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MINI-REVIEWS

Plant-derived nanopesticides for agricultural pest control: challenges and prospects

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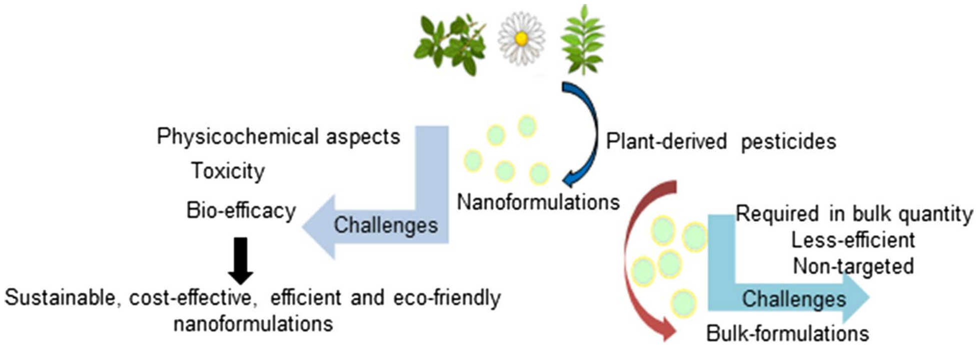
Abstract

As compared to bulk form of pesticides, plant-derived nanopesticides through controlled and sustained release of toxicant have been found to be more effective in reducing pest population and plant infestation levels. Particularly, polymer-based nanoformulations have been commercially exploited for the encapsulation of neem-derived products (seed kernel oil, extract of seed, leaf or bark gum, azadirachtin) compared to other plants. The main concerns yet to be solved include risk assessment to environmental and/or human health and nontarget organisms. There is an urgent need to develop safe and promising formulations and execute regulatory framework for nanopesticides as they have different properties and are applied in small quantity. The current application of nanopesticides in agriculture and their consequences is reviewed here with a perspective of replacing or at least reducing chemical pesticides with precautionary measures.

Graphic abstract



Keywords Nanopesticides · Nanoformulation · Plant-derived products · Bioefficacy · Active ingredient, toxicity

Introduction

Nanotechnology has recently been introduced in agriculture to enhance crop protection by the way of remediation of harmful pesticides and to prepare new pesticide formulations to ease application with controlled delivery on plants and grains. Consequently, there is an increasing interest among researchers and extension agents to use nanopesticides which consist of organic and inorganic constituents having nano-sized particles of a pesticide active ingredient (AI) or other small engineered structures having pesticide properties [1]. Nanopesticides showed in some instances

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higher or similar bioefficacy in pest mortality compared to conventional pesticides as recently discussed by Kah et al. [2] and Rani and Sushil [3]. Field bioefficacy and potential impact of nanopesticides on ecosystems may be different from that obtained in laboratory trials because nanoformulations can decrease or increase the mobility of the AI [2]. Nanoformulation with the property of sustained release and with boarder applicative potentials at large scale is urgently needed though several studies have shown that nanoformulations can escape drift and volatile losses during application [4].

Information on synthesis, characteristics and nanoformulations or nanoparticles of a few biopesticides based on plant-derived products (PDP) is available [5–10]. Currently, nanotechnology seems to be unsafe to nontarget organisms, humans and environment [11, 12]. No systematic comparative study of PDP nanopesticides and synthetic or other commercial products has been carried out. It is expected that the future nanotechnology measures would improve formulations and application techniques to reduce the load of chemicals in agriculture and the treatment cost while increasing the yield potential of food crops [4]. Moreover, crop and grain protection can be improved by enhancing the selectivity, bioefficacy and longevity of PDP by encapsulation and other processes with due consideration to impact on the environment, agro-ecosystems and humans [13, 14]. Application of nanopesticides in plant protection attracted attention of the researchers and farmers and has been recommended for cost-efficient sustainable agriculture. The objective of this mini-review is to discuss current practices of plant-derived nanopesticides (being environmentally friendly and safe to nontarget organisms) against insect and mite pests, to point out whether their applications have undesirable side effects and to describe caution about its future expansion in field crops and storage structures.

