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# Sustainable and Novel Eco-friendly Approaches Towards Integrated Disease and Vector Management

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## Abstract

Herbal medicine has been used since time immemorial for treating a large number of human ailments. Despite the widespread use of western system of medicine, in recent years, most people even in the western world resort to herbal medicines as holistic, inexpensive treatments allude the common man. In addition, western medicine does not offer solutions to chronic incurable diseases and other such problems that confront humanity. Most patients undergoing cancer therapy or treatment for AIDS, rheumatoid arthritis, etc. use herbal medicines in the hope of a cure irrespective of the recommendation by the physician. Many pesticides are known to create significant health risks like birth defects, nervous system breakdown and cancer. The only way out is the use of herbal biomedicines and herbal pesticides.

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## 2.1 Introduction

Presently, there is a paradigm shift from the use of synthetic drugs to the acceptability of herbal biomedicines. This change of trend is due to the realization of harmful effects of synthetic drugs and the searching for alternative ways of cure. The market for herbal biomedicine for human and animal con-

sumption is growing. Similarly, the demand for herbal insecticides is on the rise. Worldwide, herbal biomedicines have an estimated annual growth rate between 5 % and 15 %, and the global total herbal drug market is about US \$62 billion. In India, the value of herbal product trade is estimated to be approximately US \$10 billion per annum and US \$1.1 billion is the annual export value, while for China, it is US \$48 billion with an export value of US \$3.6 billion. Apart from India, currently, the United States is the largest market for Indian herbal products accounting for about 50 % of the total exports. Traditional Chinese medicine (TCM) and herbal medicines from Japan, Hong Kong, Korea and Singapore find extensive use in the United States (Citarasu 2010).

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At the global level, there is a shifting from antibiotics over to natural products due to the development of multidrug resistance in pathogens. Herbal medicine is comparatively low in cost, although it is becoming an advanced way of traditional phytotherapy. Plants are the potential store of safer and cheaper chemicals and cure various diseases due to their active principles having antioxidant and anti-microbiological activities. The occurrence of active principles like alkaloids, flavonoids, pigments, phenolics, terpenoids, steroids and essential oils in plant products is reported to promote various activities like antistress, growth promotion, appetite stimulation, tonic and immunostimulation, aphrodisiac and antimicrobial properties (Citarasu 2010).

In addition, serious environmental problems have been encountered as a result of intensive application of pesticides in modern agriculture (Dua et al. 1998; Waliszewski et al. 1999; Singh et al. 2004). Some of the pesticides are highly persistent compounds and pose immense environmental concerns, and some examples are pentachlorophenol (PCPs), polychlorinated biphenyls (PCBs), atrazine (S-triazines), organochlorines (OCs), organophosphates (OPs) and carbamates. The use of these pesticides in agriculture contaminates the adjoining freshwater bodies posing threat to potential freshwater organisms especially important animals, fishes and prawns (Saravanan et al. 2003; Selvarani and Rajamanickam 2003; Park et al. 2004). Recently, the uses of herbal products have got unparalleled momentum throughout the world. Herbal biomedicines are increasingly finding applications for prophylactic and therapeutic purposes, often even for diseases for which treatment modalities are unavailable or ineffective.

On the other hand, the problems associated with the use of synthetic pesticides and insecticides are manifold. Many pesticides are known to create significant, known health risks to people, including birth defects, damage to the nervous system, disruption of hormones and endocrine systems, respiratory disorders, skin and eye irritations and various types of cancer. Also, exposure to persistent organic pollutants through diet has been known to cause breast and other types of cancer, immune system suppression, nervous

system disorder, reproductive damage and disruption of hormonal systems (Kristin 2000). An alternate strategy to overcome the problems associated with the use of synthetic insecticides and pesticides is the use of green herbal insecticides for integrated management and vector control.

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## 2.2 Herbal Biomedicines

An overview of herbal biomedicines as antibacterial, antiviral, antifungal and growth-enhancing agents and as immunostimulant, antistress and appetizing agents as per Citarasu (2010) is provided below.

