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Bioefficacy of botanicals with special emphasis on *Cassia fistula* and nano-formulations on survival, growth, and development of insects: A sustainable approach of integrated pest management

Priyanka Saini[1] and Kamal Kumar Gupta[2]*

[1]Insect Reproduction Laboratory, [2]Department of Zoology, Deshbandhu College, University of Delhi, New Delhi 110019, India

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Insects are the most adaptable creatures found all over the world. They affect both the quality and quantity of many crops. The plant contains various secondary metabolites that can hamper insect molting, metamorphosis, growth and development. *Cassia fistula* is a rich source of amino acids, carbohydrates, fatty acids, flavonoids, proanthocyanidins, and polyphenols, which possess antimicrobial and anti-inflammatory activities. Also, the antifeedant, larvicidal, ovicidal, nymphicidal, and adulticidal properties of these phytocomponents have been documented. Nanoformulations based on plant decoction can act as potent insecticidal agents against insects. Silver nanoparticles (AgNPs) synthesised from *C. fistula* fruit pulp extract drastically affected the midgut wall of insects and altered their growth and reproduction, ultimately leading to insect death. The potentials of botanicals, *C. fistula,* and nano-formulations of plant extracts were explored in Insect pest management.

Keywords: *Cassia fistula*, Insecticidal activity, Nanoparticles, Phytochemical constituents

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Introduction

Insects constitute the most common animal group found almost everywhere on the earth. Almost 5.5 million insect species have been identified, and it is expected that approximately 10 million species need to be described[1,2]. The insects pose serious challenges to humans as they cause significant damage to agricultural products and spread many human and livestock diseases[3]. More than 9000 species of insects and mites have been reported to harm crops globally[4]. A report estimated that 20 to 40 per cent of global crop production loss is due to insect pests[5]. Crop loss includes both a reduction in quantity and quality[6]. Besides direct losses, insect pests also cause indirect losses by contaminating agricultural products with body parts, exoskeletons, eggs, faeces, etc. Moths such as cutworms, armyworms, earworms, and borers are the most common groups of crop-damaging insects. This is followed by beetles (rootworms, wireworms, grubs, grain borers) and weevils; sap-sucking bugs are another important group of insects causing damage to agricultural crops[2]. Many insects also affect human health directly or indirectly. They can bite, sting, parasitise, cause allergic reactions, and spread several vector-borne diseases to humans.

The use of chemical insecticides is the most prevalent method of insect control worldwide. It mainly includes four groups of chemical insecticides: organochlorines, organophosphates, carbamates and pyrethroids. Organochlorine insecticides such as DDT and chlordane are now banned for agricultural use due to their persistence, bioaccumulation and biomagnifications, environment contamination and development of resistance mechanisms in insect pests. Organophosphate and carbamate seriously affect insects' nervous system; they disrupt the level of acetylcholinesterase (AChE) enzyme and block the action of the acetylcholine, resulting in its accumulation at synapses and neuromuscular junction. The agglomeration of acetylcholine results in overexpression of muscarinic and nicotinic acetylcholine receptors that causes various effects on humans such as salivation, lacrimation, urination, diarrhoea, miosis tremors, muscle fasciculation, and convulsions. Organophosphates and carbamates also alter the learning and memory of the brain by different mechanisms[7-12]. Pyrethroids are also toxic to animals and humans[13-15]. The toxic effects include neurotoxicity, skin contact toxicity, respiratory

*Correspondent author
Email: kgupta@db.du.ac.in

toxicity and reproductive system toxicity[16-19].

The chemical pesticides used in insect control, in general, are not safe as they cause environmental contamination, bioaccumulation, biomagnification, threat to non-target organisms and beneficial insects, serious human health problems, and pest resistance and resurgence. Agriculture workers almost live in direct contact with chemical pesticides in open fields and greenhouses that can cause various skin diseases, endocrine disruption, and other health hazards. The general population gets pesticide residues contained in food and drinking water, which adversely affects their health. The effects of insecticides on human health are immense, depending on the chemical toxicity and length and magnitude of exposure. Chemical pesticides contaminate water, soil, and air by leaching, runoff, and spray drift. More than 98% of sprayed insecticides reach a destination other than their target species[20]. Runoff carries insecticides into aquatic environments while the wind carries them to other fields, grazing areas, and human settlements, potentially affecting non-target species such as fishes, birds, honey bees and other beneficial insects. Insecticides also cause harmful effects on plants, such as poor root hair development, shoot yellowing, and reduced plant growth; they interfere with the process of nitrogen fixation. Repeated and indiscriminate use of insecticide also resulted in the development of resistance in pest species[20]. Therefore, an environment-friendly, sustainable and cost-effective strategy is needed for insect control.

Integrated pest management (IPM) is an holistic approach to pest management that involves the utilisation of multiple techniques and methods of pest control to maintain the pest populations below the economic threshold level (EIL). IPM includes five basic components: acceptable pest levels, preventive cultural practices, monitoring, mechanical and biological control, and appropriate use of pesticides[21]. The main aim of pest control under the concept of integrated pest management is to achieve crop production in a way that maximises crop output without adversely affecting the environment and non-target organisms. Pest control measures of IPM include biological control, cultural control, plant resistance, genetic modifications, use of pheromones, growth regulators and other new environment-friendly and sustainable methods.

