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BOTANICAL PESTICIDES: ENVIRONMENTAL IMPACT

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ABSTRACT

The insecticidal properties of natural plant products have been known since ancient times. It is estimated that over 2,000 plant species possess biological activity against insects, and the principal chemicals that impart such activity include alkaloids, terpenoids, acetogenins and flavonoids. Among the various plant products used as insecticides, nicotine from Nicotiana tabacum *and pyrithrins from* Chrysanthemum cinerariaefolium *are the most prominent. Pesticide formulations developed from neem* (Azadirachta indica)*, karanja* (Pongamia glabra)*, and custard apple* (Annona squamosa) *have also shown promise for pest management. Despite voluminous information on the usefulness of these products as pest control chemicals, their exploitation in practical agriculture is limited due to low toxicity, latent period of action, short shelf-life, rapid degradation, and limited spectrum of activity. However, there is a general prevailing belief that natural plant products are easily biodegradable, and thus, are considered safer as compared to synthetic pesticides. However, there is little information on their metabolism in soil, water and plants. Although considered safe to nontarget natural enemies of crop pests, plant products might still have the same toxic and anti-molting effects on these organisms as on the target arthropods, in addition to their indirect effects through sub-optimal prey. There is very little information on the effects of these products on the activity of microbes in the soil, and on the aquatic organisms. Large-scale use of natural plant products may also have disorienting effects on the foraging behavior of honeybees and other pollinators. Therefore, there is a need to generate information on natural plant products relative to their metabolic products, acute and chronic toxicity, mutagenesis, allergenicity, and teratogenicity as in the case of synthetic*

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pesticides, with due consideration for their safety to the environment to place these chemicals on a sound footing for pest management and sustainable crop production. This chapter reviews the current literature on various aspects of plant products for plant protection.

Introduction

Synthetic insecticides have been used over the past 50 years for pest management in order to stabilize crop production. However, large-scale and indiscriminate use of synthetic insecticides has led to adverse effects on the nontarget organisms, pesticide residues in food, pest-resurgence, development of insect resistance, toxic effects on human beings, and environmental pollution (Regnault-Roger 1997). With the evolution of insect resistance to insecticides, it has become quite difficult to control certain insect pests by currently available chemical insecticides. Therefore, there is an urgent need to develop alternate methods of pest control, and it is in this context that greater effort has now been placed on the use of biopesticides, natural plant products, natural enemies, and insect-resistant varieties for pest management. Among the alternative strategies, natural plant products have been found to be quite effective, biodegradable, and safer to the environment (Leatemia and Isman 2004; Isman 2006).

Botanical pesticides have been used for insect control since ancient times, especially in societies with a strong herbal tradition (Yang and Tang 1988). Concoctions of inorganic and organic materials were used by rice farmers for insect control in Southeast Asia (Maata 1987). Traditionally, the pest habitats were treated with leaves, stems, seeds, roots, or other plant parts or products known to kill or repel insect pests (Sharma et al. 1999; Isman 2000). Botanical pesticides have been reported to be effective against nematodes (Tsao and Yu 2000; Wiranto et al. 2009; Ononuju and Nzenwa 2011), insects (Isman 2006; Nathan et al. 2006; Akhtar et al. 2008; Baskar et al. 2009; Pavela 2011; Moawad and Al-Barty 2011), mites and ticks (Kim et al. 2004), and plant pathogens (Isman 2000). Different plant parts such as roots or rhizomes of derris (Cabizza et al. 2004), flowers or buds of pyrethrum (Glynne-Jones 2001), and seeds and leaves of various plants (Nathan et al. 2006; Baskar et al. 2009) have been used for insect control.

Plant secondary metabolites such as coumarins, furanocoumarins, terpenoids, alkaloids, and polyphenols have been found to kill or reduce/inhibit feeding, egg-laying, and growth and development of insects. These secondary metabolites exhibit repellent, antifeedant, and growth inhibiting effects against insect pests (Table 1; Isman 2000, 2006; Koul et al. 2004; Nathan et al. 2006; Pavela 2011; Moawad and Al-Barty 2011). Although insecticidal properties of several plant species have been known since ages, only a handful of them have been successfully exploited in insect management programs. Azadirachtin obtained from *Azadirachta indica* A. Juss, nicotine from *Nicotiana tabacum* L., pyrethrins from *Chrysanthemum*

Table 1: Botanical pesticides used for pest management.

Plant species	Insect against which effective	Host crops	Reference
Neem	*Sogatella furcifera*	Rice	Shukla et al. (1991)
	Leptinotarsa decemlineata	Potato	Zehnder and Warthen (1990)
	Plutella xylostella	Cabbage	Shukla et al. (1991)
	Helicoverpa armigera	Cotton	Sharma et al. (1984)
	Spodoptera litura	Groundnut	Joshi and Sitaramaiah (1979)
	Myzus persicae (Sulzer)	Tomato	Pavela (2009)
	Pseudaletia unipuncta (Haw.)	Wheat	Akhtar et al. (2008)
	Trichoplusia ni (Hub.)	Cabbage	Akhtar et al. (2008)
	Sahlbergella singularis (Haglund)	Cocoa	Asogwa et al. (2010)
	Cnaphalocrocis medinalis (Guenee)	Rice	Nathan et al. (2006)
	Schistocerca gregaria	Maize	Butterworth and Morgan (1971)
	Mythimna separata	Sorghum	Sankaram et al. (1987)
Atalantia monophylla (L.)	*H. armigera*	Cotton	Baskar et al. (2009)
Pongamia glabra	*M. persicae*	Tomato	Pavela (2009)
	S. litura	Groundnut	Behera and Satapathy (1997)
	H. armigera	Cotton	Murugun and Babu (1998)
Chrysanthemum	*M. persicae*	Tomato	Pavela (2009)
cinerariifolium	*Spodoptera littoralis*	Bean	Pavela (2009)
Melia azedarach	*P. unipuncta*	Wheat	Akhtar et al. (2008)
	T. ni	Cabbage	Akhtar et al. (2008)
	P. xylostella	Cauliflower	Charleston et al. (2005)
	Brevicoryne brassicae	Cabbage	Mekuaninte et al. (2011)
Ailanthus excels Roxb.	*P. unipuncta*	Wheat	Akhtar et al. (2008)
	T. ni	Cabbage	Akhtar et al. (2008)

Table 1: (*Contd...*)