### 2.2.1 Antibacterial Agents

The herbal compounds responsible for antibacterial activities include mainly phenolics, polysaccharides, proteoglycans and flavonoids present in plants. The antibacterial active principles of the herbal products may act by breaking the cell wall, by blocking DNA and protein synthesis and by inhibiting the enzyme synthesis and then interfering the cellular signalling mechanism. Also, it has been proposed that the means of the antimicrobial effects engage the inhibition of various cellular processes, followed by an increase in plasma membrane permeability and finally ion leakage from the cells. The antagonistic effects of the methanolic extracts of *Coleus aromaticus* of Lamiaceae and *Tabernaemontana divaricata* of Apocynaceae family were found to be most effective against the fish pathogen *Aeromonas hydrophila*. *Ocimum basilicum* extracts, specially ethanol, methanol and hexane extracts, have shown excellent in vitro antimicrobial properties. Another example is of Indian almond, *Terminalia catappa*, where the extract at a concentration of 0.5 mg ml<sup>-1</sup> has shown the growth inhibition of two strains of *A. hydrophila* (Citarasu 2010).

### 2.2.2 Antiviral Agents

Many herbs have potent antiviral activities. Oleuropein derived from olive tree leaf (*Olea*

*europaea*) was found to control salmonid rhabdovirus. White spot syndrome virus (WSSV) was effectively suppressed by the methanolic extracts of the herbs *Acalypha indica*, *Cynodon dactylon*, *Picrorhiza kurroa*, *Withania somnifera* and *Zingiber officinalis*. Strong antiviral activity against WSSV was shown by 20 species of Indian traditional medicinal plants such as *Aegle marmelos*, *C. dactylon*, *Lantana camara*, *Momordica charantia* and *Phyllanthus amarus* in the form of petroleum ether, benzene, diethyl ether, chloroform, ethyl acetate, methanol and ethanol extraction. The mode of action of the herbal active compounds includes inhibition or blocking of the transcription rate of the virus and thereby reducing the replication rate in the host cells (Citarasu 2010).

### 2.2.3 Antifungal Agents

Fungi are increasingly becoming resistant to conventional drugs, and the limited numbers of antifungals currently used are showing side effects. The fungal infections, whether superficial or systemic, often pose considerable management problems and are still a major concern. Hence, the substitute 'herbal formulations' have become an option of improved interest. Many different plant extracts have been tested for in vitro antifungal activity. For example, the plant *Datura metel* L. is a source of novel antifungal molecule, 2-(3,4-dimethyl-2,5-dihydro-1H-pyrrol-2-yl)-1-methylethyl pentanoate. It is reported to show anti-*Aspergillus* properties and also possess activities against ten clinical isolates of *Candida* and 19 clinical isolates of *Aspergillus* and also against a few marine fungi. *O. basilicum* extracts were effective in controlling the pathogens *Aspergillus flavus* and *Fusarium oxysporum* (Citarasu 2010). Herbal-based fungicidal products like coconut diethanolamide, *Azadirachta siamensis* and *Melaleuca alterniflora* along with an amalgamation of synthetic fungicide showed prominent fungicidal activities against *Aphanomyces invadans*. The mode of action of the herbal antifungal agent is by altering cell permeability, cell wall lysis, affecting metabolism, and RNA and protein synthesis (Citarasu 2010).

### 2.2.4 Growth-Enhancing Agents

Many herbal products like those based on *Hygrophila spinosa*, *Withania somnifera*, *Zingiber officinalis*, *Solanum trilobatum*, *Andrographis paniculata*, *Psoralea corylifolia*, *Eclipta erecta*, *Ocimum sanctum*, *Picrorhiza kurroa*, *Phyllanthus niruri*, *Tinospora cordifolia*, etc. have the potential of growth promotion, anti-stress activities, immunostimulation and antibacterial properties. Livol (IHF-1000), a well-explored commercial herbal growth promoter, drastically improved digestion, and the dietary ginseng herb greatly improved the growth performance, diet consumption efficiency and also haematological indices. Stressol-I and stressol-II, the herbal products enriched with *Artemia nauplii*, increased the growth rate significantly and reduced the osmotic stress in *Penaeus indicus*. Similarly, the herbal product 'Tefroli' improved the growth rate and moulting competence when fed to *Penaeus monodon* postlarvae and 'Trasina', a well-known herbal product, improved the growth and stress tolerance efficiencies radically (Citarasu 2010).

