis of the DNA fragmentations was accomplished by agarose gel electrophoresis, and light microscopy was used to observe morphological changes of promastigotes. The results revealed that *L. major* promastigotes and amastigotes are sensitive to saffron at different concentrations and time dependent manner, with apoptotic features including DNA laddering, cytoplasmic shrinkage, and externalization of phosphatidylserine. IC<sub>50</sub> and ED<sub>50</sub> of this extract after 48 h of incubation was 0.7 and 0.5 mg/ml respectively [104-105].

Safranal isolated from *Crocus sativus* extract exhibited insecticidal and pesticidal effect. This fact could present saffron as safe and effective herbal insecticide and pesticide which was more environment friendly than other synthetic insecticides [106].

#### *Cuminum cuminum*

The electrophysiological, behavioural (repellency, irritancy) and toxic effects of the of *Cuminum cuminum* essential oils was studied against *Anopheles gambiae* strain (Kisumu). Aldehydes elicited the strongest responses and monoterpenes the weakest responses in electroantennogram (EAG) trials. However, EAG responses did not correlate consistently with results of behavioral assays. In behavioral and toxicity studies, several of the single compounds exhibited repellency, irritancy or toxicity in *An. gambiae*; however, the activity of essential oils did not always correlate with activity expected from the major components. The biological activity of essential oils appeared complex, suggesting interactions between individual compounds and the insect. Data also indicated that the three effects appeared independent, suggesting that repellency mechanism(s) may differ from mechanisms of irritancy and toxicity [107-108].

Fumigant activity of essential oil vapours distilled from cumin was recorded against the eggs of two stored-product insects, the confused flour beetle, *Tribolium confusum*, and the Mediterranean flour moth, *Ephestia kuehniella*. The exposure to vapours of essential oils resulted in 100% mortality of the eggs at a concentration of 98.5 µl cumin essential oil/l air [109-110].

#### *Cupressus sempervirens*

The ethanol extract of the powdered cones of *Cupressus sempervirens*, collected from Oxford, Mississippi, exhibited potent antiparasitic activities. Bioassay-guided fractionation using a centrifugal preparative thin-layer chromatography led to isolation

of many diterpenes, 6-deoxytaxodione (11-hydroxy-7, 9(11), 13-abietatrien-12-one), taxodione, ferruginol and sugiol. 6-deoxytaxodione (11-hydroxy-7, 9(11), 13-abietatrien-12-one) and taxodione, displayed potent antileishmanial activity with half-maximal inhibitory concentration (IC<sub>50</sub>) values of 0.077 µg/ml and 0.025 µg/ml, respectively, against *Leishmania donovani* promastigotes, compared to those of the standard antileishmanial drugs, pentamidine (IC<sub>50</sub> 1.62 µg/ml) and amphotericin B (IC<sub>50</sub> 0.11 µg/ml) [111-112].

Ethanol, acetone and petroleum ether extracts of leaves from the Egyptian *Cupressus sempervirens* were tested against 3<sup>rd</sup> instar larvae of the mosquito *Culex pipiens*. The obtained results indicated that petroleum ether extracts were more efficient than ethanol and acetone extracts. The toxicity, based on LC<sub>50</sub> values, were: ethanol (LC<sub>50</sub> 263.6ppm) > acetone extract (LC<sub>50</sub> 104.3ppm) > petroleum ether extracts (LC<sub>50</sub> 37.8 ppm). A remarkable reduction in both the pupation percent and adult emergence was obtained. Moreover, all extracts exerted a delayed toxic effect on the pupae and adults after treatment of larvae. Furthermore, various degrees of morphogenic abnormalities were observed in the immature and adult stages [113].