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Plant species	Insect against which effective	Host crops	Reference
M. volkensii	*P. unipuncta*	Wheat	Akhtar et al. (2008)
	T. ni	Cabbage	Akhtar et al. (2008)
Trichilia americana	*P. unipuncta*	Wheat	Akhtar et al. (2008)
(Sesse and Moc.)	*T. ni*	Cabbage	Akhtar et al. (2008)
Annona squamosa	*L. decemlineata*	Potato	Moeschler et al. (1987)
	P. xylostella	Cauliflower	Leatemia and Isman (2004)
	Brevicoryne brassicae	Cabbage	Dadang et al. (2009)
	Bruchus chinensis	Bean	Ahmad et al. (1984)
	Coccus viridis	Cacaoq	Ahmad et al. (1984)
	Dysdercus koenigii	Cotton	Ahmad et al. (1984)
	Euproctis fraterna	Mango	Ahmad et al. (1984)
	Nilaparvata lugens	Rice	Ahmad et al. (1984)
	S. litura	Groundnut	Ahmad et al. (1984)
	S. furcifera	Rice	Ahmad et al. (1984)
	Chilo partellus	Sorghum	Sharma et al. (1999)
	M. separata	Sorghum	Sharma et al. (1999)
	Melunaphis sacchari	Sugercane	Sharma et al. (1999)
	Calocoris angustatus Leth.	Sorghum	Sharma et al. (1999)
	Crocidolomia pavonana	Cabbage	Dadang et al. (2009)
Rhododendron molle (G. Dorn)	*Pieris rapae* L.	Cabbage	Zhong et al. (2001)

cinerariaefolium L. and rotenone from the rhizomes/roots of *Derris* and *Lonchocarpus* are the most important plant based insecticidal compounds with broad spectrum activity. Several plant products are currently being investigated for utilization in pest management. Amongst them, neem (*A. indica*) and Chinaberry (*Melia azedarach* L.) have been the focus of a large number of studies over the past three decades. They contain terpenoids that are repellents, antifeedants, growth inhibitors, and oviposition suppressants (Sharma et al. 1984, 1999; Parmar and Singh 1993). Acetogenins from *Annona* spp. and *Asimina* sp. has also shown promise for pest control (Sharma et al. 1999). Acetogenins act on mitochondria, resulting in toxic effects on insect pests (Gonzalez-Coloma et al. 2002). Limonin from *Citrus paradisi* Macfad. acts as an antifeedant/growth inhibitor (Bentley et al. 1990). Plumbagin from *Plumbago zeylanica* L. and karanjin from *Pongamia glabra* (L.) exhibit insect antifeedant and toxic properties (Sharma et al. 1984; Kumar and Singh 2002). Isobutyl amides from *Piper* sp. are neurotoxins (Tokunaga et al. 2004). These and several other compounds of plant origin have potential for insect pest management. For commercial exploitation, the natural plant products should have the following desirable characteristics:

- Safer to plant and animal life.
- Rapidly biodegradable.
- Potential for cultivation.
- Availability of standardized procedures for quantifying biologically active components.
- Potential for synthesis of biologically active compounds.
- No or less residues and nontarget effects.

Botanical Pesticides

Neem

Neem (*A. indica*), a member of the mahogany family Meliaceae, is one of the earliest used botanicals for pest control (Schmutterer 1990; Isman 2000, 2006). An age-old practice in India is to mix neem leaves with stored rice grain or to crush neem fruits on storage facility walls to prevent insect damage (Pradhan et al. 1962). Sometimes, the plant materials are chopped or ground into a powder or extracted as a liquid for use. Pesticides developed from neem have been used against a number of insect pests globally (Singh and Kataria 1991; Isman 2006; Nathan et al. 2006; Hasan and Ansari 2011).

Diverse mode of action of neem such as repellency and phagodetterance (Sharma et al. 1984; Bomford and Isman 1996; Isman 2006), growth inhibition and abnormal development (Meisner et al. 1976; Bomford and Isman 1996; Isman 2006), and oviposition suppression (Joshi and Sitaramaiah 1979; Sharma et al. 1984; Kraus 2002) has given it a prime importance for controlling insect pests. Several biologically active compounds have been

isolated from different parts of the neem tree. Azadirachtin (Fig. 1) is the most potent growth regulator and antifeedant (Butterworth and Morgan 1971; Isman 2006; Nathan et al. 2006). The dramatic feeding deterrent effect of azadirachtin on the desert locust, *Schistocerca gregaria* Forsk. (at 0.04 ppm) has been observed and correlated with the evolution of locusts with the neem tree (Butterworth and Morgan 1971). Removal of sensory parts from the mouth of *S. gregaria* resulted in azadirachtin toxicity effects similar to the normal insects. A number of terpenoids have been isolated from neem kernels. These include salanins, salanols, salanolactomes, vepaol, isovepaol, epoxyazadiradione, azadiradione, gedunin, 7-deacetylgedunin, etc. Epoxyazadiradione, azadiradione, nimbin, gedunin, and 7-benzoylgedunin isolated from neem kernels have shown antifeedant effects against the Oriental armyworm, *Mythimna separata* (Walk.) (Sankaram et al. 1987).

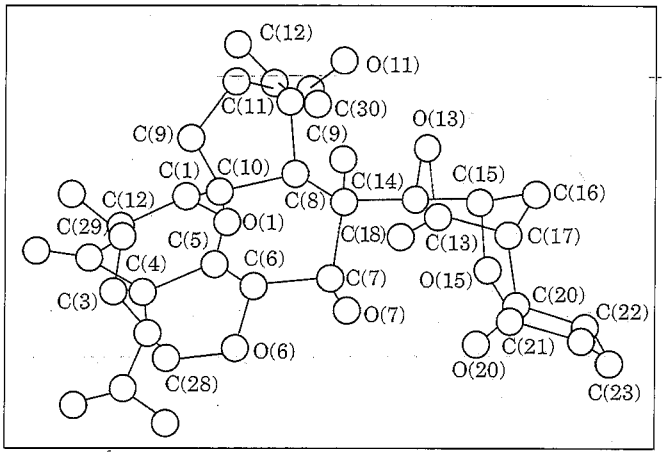

Fig. 1: Azadirachtin - the most active pesticide compound from the neem tree.

Several formulations based on neem have been developed and evaluated for pest management. Neem EC (emulsified concentrate 0.5 and 1%) has been reported to be effective against corn leaf aphid, *Rhopalosiphum maidis* (Fitch) and yellow sugarcane aphid, *Melanaphis sacchari* Zehnt. on sorghum (Srivastava and Parmar 1985). Ethanol extract of neem seed kernels (2%) has been reported to be effective against *Helicoverpa armigera* (Hub.), *Maruca vitrata* (Geyer), and *Melanagromyza obtusa* Malloch on pigeonpea. Neem oil at 2% concentration was effective only against *M. obtusa* (Singh et al. 1985). Neem oil and neem seed kernel extract (NSKE) at 5% concentration sprayed at 10-day intervals gave a two-fold reduction in *H. armigera* infestation in chickpea. Neem EC and WDP (wettable dry powder) accorded 40–60% reduction in pod borer infestation as compared to the untreated control, while the product Neemguard was ineffective (Sinha 1993). Neem extract showed moderate activity, while Neemark® and neem oil were ineffective against these insects (Sharma et al. 1999).