Use of botanicals in insect control

Plants have developed a variety of structural and chemical defence mechanisms against insect attacks[22]. The chemical defence mechanisms include a variety of secondary metabolites and proteins that adversely affect insect growth, development, metabolism and reproduction[23].

A variety of phytochemicals present in the plants are responsible for feeding deterrence to insects. Arivoli *et al.*[24] studied the antifeedant activity of 25 different plant extracts against the third instar larvae of *Spodoptera litura* and reported the highest antifeedant activity in ethyl acetate extract of *Strychnos nux-vomica*, *Vitex negundo*, *Murraya koenigii*, *Zanthoxylum limonella* and *Abrus precatorius*. Similarly, the larvae of the Colorado potato beetle, *Leptinotarsa decemlineata* showed antifeedant activity against the plant extracts of *Angelica archangelica, Grindelia camporum* and *Inula auriculata*. Leatemia *et al.*[25] reported the antifeedant activity of seed extract of *Annona squamosa* in a leaf disc choice assay against *Plutella xylostella* L. and *Trichoplusia ni* (Hübner) and found that crude extract inhibited the feeding of fourth-instar larvae. Ragesh *et al.*[26] observed antifeedant activity of crude hexane extract of *Ageratum conyzoides* against fifth instar larvae of *Helicoverpa armigera*.

Many of the plant products possess growth inhibitory and growth disruptor activities. Boussaada *et al.*[27] reported growth inhibitory activities in the methanol extract of *Mantisalca duriaei* and petroleum ether, chloroformic and methanolic extracts of *Rhaponticum acaule* against *Tribolium castaneum*. Similarly, Saxena *et al.*[28] studied the effect of five plant extracts viz. *Eichhornia crassipe, A. conyzoides, Cleome icosandra*, *Tagetes erectes* and *Tridax procumbens* on fourth instar larvae and adult female mosquito *Culex quinquefasciatus* and reported inhibition of growth in the treated larvae. These plant extracts also showed juvenile hormone-mimicking activity in the larvae. Some changes like defective egg rafts, larval-pupal intermediates, demalanised pupae, and adults with deformed flight muscles were observed after treatment[28]. Leaf extract of *Glycosmis pentaphylla* was found to be responsible for increased larval duration, mortality and development anomalies in the larvae of *C. quinquefasciatus, An. stephensi* and *Ae. aegypti*[29]. Leaf extract of *G. pentaphylla* resulted in a decrease in weight gain and metamorphosis in treated castor semilooper, *Achaea janata*[30]. Treatment of sixth instar larvae and freshly moulted pupae of *S. litura* with the root extract of Ashwagandha, *Withania somnifera* caused morphological and developmental anomalies like ecdysial failure, formation of larval-pupal and pupal-adult intermediates, abnormal pupae and adultoids. The extract was more toxic to the pupae than the larvae of *S. litura*[31]. Azadirachtin, an insect growth regulator derived from *Azadirachta indica* inhibited oviposition in the mature females of *Locusta migratoria.* Radioimmunoassay results revealed that only traces of ecdysteroids were present in the ovary of treated adults[32]. Leaf ethanolic extracts of *Petiveria alliaceae* and *Trichilia arborea* were reported to possess the highest toxicity against eggs and nymphs of *Bemisia tabaci*[33].

Annona muricata extract caused mortality in the nymphs of potato psyllid, *Bactericera cockerelli*[34]. Chinaberry, geranium, onion and garlic plant extracts showed the highest toxicity against the second-instar larvae of *Tuta absoluta*[35]. Bioinsecticidal effects of methanol extracts of seven different plants such as *Centaurium erythraea*, *Peganum harmala*, *Ajuga iva*, *Aristolochia baetica*, *Pteridium aquilinum* and *Raphanus raphanistrum* extracts were studied against the *T. castaneum*. Plant extract of *C. erythraea* was more toxic than that of *P. harmala*. *L. arborescens, P. aquilinum* and *A. iva* extracts shortened the larval period while they extended the period with *R. raphanistrum* and *P. harmala* extracts. Treated larvae showed a decrease in the activity of enzyme α-amylase as compared to control[36]. A study showed that *Artemisia annua* extract showed detrimental effects on the digestive enzymatic profiles of *Eurygaster integriceps*. Treated adults showed a reduction in the activities of digestive enzymes such as α-amylase, α- and β-glucosidases, protease and lipase[37].

Biochemical constituents of *Cassia fistula*

Cassia fistula L. (Family: Fabaceae), commonly called Indian Laburnum or Golden shower tree, is an ornamental tree of forests and parks. It contains various types of secondary metabolites with medicinal properties[38]. The different parts of *C. fistula* contain a variety of phytochemicals that possess various pharmacological properties. Besides its therapeutic uses, *C. fistula* extract can be used as a good pest control agent in India. It has shown activities like antifeedant, ovicidal, larvicidal, pupicidal and adulticidal against many insects[39].