### 2.2.5 Immunostimulant, Antistress and Appetizing Agents

The methanolic extracts of five herbal medicinal plants, viz., *Cynodon dactylon*, *Aegle marmelos*, *Tinospora cordifolia*, *P. kurroa* and *Eclipta alba*, showed better performance of haematological, biochemical and immunological parameters when fed to shrimps. Extracts of the herbs *O. sanctum*, *W. somnifera* and *Myristica fragrans* were efficient in improving the immune parameters like bactericidal activity, phagocytic activity and serum albumin-globulin (A/G) ratio against *Vibrio harveyi*. The immunostimulants obtained from herbs like *Emblica officinalis*, *Cynodon dactylon* and *Adhatoda vasica* found to improve the immune system and reduce microbial contamination in the goldfish *Carassius auratus*. Dietary intake of *O. sanctum* also enhanced the immunostimulatory effects, antibody response and disease resistance. Herbs like *Tinospora cordifolia* and *Picrorhiza kurroa* have been used as

an antistress agent and are known to have the ability to scavenge free radicals, and the mode of action is similar to superoxide dismutase and metal ion chelators. Herbal drugs also act as appetite stimulators as they improve the performance by increasing gut secretions. Intake of some hot spices increases the salivation and, hence, improves digestibility by increasing enzyme production (Citarasu 2010).

### 2.3 Herbal Insecticides

Herbal insecticides have an unbeaten track record in insect pest control. However, as of now herbal insecticides are of a small part of the whole insecticide/pesticide industry as large part is covered by synthetic ones. Recently, public concern about the use of synthetic insecticides has grown dramatically resulting in organic agriculture, restricting synthetics and following herbal insect pest control. In many parts of Europe and North America, the use of synthetic pesticides are now excluded in urban areas favouring unconventional control measures such as biopesticides, biocontrol and other methodologies.

Some of the advantages of plant-derived pesticides are that they are selectively toxic, do not bioaccumulate and exhibit relatively short persistence in the environment (Shanker and Solanki 2000) and food chain. There are constant attempts going on for searching new classes of insecticides derived from plants having low toxicity and less persistence in nature (Singh et al. 1996; Kloos and Mc Cullough 1987) like alpha-terthienyl (Nivsarkar et al. 2001). Many plant products like alkaloids, vegetable oils, triterpenoids, rotenone and azadirachtin have been used in the development of alternative pest control agents (Shanker and Solanki 2000). The reasons that have prompted the use of plant products and their encouragement by different countries are because of their properties, like high pesticidal activities, fast availability, easy biodegradability with less danger of environmental contamination, little or no mammalian toxicity, solubility in water, low cost, etc.

The long history of safety of the natural products has provided a lot of confidence for their further exploration. For example, many new

botanical pesticides, such as piperamides and alpha-terthienyl, show that they are degraded in the environment in a couple of hours or days. Phytochemicals in botanical extracts are diverse, and the presence of many analogues of one compound increases the efficacy of plant extracts through analogous cooperation and the evolution of pesticide resistance under selection pressure in course of time. Moreover, there is immense scope of deriving many more new novel compounds having insect repellent or killing properties as huge diversity of novel phytochemicals is available. The process of coadaptation is never ending across the plant kingdom for defence against insect pests and diseases, and therefore, plants possibly synthesize a number of such compounds (Arnason et al. 2015).

There are reports of plant-derived compounds as insect behaviour modifying antifeedants, essential oils as repellent as well as insecticides and many more compounds with novel modes of action. Despite these developments, the herbal pesticide market has not as grown as much as for synthetics, even today. The main reasons behind this are the barriers of costs involved in toxicology testing for new herbal products, cost-effective supply of plant product, quality control and lack of stability, competition from other biopesticides and biocontrol agents (Arnason et al. 2015).

Plants, the richest source of renewable bioactive organic compounds, produce around 40,000 compounds, of which around 10,000 are secondary metabolites and responsible for defensive activities (Cooper and Johnson 1984). Many plant-derived defensive chemicals of various categories causing behavioural and physiological changes in pests have been already identified and explored. A few of these important bio-compounds (Singh et al. 2010; Bernhoft 2010) are described below:

- (a) *Alkaloids*: Alkaloids are naturally occurring organic bases with at least one nitrogen atom either in the heterocyclic ring or linked to an aliphatic skeleton. These are colourless, crystalline, nonvolatile solids, with little solubility in water but having good solubility in ethanol, ether and chloroform.
- (b) *Glycosides*: Various types of secondary metabolites joining to a mono- or oligosac-

