



Botanical insecticides in sustainable insect pest management: Phytochemistry, modes of action, field performance and translational challenges – An review

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Abstract

Insect pests remain a leading constraint on global food production, storage and public health, while the overreliance on synthetic insecticides has produced resistance, residues, loss of beneficial fauna and regulatory withdrawal of several active ingredients. Plant-derived insecticides, or botanicals, are increasingly viewed as components of integrated pest management (IPM) because they are derived from the chemical defences that plants evolved against herbivores, often act through multiple physiological targets, and generally degrade rapidly in the environment. This review synthesises current knowledge on the evolutionary and chemical basis of botanical insecticides, the major compound classes (limonoids, pyrethrins, essential-oil monoterpenoids and phenylpropanoids, alkaloids, acetogenins, piperamides, saponins, proteins and insect-hormone mimics), their neurotoxic, antifeedant, growth-regulating, repellent and synergistic modes of action, and their performance against field, storage and vector pests. Non-target effects, resistance risk, formulation and nanoencapsulation strategies, regulatory and commercialisation barriers, and the specific context of smallholder and Indian agriculture are discussed. A critical appraisal highlights recurring weaknesses in the literature, including poorly characterised extracts, unrealistic doses and absent standardisation, and proposes a research agenda for making botanical insecticides reliable, scalable and registrable.

Keywords: Azadirachtin, botanical insecticides, insect resistance, IPM, mode of action, nano formulation, pyrethrum

Introduction

Insects compete with humans for food at every stage from field to granary, and they transmit pathogens that cause some of the greatest burdens of human and animal disease. Oerke (2006) ^[41] estimated that actual losses to pests in the major crops, even with existing crop protection, range from roughly a quarter to two-fifths of attainable production depending on the crop, and more recent global assessments of five staple crops confirm that pests and pathogens continue to cause substantial yield losses (Savary *et al.*, 2019) ^[52]. In India, changing cropping systems, climate and input use have altered the pest spectrum and intensified losses (Dhaliwal & Koul, 2010) ^[13]. Since the mid-twentieth century the principal response has been synthetic chemistry. The benefits are undeniable, but so are the costs. Pesticide use has been associated with environmental contamination, residues in food and risks to human health (Carvalho, 2017) ^[7], and with declines in beneficial and non-target insects (Sánchez-Bayo & Wyckhuys, 2019) ^[51]. Resistance has evolved in numerous pest species and in vectors of human disease (Hemingway & Ranson, 2000) ^[24], leading to what Gould *et al.* (2018) ^[22] describe as a “wicked” sociobiological problem requiring diversified management rather than a single chemical solution. This context has renewed interest in natural products as a source of pest control agents. Natural products have long supplied commercial crop protection agents and templates for synthetic analogues (Gerwick & Sparks, 2014) ^[20]. Within this group, botanical insecticides are formulations or purified compounds obtained from plants that are used to kill, deter, repel or disrupt the development of insects

(Isman, 2006) ^[29]. They are attractive for several reasons: structural diversity that can overcome target-site resistance, multiple simultaneous modes of action, rapid environmental breakdown, compatibility with organic production and, in many regions, local availability that suits smallholder farming (Stevenson *et al.*, 2017) ^[59]. Nevertheless, the gap between the volume of published bioassays and the number of commercial products is large. Isman and Grieneisen (2014) ^[31] analysed thousands of botanical insecticide papers and concluded that many offered limited useful data, a theme revisited by Isman (2020) ^[30] in assessing whether botanicals have fulfilled their promise. Translating laboratory activity into registered, standardised, stable and economical products demands attention to chemistry, ecology, formulation and regulation together.

Chemical Defence in Plants: The Evolutionary Basis of Botanical Insecticides

1. Secondary metabolites as defence

Plants cannot flee herbivores and therefore rely on constitutive and inducible chemical defences. Secondary (specialised) metabolites such as terpenoids, alkaloids, phenolics, glucosinolates and cyanogenic glycosides deter feeding, intoxicate herbivores, impair digestion or disrupt hormonal regulation (Wink, 2003) ^[65]. Terpenoids alone encompass tens of thousands of structures with roles in direct defence, in signalling and in attracting natural enemies. Defensive proteins, including protease inhibitors, lectins and enzymes, add a further layer by interfering with insect digestion (Carlini & Grossi-de-Sá, 2002) ^[6].