A variety of primary and secondary metabolites have been reported in different plant parts of *C. fistula* (Table 1). It contains free amino acids such as phenylalanine, methionine, glutamic acid and proline, oxalic acids, tannins, flavonoids, proanthocyanidins, polyphenols, linoleic acid, oleic acid, stearic acid, oxyanthraquinones, anthraquinones derivatives, essential oils and terpenoids; these chemicals contribute to antimicrobial, anti-inflammatory, antifungal, antitumor, antioxidant, and insecticidal properties[38]. Chemical structures of phytochemicals present in different parts of *Cassia fistula* are summarised in Fig. 1. *C. fistula* is reported to have rhein glycosides, fistulic acids, sennosides A, and B, flavanoid-3-ol derivatives, ceryl alcohol, kaempferol, bianthraquinone glycosides, fistulin, volatile components, phytol, 2-hexadecanone, crystals and 4-hydroxy benzoic acids hydrate[40,41]. Proanthocyanidins are abundantly present in the leaves, flowers and pods, while phenolic compounds are present in the leaves[42]; sennosides B, oxalic acids, tannins, oxyanthraquinones, and anthraquinones are present in both the leaves and the fruits of *C. fistula*[43]. Anthraquinone derivative compounds such as emodin showed the highest insecticidal activity against *Nilaparvata lugens* followed by chrysophanol, physcion, rhein and aloe-emodin. Larvicidal activity of emodin has also been reported against the fourth instar larvae of *A. aegypti, Aedes togoi* and *Culex pipiens pallens*[44]. Further, emodin also caused the change in the level of acetylcholinesterase (AChE) and glutathione S-transferases (GST) against *N. lugens* and *Mythimna separata*. Polyphenolic compounds and tannins were reported to inhibit the activity of detoxifying enzymes like glutathione S-transferases (GSTs), cytochrome P450 monooxygenase (CYP450), carboxylesterase (CarE), and acetylcholinesterase (AChE) against the fourth instar larvae of *Hyphantria cunea* in a concentration-dependent manner. Mycotoxins, kojic acid and oxalic acid, affected the biological fitness of *Lygus hesperus* and showed detrimental effects on its growth and development[45]. Various other secondary metabolites, such as hextriacontanoic, triacontanoic, nonacosanoic and heptacosanoic acids, were reported in the cuticular wax of leaves[39]. Fruit of *C. fistula* possessed ceryl alcohol, kaempferol, rhein and bianthraquinone glycoside, fistulin, beta-sitosterol, triacontane, nonatetracontanone, 2-hentriacontanone[46]. Hentriacontane and triacontane exhibited larvicidal activity against *Spodoptera frugiperda*, *Tenebrio molitor* and *Drosophila melanogaster*[47]. Some of the essential oils present in the leaves include eugenol, phytol,

Table 1 — Phytoconstituents present in *C. fistula*

S. No.	Chemical nature of Compound	Plant Part	Chemical present	Molecular formula	Biological activity	References
1	Polyphenol	Stem	Flavonol	$C_{15}H_{10}O_3$	Insecticidal, Growth and development inhibitor	78,80
		Leaves	Tannin	$C_{76}H_{52}O_{46}$	Growth inhibitor Affects the activity of detoxification and acetylcholinesterase enzyme	123
		Flower	Kaempferol	$C_{15}H_{10}O_6$	Insecticidal Growth and development inhibitor Affects ecdysteroid titer	80,86
			Quercitin	$C_{15}H_{10}O_7$	Growth disrupter and development suppressor Affects the activity of antioxidant and detoxifying enzymes in insects	78,82
2	Phenol	Stem	Xanthone	$C_{13}H_8O_2$	Growth inhibitor and Larvicidal	57
		Pod	Catechins	$C_{15}H_{14}O_6$	Growth inhibitor	57
3	Benzopyran	Seed	Coumarin	$C_9H_6O_2$	Growth and development inhibitor Aphicidal	124,125
			Chromone	$C_9H_6O_2$	Antifeedant	126
4	Anthraquinone	Seed	Emodin	$C_{15}H_{10}O_5$	Larvicidal	44
		Pod	Rhein	$C_{15}H_8O_6$	Antifeedant and larvicidal	64
		Leaves	Physcion	$C_{16}H_{12}O_5$	Insecticidal and antifungal Tyrosinase enzyme inhibitor	127,128
		Fruit	Anthraquinone	$C_{14}H_8O_2$	Insecticidal and larvicidal	127,129
5	Terpene	Leaves	Camphor	$C_{10}H_{16}O$	Larvicidal	49
			Limonene	$C_{10}H_{16}$	Insecticidal, repellent Antimicrobial	130-132
			Linalool	$C_{10}H_{18}O$	Oviposition deterrant Insecticidal Antimicrobial	50,51
		Root	Betulinic acid	$C_{30}H_{48}O_3$	Growth inhibitor and development suppressor	55
6	Alkane	Pod	2- hentriacontanone	$C_{31}H_{62}O$	Involved in the accurate and quick identification of mate-specific partners in mosquito	133
		Fruit	Triacontane	$C_{30}H_{62}$	Insecticidal Molting disruption and growth inhibitor	47
7	Sterol	Fruit	Beta-sitosterol	$C_{29}H_{50}O$	Larvicidal and pupicidal Affects the activity of midgut enzymes	52
		Root	Stigmasterol	$C_{29}H_{48}O$	Insecticidal, Repellant Acetylcholinesterase inhibitor	88
8	Fatty acid	Seed	Linoleic acid	$C_{18}H_{32}O_2$	Larvicidal and insecticidal	79
			Oleic acid	$C_{18}H_{34}O_2$	Insecticidal	134
9	Carboxylic acids	Leaves	Oxalic acids	$C_2H_2O_4$	Detrimental effects on the biological fitness of insects	45
10	Alkyl benzene	Leaves	Eugenol	$C_{10}H_{12}O_2$	Insecticidal	135
11	Benzyl alcohol	Leaves	Salicyl alcohol	$C_7H_8O_2$	Insecticidal	136
12	Phenolic aldehyde	Seed	Isovanillic acid	$C_8H_8O_4$	Insecticidal and Fungicidal	137
13	Fatty alcohol	Stem	Hexacosanol	$C_{26}H_{54}O$	Acetylcholinesterase inhibitor	88