Important physicochemical aspects of conventional and nanoforms of pesticides

Molecular and physicochemical aspects of agrochemicals (ACs) including pesticides basically determine their applicative potentials, environmental fate and effects on an agroecosystem. Irrespective of the form of formulation (conventional or nano), it is imperative to consider and discuss the molecular and physicochemical aspects of a pesticide before using for crop protection. In the recent time, different schools of thoughts have expressed their views on the pros and cons of switching from conventional form to nanoform of a pesticide. However, one obvious and serious concern that is yet to be addressed is the toxicity of nanoformulations of insecticides that originate from their persistence in environment and mobility into soil. In fact, nanopesticides must be analyzed for some of the very basic molecular and physicochemical aspects that determine their efficacy, stability and environmental and/or human safety. In the next few subsections, readers are navigated through the some of the fundamental properties of a pesticide that categorically decides its suitability for nanoform or not and how these aspects can be applied in designing nanoformulations.

Chemical structure and chemical composition

Molecular geometry, freedom of rotation, chains, branches and/or rings of bonded atoms and elemental composition play a decisive role in the applied domain of a pesticide [15, 16]. Variation in functional groups causes difference in solubility and reactivity of pesticides. So far, no study has been carried out to find whether conventional and nanoforms make sense in enhancing or diminishing the effects of chemical structure and composition on the biological and chemical reactivity of pesticides which can predict the degree of interaction with environment.

Water solubility

Water solubility of a pesticide is of paramount importance for its action. From chemistry point of view, highly water-soluble pesticides will be less volatile, more reactive and environmentally unstable or less persistent. It is obvious that nanoform has higher surface area as compared to bulk form of an insecticide; however, it will be pertinent to discussing how downsizing can help in manipulating the solubility. Nanoentities are generally dispersed in a suitable solvent (hydrophilic or hydrophobic) according to their surface property. Nanotechnologist better term them as 'colloidal dispersion,' not 'colloidal solution.' A solvent/solvent system that facilitates excellent dispersion to nanoentities is a common ground of choice. Nanoformulation of an insecticide can be designed either as (a) carrier + payload or as (b) direct application. In the first case, the dispersion of the payload (insecticide) in water will be influenced by the solubility property of the carrier molecule as well. Once released from the matrix of the carrier, the dispersion of the payload becomes more dependent on its size range and is governed by colloidal principles. For conventional form of an insecticide, solubility simply follows the chemistry principle 'like-dissolves-like.' An insecticide in nanoform (suppose nanoform of glyphosate without carrier) will simply be dissolved after contact with water. So, dispersion and solubility are the two distinct consequences that can define the appropriateness of selection of nanoform over bulk or conventional form for any insecticide. It is worth mentioning that most of the nanoformulations of ACs reported so far are based on 'carrier + payload' module that makes sense only in terms of more accessibility or more bioavailability. Thus, water solubility of a pesticide seems to remain unaffected by its physical forms (nano or bulk) of application.

Volatility or air solubility

Functional efficiency of a pesticide is influenced by its volatility or air solubility which is expressed as the log of vapor pressure (VP). A pesticide with higher VP will turn into gas faster and thus will be lost before reaching the target [17]. One of the important nanosafety aspects of application of nanomaterials is the less volatility or good solubility, preferably in water. For long-term protection, pesticides should have lower VP. Based on the climatic conditions, the volatility also keeps changing. Higher temperature (tropical climates) will cause faster conversion of a liquid pesticide to gas phase. Moreover, volatilization of pesticide is also dependent on the site (e.g., foliage, soil, etc.) of application. With higher surface area, nanopesticides might evaporate at faster rate than conventional forms. ACs in nanocomposite forms have shown lower volatilization compared to a control [18]. However, control of volatilization also needs to be investigated for nanoformulation without a matrix. Rate of volatilization is also dependent on the mode of application. A nanopesticide applied into soil (incorporated mode) will have to be first desorbed from soil particles, followed by movement along the soil–air interface and volatilization [19]. This established fact can be explored for manipulating desorption kinetics and soil surface movement of nanopesticide by changing surface properties such as surface charge, surface functionalization, particle size and surface energy.