2. Constitutive and induced defence

Herbivory triggers jasmonate- and salicylate-regulated signalling cascades that raise the production of toxins and defensive proteins and release volatiles that recruit predators and parasitoids (Howe & Jander, 2008) ^[25]. Reviews of plant defence mechanisms emphasise that these responses involve morphological barriers, biochemical toxins and tritrophic effects acting together (War *et al.*, 2012) ^[64]. Because the compounds used in botanical insecticides are the same ones that plants deploy at tissue-specific concentrations, understanding where and when they are produced guides the choice of plant part, harvesting time and extraction method.

3. Insect perception and adaptation

Insects detect plant chemistry through contact and olfactory chemoreceptors, so deterrence is frequently mediated by gustatory sensilla before any toxic effect develops (Chapman, 2003; Schoonhoven *et al.*, 2005) ^[9, 54]. Insects, in turn, have evolved detoxification systems and sequestration or avoidance strategies, which explains why specialist herbivores may be insensitive to the defences of their hosts and why susceptibility to a botanical differs widely between species (Schoonhoven *et al.*, 2005) ^[54]. This coevolutionary perspective has inspired the design of botanicals and the search for compounds against which pests lack pre-adapted defences (Miresmailli & Isman, 2014) ^[31].

Historical Development and Commercial Status

Plant materials have been used against insects for millennia, including pyrethrum flowers, hellebore, tobacco, derris and neem, and these formed the basis of early commercial insecticides (Casida, 1980; Schmutterer, 1990) ^[8, 53]. Indian agriculture has a particularly deep ethnobotanical tradition

involving neem, sweet flag, custard apple and other species, documented in the context of modern pest management by Dhaliwal and Koul (2010) ^[13]. The arrival of DDT and other synthetics in the 1940s displaced most botanicals, but concern over environmental and health impacts revived interest from the 1970s onwards. By the early twenty-first century, only a handful of botanical active ingredients held significant market share. Isman (2006) ^[29] identified pyrethrum, neem (azadirachtin), rotenone, essential oils and, more regionally, ryania and sabadilla as the principal commercial botanicals, and noted that regulatory costs and supply constraints limited expansion. Nicotine, once widely used, has been withdrawn in many jurisdictions on toxicity grounds, and rotenone has been restricted because of mammalian toxicity concerns (Isman, 2006; Betarbet *et al.*, 2000) ^[4, 29]. Since then, essential-oil-based products have grown in the market, particularly in the United States, where several oils qualify under minimum-risk exemptions, and in organic and home-and-garden segments (Regnault-Roger *et al.*, 2012). Pavea (2016) ^[45, 50] reviews the present position of plant extracts as commercial botanical insecticides and the products that reached the market in Europe and elsewhere. In biopesticide terms, botanicals still represent a small share compared with microbial agents (Glare *et al.*, 2012) ^[21], which indicates both a constraint and an opportunity for growth.

Major Classes of Insecticidal Phytochemicals

Botanicals can be organised by chemical class. Table 1 summarises representative plants, active constituents and principal targets, and the subsections below discuss the most important groups.

Table 1: Representative botanical insecticides, active constituents and primary modes of action

Botanical source	Key active constituents	Chemical class	Principal mode of action	Key references
<i>Azadirachta indica</i> (neem)	Azadirachtin, salannin, nimbin	Limonoid (tetranortriterpenoid)	Antifeedant; endocrine disruption of moulting and reproduction	Schmutterer (1990) ^[53] ; Mordue (Luntz) & Blackwell (1993) ^[40]
<i>Chrysanthemum cinerariifolium</i>	Pyrethrins I and II, cinerins, jasmolins	Ester of chrysanthemic/pyrethric acid	Prolonged opening of voltage-gated sodium channels	Casida (1980); Davies <i>et al.</i> (2007) ^[8, 11]
<i>Derris</i> and <i>Lonchocarpus</i> spp.	Rotenone	Isoflavonoid	Mitochondrial complex I inhibition	Isman (2006) ^[29]
<i>Nicotiana</i> spp.	Nicotine	Pyridine alkaloid	Nicotinic acetylcholine receptor agonism	Tomizawa & Casida (2005) ^[62]
Lamiaceae, Myrtaceae, Apiaceae (essential oils)	Thymol, carvacrol, eugenol, linalool, 1,8-cineole, menthol	Monoterpenoids, phenylpropanoids	Octopamine/GABA receptor modulation; AChE inhibition; fumigant and repellent action	Isman (2000); Regnault-Roger <i>et al.</i> (2012) ^[28, 50]
<i>Piper</i> spp.	Piperine and related piperamides	Amide alkaloids	Neurotoxicity; synergism	Scott <i>et al.</i> (2008) ^[55]
Annonaceae (e.g., <i>Annona squamosa</i>)	Annonaceous acetogenins	Polyketide-derived lipids	Mitochondrial complex I inhibition	Bermejo <i>et al.</i> (2005) ^[3]
Balsam fir, <i>Ageratum</i> spp.	Juvabione, precocenes	Juvenoid and anti-juvenoid compounds	Juvenile hormone disruption	Sláma & Williams (1966); Bowers <i>et al.</i> (1976) ^[5, 56]
Various plants	Protease inhibitors, lectins	Proteins	Digestive interference; gut binding	Carlini & Grossi-de-Sá (2002) ^[6]