camphor, limonene, salicyl alcohol, and linalool[48]. Camphor, an essential oil, exhibited larvicidal activity against the third instar larvae of *Lucilia sericata*. Scanning electron microscopy results indicated that treated larvae showed cuticular inflammation and contortion[49]. Linalool showed oviposition-deterrent and repellent properties against *Ceratitis capitata*[50,51]. Eugenol, isoeugenol and methyl eugenol affected the

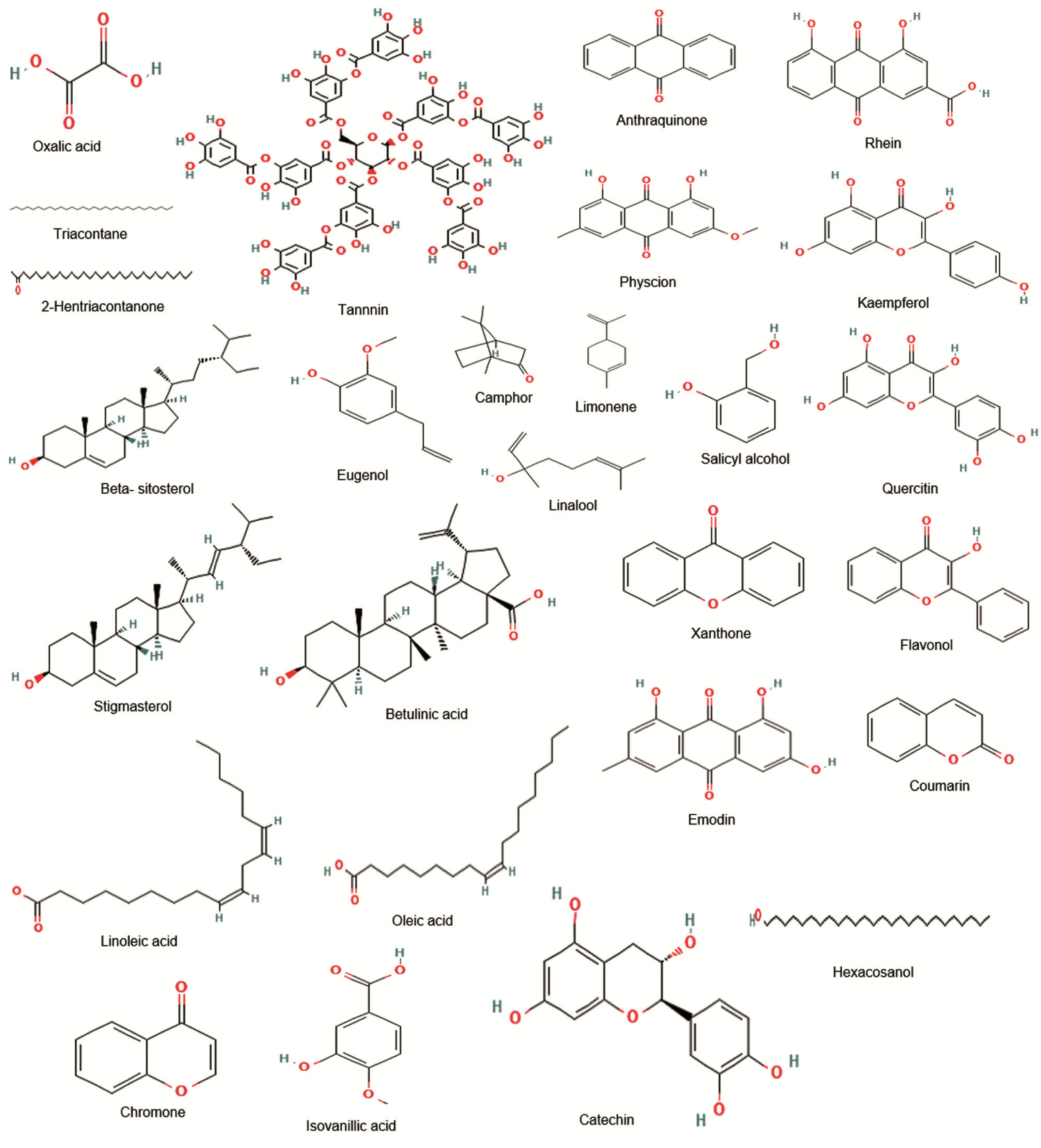

Fig. 1 — Chemical structures of phytocomponents present in different parts of *Cassia fistula* (Source: PubChem).