Nature of formulation

The general recommendations for preferred nature of formulations of pesticides are emulsion, granular or pellets, which are attributed to less drift and volatile losses during application. Other nature of formulations, such as dusts, sprayable liquid, wettable powders and liquid mixtures, is not recommended because of their susceptibility to drift, volatilization and runoff losses [20]. Several recent studies have shown that nanoformulations of pesticides can escape drift and volatile losses during application [21].

Stability of nanopesticides

Kinetic stability of colloidal dispersion is must for targeted application. Nanopesticides, particularly the liquid formulations, are governed by the colloidal principles concerning the physics of intermolecular and interfacial forces including van der Waals forces, electrostatic forces, surface tension and strong forces. Unstable colloidal dispersion forms nanoagglomerates, followed by aggregates, and this reduces the functional efficiency. In general, the colloidal stability of nanopesticides will be governed by the following equation and the value of Debye length (κ^{-1}) can influence the stability of nanopesticides in a dispersed medium [21]

$$\kappa^{-1} = \sqrt{\frac{\varepsilon_r \varepsilon_{0k_{\mathrm{B}}T}}{2 \times 10^3 N_{\mathrm{a}} e^2 I}} \tag{1}$$

where I is the ionic strength of the electrolyte in molar units, ε_0 permittivity of free space, ε_{r} dielectric constant, k_{B} Boltzmann constant, T absolute temperature in Kelvin, N_{a} Avogadro number and e Elementary charge.

Based on the ionic strength of the dispersion medium, the value of κ^{-1} can change and causes respective changes in the particle–particle interactions. As it can be predicted from Eq. (1), an increase in the ionic strength (I) will result in a decrease in the value of (κ^{-1}). This will finally lead to a decrease in the electrostatic interactions and starts aggregation. For each colloidal system, the threshold ionic concentration at which aggregation starts is called as critical coagulation concentration (CCC) and it is imperative to have this information for nanopesticides.

Apart from the Debye length, kinetic stability of nanopesticide can also be influenced by thermal energy, energy barrier and interaction energy [21]. Thermal energy is expressed as follows:

$$\text{Thermal energy} = k_{\mathrm{B}}T \tag{2}$$

where k_{B} is the Boltzmann constant and T Temperature.

The expression for energy barrier can be given as follows:

$$\text{Energy barrier} = \Delta E_{\mathrm{c}} \tag{3}$$

where E is the interaction energy.

In a colloidal system, based on the nature of particle–particle interactions, the dispersion might be stable or unstable. In the first case, value of ΔE_{c} should be greater than that of $k_{\mathrm{B}}\,T$, while the reverse case will cause unstable dispersion. Mathematically, these two cases can be expressed as follows:

$$\Delta E_{\mathrm{c}} \gg \Delta k_{\mathrm{B}}T \, : \text{ Stable dispersion}$$

$$\Delta E_{\mathrm{c}} \sim k_{\mathrm{B}}T \, : \text{ Unstable dispersion}$$

The interface domain discussed under this subsection is pertinent and of serious concern for better understanding the fate of nanopesticides in the post-application phase and also important for standardization of technical features nanopesticides based on the nanoscience and colloidal science principles.

Potential of nanopesticides for agricultural pest control

The mechanism of actions of metabolites (alkaloids, flavonoids, terpenoids) present in PDP can vary due to the complex mixture of compounds which act in various ways on insects such as antifeedant, repellent, oviposition deterrent, insect growth regulator and toxic [22]. Isman commented that PDP or botanicals have not moved from the laboratory to the farm [23]. In fact, with introduction of organic farming in developing countries, conventional plant products (crude oil, seed cake, water extracts) and commercial formulations (wettable granules, AI, emulsifiable concentrates, solvent-based extracts) are routinely applied by small and marginal farmers [22]. In some instances, the conventional PDP proved as effective as commercial/formulated formulations [24]. Similarly, essential oils (EOs) performed better in bioefficacy than extracts probably because of mixed contents of AI and other allelochemicals which may have synergistic effect [25].