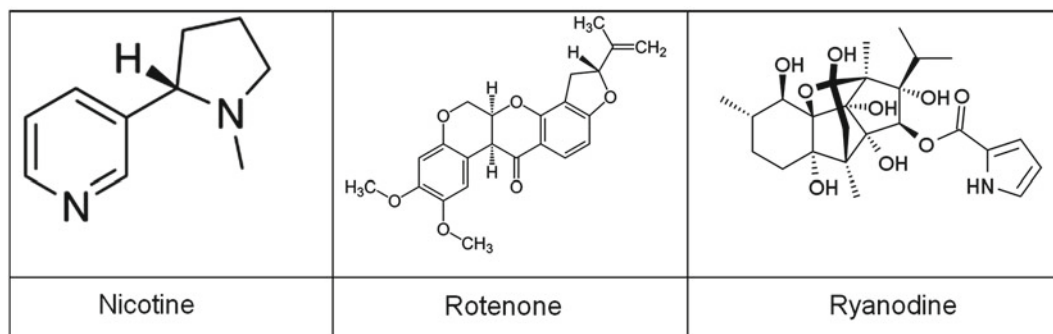
- charide or to uronic acid make the glycosides, which are composed of two parts called the glycone and aglycone. The major groups of glycosides are cardiac glycosides, cyanogenic glycosides, glucosinolates, saponins and anthraquinone glycosides. Furthermore, flavonoids frequently occur as glycosides.
- (c) *Flavonoids*: Flavonoids are C<sub>15</sub> compounds (exclusive of O-alkyl groups and secondary substituents), composed of two phenolic nuclei connected by three carbon units.
- (d) *Saponins*: Saponins are naturally occurring plant glycosides consisting of a sugar moiety and an aglycone unit. The saponins having toxic activity are the monodesmosidic saponins (sugar moiety only at position C-3); on the other hand, bidesmosidic saponins (sugar moiety both at C-3 and C-28) are inactive.
- (e) *Tannins*: Tannins are complex phenolic compounds, which can be divided into two groups, (i) the esters of gallic acid and also glycosides of these esters known as the hydrolysable tannins and (ii) polymers derived from various flavonoids, the condensed tannins.
- (f) *Resins*: Resins are complex lipid-soluble mixtures consisting of diterpenoid, triterpenoid, monoterpenoid and sesquiterpenoid. Resins are mostly present in woody plants, but resins to some extent are also present in herbaceous plants. Most resins are having properties like antimicrobial and wound healing, and they are generally safe in handling, but reports of contact allergy are there.
- (g) *Lignans*: Lignans are lipophilic, are composed of two phenylpropanoid units forming an 18-carbon skeleton, have various functions related to plant cell membranes and are present in highly concentrated oil seeds.
- (h) *Iridoids*: Iridoids are the monocyclic monoterpenoids, which possess a lactone ring as a replacement of the  $\rho$ -menthane skeleton.
- (i) *Furanocoumarins*: Furanocoumarins are those compounds in which the 1,2-benzopyrene skeleton is fused with a furan ring.
- (j) *Diterpenoids*: Diterpenoids have a general molecular formula of C<sub>20</sub> H<sub>32</sub>, are not steam volatile and are usually obtained from plants. A new class of diterpenes which are esters of phorbol possess high toxicity against pests.
- (k) *Monoterpenoids*: Monoterpenoids are the major constituents of essential oils and are made up of two isoprene units (C<sub>10</sub> H<sub>16</sub>).
- (l) *Sesquiterpene lactones*: Sesquiterpenoid lactones possess a sesquiterpene skeleton having an additional lactone ring.
- (m) *Proteins and peptides*: There are proteins and peptides with bioactivity which are not hydrolysed in the digestive tract and exert their specific action, for instance, ricin in seeds of *Ricinus communis* (castor bean).