growth rate and food consumption activity of the adults and larvae of *Sitophilus zeamais* and *T. castaneum* also showed contact toxicity. Polyphenols like quercitin were abundantly present in the flower of this plant[42]. A combined treatment of flavonoid compound quercetin and nuclear polyhedrosis virus of *Bombyx mori* (BmNPV) was reported to have synergistic effects on the growth and development of silkworm *B. mori.* The activities of some detoxifying enzymes such as glutathione S-transferase (GST), carboxylesterase (CarE), acetylcholinesterase (AChE), and malondialdehyde (MDA) and antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), peroxidase (POD) were significantly changed in treated larvae of *B. mori* that increased reactive oxygen species. Flowers also contain aurantiamide acetate, β-sitosterol and its β-D-glucoside[39]. In a study, it was shown that β-sitosterol affected the growth and development of larvae of *H. armigera*. A significant decrease in the activities of midgut enzymes like alanine aminotransaminase (ALT), aspartate aminotransaminase (AST) and alkaline phosphatase (ALP) was also observed[52]. Roots of *C. fistula* have β-sitosterol, stigmasterol. β-sitosterol-3-O-β-glucopyanoside, lupeol, betulinic acid, fistucacidin[39,53], and rhamnetin 3-O-gentiobioside[54]. It was reported that betulinic acid, a terpenoid compound, affects the growth and development of larvae and pupae of *S. litura*, resulting in the formation of larval-pupal and pupal-adult intermediates[55]. In stem bark, polyphenolic compounds like anthraquinones, proanthocyanidin, xanthones, alkaloids and flavonols are abundantly present[56,42]. Xanthone derivative compound α-mangostin was shown to possess potent larvicidal activity against the larvae and adults of the Colorado potato beetle, *L. decemlineata*[57]. Various types of essential oils are present in the flower extract, like (E)–nerolidol and 2-hexadecane[39,48,58]. Major fatty acids found in the seeds of *C. fistula* are linoleic acid, oleic acid, stearic acid and palmitic acid; caprylic acid and myristic acid are in minor amounts[39]. The various types of compounds like triterpene, lupeol; emodin, physcion, citreorosein, rhein, ziganein, coumarins, scopoletin, chromones, isovanillic acid and vanillic acid are present in the aril of seeds of *C. fistula*. Other compounds of seeds are galacto-mannas[59], globulin, albumins, cephalins and lecithins[43]. The root bark contains four main compounds tannin, phlobaphenes, oxyanthraquinone, and flovefin. Pods have other types of compounds such as catechins, arabinopyranoside, 5-nonatetracontanone, 2-hentriacontanone, barbaloin, formic acid, butyric acid, oxalic acid, β-sitosterol[43], sennidin, aloin, emodin, aloe-emodin, physcion, sennosides A & B, rhamnetin 3-O-gentiobioside and chrysophanic acid[53]. Fruit pulp has anthraquinone, glucose, alkaloids, pectin and calcium[56,41]. Palmitic acid is present in root bark[60]. Heartwood of *C. fistula* is reported to have an optically inactive compound leucoanthocyanidin- 5, 4′ -dihydroxyflavan-3, 4-diol, 3, 4, 7, 8, 4′ pentahydroxyflavan and fistucacidin[56,61,62].

Impact of *C. fistula* on insect bioactivities

Antifeedant activity

Antifeedants are natural or synthetic substances that stop or inhibit insect feeding. Extracts of *C. fistula* have been shown to possess antifeedant activity against a variety of insects. Arivoli *et al.*[63] reported the antifeedant and feeding deterrence activity of hexane extract of *C. fistula* against *S. litura.* Similarly, its flower extract showed antifeedant activity against *S. litura* and *H. armigera*[64]. In another investigation, the antifeedant activity and toxicity potential of ethyl acetate, hexane, chloroform and methanol extracts were evaluated against the fourth instar larvae of *S. litura* It was observed that the methanol extract showed excellent antifeedant and toxicant activity against the larvae of *S. litura,* with an antifeedant index of 73.2%. Leaf extract of *C. fistula* had shown antifeedant activity in *Sitophilus granarius* in a dose-dependent manner[65].