Neem products have also been used for health applications such as antiviral and antifungal treatments and dental hygiene. Millions of people in Asia and Africa brush their teeth and gums with neem tree twig (Alam 1991; Khan 2006). Extracts from neem fruits are used in toothpaste, body soap, skin ointment, and other preparations. *Ayurvedic* system of medicine, practiced in India for about 2,000 years, uses combinations of herbs, purgatives, rubbing oil, and other concoctions to prevent and cure human illness (Khan 2006). Neem extract has been found to inhibit the Ranikhet viral disease of poultry (1 mg per embryo), and reduces virus multiplication by 70%, and reduces the cholesterol and triglyceride levels in rats (Sankaram et al. 1987). Neem extract also inhibits the growth of *Klebsiella pneumonia* Trev., *Candida albicans* Berk., *Cryptococcus neoformans* Vuill, and *Trichophyton mentagrophytes* Priest, but is not active against *Escherichia coli* Cast. et Chalmers, *Pseudomonas aeruginosa* Migula, *Staphylococcus aureus* Rosen., and *Aspergillus fumigatus* Fres. (Sankaram et al. 1987).

Custard apple

Custard apple (*Annona* species) grows widely in India and Africa. Family Annonaceae includes the sweetsop (*Annona squamosa* L.) and soursop (*A. muricata* L.). Insecticidal properties of *Annona* spp. have been studied for nearly 50 years (Puttarudriah and Bhatta 1955). Extracts of *Annona reticulata* L. and *A. squamosa* have been used against many insect pests including cabbage aphid, *Brevicoryne brassicae* L.; pulse beetle, *Bruchus chinensis* (L.); green scale, *Coccus viridis* (Green); cotton stainer, *Dysdercus koenigii* Fab.; hairy caterpillar, *Euproctis fraterna* M.; brown plant hopper, *Nilaparvata lugens* (Stal.); saw toothed grain beetle, *Oryzeaphilus surinamensis* (L.); diamond back moth, *Plutella xylostella* (L.); white backed plant hopper, *Sogatella furcifera* (Horv.), and tobacco caterpillar, *Spodoptera litura* (Fab.) (Ahmad et al. 1984). The biological effects of custard apple are due to direct toxicity to insects (Isman 2006). Acetogenins (long chain fatty acids) and their derivatives present in the seeds of *Annona* are responsible for insecticidal activity (Rupprecht et al. 1990). Acetogenins block the electron transport chain, and thereby also block the production of energy in both insects and mammals (Londershausen et al. 1991). Annonin, asimicin, bullatacin, isobullatacin, desacetyluvaricin, and isodesacetyluvaricin have been isolated from *Annona*. Asimicin has been characterized from the bark of *Asimina triloba* (L.) (Alkofahi et al. 1989). Bullatacin and bullatacinone have been isolated from *Asimina bullata* A. Rich. Bullatacin is a diastereomer of asimicin. Bullatacinone represents bullatacin with the lactone cleaved and reformed at 4-OH. Bullatacin acts as a pesticide at a concentration of 1 ppm (Hui et al. 1989). Several fractions of custard apple seed extract have been found to be effective against many insect pests including *M. separata* and the sugarcane aphid, *M. sacchari* (Sharma et al. 1999). Custard apple seed extract also shows synergistic activity in combination with neem seed kernel extract against *Callosobruchus chinensis* (L.), *Rhyzopertha dominica*

(Fab.), *Musca domestica nebula* (Fab.), and *P. xylostella* (Quadri and Rao 1977; Laetemia and Isman 2004). *Annona squamosa* and *Piper retrofractum* Vahl extracts in mixture, and *A. squamosa* extracts individually are more effective against *Crocidolomia pavonana* (F.) and *P. xylostella* than the synthetic insecticides (Dadang et al. 2009).

Rotenone

Rotenone is derived from the roots or rhizomes of the tropical legumes such as *Derris, Lonchocarpus*, and *Tephrosia*. It has been used as an insecticide for more than 150 years. However, it has been known as a fish poison for a long time (McClay 2000; Isman 2006). Rotenone inhibits mitochondrial respiration. It blocks the NADH oxidation by the NADH-ubiquinone oxide reductase enzyme complex, which in turn inhibits mitochondrial respiration, thereby, reducing the ATP synthesis (Hollingworth et al. 1994; Chauvin et al. 2001). It readily breaks down on exposure to sunlight within 6–7 days, and is rapidly broken down in soil and in water with a half life of 1–3 days (Walker et al. 1992).

Pyrethrum

Pyrethrum is an oleoresin extracted from the flowers of pyrethrum daisy, *C. cinerariaefolium*. The flowers are powdered and extracted with either hexane or some other solvents of low polarity (Casida and Quistad 1995; Glynne-Jones 2001). The extract contains three esters of chrysanthemic acid and three esters of pyrethric acid. The esters such as pyrethrins I and II are most abundant and account for most of the insecticidal activity. Commercial pyrethrum formulations contain 20–25% pyrethrins, which are known for their quick knockdown effect, mostly on flying insects (Casida and Quistad 1995). Pyrethrum has been used to control a wide-range of insect pests including true bugs, caterpillars, beetles, aphids, flies, mites, whiteflies, thrips, and leafhoppers (Casida 1973). However, it is not very effective against flea beetles, imported cabbageworm, diamondback moth, aphids and lygus bugs (Casida 1973). Pyrethrins are neurotoxic and block the voltage gated sodium-channels (Casida 1973).

Nicotine

Nicotine is an alkaloid obtained from aqueous extracts of tobacco plants namely *N. tabacum, Nicotiana glauca* Graham or *Nicotiana rustica* L. Nicotine has long been used as an insecticide (Schmelz 1971). The liquid concentrate of nicotine used as insecticide is nicotine sulfate. Nicotine is neurotoxic and acts on nicotinic acetylcholine receptors (Hayes 1982; Isman 2006).

Botanical pesticides have low or no residual effect, and are generally considered to be non-persistent under field conditions as they are readily degraded by light, oxygen, and micro-organisms into less toxic products

(Isman 2006). They are regarded as an ideal arsenal for insect control because of their occurrence in nature and are renewable. Although botanical pesticides have been found to be safer than the synthetic pesticides, there are a number of reports about their toxicity to some beneficial natural enemies, soil organisms, aquatic species, and to warm blooded animals including human beings. However, their occurrence in nature is no guarantee that they are always environmentally friendly and safe to the nontarget organisms including natural enemies, aquatic organisms, soil organisms, and warm blooded animals.

Environmental Effects of Botanical Pesticides

Natural enemies of crop pests

Long-term effects of plant products on natural enemies, aquatic and soil organisms, and other beneficial insects need special investigation. Study of direct and indirect effects of botanicals on natural enemies is important to understand their biological activity and their usefulness for pest management. Although many nontarget organisms are affected by pesticides, the two groups of organisms that have received much attention are the natural enemies and plant pollinators because of their potent roles on the environment (Van Driesche and Bellows 1996). Effect of neem and other botanicals on some nontarget organisms has been studied, which has led to suspicion regarding their safety to the natural enemies (Stark et al. 1992; Lowery and Isman 1995; Spollen and Isman 1996; Ruiu et al. 2008; Defago et al. 2011). A number of reports have been published on the negative effects of botanicals including azadirachtin on parasitoids and predators (Tables 2 and 3). However, in most of the cases, the natural enemies have been found to be less susceptible than their insect hosts (Hoelmer et al. 1990; Schmutterer 1997; Simmonds et al. 2000; Condor Golec 2007).