1. Limonoids: neem and related Meliaceae

Neem (*Azadirachta indica* A. Juss.) is the most widely used botanical insecticide worldwide. Its seed kernels contain azadirachtin and related tetranortriterpenoids that produce antifeedant and growth-disrupting effects at very low doses (Schmutterer, 1990) ^[53]. Azadirachtin was first isolated through its feeding-suppressant effects on locusts (Mordue (Luntz) & Blackwell, 1993) ^[40], and subsequent work showed that it interferes with the neuroendocrine regulation

of ecdysteroid and juvenile hormone titres, causing moulting abnormalities, reduced fecundity and sterility (Mordue (Luntz) & Blackwell, 1993) ^[40]. Neem oil additionally acts through physical and contact effects. Recent assessments of azadirachtin-based products highlight both their favourable ecological profile and the need for careful risk assessment for aquatic and beneficial organisms (Kilani-Morakchi *et al.*, 2021) ^[34]. Limonoids from other Meliaceae and Rutaceae also show antifeedant and

insecticidal activity. A practical difficulty is variability in azadirachtin content with genotype, geography, storage and extraction (Gahukar, 2014)^[19].

2. Pyrethrins

Pyrethrins from the flowers of *Chrysanthemum cinerariifolium* (Trevir.) Vis. are among the oldest and most commercially successful botanical insecticides. They act on voltage-gated sodium channels, delaying channel closure and causing repetitive firing, hyperexcitation and knockdown (Davies *et al.*, 2007)^[11]. Their rapid action, low mammalian toxicity at typical doses and fast photodegradation are advantages, while photolability and cost motivated the development of synthetic pyrethroids (Casida, 1980)^[8]. Synergists such as piperonyl butoxide inhibit detoxifying monooxygenases and extend activity; the resulting pyrethroid class illustrates how a botanical lead became a dominant synthetic group, but also how heavy use selected for target-site and metabolic resistance (Davies *et al.*, 2007; Sparks & Nauen, 2015)^[11, 58].

3. Essential oils and their constituents

Essential oils are volatile mixtures dominated by monoterpenoids, sesquiterpenoids and phenylpropanoids, obtained from aromatic plants of the Lamiaceae, Myrtaceae, Lauraceae, Apiaceae, Poaceae, Rutaceae and other families. Their insecticidal, repellent and antifeedant potential has been reviewed extensively (Isman, 2000; Regnault-Roger *et al.*, 2012)^[28, 50]. Efficacy is often attributable to a few major constituents such as thymol, carvacrol, eugenol, linalool and 1,8-cineole, but whole oils may outperform single compounds because of synergism among constituents (Hummelbrunner & Isman, 2001)^[26]. Commercial interest is supported by the low toxicity of many oils to mammals and by their regulatory status in some markets.

4. Alkaloids and rotenoids

Nicotine acts as an agonist at insect nicotinic acetylcholine receptors, and its mechanism informed the discovery of neonicotinoid insecticides (Tomizawa & Casida, 2005)^[62]. Rotenone, obtained from legumes such as *Derris* and *Lonchocarpus*, inhibits mitochondrial complex I and has been used widely in organic agriculture and fish management. It is highly toxic to fish, and experimental work linking chronic systemic exposure to Parkinson-like pathology in rodents (Betarbet *et al.*, 2000)^[4] contributed to restrictions on its use. These examples show that natural origin does not guarantee safety, which is a recurrent theme in the regulatory literature (Isman, 2006)^[29].

5. Acetogenins, piperamides and saponins

Annonaceous acetogenins are potent inhibitors of mitochondrial complex I in the electron transport chain and show insecticidal and cytotoxic activity (Bermejo *et al.*, 2005)^[3]. Piperamides from *Piper* species, including piperine, show neurotoxic and synergistic activity and have been proposed as botanical leads (Scott *et al.*, 2008)^[55]. Saponins disrupt membranes by complexing with sterols, which affects gut integrity, feeding and growth (Francis *et al.*, 2002)^[18].