Ovicidal, larvicidal, pupicidal, and adulticidal activities

Larvicidal and ovicidal activity of *C. fistula* methanolic leaf extract has been reported against the *C. quinquefasciatus* and *A. stephensi*[66]. Crude flower extract showed potent larvicidal effects against the *Culex tritaeniorhynchus*, *Ae. albopictus* and *A. subpictus*[67]. Similarly, Abutaha *et al.*[68] reported potent ovicidal activity of hexane-methanol soluble fraction (HMSF) and larvicidal activity in chloroform-methanol soluble fraction (CMSF) of the fruit against *C. pipiens*. Hexane-methanol soluble fraction had high pupicidal activity and adulticidal activity[68]. Also, the extract caused 100% mortality in the third larval instar of *C. quinquefasciatus* within 72 hours of treatment[69]. Leaf extract was reported to have adulticidal activity against *A. stephensi*[70]. In *Dysdercus koenigii*, the hatching success of eggs treated with *C. fistula* leaf extract decreased with the increasing concentration of the extract[71]. The methanolic bark extract also inhibited the metamorphosis in *D. koenigii* and affected reproduction adversely[72]. The seed extract showed potent ovicidal activity against the rice moth *Corcyra cephalonica*[73], and the leaf extract hindered the oviposition process in *Callosobruchus maculatus*[74]. Treatment of *S. frugiperda* with hexane and ethanol extract of seeds of *C. fistula* resulted in a reduction in pupation, oviposition, hatchability and increased sterility[75].

C. fistula extract contains flavonoids such as chlorogenic acid, quercetin and rutin. These flavonoids have been reported to affect the survival and growth of many lepidopteran pests, such as *H. armigera* and *S. litura*. Consequently, the larval period of *H. armigera* larvae treated with rutin increased[76]. Chlorogenic acid and quercetin-treated *H. armigera* moth failed to reproduce. In *S. litura*, rutin reduced larval growth and development and produced malformed adults[76]. Two trypsin inhibitors, CFTI-1 and CFTI-2, were reported and isolated from the seeds of the *C. fistula*; in *H. armigera*, these trypsin inhibitors inhibited the activity of midgut trypsin-like proteases. It was also reported that CFTI-1 was responsible for decreasing the larval weight, fecundity and fertility of moths in a dose-dependent manner[77]. Quercitin, a flavonoid reported in *C. fistula,* had an impact on the growth and development of larvae of *S. litura*. Significant changes were observed in different parameters of growth and development of treated insects, such as pupal weight, survival rate, fecundity, egg hatchability, and population growth index. Also, different cell organelles were degenerated, as reflected by histological studies[78]. Toxicity bioassay of linoleic acid against the larvae of *S. littoralis* indicated its potent toxicity against the larval instars; the larval body weight was also decreased[79]. The larvae of gypsy moth, *Lymantria dispars,* when feeding on low concentrations of emodin showed a prolonged development period; high concentration of emodin induced mortality within 2-3 days.

There are reports that showed that various flavonoids (rutin, chlorogenic acid, quinic acid, caffeic acid, naringenin, quercitin, kaempferol, myricetin, catechin, and ferulic acid), lectins (groundnut leaf lectin, concavalin A) and phenyl β-D-glucoside affect survival, growth, and the activities of some digestive and detoxifying enzymes of the larva of *S. litura*[80]. A significant reduction in the activities of some enzymes, such as serine protease, trypsin and esterase, was observed in flavonoid-treated larvae. Larval growth and development were drastically affected in *S. litura* larvae fed on a diet containing groundnut leaf lectin, concavalin A[80]. In a study conducted on pea aphid, *Acyrthosiphon pisum*, the results showed that quercitin-fed larvae had increased development time, pre-reproductive period and mortality and decreased fecundity[81]. Although the probing and feeding behaviour of adult apterae was observed, salivation and passive fluid ingestion were completely stopped after treatment with higher concentrations of quercitin[81]. Quercitin-fed insects showed significant changes in the activities of some enzymes, such as superoxide dismutase, catalase, peroxidase, carboxylesterase, and glutathione S-transferase in *B. mori*[82]. Long-term exposure to quercitin also suppresses the expression of immune-related genes that drastically affect the growth and development of silkworms[82]. Another finding revealed that quercitin significantly changed the activity of carboxylesterase (CarE) and glutathione S-transferase(GST) enzymes in tobacco white fly *B. tabaci*[83]. Polyphenolic compounds modulate endogenous signal transduction pathways, interfering with the biosynthesis, secretion, transport, and metabolism of reproduction-linked hormones[84]. Reduced secretion of regulatory hormones reduced ovarioles growth, which resulted in low egg output in mosquitoes[85]. Effects of sublethal concentrations of proanthocyanidins were studied in the malarial vector *A. gambiae,* and results demonstrated that the proanthocyanidins decreased the growth and development of the mosquito and affected its reproductive fitness. Proanthocyanidins decrease the process of JH biosynthesis and detoxifying enzymes in treated larvae of *A. gambiae,* resulting in impaired metamorphosis, a reduction in JH levels, and a delayed development period. Proanthocyanidins tend to generate highly reactive free radicals due to their instability in the high pH of insect midguts, which generates oxidative stress[85]. Kaempferol affects ecdysteroid titer in the ovaries, hemolymph, and oocyte size in *H. armigera*. Feeding on food containing kaempferol caused a decrease in tachykinin-4 (a neuropeptide) level of the brain and hemolymph that led to decreased ecdysteroid titer in the ovary and hemolymph. Finally, the decrease in ecdysteroid titer resulted in a smaller oocyte[86]. Among the multiple approaches, protease inhibitors can act as potent biopesticides for controlling pest species. Sublethal doses of essential oils present in *C. fistula* were tested against the termite *Odontotermes feae.* The result showed that essential oils were toxic and caused a decrease in the glutathione S-transferase(GST) enzyme activity in treated termites[87]. Toxicity bioassay also revealed that flavonoids, quercetin dehydrate, rutin hydrate and naringine present in the *C. fistula* induced mortality in *Eriosoma lanigerum.* The stigmasterol and 1-hexacosanol (Fig. 1) derived from *Chromolaena odorata* plant resulted inhibition of the activity of acetylcholinesterase enzyme in larvae, which caused mortality in the larva of *C. quinquefasciatus, A. aegypti* and *Chironomus riparius*[88].