Predators

Neem seed kernal extract (10%) resulted in 73.3% mortality of the coccinellid, *Adonia variegata* (Goeze) compared to 65.0% mortality with neem oil (5.0%) (Swaminathan et al. 2010). NSKE resulted in 72.0% reduction in feeding, followed by 68% reduction with neem oil. Aqueous suspension of ground neem seeds caused a 50% reduction in the number of aphids consumed. The coccinellid predator *Delphastus pusillus* (LeConte) avoided the eggs of whitefly, *Bemisia tabaci* (Gen.) treated with neem (Margosan-O) for 1 day, but resumed feeding the next day (Hoelmer et al. 1990). Neem oil (50% EC) had no effect on the predatory green lacewing, *Chrysoperla carnea* (Stephens), but was more toxic than malathion to predatory black mirid, *Tytthus parviceps* (Reu.) (IRRI 1992). Several studies have been carried out on the biological activity of neem based formulations on ladybird beetles (Banken and Stark 1998; da Silva and Martinez 2004) and imagos (Roger et al. 1995; Smith and Krischik 2000; Ulrichs et al. 2001). NeemAzal-S reduces the

Table 2: Effect of botanical pesticides on insect parasitoids.

Plant species	Parasitoid affected	Host insect	Reference
Neem	*Telenomus remus*	*Spodoptera frugiperda*	Joshi et al. (1982)
	Encarsia formosa Gahan	*Bemisia tabaci*	Feldhege and Schumutterer (1993)
	Encarsia pergandiella Howard	*B. tabaci*	Stansly and Liu (1997)
	Opius concolor Szepligeti	Olive fly	Vinuela et al. (2000)
	Pholeaster glomeratus (L.)	*Pieris brassicae*	Osman and Bradley (1993)
	Muscidifurax raptor	Fly	Ruiu et al. (2008)
	Goniozus triangulifer	*Marasmia patnalis*	Lamb and Saxena (1988)
	Psyttalia incise (Silvestri)	*Dacus dorsalis* Hend.	Stark et al. (1992)
	Hyposoter didymator (Thunberg)	*Spodoptera exigua*	Schneider et al. (2003)
	Tetrastichus howardi	*Chilo suppressalis*	
	Trichogramma cacoeciae		Saber et al. (2004)
	Cotesia plutellae	*Plutella xylostella*	Loke et al. (1992)
	Trichogramma chilonis	*Helicoverpa armigera Spodoptera litura*	Raguraman and Singh (1999)
	Campoletis chlorideae	*H. armigera, S. litura*	Rao et al. (2008)
Nicotiana tabacum	*Uscana lariophaga* (Steffan)	*Callosobruchus maculatus* (Fab.)	Boeke et al. (2003)
Mentha spicata	*T. chilonis*	*H. armigera, S. litura*	Solayappan et al. (2001)
Tephrosia vogelii (Hook)	*U. lariophaga*	*C. maculatus*	Boeke et al. (2003)

Table 3: Effect of botanical pesticides on predatory insects.

Plant species	Predator affected	Host insect	Reference
Neem	*Chrysoperla carnea*	Aphids	Schneider et al. (2003)
	Coccinella septempunctata	Aphids	Medina et al. (2001)
	Coccinella undecimpunctata	Aphids	Vinuela et al. (2000)
	Eupeodes fumipennis (Thompson)	Aphids	Banken and Stark (1997)
	Adonia variegata	Aphids	Swaminathan et al. (2010)
	Delphastus pusillus	Whitefly	Hoelmer et al. (1990)
	Tytthus parviceps	Leaf hopper	IRRI (1992)
	C. undecimpunctata	Aphids	Ahmad et al. (2003); Zaki (2008)
	C. carnea	Aphids	Ahmad et al. (2003); Zaki (2008)
	Cryptolaemus montrouzieri	Mealy bug	Simmonds et al. (2000)
	Hippodamia variegata	Aphids	Hamd et al. (2005)
	Cheilomemes sexmaculatus	Aphids	Regupathy and Ayyasamy (2005)
	Coccinella transversalis	Aphids	Regupathy and Ayyasamy (2005)
	Micraspis discolor	Aphids	Regupathy and Ayyasamy (2005)
	Ipheseius degenerans (Berlese)	Thrips	Lowery and Isman (1995)
	Neoseiulus cucumeris (Oudemans)	Mites	Lowery and Isman (1995)
Melia azedarach	*C. undecimpunctata*	Aphids	Zaki (2008)
	C. carnea	Aphids	Zaki (2008)
Melia volkensii	*Chilocorus bipustulatus* var. *iranensis*	*Parlatoria blanchardi*	Peveling and Ely (2006)
	Coccinella spp.	Aphids	Smith and Krischik (2000)
Bougainvillea spectabilis	*C. carnea*	Aphids	Ravikumar et al. (1999)
Vitex negundo	*C. carnea*	Aphids	Ravikumar et al. (1999)
Garlic crude extract	*C. carnea*	Aphids	Nasseh et al. (1993)
	C. septempunctata	Aphids	Nasseh et al. (1993)

population of *Coccinella undecimpunctata* L. and *C. carnea* on cabbage (Zaki 2008). The mortalities of *C. carnea* and *C. undecimpunctata* reared on hosts treated with ethanol extracts of neem fruits and *M. azedarach* flowers in petroleum ether were 33.3 and 81.5%, respectively (Zaki et al. 2008). Azadirachtin also affects the coccinellid predator, *Cryptolaemus montrouzieri* Mul. (Simmonds et al. 2000). Neem oil reduced the hatching rate of *C. septumpunctata* and *C. carnea,* and resulted in morphological deformities in the adults (Ahmad et al. 2003), and a slight reduction in the number of pupae and adults of *C. carnea* (Medina et al. 2001, 2004). Direct spray of neem extract and neem oil in the laboratory caused high mortality and morphogenic defects in the larvae and adults of *C. carnea* and *C. septumpunctata* (Kaethner 1991). Azadirachtin and neem seed oil significantly reduced the survival of first-instars of *Harmonia axyridis* (Pallas), however, only azadirachtin reduced third-instar survivorship (Kraiss and Cullen 2008). NeemAzal T/S has been reported to be more harmful to the predator, *Hippodamia variegata* (Goeze) than neem seed water extract when different stages of the beetle were fed on the aphid, *Aphis gossypii* Glover sprayed topically (Hamd et al. 2005). Neem has also shown strong growth-regulating effects on the larvae of green lacewing, *C. carnea* and ladybird beetle, *C. septempunctata* (Schmutterer 1990). Crude extract of *Annona* leaves has been found to be toxic to *C. carnea* and *Orius insidiosus* (Say) (Leatemia and Isman 2004). However, *C. carnea* larvae were less susceptible to the extracts than *O. insidiosus* adults. Duso et al. (2008) reported that pyrethrins and rotenone were highly toxic to the predatory mite, *Phytoseiulus persimilis* Evans.