6. Proteins and insect-hormone mimics

Plant protease inhibitors, lectins, ribosome-inactivating proteins and chitin-binding proteins impair digestion and gut function and have been exploited both as sprays and in

transgenic crops (Carlini & Grossi-de-Sá, 2002)^[6]. Phytoecdysteroids mimic moulting hormones and are present in many plants as defensive compounds (Dinan, 2001)^[14]. Juvabione, discovered serendipitously through the “paper factor” that prevented development of the bug *Pyrrhocoris apterus* (Sláma & Williams, 1966)^[56], and precocenes, which act as anti-juvenile hormones (Bowers *et al.*, 1976)^[5], demonstrate that plants also produce compounds that interfere with insect endocrine systems.

Modes of Action

The complexity of plant extracts means that a single botanical may act at several levels. Rattan (2010)^[49] reviews the mechanisms of insecticidal plant metabolites, and the principal categories are outlined below.

1. Neurotoxic action

The insect nervous system is the main target of many botanicals. Pyrethrins prolong sodium channel opening (Davies *et al.*, 2007)^[11], and nicotine activates nicotinic acetylcholine receptors (Tomizawa & Casida, 2005)^[62]. Essential-oil constituents act on several neural targets. Enan (2001)^[16] proposed octopaminergic sites of action for essential-oil constituents. Thymol is a positive allosteric modulator of GABA-gated chloride channels, including those of *Drosophila* (Priestley *et al.*, 2003)^[47], and monoterpenoids also act on insect GABA receptors. Inhibition of acetylcholinesterase (AChE) by plant compounds is well documented (López & Pascual-Villalobos, 2010)^[37], and kinetic analysis of monoterpenoids has clarified how they inhibit the enzyme and why this is relevant to pest control (López & Pascual-Villalobos, 2010)^[37].

2. Antifeedant and deterrent effects

Antifeedants inhibit feeding without necessarily killing the insect and are especially relevant to crop protection because feeding damage, not mortality, determines yield loss. Koul (2008)^[36] provides comprehensive coverage of antifeedant chemistry and physiology. Deterrence can arise from stimulation of deterrent-sensitive gustatory neurons or from suppression of phagostimulant neurons (Chapman, 2003)^[9]. Azadirachtin is a classic example, with potency depending strongly on species (Mordue (Luntz) & Blackwell, 1993)^[40]. Antifeedants are attractive for IPM but depend on adequate coverage and the absence of alternative feeding sites, and sublethal effects must be considered alongside mortality.

3. Growth regulation and endocrine disruption

By mimicking or disrupting insect hormones, some botanicals interfere with moulting, metamorphosis and reproduction. Azadirachtin affects ecdysteroid and juvenile hormone release (Mordue (Luntz) & Blackwell, 1993)^[40], phytoecdysteroids mimic moulting hormones (Dinan, 2001)^[14], and juvabione and precocenes act on the juvenile hormone system (Sláma & Williams, 1966; Bowers *et al.*, 1976)^[5, 56]. Such effects are slow compared with neurotoxins, so growers accustomed to rapid knockdown must be informed about expected symptom development.

4. Respiratory, digestive and physical action

Rotenone and acetogenins inhibit mitochondrial complex I, depriving cells of ATP (Bermejo *et al.*, 2005; Isman, 2006)^[3, 29]. Protease inhibitors and lectins act in the gut (Carlini &

Grossi-de-Sá, 2002)^[6], while saponins disrupt membranes (Francis *et al.*, 2002)^[18]. Oils can also kill soft-bodied insects and mites physically by blocking spiracles and disrupting cuticle, as with neem oil emulsions. Enhanced cuticular penetration is a further mechanism. In *Trichoplusia ni*, the synergy among constituents of rosemary oil was attributed to improved cuticular penetration of the active compound (Tak & Isman, 2015)^[60].

5. Repellence and oviposition deterrence

Repellents reduce contact between insects and hosts and are a major application of essential oils, notably for mosquitoes and other biting insects (Maia & Moore, 2011; Benelli & Pavela, 2018)^[2, 38]. The duration of protection remains the principal limitation of plant-based repellents because of volatility. Oviposition deterrence and altered egg-laying behaviour have been demonstrated for essential-oil components against stored-product beetles (Papachristos & Stamopoulos, 2002)^[43].

6. Synergism and multi-target activity

Synergistic interactions among constituents are a defining feature of botanicals and a possible reason for their slower resistance evolution. Mixtures of monoterpenoids showed synergistic, antagonistic and additive effects against lepidopteran larvae depending on composition (Hummelbrunner & Isman, 2001)^[26], and the rosemary oil work cited above provides a mechanistic explanation through enhanced penetration (Tak & Isman, 2015). Miresmailli and Isman (2014)^[31, 60] argue that mimicking the multi-component, multi-target character of plant defence is a design principle for next-generation botanicals.