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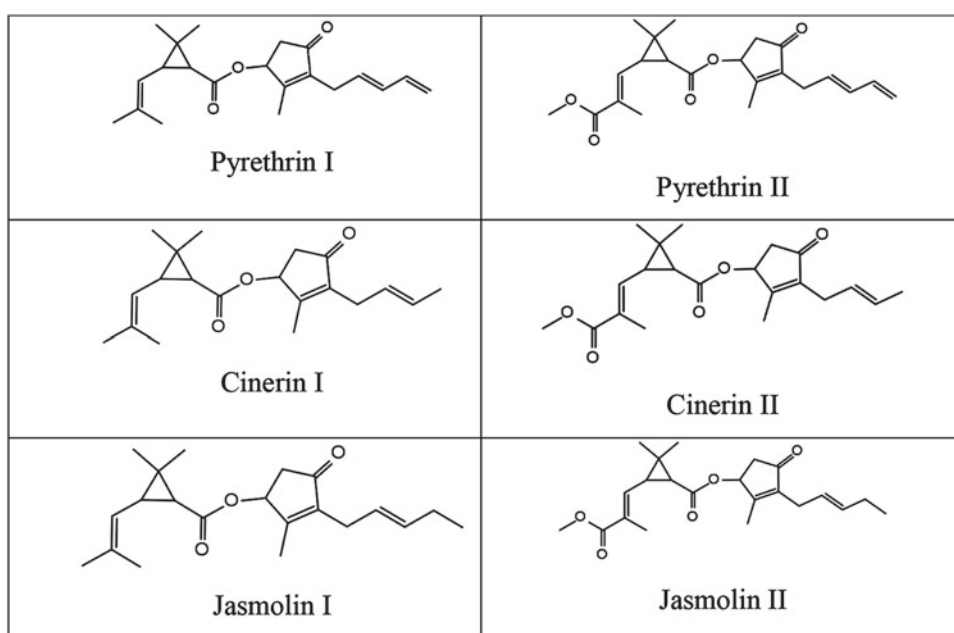
## 2.4 Conventionally Used Herbal Insecticides

Some of the conventionally used herbal insecticides/pesticides include nicotine, rotenone, ryania, sabadilla and pyrethrum. Nicotine (Fig. 2.1), an alkaloid obtained from the leaves of tobacco plants (*Nicotiana tabacum*), is an effective insecticide/pesticide. The insecticide resulting from extracts of the tropical legumes *Derris* and *Lonchocarpus* is named as rotenone (Isman 2006). The main active principle, the isoflavonoid rotenone (Fig. 2.1), is extremely poisonous to insects and fish, due to its fast uptake and inhibitory activity of respiratory electron transport at site 1 (Arnason et al. 2015).

The extract from the South American shrub *Ryania* sp. is known as ryania and contains the diterpene alkaloid ryanodine (Fig. 2.1). It is a contact and stomach poison against horticultural and ornamental crop pests that acts by blocking Ca<sup>++</sup> ion channels. The seed extract of the neotropical lily *Schoenocaulon officinale* is known as sabadilla. It contains veratridine alkaloids having a neurotoxic mode of action. The extract is a valuable contact insecticide against a number of agricultural insect pests, viz., lepidoptera, leafhoppers and thrips. However, the market for these products is relatively small (Arnason et al. 2015).



**Fig. 2.1** Conventional herbal insecticides/pesticides (Source: Wikipedia 2015)



**Fig. 2.2** Important conventional herbal insecticide, pyrethrins from *Chrysanthemum cinerariifolium* (Source: Wikipedia 2015)

The most important traditional herbal insecticide is pyrethrum. It is derived from African daisy, *Chrysanthemum cinerariifolium*. The plant produces an insecticidal oleoresin which is extracted in organic phase. The pyrethrum extract contains six major pyrethrin compounds: pyrethrins I and II, jasmolins I and II and cinerins I and II (Fig. 2.2).

Pyrethrin is specially known for its quick knockdown of flying insects as well as a wide variety of home and garden pest insects. It acts

via the insect nervous system at the  $\text{Na}^+$  channels and has low mammalian toxicity, but does cause significant toxicity to fish and aquatic invertebrates. However, due to the growth of more stable and active synthetic pyrethroids, the market for natural pyrethrum dropped. Now natural pyrethrin is showing more application due to its application in natural pest control methods (Arnason et al. 2015).

Some of the important plants, products and their biological activities are enumerated in Table 2.1.



**Table 2.1** Some important plants, active components and their biological activities (Source: Pino et al. 2013 supplemented and modified by the authors)