In agriculture, chemical pesticides are extensively applied by farmers due to availability of ready-made formulations and quick 'knockdown effect' on insect life stages. Often, the applied pesticides do not reach the targeted plant parts and the dose/concentration of AI is not supplied in required quantity to control insects because > 90% of applied pesticides are lost to the air during the application and as runoff, not only in the air, but also in the soil and water [26, 27]. Moreover, whenever farmers do not follow recommended mixtures, doses (misuse or overuse), application techniques and safety measures, the repeated applications result in rapid buildup of insect resistance, content of harmful pesticide residues on/in plant parts, and can cause harm to the environment, nontarget organisms and humans [22]. For example, application of popular neonicotinoids in agriculture is debatable because of danger to honeybees [28]. Continuous efforts are therefore being made by the government departments and extension agencies to reduce the number of applications of synthetic pesticides. Besides, there is a worldwide movement to shift chemical-based plant protection to green technology (e.g., biopesticides, PDP, semiochemicals, etc.) [7]. Plant products degrade rapidly by sunlight leaving less persistence in the environment, lower likelihood of the target organisms developing resistance, low residual toxicity and comparative safety to nontarget organisms [22].

Compared with conventional pesticides, the improved properties in PDP nanotechnology are attributed to controlled system releasing small-sized molecules at the site of action, enhancing the target specificity, optimizing the action of the AI, minimizing the residual impacts and improving both the physicochemical stability and effectiveness of AI [27, 29]. It is presumed that nanopesticides have low impact on environment and human health and presents reduced toxicity to animals and nontarget organisms [29]. Overall, nanopesticides showed enhanced biocompatibility, biodegradation, efficient delivery of AI and ability to modify. As such, aqueous extract or extract in solvents, seed/seed kernel oil and essential oils of plants have been experimented as nanopesticides in the form of formulations/emulsion, particles and capsules on ten crop pests and four storage pests.

Control of crop pests

Stem, leaf and fruit/seed feeding insects

Giongo et al. [30] evaluated AZ on corn plants at laboratory scale and in greenhouse against fall armyworm, *Spodoptera frugiperda* (J.E. Smith) in Brazil. At laboratory scale, corn leaves treated with four nanoformulations containing 3.87 mg AZ/l were offered to first instar larvae for 10 days. In all five bioassays, nanoformulations proved inferior (45.0–75.0% mortality) compared to organic NO (56.2–100% mortality). However, there was a significant decrease in larval weight after application. In greenhouse experiment, corn plants were sprayed with seven formulations of nanocapsules and nanospheres containing neem leaf extract (NLE) or NO and surfactant (Tween 80). All nanoformulations presented lower or no efficiency probably due to low degradation rate of the polymers. Nanocapsules were composed of polymeric layer coating of a mixture of commercial NO and neem seed kernel extracts (NSKE), whereas nanospheres contained polymetric matrix containing only NSKE. Three polymers, viz. PCL, poly (beta) hydroxybutyrate (PHB) and poly (methylmethacrylate) (PMMA), proved quite effective, indicating that they can be used for encapsulation. There was reduced structural stability of nanocapsules when prepared with polyvinyl acetate (PVA) instead of Tween 80 leading to better release. Similarly, most of the nanoformulations in suspension were more effective than in the powder formulations.

In another study, silver nanoparticles synthesized with the aqueous leaf extract (5, 10, 20, 30, 40, 50 mg/ml) of *Aristolochia indica* L. were applied against third instar larvae of cotton bollworm/gram caterpillar, *Helicoverpa armigera* (Hb.) [31]. Maximum antifeeding activity of 72.2%, 92.4%, 97.3% and 4.3% was observed in crude aqueous (50 mg/ml), Ag nanoparticles (112 nm size), AZ (50 ml/l) and $AgNO_3$ (50 mg/ml), respectively [31]. Similarly, larval mortality was 87.7%, 100%, 100% and 2.6% for these four products. Ag nanoparticles showed better efficacy in terms of LC_{50} than $AgNO_3$ or AZ. On the contrary, the cytotoxic activity was lower with TC_{50} values of > 100 µg/ml and 89 µg/ml for extract and Ag nanoparticles, respectively.