Efficacy Against Major Pest Groups

1. Field and horticultural pests

Field performance of botanicals is variable, and effect sizes depend on pest, crop, formulation and application schedule. Neem products are effective against many Lepidoptera, aphids, whiteflies, leafminers and thrips when applied with adequate coverage, but are slower than synthetic neurotoxins (Schmutterer, 1990; Isman, 2006)^[29, 53]. Rosemary and thyme oils have shown activity against lepidopteran larvae such as *Spodoptera littoralis* and *Trichoplusia ni* (Tak & Isman, 2015)^[60]. In sub-Saharan

Africa, extensive trials of pesticidal plant extracts demonstrate practical value. Extracts of locally available plants reduced pest damage and increased legume yields without harming beneficial arthropods (Tembo *et al.*, 2018)^[61], and protected cabbage against key pests in a tritrophic evaluation (Amoabeng *et al.*, 2013). Dougoud *et al.* (2019)^[1, 15] reviewed the efficacy of homemade botanical insecticides based on traditional knowledge and found that, although many preparations are effective, reproducible data and dose standardisation are often lacking. Nanoformulated essential oils have also shown promise against whiteflies (Christofoli *et al.*, 2015)^[10].

2. Stored-product pests

Stored grains are a particularly suitable target for botanicals because they are a high-value commodity held in enclosed environments, where volatile fumigants remain effective and regulatory demands for residues are stringent. Rajendran and Sriranjini (2008)^[48] review plant products as fumigants for stored-product pests. Essential oils and constituents have been shown to be toxic, repellent or reproduction-inhibiting to beetles such as *Sitophilus* spp., *Tribolium* spp., *Callosobruchus* spp. and *Acanthoscelides obtectus* (Papachristos & Stamopoulos, 2002)^[43]. Many of these studies identify phenylpropanoids such as eugenol, or monoterpenoids, as the active components. Practical obstacles include loss of volatiles from permeable storage, effects on grain odour and taste, and safety limits for repeated human exposure.

3. Mosquitoes and other medically important insects

Botanical derivatives have long been investigated against mosquito larvae, adults and oviposition. Essential oils from diverse plants show larvicidal activity against *Aedes*, *Anopheles* and *Culex*, and Pavela (2015)^[44] reviewed their prospects as eco-friendly larvicides. Beyond mosquitoes, Benelli and Pavela (2018)^[2] reviewed essential oil toxicity and repellency against blood-sucking insects including flies, bugs and lice. Because resistance to synthetic insecticides is widespread in vectors (Hemingway & Ranson, 2000)^[24], botanicals could complement vector control, although protective duration and standardised field testing remain constraints (Maia & Moore, 2011)^[38]. The main pest groups discussed in this section are summarised in Figure 1.

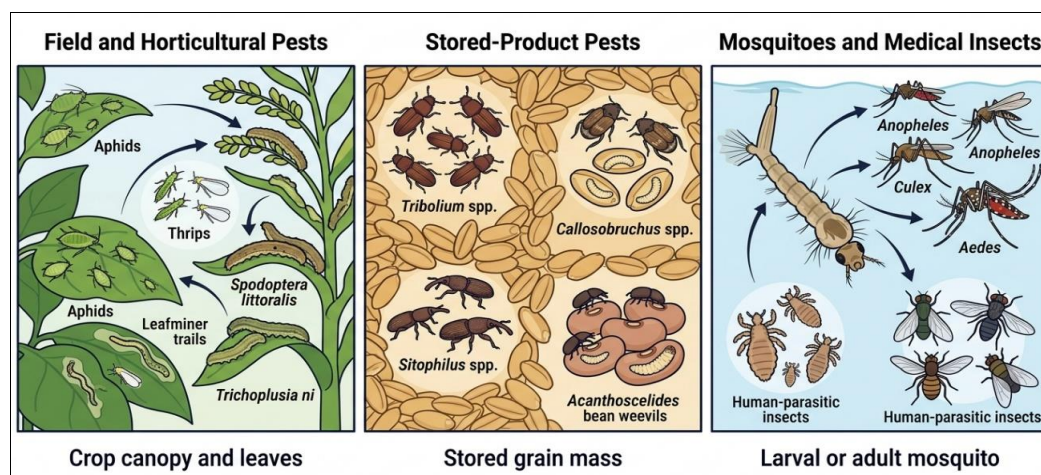


Fig 1: Major pest groups targeted by botanical insecticides: field and horticultural pests, stored-product pests, and mosquitoes and other medically important insects (schematic illustration)