Plant	Product	Bioactive component(s)	Biological activity	Mode of action	References
<i>Capsicum</i> spp. ( <i>Capsicum frutescens</i> Mill.)	Capsicum oleoresin	Capsaicin	Repellent, fungicide, nematocide, bactericide	Neurotoxic, repellent	Copping and Duke (2007), Dayan et al. (2009)
<i>Syzygium aromaticum</i> , <i>Eugenia caryophyllus</i> Spreng	Clove essential oil	Eugenol (mixture of several predominantly terpenoid compounds)	Insecticide, herbicide	Neurotoxic, interference with neuromodulator octopamine	Isman (2006), Copping and Duke (2007), Dayan et al. (2009), Fischer et al. (2013), Isman and Machial (2006)
<i>Thymus vulgaris</i> L., <i>Thymus</i> spp.	Thyme essential oil	Thymol, carvacrol	Insecticide, fungicide, herbicide	Neurotoxic, interference with GABA-gated chloride channels	Copping and Duke (2007), Dayan et al. (2009), Fischer et al. (2013)
<i>Rosmarinus officinalis</i>	Rosemary essential oil	1,8-cineole (borneol, camphor, monoterpenoids)	Insecticide, acaricide, fungicide	Octopamine antagonist; membrane disruptors, others	Dayan et al. (2009), Fischer et al. (2013), Isman and Machial (2006)
<i>Cinnamomum zeylanicum</i>	Cinnamon essential oil	Cinnamaldehyde	Insecticide, herbicide	Octopamine antagonists; membrane disruptors, others	Dayan et al. (2009), Fischer et al. (2013)
<i>Cymbopogon nardus</i> , <i>Cymbopogon citratus</i> Stapf., <i>Cymbopogon flexuosus</i> DC	Lemon grass essential oil	Citronellal, citral	Insecticide, herbicide	Octopamine antagonists; membrane disruptors, others	Dayan et al. (2009), Fischer et al. (2013)
<i>Mentha species</i> (mint)	Mint essential oil	Menthol	Insecticide	Octopamine antagonists; membrane disruptors, others	Dayan et al. (2009), Fischer et al. (2013)

(continued)

Table 2.1 (continued)

Plant	Product	Bioactive component(s)	Biological activity	Mode of action	References
<i>Cassia tora</i> L., <i>Cassia obtusifolia</i>	Cinnamaldehyde	Cinnamaldehyde	Fungicide, insect attractant	Disruption of the fungal membranes, repellent and attractant	Copping and Duke (2007), Dayan et al. (2009)
<i>Reynoutria sachalinensis</i> (Fr. Schm.) Nakai	Extract of giant knotweed	Physcion, emodin	Fungicide, bactericide	Induction of SAR (phenolic phytoalexins)	Dayan et al. (2009), Regnault-Roger (2012)
<i>Macleaya cordata</i> R. Br.	Pink plume poppy extract	Alkaloids, sanguinarine chloride and chelerythrine chloride	Fungicide	Induction of SAR (phenolic phytoalexins)	Dayan et al. (2009), Regnault-Roger (2012)
<i>Trigonella foenum-graecum</i> L.	Stifenia	Alkaloids	Fungicide	Stimulation of plant defence	Regnault-Roger (2012)
<i>Derris indica</i> (Lam.) Bennet	Karanjin	Karanjin	Insecticide, acaricide	Antifeedant/repellent, insect growth regulator	Copping and Duke (2007)
<i>Mentha piperita</i> L.	Phenethyl propionate	Phenethyl propionate	Insecticide, insect repellent, herbicide	Repellent	Isman (2006), Copping and Duke (2007), Dayan et al. (2009)
<i>Simmondsia californica</i> Nutt., <i>S. chinensis</i> Link.	Jojoba essential oil	Straight-chain wax esters	Fungicide, insecticide	B suffocation (eggs and immature life stages), repellent, blocking access to oxygen	Copping and Duke (2007), Dayan et al. (2009)
<i>Tanacetum cinerariifolium</i> (Trevisan) Schultz-Bip	Pyrethrum	Ester of chrysanthemic acid and permethric acid (pyrethrins I and II, cinerins I and II, jasmolins I and II)	Insecticide, acaricide	Axonic poisons (sodium channels agonists)	Isman (2006), Copping and Duke (2007), Isman and Paluch (2011), Dayan et al. (2009)