#### *Cymbopogon schoenanthus*

The anthelmintic potential of *Cymbopogon schoenanthus* essential oil was evaluated in lambs experimentally infected with *Haemonchus contortus*. Two-month-old lambs with mean body weight (BW) of 22.5 kg were experimentally infected with a multidrug-resistant *Haemonchus contortus* strain. Infected animals were dosed orally with *Cymbopogon schoenanthus* essential oil. Eighteen animals were allocated into three groups of six animals, and each received one of the following treatments: Group 1 - control (10 ml of water), Group 2 - *Cymbopogon schoenanthus* essential oil (180 mg/kg bw); and Group 3 - *Cymbopogon schoenanthus* essential oil (360 mg/kg bw). Animals received the oil once a day for 3 consecutive days. Lambs were evaluated clinically for blood biochemistry before and at 1, 5, 10, 15, 20 days after treatment. No statistically significant reduction in fecal egg count, packed cell volume or total worm count was observed after treatments. Also, no statistical difference among group means for blood levels of urea, creatinine, albumin, alkaline phosphatase, aspartate aminotransferase and gamma glutamyl transferase was found. Larval development assay (LDA) and egg hatch assay (EHA) were performed from feces of treated animals at 1, 5, 10 and 15 days after essential oil administration. An inhibition in LDA was observed 1 day after the 3-day treatment in larvae from feces of animals treated with 360 mg/kg essential oil [113].

*Cymbopogon schoenanthus* essential oils were evaluated against developmental stages of trichostrongylids from sheep naturally infected (95%

*Haemonchus contortus* and 5% *Trichostrongylus* spp.) using egg hatch assay (EHA), larval development assay (LDA), larval feeding inhibition assay (LFIA), and larval exsheathment assay (LEA). *Cymbopogon schoenanthus* essential oil showed a good activity against ovine trichostrongylids. It had LC<sub>50</sub> value of 0.045 mg/ml in EHA, 0.063 mg/ml in LDA, 0.009 mg/ml in LFIA, and 24.66 mg/ml in LEA [114].

The insecticidal activity of crude essential oil extracted from *Cymbopogon schoenanthus* and its main constituent (piperitone), was assessed on different developmental stages of *Callosobruchus maculatus*. Piperitone was more toxic to adults with LC<sub>50</sub> value of 1.6 µg/ml vs. 2.7 µg/ml obtained with the crude extract. Piperitone inhibited the development of newly laid eggs and of neonate larvae, but was less toxic than the crude extract to individuals developing inside the seeds [115].

*Cymbopogon schoenanthus* essential oils from Benin Republic in west Africa displayed about 100% mortality rate against adult *Anopheles gambiae* [116].

The efficacies of essential oils of nine plant species, which were traditionally used to avoid mosquito bites in Benin, were investigated. These oils were tested on susceptible "kisumu" and resistant "ladji-Cotonou" strains of *Anopheles gambiae*. The results showed that *Cymbopogon schoenanthus* was a potential promising plant source alternative to pyrethroids, for the control of the *Anopheles malaria* vector in Benin. The efficacy of essential oil was possibly attributed to its chemical composition in which major and/or minor compounds have been shown insecticidal activities on various pests and disease vectors such as *Anopheles* [117].

The effect of camelgrass (*Cymbopogon schoenanthus*) oil on *Anopheles* mosquito and its larvae was tested to evaluate its repellence property. Different quantities of the oil extract viz: 10ml, 5ml and 1ml was introduced into two sets of twelve beakers each containing twenty larvae and adult mosquito. Mortality rate was recorded at certain time intervals. Application of the oil extract on adult mosquitoes and larvae caused 100% mortality. The maximum mortality time taken was 15 minutes for the adult mosquito and 18 minutes for the larvae. The minimum mortality time taken was 3 minutes. The rapid mortality recorded in respect to both larvae and adult of *Anopheles* mosquito indicated high insecticidal and larvicidal properties of the chemical compounds present in the oil of the grass species [118].