Nanoformulations in insect management

In the recent past, there has been considerable research interest in the area of controlling insect pests by using nanoparticles[89]. Nanoparticles can be synthesized by a single-step green synthesis process in which secondary metabolites present in plant extracts can be used to reduce metal ions of nanoparticles. Different types of reducing agents involved in the process are alkaloids, phenolic compounds, terpenoids and co-enzymes. The process is quick, environmentally amiable, and can easily be conducted at room temperature and under pressure. By the biogenic reduction method, large quantities of nanoparticles with well-defined sizes and morphology can be synthesized[90]. Different plant extracts have a variety of reducing and stabilizing agents that can influence the characteristics of the nanoparticles[91]. Typically, this process involves mixing the aqueous extract with an aqueous solution of the relevant metal salt. A variety of plant extracts have been used successfully to make nanoparticles. Nanoparticles can be synthesized using various elements like copper, zinc, titanium, magnesium, gold, and silver; silver nanoparticles have more promising results against bacteria, viruses and other microorganisms[92,93]. Nanoparticles can be synthesized by 'Top-down' and 'Bottom-up' approaches[94]. In the top-down approach, the bulk material is reduced to a smaller size by various physical and chemical actions, while in the bottom-up approach, nanoparticles are synthesized with the help of aggregation of small atoms[95]. Plant-mediated nanoparticles have advantages as they are cheap to make, less toxic and have wider application against various microorganisms and insects[96].

Characterization of nanoparticles

Nanoparticles are characterized using various techniques such as UV–visible spectrophotometry, dynamic light scattering (DLS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), Fourier transform infrared spectroscopy (FTIR), powder X-ray diffraction (XRD) and energy dispersive spectroscopy (EDS)[97-99]. Surface charge and the size distribution of the particles present in liquid are identified by dynamic light scattering (DLS)[100]. Morphological characterization of nanoparticles can be done by scanning electron microscopy and transmission electron microscopy[101]. FTIR spectroscopy can detect the surface chemistry of synthesized nanoparticles like attached functional groups and chemical residues on the surface of nanoparticles[102]. XRD is involved in the identification of the crystal structure of the nanoparticles[103]. Another technique used to characterize the nanoparticles is energy dispersive spectroscopy (EDS), which can be used to detect the elemental composition of nanoparticles[104].

Insecticidal activity nanoparticles against insect pests

Several research studies have been conducted to detect the toxicity of nanoparticles against a wide number of insect pests and vectors. AgNPs synthesised from the leaf extract of *Nelumbo nucifera.* showed tremendous larvicidal activity against the third instar larvae of mosquito *A. subpictus* and *C. quinquefasciatus*[105]. Toxicity bioassay of AgNPs synthesised from the leaf extract of *A. squamosa* against *A. aegypti* and *A. stephensi* showed 70 to 100% mortality of larvae[106]. Silver nanoparticles synthesised from the *C. fistula* fruit pulp inhibited the growth of I-IV instar larvae and pupae of *A. albopictus* and *C. pipiens pallens*[107]. AgNPs synthesised using leaf extract of *Azadirachta indica* showed potent larvicidal activity against *C. quinquefasciatus*[108]. Exposure of *D. melanogaster* to sublethal doses of silver nanoparticles showed detrimental effects on its development[109]. Carbon-dot silver nanohybrid synthesised using potatoes, *Solanum tuberosum* showed tremendous larvicidal and pupicidal activity against *A. stephensi* and *C. quinquefasciatus*[110]. Zinc oxide nanoparticles formed using the leaf extract of *Lobelia leschenaultiana* showed deleterious effects on the third instar larvae of *A. aegypti* that led to shrinkage in the abdominal region, change in the shape of the thorax, damage to the midgut, and loss of lateral hairs, anal gills and brushes of treated larvae[111]. Silver and zinc nanoparticles fabricated using *Moringa oleifera* leaf extract showed larvicidal and pupicidal toxicity against *Musca domestica*. Toxicity bioassay also revealed a significant reduction in the egg hatchability and fecundity of females[112].