<i>Azadirachta indica</i> A. Juss	Neem (neem oil, medium polarity extracts)	Azadirachtin, dihydroazadirachtin, variety of triterpenoids (nimbini, salannin and others)	Insecticide acaricide, fungicide	Moulting inhibitors (ecdysone antagonists), antifeedant/repellent, physical smothering and desiccation	Isman (2006), Copping and Duke (2007), Isman and Paluch (2011), Dayan et al. (2009)
<i>Derris</i> , <i>Lonchocarpus</i> and <i>Tephrosia</i> species	Rotenone	Rotenone, deguelin (isoflavonoids)	Insecticide, acaricide	Mitochondrial cytotoxin	Isman (2006), Copping and Duke (2007), Isman and Paluch (2011)
<i>Nicotiana</i> spp.	Nicotine	(S)-isomer, (RS)-isomers and (S)-isomer of nicotine sulphate	Insecticide	Neurotoxin (acetylcholine agonist)	Isman (2006), Copping and Duke (2007), Isman and Paluch (2011), Dayan et al. (2009)
<i>Ryania</i> spp. ( <i>Ryania speciosa</i> Vahl)	Ryania	Ryanodine, ryania, 9,21-didehydroryanodine (alkaloids)	Insecticide	Neuromuscular poison (calcium channel agonist)	Isman (2006), Copping and Duke (2007), Isman and Paluch (2011), Dayan et al. (2009)
<i>Schoenocaulon</i> spp. ( <i>Schoenocaulon officinale</i> Grey)	Sabadilla	Mixture of alkaloids (cevadine, veratridine)	Insecticide	Axonic poisons (sodium channels agonists, heart and skeletal muscle cell membranes)	Isman (2006), Copping and Duke (2007), Isman and Paluch (2011), Dayan et al. (2009)
<i>Quassia</i> , <i>Aeschriton</i> , <i>Picrasma</i>	Quassia	Quassin (triterpene lactone)	Insecticide	Unknown	Isman (2006), Isman and Paluch (2011)

## 2.5 Future Areas of Focus

### 2.5.1 Photodynamic Killing of Insects

The first scientific documentation showing toxicity of sunlight to biological system was provided by Marcacci (1888) by reporting that the fermentation of plant alkaloids as well as amphibian eggs becomes more important under UV/visible light than in the dark. Many phytochemicals are documented as having photochemically active substances, which can be lethally toxic to insects. The major phytotoxin-producing plant family is known to be the sunflower family, Asteraceae.

Moreover, many photosensitizing agents have been shown to be accumulated in significant amounts by a variety of insects when given in association with suitable attractants. The follow-up exposure of such insects to UV/visible light leads to mortality. Two very important photosynthesizers, known to have very high photoinsecticidal activity, are xanthenes (e.g. phloxin B) and porphyrins (e.g. haematoporphyrin). The very high photobleaching of xanthenes and porphyrins when illuminated by visible light, and no major toxicity of such compounds in the dark, makes these as ideal photoinsecticidal agents due to least environmental impact of such compounds (Amor and Jori 2000).

### 2.5.2 Genetically Engineered Plants for Pest Management

Genes conferring resistance to insect pests have been inserted into several crops, e.g. *cry* genes from *Bacillus thuringiensis* (Bt) have shown considerable potential for pest management especially in crops like cotton and maize (Sharma et al. 2007). The Bt-transgenic crops have been shown to have better yield as well as insect-resistant trait, but detailed in-depth studies regarding their effect on nontarget species need to be evaluated in detail. Moreover, a number of ecological and economic issues need to be considered while considering the use of transgenic crops for pest management

(Sharma and Ortiz 2000). Also, the regulatory issues are of major concern in this regard. Currently, transgenic plants for crop protection have been developed using genes encoding for protease inhibitors, plant lectins, secondary plant metabolites, vegetative insecticidal proteins and RNAi technology.

### 2.5.3 LLIN with Herbal Insecticides

Long-lasting insecticidal nets (LLINs) are impregnated with synthetic pyrethroids and are wash proof till 20 times. Although pyrethroid use are considered to be very safe for human beings, LLINs with herbal insecticides would be more acceptable, keeping in mind the eco-friendliness and almost negligible toxicity. The LLIN developed by Defence Research and Development Organisation, India, known as 'Defender Net', is in very high demand; however, if instead of synthetic pyrethroids, herbal insecticides are used, its user-friendliness would increase manifold. Several essential oils like patchouli, together with citronella, clove and makaen, have been shown to have mosquito repellent activities, which could be of immense use if explored for using in LLINs. Endeavours in this direction need to be focussed.

### 2.5.4 Herbal Therapeutics for Vector-Borne Diseases

Plant products, especially essential oils, are a potential source of mosquito control due to their insecticidal properties (Benner 1993). Essential oils are naturally occurring, volatile, complex compounds with strong odour and are present in aromatic plants as secondary metabolites (Madhumathy et al. 2007). Amongst higher plants, about 17,500 aromatic plant species and about 3,000 essential oils are known, of which 300 are commercially important for pharmaceuticals, cosmetics and perfume industries and also having insecticide/pesticide potential (Palanisami et al. 2014). Some of the essential oils constitute even better alternatives or complementary to

synthetic compounds for vector control without showing the same secondary effects. A better understanding of their mode of action would help in exploring their further potential in controlling vector-borne diseases as well as application in human health, agriculture and the environment (Karmegan et al. 1997).