Recently, Kamaraj et al. [10] prepared neem bark gum extract nanoformulation (NGNF) with $TiCl_4$ as carrier and evaluated its impact on larval feeding, and larval and pupal mortality in two important polyphagous insect pests, *H. armigra* and *Spodoptera litura* (Fb.) [10]. In NGNF, the major compounds identified were fatty acids (hexadecenoic acid, oleic acid and ricinoleic acid). Application at 100 ppm showed significant difference in the activity of detoxifying enzymes in the larval gut reflected by 100% antifeeding activity compared to 74.8–82.2% with simple neem gum extract (NGE) and 68.2–76.8% with AZ, both at 100 ppm. Larvae of *H. armigera* treated with NGNF at 100 ppm in second, third and fourth instars were killed up to 100%, 96.4% and 92.4%, respectively. The mortality level in *S. litura* was 100%, 90.5% and 86.8% for the three instars, respectively. This treatment was followed by NGE with 68.4–56.5% antifeeding activity in both insects. Mortality in pupae of both insects was 100% in NGNF at 100 ppm, followed by 68.4% and 72.1% at 100 ppm in NGE. Apart from mortality, different degrees of abnormalities (larval–pupal intermediate, pupal–adult intermediate) were observed in NGNF-treated larvae. LC_{50} values for *H. armigera* were 10.20 ppm and 38.36 ppm for NGNF and neem gum, respectively, whereas these values for *S. litura* were 12.49 and 42.80 ppm, respectively. In all parameters, NGNF proved superior to NGE and $TiCl_4$ [10]. The detoxification of metal through feces was higher in NGNF than in NGE. Thus, the nanoformulation was completely detoxified and proved safe for nontarget organisms.

Forim et al. prepared poly (alpha-caprolactone) (PCL) nanoparticles and powder form containing AZ and tested against the larvae of diamondback moth, *Plutella xylostella* (L.) [32]. The nanoparticles of particle size of 245 nm showed reasonable stability of AZ in the presence of UV radiation and increased its dispersion in aqueous extract with 100% mortality at 5000 mg AZ/kg. The tomato borer, *Tuta absoluta* (Mayrick), is an important pest of tomato and other vegetables. Compolo et al. [33] evaluated nanoparticles of essential oils (EONP) extracted from peels of three citrus species for contact toxicity to eggs and adults and for ingestion toxicity to larvae. Significant results were obtained in sweet orange, *Citrus sinensis* (L.) with 40.4% versus 22.1% in EO for egg morality and 46.0% versus 24.0% in EO for adult morality [33]. On the contrary, EONP of mandarin, *Citrus reticulata* Blanco, resulted in higher mortality (62.0% versus 18.0% in EOs) in larvae. The EO nanoparticles of lemon, *Citrus limon* (L.), were less effective than EOs in reducing pest population. Al-Barly and Hamza assessed larvicidal effect of aqueous extract of *Moringa oleifera* Lam. leaves using TiO_2 nanoparticles as carrier against the red palm weevil, *Rhynchophorus ferrugineus* Olivier [34]. When extract was applied topically to the larvae at 50, 75,100,150 and 200 mg/l, the dose of 75 mg proved the most effective with 40.0% mortality 2 days after application and 100% mortality 10 days after application. This plant is readily available in villages, and extraction can be done at local level.