Mechanism of action of nanoparticles against insect larvae

The mechanism of action of nanoparticles against insects is summarised in Fig. 2. The precise mechanism of action of nanoparticles against insects is not fully understood. AgNP-treated larvae also showed morphological changes like depigmentation, necrosis, and disintegration of muscle layers[113,114]. Nanoparticles also affect the growth and development of many insect pests. SiO_2 and Al_2O_3 nanoparticles

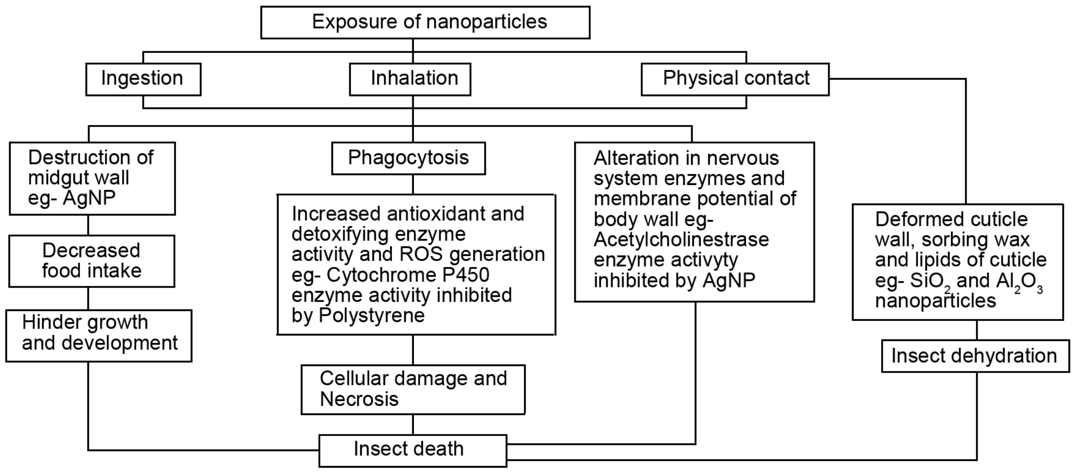

Fig. 2 — The mechanism of action of nanoparticles against insects.

bind with the insect cuticle, resulting in the physico-sorption of waxes and lipids, leading to insect dehydration.

AgNPs synthesised from plant extract have been reported to drastically affect the midgut wall of insects. AgNPs synthesised using *C. fistula* resulted in the formation of multiple lesions in the midgut epithelium of insects, degradation of the gut membrane and broken brush border[115]. Similarly, silver nanoparticles synthesised from the extract of *Hedychium coronarium* rhizome caused damage to midgut epithelial cells and vesicles of the fourth instar larvae of *A. aegypti*[116]. In a study, silver nanoparticles synthesised using the *Punica granatum* peel extract were reported to decrease the activities of enzymes such as amylase, protease, lipase, and invertase in the third instar larvae of *S. litura*[117]. Also, gold nanoparticles synthesised from the latex of *Jatropha curcas* inhibited the activity of trypsin enzyme in *A. aegypti*, as well as beetle and mealy bugs[118]. Trypsin inhibitory activity of gold nanoparticles affected insect development and reproduction[119]. Yasur *et al.*[120] reported that silver nanoparticles increased oxidative stress and some antioxidant enzymes in the larvae of *S. litura* and *A. janata*. Further, AgNPs-treated mosquito larvae showed a decrease in the activity of superoxide dismutase and tyrosinase enzymes[109,121,122]. In *Drosophila*, silver nanoparticles increase the production of reactive oxygen species in the fly tissues, leading to the initiation of apoptosis, DNA damage, and autophagy[109]. Both silver and graphene oxide nanoparticles increase the oxidative stress in the treated insects, which leads to cell death[119]. Cytochrome P450 enzyme is inhibited by polystyrene nanoparticles[119]. In *M. domestica*, the larvae treated with silver and zinc nanoparticles fabricated using *M. oleifera* leaf extract showed a reduction in the activities of enzymes such as esterases, acetylcholinesterase, and glutathione S-transferase[112]. Also, AgNP fabricated using *C. fistula* showed a reduction in the activities of acetylcholinesterase and carboxylesterase and protein content in *A. albopictus* and *C. pipiens pallens*[107].

Conclusion

Plants have different types of metabolites that can affect insect growth and development. *C. fistula* is an abundant source of carbohydrates, fatty acids, flavonoids, tannins, oxalic acids, anthraquinones, etc. Larvicidal activities of different plant parts of *C. fistula* have been reported in many species of lepidopteran, dipteran, hemipteran, and coleopteran pests. Nanoparticles synthesized from different plant extracts can act as a novel approach for controlling different insect pests. Silver nanoparticles (AgNPs) synthesized from *C. fistula* fruit pulp extract drastically affected the midgut wall of an insect and altered its growth and reproduction. Thus, AgNPs synthesized using plant extracts can be explored as novel molecules for insect pest management in future. The present review summarises the phytochemical investigation and biological activities of *C. fistula* and its importance in 'Insect Pest Management'.

Conflict of interest

The authors declare that they have no conflict of interest.

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