Parasitoids

Pure neem oil is more toxic than emulsifiable concentrate formulation, despite having lower concentration of azadirachtin (Ahmad et al. 2003; Isman 2006). Azadirachtin-based insecticide resulted in reduced life span and reproduction rate of the pupal parasitoid, *Muscidifurax raptor* Girault et Sanders (Ruiu et al. 2008). The parasitoid adults fed on azadirachtin treated artificial diet were susceptible to the azadirachtin-based formulation. The LC_{50} value for *Trichogramma cacoeciae* Marchal was 13.3 mg [AZ]/ml (Saber et al. 2004). Neem based formulations resulted in reduced emergence of the braconid wasp, *Cotesia plutellae* Kurdj. (Loke et al. 1992), and reduced fecundity in the bethylid wasp, *Goniozus triangulifer* Kieffer (Lamb and Saxena 1988). Neem had a longer lasting impact on the larval parasitoid, *G. triangulifer* of the rice leaf folder, *Marasmia patnalis* Brad. (Lamb and Saxena 1988). Emergence of adult parasitoids from neem-treated pupae and fecundity of the emerging adults were also reduced. Neem oil (50% EC) has been found to be nearly as toxic as chlorpyriphos to *Tetrastichus howardi* (Olliff) (IRRI 1992). Neem seed kernel extract (5%) also altered the sex ratio of *T. howardi* adults that emerged from treated pupae of the striped stem borer, *Chilo suppressalis* (Walk.), whereas neem oil reduced the emergence and longevity of the scelionid parasitoid, *Telenomus rowani* (Gahan) (IRRI

1992). Neem products reduced the parasitization of *H. armigera* larvae by *Campoletis chlorideae* Uchida up to 20% (Rao et al. 2008).

Larval parasitization, mostly by *Apanteles ruficrus* Hal. of the Oriental armyworm, *M. separata* was lower in the neem-treated plots than in the untreated control plots (Sharma et al. 1999), either due to premature death of the larvae or repellent effects of neem extracts on the parasite. Reduced parasitism by ichneumonid, encyrtid, and braconid hymenopterans has also been reported for rice leaf folder, *C. medinalis* (Saxena et al. 1981). Zaki (2008) reported that the numbers of the two parasitoids, *Diaeretiella rapae* (McIn.) and *Eretmocerus mundus* Mercet decreased after the application of Neemazal-S. Treatment of cabbage with botanical insecticide resulted in reduction of hind tibia length in males of the parasitoid, *C. plutellae* emerging from *P. xylostella* larvae fed on the treated cabbage, which resulted in a strong reduction in their fitness since the mating potential is correlated with overall body size (Charleston et al. 2005). Neem has also been found to be more toxic to the females than the males of the egg parasitoid, *Trichogramma chilonis* Ishii (Raguraman and Singh 1999). Neem adversely affected the coreid bug parasitoid, *Gryon fulviventre* (Craw.) (Mitchell et al. 2004), and reduced the longevity of the citrus aphid parasitoid, *Lysiphlebus testacipes* (Cresson) (Tang et al. 2002). Emergence of tephritid fruit fly parasitoids, *Psytalia incisi* (Silvestri), *Diachasmimorpha longicaudata* (Ashmead) and *Diachasmimorpha tryoni* (Cameron) were reduced when fed on azadirachtin-treated host flies (Stark et al. 1992). Commercial botanical insecticides such as Neemark, Repellin, Welgro, neem seed kernel suspension, nicotine sulfate and Neemrich repelled *Chrysoperla* from treated cotton field (Yadav and Patel 1990).

Toxicity of different oil formulations of *Melia volkensii* Gurke seed extract on the ladybird predator, *Chilocorus bipustulatus* var. *iranensis* L. of the date palm scale, *Parlatoria blanchardi* (Targioni Tazz.) have been studied by Peveling and Ely (2006), and on coccinellid species by Smith and Krischik (2000). Azadirachtin reduced the longevity and progeny size per female of the braconid wasp, *Opius concolor* Szepl. (Viñuela et al. 2000), and survival and adult emergence of *Podisus maculiventris* (Say) (Viñuela et al. 2001). Nemento (combination of neem seed kernel and *Mentha spicata* L. leaf extracts, and tobacco) resulted in greater mortality of *T. chilonis* and *C. scelestes* Banks (Solayappan et al. 2001). Neem oil and lufenuron were found to be less harmful to *Trichrogramma pretiosum* Riley and *Trichrogramma exiguum* Pinto and Platner, when applied to the eggs before parasitism, however, its toxicity increased when the wasps were in contact with the eggs after parasitism (Thuler et al. 2007). Direct contact of pyrethrum to beneficial wasps could be highly toxic (Cox 2002). *Melia azedarach* extract when included in the food caused higher mortality of the parasitoid, *C. ayerza* (Brèthes) (Defago et al. 2011). Dust formulation (25%) of *Bougainvillea spectabilis* (Wild.) caused 10 to 16% mortality of different instars of *C. carnea* (Ravikumar et al. 1999), while the aqueous extract (2%) of *Vitex negundo* L.

caused 26.6% adult mortality. Garlic crude extract (1.25 to 5.0%) killed 16 to 65% and 4 – 20% of *C. carnea* and *C. septumpunctata*, respectively (Nasseh et al. 1993). Leaf fractions of *Peganum harmala* L. have shown a significant effect on adult emergence of the parasitoid, *Microplitis rufiventris* Kok. (Shonouda et al. 2008).

Effects on honeybees/pollinators

Little attention has been paid to the effects of neem and other botanical pesticides on the honeybee, *Apis mellifera* L. and other pollinators. Neem formulation, Margosan-O is non-toxic to worker honeybees when applied at doses of up to 4,418 ppm azadirachtin/ha (Schmutterer and Holst 1987). Three sprays of an enriched formulation of neem seed kernel extract (AZT-VR-K) at 500 ppm/litre on tansy phacelia, *Phacelia tanacetifolia* Benth. and other plants in full bloom had no negative effects on the queen, and about 3,000 worker bees in a screen house study. However, some damage was observed in two smaller colonies consisting of a queen and about 200 to 300 workers, where a number of young bees were unable to emerge from the cells (Schmutterer and Holst 1987). Peng et al. (2000) reported the LC_{50} of 180.92 ng ml^{-1} (purified azadirachtin) and 100.13 ng ml^{-1} (formulated Azadirachtin) against honey bees. Larvae were more sensitive than the adults. High toxicity of pyrethrum has been observed with the average lethal dose (LD_{50}) for honeybees at 0.022 mg per bee (Casida and Quistad 1995). Further, the direct contact of honeybees to pyrethrum may have greater toxicity (Cox 2002). Higher residue of rotenone in honey and wax, and a reduction in adult population was observed by Satta et al. (2008). Rotenone (1%) has also been found to cause severe mortality of brood and adult bees (Gregorc and Skerl 2007).