Non-Target Effects and Safety

A common assumption holds that botanicals are inherently safe. The evidence is more nuanced. Many have low acute mammalian toxicity and short environmental persistence, but several are toxic to fish and aquatic invertebrates (rotenone), to humans (nicotine) or to bees and natural enemies at certain doses (Isman, 2006; Pavela & Benelli, 2016) [29, 46]. Sublethal effects on beneficial arthropods, including altered fecundity, behaviour and foraging, can be as important as lethality (Desneux *et al.*, 2007) [12]. Selectivity is often a result of ingestion versus contact exposure, and trials of pesticidal plants in Africa observed reduced harm to beneficial arthropods compared with synthetic comparators (Tembo *et al.*, 2018; Amoabeng *et al.*, 2013) [1, 61]. Risk assessment for azadirachtin shows low toxicity to many beneficials but potential effects on aquatic organisms and some predators (Kilani-Morakchi *et al.*, 2021) [34]. A responsible approach therefore requires pest- and context-specific ecotoxicology, and the broader environmental benefit must be weighed against these data (Carvalho, 2017) [7].

Resistance to Botanical Insecticides

Because botanicals are frequently complex mixtures acting on multiple targets, resistance is generally expected to evolve more slowly than to single-target synthetics, but it is not impossible. Selection of the green peach aphid, *Myzus persicae*, with azadirachtin for about 40 generations produced only modest resistance (Feng & Isman, 1995) [17]. Pyrethroids, the synthetic analogues of pyrethrins, illustrate the opposite case, as their heavy use has selected for target-site and metabolic resistance worldwide (Davies *et al.*, 2007; Hemingway & Ranson, 2000). Isman (2020) [11, 24, 30] notes that field resistance to multi-component botanicals is rare but that purified single actives risk the same trajectory as synthetics. The Insecticide Resistance Action Committee classification, which groups compounds by mode of action to guide rotations, now includes azadirachtin and other natural products (Sparks & Nauen, 2015) [58], and rotation or mixtures with differing modes of action should be part of resistance-management strategies (Gould *et al.*, 2018) [22]. Figure 2 contrasts these cases and summarises the main resistance-management options.

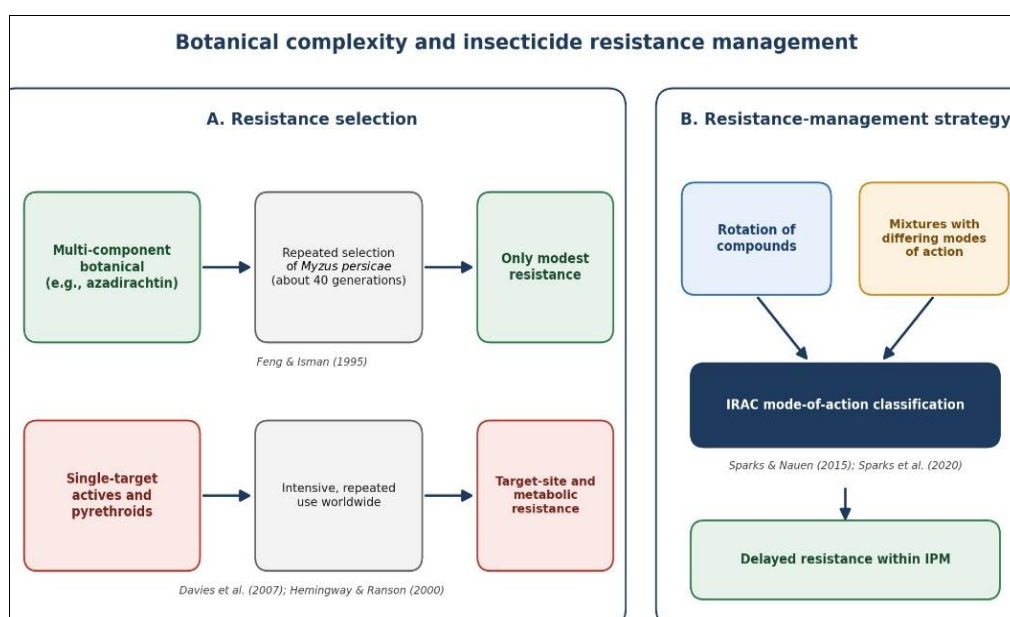


Fig 2: Resistance selection under botanical and single-target insecticides (A) and resistance-management strategies based on rotation and mixtures of compounds with differing modes of action (B). Based on Feng and Isman (1995), Davies *et al.* (2007) and Sparks and Nauen (2015) [11, 17, 58].