Leaf sap-sucking insects and mite

While comparing the bioefficacy of Ag and Ag–Zn nanoparticles with imidacloprid against Nerium aphid, *Aphis nerri* Boyer de Fonscolombe, a major pest of ornamental plants in Brazil, Rouhani et al. [35] observed that imidacloprid caused highest mortality of 11.0% at 1 µl/ml (LC_{50} of 0.13 µl/ml), whereas nano-Ag and nano-Ag–Zn caused mortality of 9.6% at 700 mg/ml (LC_{50} of 424.67 mg/ml) and 8.6% at 700 mg/ml (LC_{50} of 539.46 mg/ml), respectively. Pascual-Villalobos et al. [36] tested nanoemulsions of essential oils extracted from aniseed/anise (*Pimpinella anisum* L.), lemongrass and peppermint at laboratory level against oat aphid, *Rhopalosiphum padi* L. At a lower dose of 0.02 $\mu l/cm^2$ of treated leaf, EO cis-jasmone showed 68.8–100% repellency to wingless females, whereas at high dose of 0.15 $\mu l/cm^2$ it proved toxic and killed aphids (LD_{50} of 0.11 $\mu l/cm^2$). When surfactant lecithin (ratio of 1:2) or lecithin + glycerol (ratio of 1:2:1) in addition to AI were mixed in EO, emulsion produced more stable and active formulation. Also, small particles showed greater activity than the large ones. These criteria are important for nanopesticides to be effective and persistent under field conditions.

A mixture of ZnO (28%) + TiO_2 (70%) + Ag (2%) caused 100% mortality (LD_{50} value of 195.27 mg/l) in western flower thrip, *Frankliniella occidentalis* Pergande at laboratory level [35]. To control cotton whitefly, *Bemisia tabaci* (Genn.), Christofoli et al. [37] evaluated insecticidal effect of nanospheres containing essential oils (B-elemene, alpha-elemene, B-caryophyllene, D-geracrene) from *Zanthoxylum rhoifolium* Lam. Encapsulation (particle of < 50 nm) exhibited significant reduction ($> 95.0\%$) in fecundity and nymph populations. Similarly, Samith et al. [38] found significantly higher mortality in pistachio psylla, *Agonoscena pistacie* Burelhardt and Lauerer by applying nano-ZnO and nano-ZnO–Al_2O nanoparticles than amitraz, a common insecticide applied against this pest in Iran. The citronella EOs encapsulated in zein nanoparticles were highly repellent to a red spider mite, *Tetranychus urticae* Koch, which is a major pest of crucifers and other agricultural crops [39].

Control of storage pests

While studying bioefficacy of plant-mediated Ag nanoparticles against rice weevil, *Sitophilus oryzae* (L.), an aqueous extract of *Euphorbia prostrata* Aiton leaves was the most effective with 100% mortality on 7th day of treatment

[40]. On 14th day, aqueous extract and $AgNO_3$ resulted in total pest mortality. The LD_{50} values for aqueous extract, $AgNO_3$ solution and synthesized Ag nanoparticles were 213.32 mg, 247.90 mg and 44.69 mg/kg, respectively. The corresponding LD_{90} values were 1648.08 mg, 2675.13 mg and 168.28 mg/kg. In another study, Sankar and Abideen studied pesticidal effect of green synthesized Ag and lead nanoparticles using mangrove plant, *Avicennia marina* (Forssk.) Vierh extract, and reported 100% mortality in *S. oryzae* adults within 4 days of treatment [41].

Nanoparticles (240 nm size) loaded with garlic (*Allium sativum* L) essential oil using polyethylene glycol as carrier killed > 80.0% of adults (11.0% mortality in the control) of red flour beetle, *Tribolium castaneum* Herbst, after 5 months. This action was attributed to slow with controlled dispersion and persistent release of AI from the nanoparticle [42]. Nenaah studied toxicity and growth inhibitory activities in *T. castaneum* of nanoemulsions of EOs extracted from three *Achillea* species [43]. Among them, *A. biebersteinii* Afan. showed greater effectiveness in adults than larvae in laboratory with three application techniques. The LC_{50} values for larvae and adults were 47.8–62.3 µg/mg and 21.8–50.7 µg/mg insect in topical application, 41.7–93.2 µl/l and 36.1–80.6 µl/l air in filter paper impregnation and 11.0–27.5 µl/l and 8.8–21.3 µl/l air in fumigation of nanoemulsion. Additionally, grains treated with nanoemulsion exerted certain actions such as prolongation of larval development period and life span of adults and significant reduction in the progeny of F1 generation.