Effects on earthworms

Treatment of soil with either ground neem leaves or ground neem seed kernels (each treatment consisted of 5% by volume of the treated soil) slowed down the entry of the earthworm, *Eisenia foetida* (Savi.), indicating a short-term repellency effect. However, the earthworm population in neem-treated soil (both treatments) gained significantly more weight after 4 weeks than in the control plots, and the survival and fecundity of earthworms in the neem-treated soil were significantly greater than the untreated soil (Rossner and Zebitz 1987). Earthworm, *Lampito mauritii* Kin. in pots with 40 g neem cake/kg soil died after 20 days of exposure (Bakthavathsalam 2003; Bakthavathsalam and Ramakrishnan 2004). A reduction of 78 and 61% in cocoon production, and 75 and 71% in hatching over control were noted in the worms kept in pots with 20 and 4 g of neem cake/kg soil, respectively. There were no adverse effects on the growth rate. Aqueous and alcohol extracts of *Chromolaena odorata* (L.) leaves showed antihelminthic activity against the Indian earthworm, *Pheretima posthuma* Kinb. (Sheela and

Viswanathan 2009) due to its anatomical and physiological resemblance with the intestinal roundworm parasites of human beings. Petroleum ether, chloroform, and methanol extracts obtained from the bark and leaves of *Anogeissus latifolia* (Roxb. ex DC.) showed moderate antihelmintic activity against *P. posthuma* (Parvathi et al. 2009).

Effects on fish and other aquatic organisms

Little is known about the effects of neem products on nontarget aquatic organisms. An acute toxicity (at LD_{50}) of Margosan-O (a neem based formulation) was observed on the rainbow trout, *Salmo gairdneri* Walb. at 96 h in 8.8 ml/litre of water, and in bluegill sunfish, *Lepomis macrochirus* Rafin. at 96 h in 37 ml/litre water (Larson 1987). Young guppies, *Lebistes reticulatus* (Peters) tolerated up to 100 ppm AZT-VR-K/litre water (Zebitz 1987). Toxicity of Margosan-O to fish is probably caused by its petroleum oil content (15%) or another compound used in the formulation (Schmutterer 1990). Margosan-O is also toxic to the water flea, *Daphnia magna* Straus and other invertebrates that inhabit stagnant water (Larson 1987). Aqueous neem seed kernel extract has been reported to kill the ostracod, *Heterocypris luzonensis* Neale, which feeds on nitrogen-fixing blue-green algae (Grant and Schmutterer 1987). Recommended dose (5%) of neem seed kernel extract is toxic to Nile tilapia, *Oreochromis niloticus* (L.), but neem oil (50% EC at 3 ml/litre) did not harm the fish (Fernandez et al. 1992). In laboratory assays, the LC_{50} of neem oil for carp, *Cyprinus carpio* L. was 302.7 ppm at 24 h after treatment (Fernandez et al. 1992). There was no mortality of the Java tilapia, *Oreochromis mossambicus* (Peters) when exposed to <0.01 % neem seed kernel extract or neem oil (50% EC) (Jayaraj 1992). Significant genotoxicity was induced by azadirachtin in *O. mossambicus* (Chandra and Khuda-Bukhsh 2004). Neem seed kernel extract and neem oil were not toxic to the common rice field toad, *Bufo* sp. when used at <0.1% concentration (Jayaraj 1992). The Zebrafish, *Danio rerio* (Ham.) is more sensitive to deltamethrin than to the neem based product, Achook (Ansari and Sharma 2009). Azadirachtin-A has been reported to be toxic to the nontarget aquatic macro-invertebrates in Montana river systems in the USA. LC_{50s} (24 h) for five insect species, *Drunella grandis* (McDun.), *D. doddsi* (Needham), *Skwala parallela* (Frison), *Brachycentrus occidentalis* Banks, and *B. americanus* (Banks), and one isopod species, *Caecidotea intermedia* (Forbes) varied from 1.8 to 9.2 ppm (Dunkel and Richards 1998).

Rotenone has been used traditionally to clear ponds of unwanted organisms and trash fish, which may predate on fish when the ponds are stocked (Agbon et al. 2004). Many studies have been published regarding the effects of rotenone on the nontarget aquatic life including microorganisms, zooplankton, and phytoplankton (Melaas et al. 2001; Ling 2003; Agbon et al. 2004; Finlayson et al. 2011). Rainbow trout is drastically affected by rotenone (Finlayson et al. 2011). Aquatic invertebrates have been reported to have a wide range of sensitivity to rotenone with 96 h LC_{50}

values ranging from 0.002 to 100 ppm (Ling 2003). Bottom dwellers are less sensitive than the planktonic invertebrates, and smaller ones are more sensitive than the larger invertebrates. Invertebrates that respire through gills are more sensitive than those respiring cutaneously or through lamellae or spiracles, make use of respiratory pigments, or the ones that can breathe atmospheric oxygen. Rotenone at 1 to 1.5 ppm resulted in 100% mortality of lotic invertebrates, and >3 ppm of lentic invertebrates and aquatic adult insect taxa (e.g., Heteroptera and Coleoptera) depending on the exposure time. The fish, *Aphyosemion gardneri nigerianum* Claus. was the most sensitive to water extract of the leaves of *Tephrosia vogelii* Hook, while the mosquito larvae were the least sensitive. Nicotine was highly toxic to fish and mortality occurred within 44 h after exposure to 3.2 ppm concentration (Konar 1969).

The LC_{50} of botanical pesticides such as rutin, taraxerol and apigenin against the fresh water fish, *Channa punctatus* Bloch were 1.128, 2.407 and 2.021 mg/l, respectively at 96 h (Shahi and Singh 2010). Haemoglobin and erythrocytes in *C. punctatus* as a result of exposure to mahua, *Madhuca longifolia* (J. Konig) oil cake decreased by 23.9 and 26.66%, respectively, after 5 days at 58 ppm concentration of mahua oil cake (Chatterjee et al. 2008). However, Cd-induced toxicity in *O. mossambicus* appeared to be ameliorated to some extent by azadirachtin. *T. vogelii* water extract LC_{50} to the fish, *A. gardneri nigerianum* was 0.24 mg L^{-1} (Agbon et al. 2004). *Phytolacca dodecandra* (L Herit), a plant with molluscicidal properties is used against water flea, and it is highly toxic to fish and other beneficial aquatic organisms. It was also toxic to the alga, *Selenastrum capricornutum* Printz (Lambert et al. 1991).