The efficacy of 3% citronella candles and 5% citronella incense were evaluated in protecting subjects from bites of *Aedes* spp under field conditions. The study was conducted in a deciduous woodlot in Guelph, Ontario, Canada. Eight subjects, dressed identically, were assigned to one of 8 positions on a grid within the

study area. Two citronella candles, 2 citronella incense, 2 plain unscented candles, or no candles (i.e., non-treated controls) were assigned to 2 positions on the grid each evening. Subjects conducted 5-min biting counts at each position and performed 16 biting counts per evening. On average, subjects received 6.2 ± 0.4, 8.2 ± 0.5, 8.2 ± 0.4, and 10.8 ± 0.5 bites/ 5 min at positions with citronella candles, citronella incense, plain candles, and no candles, respectively. Although significantly fewer bites were received by subjects at positions with citronella candles and incense, than at non-treated locations, the overall reduction in bites provided by the citronella candles and incense was only 42.3 and 24.2%, respectively [119].

The insecticidal properties of the aerial part of *Cymbopogon schoenanthus* was studied experimentally. Cabbage plants were sprayed with the aqueous extracts of *Cymbopogon schoenanthus* leaves as treatment, and the damage levels of *Plutella xylostella* was assessed. *In vitro*, the emulsified essential oil concentrations were used in a contact test on the larvae in order to assess the mortality effects. The larvae survival time was only 22 seconds with *Cymbopogon schoenanthus* emulsified oil treatment (2 g/l), whilst it exceeded 44,100 seconds (over 12 hours) for the dimethoate. The nutrition test showed that at 48 h period, a significant effectiveness against larvae was observed with emulsified oil treatment 2 g/l (60% mortality) versus 10% of mortality for dimethoate. The authors concluded that *Cymbopogon schoenanthus* can validly be used as alternative in *P. xylostella* management. The results of the field experiments showed no significant difference between the treatments and the control in terms of marketable cabbages harvested [120].

#### *Cynodon dactylon*

Anthelmintic activity of petroleum ether, methanol, and water extracts of *Cynodon dactylon* was evaluated on adult Indian earthworm *Pheretima posthuma* with the use of albendazole as a standard drug. The aqueous extract of *Cynodon dactylon* exerted anthelmintic activity in comparison with the standard drug [121].

The mosquito repellent activity of volatile oils of *Cynodon dactylon* was studied against (*A. aegypti*). The distillates of the fruits of *Cynodon dactylon* were effective for 3 hours. The mixture of *C. papaya* and *Cynodon dactylon* was effective for 2.5 hours compared to that of *C. papaya* (2.5 hours) alone or *Cynodon dactylon* (1.5 hours) alone [122].

#### *Cyperus rotundus*

Hexane extract of tuber of plant *Cyperus rotundus* was tested for repellent activity against mosquito vector *Anopheles culicifacies*, *Anopheles stephensi* and *Culex quinquefasciatus*. Results showed that the tuber extracts were effective

for repellency of the entire mosquito vector even at a low dose [123].

*Cyperus rotundus* was more effective insecticidal than carbamate and has almost the same efficacy as that of organophosphate. Result showed that all the test ants died after 10s, while organophosphate ranked second with 9 ants dead after 10s, and the carbamate ranked third with seven ants dead after 12s [124].

The ovicidal and larvicidal efficacy of essential oils of the tubers of *Cyperus rotundus* was studied on eggs and fourth instar larvae of *Aedes albopictus*. The eggs and larvae were exposed to serial concentration of the oils ranging from 5-150 ppm and observed for 24 h. Oils showed remarkable ovicidal and larvicidal activities indicated by EC<sub>50</sub> values of <5 ppm and LC<sub>50</sub> and LC<sub>90</sub> values of <20 ppm [125].

Activity-guided investigation of *Cyperus rotundus* tubers led to the isolation of patchoulenone, caryophyllene alpha-oxide, 10,12-peroxycalamenene and 4,7-dimethyl-1-tetralone. The antimalarial activities of these compounds were in the range of EC<sub>50</sub> 10<sup>-4</sup> to 10<sup>-6</sup> M, with the novel endoperoxide sesquiterpene, 10,12-peroxycalamenene, exhibiting the strongest effect at EC<sub>50</sub> 2.33 × 10<sup>-6</sup> M [126].

#### Conclusion:

The paper reviewed the antiparasitic, antiprotozoal, molluscicidal and insecticidal effects of the medicinal plants to open the door for their utilization in medical applications as a result of effectiveness and safety.

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