The nanoformulations comprising NO emulsion, nonionic surfactant (e.g., alkyl poly glucoside or polysorbate 80) and water having particle size of 208–507 nm showed excellent contact toxicity against adults of *S. oryzae* with 85.0–100% mortality and *T. castaneum* with 74.0–100% mortality at 1% AZ after 2 days of exposure compared to non-formulated NO [44]. Later, Choupanian and Omar tested four formulations in filter paper experiments and six formulations for food impregnation. At a dose of 2 ml, AZ/kg food caused 100% mortality in *S. oryzae* adults after 24-h exposure. Similar results were obtained with filter paper. In both techniques, adults of *S. oryzae* were more susceptible than those of *T. castaneum* on the basis of LT_{50} values [45].

Toxicity of imidacloprid microcrystals (7 nm length) encapsulated with polysaccharides chitosan and sodium alginate to a tenebrionid beetle, *Maritanus dermestoides* Chevrolet, significantly increased in adult mortality when coated with 50% nanoparticles ($SD_3/Ag/TiO_2$–imidacloprid) compared to the 95.0% with imidacloprid alone. Capsules prolonged the release time of crystals and had the highest photocatalytic activity because of synergistic effect [46]. In Mexican bean weevil, *Zabrotes subfasciatus* (Boheman), the AZ-coated nanocapsules (particle size of 1–5 nm) showed high mortality in adults. The nanocapsules lasted for 14 days with only 20% degradation from UV radiation compared to zero stability in unencapsulated compound [47].

Current issues and challenges

We discuss below how the plant-derived nanopesticides pose certain risks of their application to agricultural crops and stored grains [4, 11, 48].

Bioefficacy

For achieving desired level of pest control, nanocarrier and AI need to be provided in required quantity because nanocarrier may have limited bioavailability. Therefore, bioavailability and durability of these components in PDP-based nanopesticides should be ascertained [4]. The commercial products, particularly those in powder formulation, showed greater UV stability than encapsulated nanoformulations [47]. In practice, farmers prefer liquid formulations. Therefore, increasing stability and persistence in solid formulations is a challenge to manufacturers. For encapsulation of hydrophilic molecules in polymer-based nanoparticles, Vrignaud et al. [49] recommended that while increasing uptake of AI for enhancing bioefficacy risks to nontarget organisms should be minimized.

Phytotoxicity

Cytotoxic and genotoxic effects in plants caused by AZ in nanoformulation have been reported by Kwankua et al. [50]. During plant development, toxicity is, however, reduced by sunlight to undetectable level. In another instance, Liu and Xing reported five types of nanomaterials (multi-walled carbon nanotubes, nanotubes, Al, Zn and ZnO), showing no adverse effect on seed germination in five vegetables and rye grass except for the inhibition by Zn in ryegrass and ZnO in corn at 2000 mg/l and termination of root elongation of all plants at this dose [51]. No phytotoxicity in corn plants treated with nanocapsules (particle size of 400 nm) containing 200 mg NO was observed, while other formulations containing a mixture of 100 NO/100 oleic acid or 150 NO/50 oleic acid led to negative effect on the physiological parameters [29].

Toxicity to nontarget organisms

In nanoformulations, addition of NO on polymeric nanocarriers (e.g., PCL, beta-cyclodextrin) showed less toxicity to *B. tabaci* parasitoids including the parasitic wasp, *Encarsia formosa* Gahan [52].

Soil-dwelling earthworms and microorganisms are exposed to plant-derived metallic nanoparticles (PMP) through dermal and respiratory routes. The uptake, bioavailability and toxicity of nanopesticides depend upon the particle number, concentration, particle size, distribution and ratio of free and engineered nanopesticide-bound AI [53]. Release of metallic nanoparticles into terrestrial environment is still disputable for safety to nontarget organisms because of persistence in environment because with soil microorganisms, PMP can have different effects on the capped phytochemicals and metal core [12]. This can inadvertently happen as soil microorganisms and earthworms transform plant debris into organic matter and initiate mineralization. Humus produced by non-enzymatic chemical reactions is also stored in the soil. Microbial decomposition of the surface-capped plant molecules will render the surface of PMP naked and ultimately less effective [12].