Effects on warm-blooded animals

Botanical pesticides have been used for many years and are well entrenched in various cultural practices, but this does not necessarily mean that they are always safe. They have been considered safe to higher animals because they are readily biodegradable in nature. However, there are a number of reports indicating that several natural plant products are toxic to warm blooded animals. Neem leaf extracts cause mitotic chromosome abnormalities in bone-marrow cells (Awasthy et al. 1995, 1999), and genotoxicity in male germ cells of mice (Awasthy 2001). Adverse effects of neem leaf extract have also been observed on head morphology and sperm count in murine germ cells (Khan and Awasthy 2003). Oral intake of neem oil has shown encephalopatic effects (Lai et al. 1990) and acute toxicity in humans (Sinniah et al. 1982). Acute toxicity of neem oil has been observed in rats and rabbits by Gandhi et al. (1988). Convulsive jerks, labored respiration, and death have been observed in mice at higher doses of neem oil (Tandan et al. 1995). Sub-acute administration of neem oil reduced the body weight in female rats (Dhaliwal et al. 1998) and lowered the glucose levels in rabbits (Khosla et al. 2000). Negative effects of azadirachtin on

liver function (Abdel Mageed et al. 2001) and on blood constituents (Radwan et al. 2001) have also been studied in rats. Tests for skin and eye irritation, inhalation, mutagenicity, and immune response were low enough to allow its registration by Environmental Protection Agency (EPA) (Larson 1987; Schmutterer 1990). Neem oil reportedly caused the death of children in India when used to cure minor ailments (Sundaravalli et al. 1952). In Malaysia, children who ingested unrefined neem oil acquired a Reye-like syndrome, a severe disorder that involves swelling of the brain, liver, and other organs (Sinniah et al. 1982). In South India where neem oil is widely used, epidemiological studies revealed that numerous deaths were caused by ingesting neem oil (Sinniah et al. 1982), possibly because of contamination of neem seeds with aflatoxin-producing strains of the fungus, *Aspergillus flavus* Joh. Hein & Fried. (Sinniah et al. 1982). When extracted from clean and fungus-free seed kernels, neem oil did not cause any oral toxicity in laboratory rats even at 5,000 mg/kg body weight (NRC 1992).

Neem formulation of AZT-VR-K at 5,000 mg/kg body weight caused no acute oral toxicity to rats or dermal toxicity to rabbits (Schmutterer 1990). Methanol neem seed kernel extract at 5,000 and 8,750 mg/kg body weight and neem oil at a concentration of 5,000 mg kg^{-1} body weight caused no acute oral toxicity to rats. Further, sub-acute injections with an aqueous neem seed kernel extract (25 and 50 g kernel/litre) caused no toxicity and when 50 g kernel/litre was applied, there was no eye irritation or dermal toxicity (Schmutterer 1990). Some birds and bats eat the pulp of neem fruits without apparent harmful effects, and in areas such as Ghana's Accra Plains, neem fruits are a main source of their diet (NRC 1992). The seed extract of *A. squamosa* has been reported to induce genetic toxicity and oxidative stress in rats (Grover et al. 2009).

Nicotine derived from the leaves of *N. tabacum* has been widely used as an insecticide against many insect pests. Although promising results have been demonstrated against many pest insects, toxicity studies on nontarget organisms have been limited (Coats 1994). The LD_{50} values for acute toxicity via oral route have been reported to be 3–188 mg kg^{-1} for different mammals (Coats 1994). Severe toxicity from dermal absorption or inhalation (by greenhouse fogging) has also been demonstrated. Nicotine is a neurotoxin, affecting primarily ganglia, and thereby, inducing rapid toxicity that leads to paralysis and eventually death within few minutes (Jaffe 1985). Nicotine has resulted in hundreds of accidental fatalities and suicides (Ray 1991). Furthermore, chronic exposure causes reproductive and cardiac disturbances (Coats 1994).

Rotenone has been found to generate reactive oxygen species (ROS) that can interact with proteins, DNA and RNA, changing their functions or inducing lipid peroxidation, eventually leading to cell death (Suzuki et al. 1997; Betarbet et al. 2000; Gao et al. 2002; Ling 2003). Rotenone also leads to some of the symptoms associated with Parkinson's disease (Betarbet et al. 2000; Caboni et al. 2004). The local effects on the body by rotenone

include conjunctivitis, dermatitis, sore throat, and congestion (Ling 2003). It also leads to mild irritation and vomiting. Inhalation can cause elevated respiration that can lead to depression and convulsions. In rats, the oral LD_{50} of rotenone ranges from 132 to 1,500 mg/kg (Hien et al. 2003). Humans are also susceptible to rotenone, and the oral lethal dose is 300 to 500 mg/kg. In mice, the induced oral LD_{50} has been found to be 350 mg/kg; rabbits have LD_{50} of 600–2,000; and guinea pigs an LD_{50} of 12–200 (Hien et al. 2003). Rotenone is highly toxic when administrated intravenously rather than orally. Teratogenic effects of rotenone have been reported in neonates from pregnant rats fed with small amounts (5 mg/kg), however, no skeletal deformities were observed at 10 mg/kg (Johnson and Finley, 1980). Ray (1991) reported that chronic toxicity of rotenone may lead to changes in liver and kidneys. LD_{50} against mammals is 25–3,000 mg kg^{-1}, depending on the origin and purity of the extract, carrier and the animal species tested (Ray 1991). Rotenone affects the respiratory tract, blocks the electron transport chain, and thereby, prevents the oxidation of NADH, and death mainly because of respiratory failure (Hollingworth et al. 1994; Sanchez et al. 2008). Carcinogenic effects of rotenone have also been reported (Coats 1994). Exposure to rotenone causes irritation of the skin. Residual effects of rotenone have been reported in some agricultural crops (Cabras et al. 2002). However, no rotenone residue was observed in two Italian olive cultivars (Casacchia et al. 2009).

Inhalation of pyrethrum causes asthmatic breathing, sneezing, nasal stuffiness, headache, nausea, lack of coordination, tremors, convulsions, facial flushing and swelling, and burning and itching sensations in humans (Extoxnet 1994; Cox 2002). The lowest lethal oral dose of pyrethrum is 750 mg/kg and 1,000 mg/kg for children and adults, respectively. In rats, the lowest lethal oral dose of pyrethrum ranges from 200 mg/kg to >2,600 mg/kg. For mice, the pyrethrum oral LD_{50} is 370 mg/kg (Extoxnet 1994; Cox 2002). Pyrethrins at higher doses may cause severe damage to immune and central nervous systems, and liver damage is more common due to poisoning by pyrethrum. It has been suggested that there is a possibility of leukemia cancer on exposure to pyrethrins (Cox 2002). No birth defects have been reported in mammals by pyrethrins (Extoxnet 1994). Casida and Quistad (1995) did not observe any teratogenic effects in rats at 600 mg/kg/day.

Crude methanol leaf extract of *T. vogelii* results in enteritis, congestion of the lungs, liver, kidneys and spleen in mice at doses ranging from 10 to 10,000 mg kg^{-1} body weight following oral administration. The median lethal dose (LD_{50}) of leaf extract was 134.16 mg/kg (Dzenda et al. 2007). Ryanodine, obtained from *Ryania speciosa* Vahl, a diterpenic alkaloid, is a neuromuscular poison (Isman 2006). Sabadilla obtained from the seeds of South American lily *Schoenocaulon officinale* A. Gray ex Benth. contains cevadine type alkaloids. The mode of action is similar to that of pyrethrins. Cevadine alkaloids are highly toxic to mammals (rat oral LD_{50} is 13 mg kg^{-1}) (Isman

2006). Some plant oils contain photoactive molecules like furocoumarins, e.g., *Citrus bergamia* Risso & Poit. essential oil contains psoralens that bind to DNA under ultraviolet light exposure, producing severe toxicity and mutagenicity (Averbeck et al. 1990). Various essential oils such as *Fusanus spicatus* R. Br., *Citrus aurantium dulcis* (L.), and *Cymbopogon citratus* Stapf. have been found to be highly cytotoxic to mammalian cells under *in vitro* conditions (Dijoux et al. 2006). Acetogenins from custard apple have also been found to be harmful to mammals. The LD_{50} value of acetogenins for mammals is <20 mg kg^{-1} (Londershausen et al. 1991).