Formulation, Stability and Nanotechnology

The principal technical challenges for botanicals are instability, volatility, low water solubility and phytotoxicity. Azadirachtin degrades under ultraviolet light, and photostabilisers have been tested to extend its field persistence (Johnson *et al.*, 2003) [32]. Essential oils are susceptible to oxidation, evaporation and polymerisation, which affects both shelf life and bioactivity (Turek & Stintzing, 2013) [63]. Standard emulsifiable concentrates, microemulsions and dusts can address some problems, but controlled-release systems offer more. Nanotechnology provides carriers such as polymeric nanoparticles,

nanoemulsions, nanogels and solid lipid particles that protect actives, regulate release and improve penetration. Oliveira *et al.* (2014) [42] reviewed encapsulation of botanical insecticides in agriculture. Christofoli *et al.* (2015) [10] reported insecticidal activity of nanoencapsulated *Zanthoxylum rhoifolium* oil against *Bemisia tabaci*. These advances should be accompanied by studies of fate, exposure and ecotoxicity of nanopesticides (Kah *et al.*, 2013) [33] and by caution about unvalidated “green nano” claims (Pavela & Benelli, 2016) [46]. Figure 3 summarises the main technical challenges and formulation strategies discussed in this section.

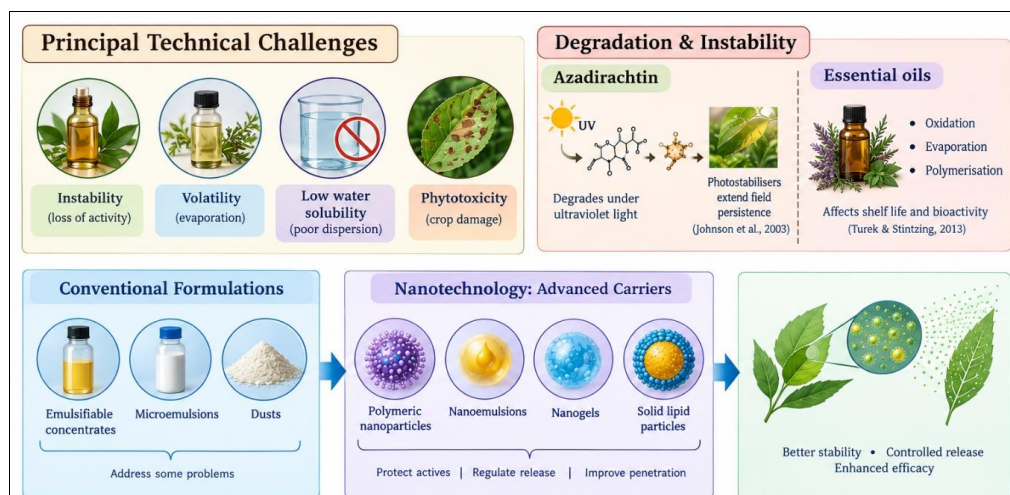


Fig 3: Technical challenges in formulating botanical insecticides, degradation of azadirachtin and essential oils, and the progression from conventional formulations to nanotechnology-based carriers (Johnson *et al.*, 2003; Turek & Stintzing, 2013) [32, 63].

Regulation, Commercialisation and the Smallholder Context

1. Regulatory barriers

In most jurisdictions, a botanical active substance is regulated like any other pesticide and must be supported by chemistry, toxicology, ecotoxicology and efficacy data. Isman (1997) [27] identified three principal barriers to commercialisation of neem and other botanicals: scarcity of renewable plant resources, lack of standardisation and chemical consistency, and the cost and complexity of registration. These barriers persist in modified form (Isman, 2006, 2020) [29, 30]. Because botanical extracts are mixtures whose composition shifts with plant origin and processing, regulators may require characterisation of multiple constituents, and the cost of registration can exceed the commercial value of a niche product. Reviews of biopesticide regulation note that streamlined pathways for low-risk products have accelerated approvals in some regions (Glare *et al.*, 2012), while Pavela (2016) [21, 45] illustrates how the status of plant extracts differs among countries. Researchers should consult current national rules, such as India's Insecticides Act and the registration process of the Central Insecticides Board and Registration Committee, before planning product development, since regulations are revised periodically.