Psquoto-Stgliiani et al. [29] showed that the nanocapsules (particle size of 400 nm) containing PCL treated with NO did not affect soil microbiota during exposure of 300 days. Similarly, the laboratory study using filter paper test and artificial soil test by Kamaraj et al. [10] showed < 10.0% mortality in African earthworm, *Eudrilus eugeniae* (Kinberg), which is a bio-indicator and sol decomposer. Low-level mortality was recorded with application of NGNF or NGE at 100 ppm compared to 100% mortality by cypermethrin (a common pyrethroid insecticide). Additionally, nanoformulations improved biomass of adult earthworms even after 72 days of exposure to treated soil [10].

In aquatic environment, the physicochemical properties of the engineered nanomaterials can influence surface charge, surface coating and other properties. Also, surface-capped plant molecules can alter the nanospecific fate of PMP while processing (e.g., homo-/hetero-aggregation, surface modification, sedimentation, dissolution, etc.) [12]. Since the nanopesticides may not be safe to environment, there is need to understand environmental fate and role of surface-capped plant molecules of plant-derived products in nanospecific processes and applicability of colloidal behavior needs to be known [12].

Toxicity to animals and humans

Since nanomaterials are innocuous in bulk form, they often become toxic when they reach nanosize. Particularly, the non-biodegradable materials (particularly metals) which accumulate and stimulate the immune system can pose an increased toxicity in soil, plants and mammals, and activity of detoxifying enzymes is altered by nanoformulations [54]. Nanotube filled with aluminosilicate can stick to plant surfaces and can enhance product stability, while their ingredients are able to stick to the surface hairs of insect pests, ultimately entering the human body and affecting certain physiological functions [11]. Apart from ingestion, nanoparticles can enter human body by inhalation or dermal contact. Inhalation toxicity due to sub-acute and chronic exposure is common among pest control operators and often poses a major health risk to field workers.

Environment

Current regulatory protocols for assessment of risk to environment are applicable only to bulk insecticides. Therefore, there is need to formulate guidelines for nanoformulations as they have different properties [55]. For future applications, the risk assessment framework is to be practiced rigorously because tests used for commercial bulk production of synthetic pesticides may not hold valid for nanoparticles [56]. Jamilek and Kralova discussed possible risks to environment, and Tiede et al., Watson et al. [59] and Kookana et al. [53] described existing regulations in the USA and Europe which can be referred as guidelines for future programs and projects [53, 57–59].

Further research on socioeconomic aspects (cost/benefit ratio of application, price of nanoformulations, acceptance by small and marginal farmers, easy and safe application techniques, local availability) would be ideal while recommending nanopesticides in agricultural crops and stored grains. In nature, interactions between nano-sized chemicals and the various climatic stresses in the agro-ecosystem are possible and may result in synergistic, antagonistic or susceptibility to environmental adverse effects and their combinations [60].

Conclusions

Nanoformulations have shown greater efficacy than commercial formulations of synthetic pesticides, and encapsulated AZ was more stable than non-capsulated form. Nanoparticles improved the stability of neem products against UV radiation and increased the dispersion in aqueous phase. However, a safe and effective delivery system for nanopesticides is needed for practical application by farmers. It seems that considering specificity and longevity of available formulations, nanocapsules are the most suitable for soil application to reduce negative environmental impacts. Also, nanotechnology may prove beneficial in precision farming by using wireless sensors and digital systems to forecast environmental conditions, to monitor population dynamics of pests and crop infestation and to organize timely and need-based applications of PDP nanopesticides. The research on nanopesticides is limited probably due to cost of formulating products. Understanding of properties and behavior of nanopesticides would provide firm basis to develop new formulations without any impact on environment, nontarget organisms and humans. Evaluation of environmental fate, uptake by plants, aquatic and terrestrial ecosystems and changes in test methodology should form research priorities. Time-to-time refinement in methodologies would make the current recommendation replicable for general use. Future recommendations would facilitate the development of regulatory approaches and a regulatory framework for the application of plant-derived nanopesticides.

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Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Research involving human participants and/or animals This article does not contain any studies with human participants or animals performed by any of the authors.

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