Nutritional studies with weanling rats have indicated good growth performance and food intake using neem oil, and the results were comparable to those fed on groundnut oil, and the cholesterol and triglycerides levels in blood serum and liver decreased in rats fed on neem oil (Sankaram et al. 1987). Protein consumption, weight gain, and protein utilization were lower in rats fed on neem meal than in rats fed on a casein diet. Feeding neem meal at 84% level of the total diet did not cause any toxic effects to the rats. Thus, neem cake obtained after extracting neem bitters can possibly be used as cattle feed. However, long-term toxicity studies need to be undertaken to recommend neem kernel meal in animal rations (Sankaram et al. 1987). Inclusion levels of neem seed cake in diet resulted in elevated protein turnover. Nitrogen catabolism was also elevated since uric acid values in neem-treated birds were higher than in the control birds (Virmani et al. 2005). Neem leaf extract treated birds showed mild depression, isolation in some birds, and lesser body weight gain after 4 weeks (Sridhar et al. 2003). Broilers (4-week-old) fed on neem seed cake (NSC) (5, 10 and 15%) exhibited decreased feed intake, dullness, depression, ruffled feathers, stunted growth, reduced body weight, and lowered head in a few birds (Lather et al. 2002).

Pest resurgence and development of resistance

Many chemical pesticides cause pest resurgence, resulting in increased rather than decreased pest populations. This is because the natural enemies of pests are killed and the fecundity of insect pests is stimulated. An important challenge is to find out whether botanical pesticides will cause resurgence of insect pests. Some researchers believe that insect resistance to neem products is unlikely, because of its multi-mortality and multi-behavior modifying factors that are more difficult for the pest to defy than the pesticides with single mechanism of action (Saxena 1989). However, Larew (1992) suggested that increased use of botanical pesticides might lead to the development of resistance in insect populations. Vollinger (1987) explored the possibility of the diamondback moth becoming resistant to neem based pesticides. In this context, the lessons learnt with the development of resistance to the bacterium, *Bt* and the transgenic plants expressing *Bt* genes should serve as a useful guideline. Although, insect populations with resistance to *Bt* have been selected under laboratory

conditions for several insect species, there is only one instance of development of resistance to *Bt* in the diamondback, *P. xylostella* under field conditions (Tabashnik et al. 1990). Thus, there is a need for more scientific investigations on the possibility of development of resistance to botanical pesticides. While there are several instances of development of resistance to synthetic pyrethroids in insects all over the world, there is no confirmed report of resistance development to natural plant products possibly because a number of molecules are present in the botanical pesticides.

Phytotoxicity

Phytotoxicity is an important feature that limits the use of neem oil. Phytotoxicity occurs quite commonly at doses that are effective against insect pests (Schmutterer 1990). Loke et al. (1992) reported that 3% neem oil was toxic to cabbage. *Brassica oleracea capitata* L. plants surviving at lower concentrations were scorched and retarded. Mustard, *Brassica juncea* Czern. plants treated with 3% neem oil had 30% mortality, and those treated with 4% neem oils suffered 40% plant mortality (Loke et al. 1992). The surviving plants were scorched, retarded, and yielded significantly less than non-treated plants. Scorching occurred at 2% and higher concentrations of neem oil (Loke et al. 1992). All the plants survived and produced a yield not significantly different from that of untreated control. However, rice grain ripened unevenly. Cabbages, Chinese mustard (*Brassica chinensis* L.) and rice seedlings sprayed with 0.5, 1.0, 2.0, 3.0 and 4.0% of neem oil exhibited phytotoxic effects, and the plants after 4 sprays showed pronounced scorching and growth retardation (Loke et al. 1992). Neem oil at >10% concentration caused higher phytotoxicity on rice (Mochizuki 1993). The neem seed extract exhibited phytotoxic effects on leaves and flowers of gerbera at 14 days after treatment (Kadam et al. 2008). The neem formulations showed higher phytotoxicity to *Prunus domestica* L. at 6.4 and 8% concentration (Bajwa and Zimmermann 1997). Mourier (1997) reported varying degrees of phytotoxicity by the neem kernel water extract on cassava at 1, 10, and 25% concentration. Limonene, a naturally occurring monoterpene found in citrus and other fruits, conifers and spices, is used as an insecticide against many insect pests including mealy bugs, scales and whiteflies (Hollingsworth 2005). Limonene solution containing 0.5% APSA-80 (all purpose spray adjuvant) was found to be highly phytotoxic to *Gardenia augusta* (L.) Merr. (Hollingsworth 2005). Moss, ferns, ginger and certain types of dracaena, and delicate flowers suffered severe damage due to limonene at 1% (Hollingsworth 2005). Ibrahim et al. (2001) observed greater phytotoxicity in strawberries due to limestone at >3% concentration, and to cabbage and carrot seedlings above 9% concentration. Xuan et al. (2004) reported phytotoxicity of *A. indica* to various crops. Phytotoxicity of oil extract of neem was observed in *Ixora coccinea* L., causing lesions in 35% of the treated leaf area (Esparza-Díaz et al. 2010). Pyrethrin, potassium salts of fatty acids, and cinnamaldehyde were consistently more phytotoxic than

the insecticides on various plants including Spanish lavender (*Lavandula stoechas* L.), oregano (*Origanum vulgare* cv. Santa Cruz), and rosemary (*Rosmarinus officinalis* L.) (Cloyd and Cycholl 2002). Despite their advantages, phytotoxicity concerns might limit the large-scale use of botanical insecticides. It is important to find ways to minimize the phytotoxic effects of botanical pesticides through the development of safer formulations.

Conclusions

Several botanical pesticides have been found to be effective in controlling insect pests. However, only a few of them have been exploited commercially. Although considered to be environmentally safe, there is limited information on the environmental effects of botanical pesticides on nontarget organisms. Botanicals are readily biodegradable, but may not necessarily be safe to certain nontarget organisms in the environment. Both "no-effect" and "slight-effect" levels of a product use should be determined, particularly for parasitoids, predators, and warm-blooded animals. It is also important to differentiate between laboratory and field experiments because some products or molecules might show divergent results under controlled and field conditions. There is a need to generate information on natural plant products relative to their metabolic products, acute and chronic toxicity, mutagenesis, allergenicity, teratogenicity, etc., as done in the case of synthetic pesticides, with due consideration for their safety to the environment to place these chemicals on a sound footing for use in integrated pest management.

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