### 2.5.5 Biolarvicides

Mosquito larvae can be controlled by bacteria such as *Bacillus thuringiensis* var. *israelensis* (*Bti*) and *Bacillus sphaericus* which act as biolarvicides. *Bacillus thuringiensis* var. *israelensis* (*Bti*) is an aerobic spore-forming entomopathogenic bacterium effective against mosquitoes and black flies. These are highly effective against mosquito larvae at very low doses; safe to other nontarget organisms, environment, man and wild life and also appropriate for community use. These biolarvicides are regarded as the most promising microbial control agent against mosquitoes and black flies for use in integrated vector control programme. Similarly, *B. sphaericus* isolated first time from United State in 1965 are also reported to be highly insecticidal against mosquito larvae (Mittal 2003).

### 2.5.6 Herbal Repellents

Herbs with repellent properties are known to play an important role by minimizing man-vector contact. Nowadays natural insect repellent products that are preferred as chemical repellents are considered not safe for public use and have unpleasant smell, oily feeling to some users and potential toxicity. Repellents of herbal origin do not show toxicity to human and domestic animals and are easily biodegradable. Also, natural products are safe for human use when compared to synthetic compounds (Das et al. 2003).

Certain plants, viz., *Zanthoxylum armatum* DC syn. *Z. alatum* Roxb. (Rutaceae), *Azadirachta indica* (Meliaceae) and *Curcuma aromatica* (Zingiberaceae), have been investigated for repellent activity against mosquitoes (Das et al. 2000); *Callistemon rigidus* (bottlebrush), *A. indica*

(neem) and *Z. armatum* (timur) have been reported to have repellent activity against land leeches also (Nath et al. 2002). Likewise, repellent action of neem oil in the form of mats and neem cream has been evaluated. Essential oil obtained from *Vitex negundo* and *Lantana camara* flowers is active against *Aedes* mosquitoes (Das et al. 2003).

### 2.5.7 Nanoparticles of Herbs for Vector Control

The activity of herbal medicines is because of the active constituents present in them, which show synergistic action and thus enhance the curative value (Lu et al. 2007; Williamson 2001). However, most of the herbal constituents are poorly water soluble because of their hydrophobic nature, which leads to decreased bioavailability. Nanoparticles are utilized to increase the herbal drug solubility and for helping in localizing the drug specificity in the body. Nanoparticulate formulations such as polymeric nanoparticles, liposomes, proliposomes, solid lipid nanoparticles and microemulsions have the potential to deliver herbal medicines effectively (Thapa et al. 2013). Hence, insecticidal herbal drugs in the form of nanoparticles will be of immense use in controlling disease vector as in the form of nanoparticles; the efficiency of insecticidal drugs will be at its best.

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## 2.6 Conclusion

Our country possesses a rich biodiversity of medicinal plants, which are used for various purposes. The active principles of the herbs have unique bioactivities, e.g. growth-promoting ability, modulating immune system, antimicrobial capability, appetizing and antistress activities. The major active principles of biomedicines include alkaloids, flavonoids, pigments, phenolics, terpenoids, starch, steroids and essential oils. The use of biomedicines will certainly reduce the use of synthetic compounds, reduce the cost and be an eco-friendly approach to solve the menace of pests.

Plants synthesize a number of secondary metabolites due to their co-evolution with insects, and these serve as defence chemicals against pest attack. Researchers have discovered a completely new paradigm for the control of vectors using secondary plant products, which may be toxic to specific vectors while harmless to nontarget organisms. More than 2,000 plant species of different families and genera have been reported to contain toxic principles effective against insects. There are many plant species containing compounds lethal to target as well as nontarget organisms, which are much below those for synthetic pyrethroids. Moreover, such products have the further advantage of biodegradability, as all such compounds are not only confined to the plants in which they are found but also get disseminated in the environment. An important issue about herbal insecticides/pesticides is that there are reports of toxicity. However, very little literature is available on their mode of action and effects on other organisms. But the hope is that they are safe, as these have been used by mankind for pest management without polluting the environment since ages.

It is anticipated that herbaceous products not only can control the plant/animal disease vectors, storage insects, predatory fishes and mosquitoes but are easily available and inexpensive and have easy biodegradability and greater acceptance amongst the users. It is apparent that with the rapid advancements in biotechnology, such valuable plant pesticide products can be sourced from industries using biotechnological methods also, other than only plant source, and thus in a plant and season-independent manner for sustainable vector management.

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