2. Plant supply, standardisation and quality control

Standardisation is a central requirement. Azadirachtin content in neem varies with provenance, season, storage and extraction (Gahukar, 2014) [19], and similar variation applies to essential oils, where chemotypes can alter composition and activity. The active principles in extracts must be identified and quantified if consistency is to be achieved. Sustainable sourcing is equally important; harvesting wild plants for pesticides can threaten local biodiversity unless cultivation or by-product use is developed (Stevenson *et al.*, 2017) [59].

3. Smallholder and low-input systems

Where synthetic pesticides are costly, poorly regulated or inaccessible, locally produced botanicals can provide pest control and income. Grzywacz *et al.* (2014) [23] argue for the use of indigenous ecological resources, including pesticidal plants, in African pest management, and Stevenson *et al.* (2017) [59] present a global vision for new products from

local uses. Sola *et al.* (2014) [57] describe the production, trade and regulatory environment for plant-based pesticidal products in sub-Saharan Africa and call for harmonised, proportionate regulation. Similar arguments apply to India, where neem, custard apple, *Pongamia*, sweet flag and many aromatic plants are widely available and traditional knowledge exists (Dhaliwal & Koul, 2010). Dougoud *et al.* (2019) [13, 15] caution, however, that the efficacy of homemade preparations varies and should be validated before promotion. The integration of botanicals into IPM, in which pest monitoring, thresholds, cultural and biological control, and selective chemical tools operate together (Kogan, 1998) [35], remains the most coherent framework for their deployment.

4. Critical appraisal of the literature

Several recurring problems limit the value of botanical insecticide research. First, a large proportion of papers screen crude extracts without phytochemical characterisation, so results cannot be replicated (Isman & Grieneisen, 2014) [31]. Second, many studies report activity at concentrations that would be impractical or uneconomical in the field, with LC50 values several orders of magnitude above those of commercial products; Pavela and Benelli (2016) [46] caution that high laboratory toxicity does not imply a viable product. Third, experiments frequently omit positive controls such as a commercial insecticide, formulation blanks and solvent controls, or use a single, highly susceptible laboratory strain of one pest. Fourth, ecotoxicological and mammalian safety data are scarce for most candidate plants, despite assumptions of safety (Isman, 2006) [29]. Fifth, field trials are fewer than laboratory bioassays, and the persistence and residue behaviour of botanicals under real conditions are rarely measured (Dougoud *et al.*, 2019) [15]. Finally, the abundance of publications on a small number of well-known plants, such as neem and a few Lamiaceae oils, contrasts with limited research on novel scaffolds and mechanisms (Isman & Grieneisen, 2014; Isman, 2020) [30, 31].

Future Perspectives

Three directions appear especially promising. The first is the use of plant chemistry as a template. Miresmailli and Isman (2014) [31] propose designing botanicals inspired by plant–herbivore interactions, and the history of pyrethroids and

neonicotinoids shows that natural leads can yield commercially significant synthetic classes (Gerwick & Sparks, 2014; Tomizawa & Casida, 2005)^[20, 62]. The second is the combination of botanicals with other IPM tools, including biological control agents, semiochemicals and selective synthetic insecticides, to deliver additive or synergistic control and delay resistance (Gould *et al.*, 2018; Kogan, 1998)^[22, 35]. The third is advanced delivery and digital precision application, in which encapsulated actives are applied at the right time and place, reducing dose and non-target exposure (Oliveira *et al.*, 2014)^[42]. Genomic tools may also identify biosynthetic pathways for high-value insecticidal compounds, opening routes to sustainable production independent of wild harvest, although such possibilities require economic validation. The overall trajectory is likely to be incremental rather than revolutionary. Botanicals are unlikely to replace synthetic insecticides wholesale, but they can be valuable niche and complementary tools, particularly in organic systems, stored-product protection, urban and public-health settings and smallholder agriculture (Isman, 2020; Pavela, 2016)^[30, 45].

Conclusions

Botanical insecticides draw on the chemical defences that plants evolved against herbivores, and they include some of the oldest and most valuable crop protection agents. Their multiple modes of action, generally rapid degradation and compatibility with IPM make them relevant to a world seeking to reduce dependence on synthetic pesticides. Yet natural origin is not synonymous with safety, efficacy is heterogeneous, and commercial success has been confined to a limited set of products, chiefly pyrethrum, neem and selected essential oils. Overcoming this gap requires rigorous, standardised and field-relevant research that integrates chemistry, ecology, formulation science and regulatory strategy. For doctoral researchers, the greatest opportunities lie in mechanism-based discovery, quality-controlled formulations, honest ecotoxicological evaluation and validation within IPM, which together can move botanicals from promising laboratory results to dependable tools for sustainable agriculture.

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