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Nanopesticides: Current status and scope for their application in agriculture

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Abstract: Nanotechnology is a rapidly evolving field that has the potential to revolutionise food systems and counter the present-day challenge of food security. It envisages taking agriculture from the era of indiscriminate natural resource use and environmental degradation to the brave new world of advanced systems with enhanced material use efficiency and targeted applications to reduce crop losses caused due to abiotic-biotic stresses as well as to give due considerations to the environment. To manage plant diseases and insect pests, pesticides are inevitably used in agriculture. However, the higher dosage of these chemicals on a per hectare basis has resulted in many environmental and health hazards. To tackle the conventional pesticide related issues, a new field of science called nanotechnology has led to the development of nanopesticides that have less active ingredients, but better efficiency. The nanopesticides contain the carrier molecule or the active nanosized ingredient with a very high surface area to the volume property that provides them unique exploitable-advantages. Several formulations, viz., nanoemulsions, nanosuspensions, nanogels, metal compound-based nanopesticides, have been developed for different modes of action and vivid applications. The biggest advantage comes due to the small size of the particles that helps in properly spreading the ingredients on the pest surface and, thus, producing a better action than conventional pesticides. The use of nanoparticles in the form of nanopesticides, nanofertilisers, and nano delivery systems is on the increase day by day due to their higher efficiency and reduced dosage requirements. However, human beings and other organisms are also getting exposed to the nano-entities during the application or afterwards. The interactions of these engineered nano-entities with biological systems are relatively unknown thus far. Therefore, before their wider usage in crop production and protection, a better understanding of their interactions, and adverse effects, if any, is also crucial for a sustainable transition.

Keywords: nano-formulations; productivity; pests; diseases; crop management

Globally, a huge part of the population is dependent on agriculture for their livelihood and is engaged in the production of food, feed, and fibre crops. The world population is expected to reach 10 billion by 2050, out of which, developing countries will contribute approximately 95% of the global population increase (Carvalho 2006). Although technological innovations are boosting crop productivity, the growth of yields of various crops has slowed down due to the degradation of natural resources, the loss of biodiversity, and the spread of transboundary pests and diseases of plants, some of which are becoming resistant to pesticides. As per an estimate, worldwide insect pests are causing a 14% loss in agricultural production, however, plant pathogens and weeds are responsi-

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ble for a 13% loss, which accounts for an economic loss of 2 000 billion USD per annum (Dhawan & Peshin 2009). To cope with the problem of insect pests, pathogens, and weeds, the application of pesticides is considered as the most feasible option to manage them. Pesticides are widely used in agricultural ecosystems to improve the yield quantity and quality due to their easy availability, effectiveness, and ease of application. With the widespread use of pesticides, agriculture today is facing major challenges of environmental contamination, pest resistance, bioaccumulation, and health hazards which need to be addressed and require immediate solutions. Amongst various options, one of the solutions that can be applied is the reduction in the quantity of pesticides applied for a crop and or used in the protection of a stored product. In this direction, nanotechnology is becoming a highly attractive tool to achieve the target of lowering the quantity of pesticide use, thereby offering new methods for the formulation and delivery of a pesticide's active ingredients, as well as novel active ingredients, collectively referred to as nanopesticides (Hayles et al. 2017).

Nanotechnologies deal with materials on a nanometre scale and are demonstrated to have great potential in providing novel solutions to pest problems (Sasson et al. 2007; Unsworth et al. 2016; Kashyap et al. 2020). The use of nanotechnologies will overcome the limitations associated with conventional pesticides by enhancing the pesticide efficacy, improving the stability of the active ingredients, reducing the required pesticide dose, and conservation of the agri-inputs (Jasrotia et al. 2018). New advanced nano-based formulations are expected to be target-specific, stable, active under different environments, cost-effective to formulate and manufacture, and preferably possess a new mode of action (Smith et al. 2008). Although nanopesticide formulations have exhibited low toxicity, good biocompatibility, and higher bioavailability, their application is still restricted because the use of nanotechnologies or nanoparticles (NPs) demands investigation into the possible toxic effects, linked to soil and water contamination. To expend the possible benefits, we need to develop nanoformulations with unique properties, like early degradation without any harmful residues and precise active ingredient release. This article presents an in-depth review of recent advancements in the field of nanopesticides with a specific focus on their advantages and limitations, followed by future perspectives.

NANOPARTICLES

Nanoparticles refer to materials having either nanoscale external dimensions or internal structures. The nanoscale may be defined as the size which generally has an upper limit of about 100 nm (Figure 1). Based on the particle size, nanoparticles have been classified into three categories: (1) ultrafine particles having a size less than 100 nm in diameter, (2) accumulation-mode particles having a size between 100 nm to 2.5 µm in diameter, and (3) coarse-mode particles having a size greater than 2.5 µm in diameter (Sioutas et al. 2005). However, Keck and Müller (2013) classified nanoparticles according to their particle sizes and biodegradability into four classes: (1) size greater than 100 nm and biodegradable, (2) size greater than 100 nm and non-biodegradable, (3) size less than 100 nm and biodegradable, and (4) size less than 100 nm and non-biodegradable. A nanosystem as a unit consists of two basic components, i.e., an active ingredient and a carrier. Currently, nanoformulations can be classified into three basic categories including (1) inorganic-based, solid and non-biodegradable nanoparticles (gold, silver, copper, iron, and silica-based nanoparticles), (2) organic-based biodegradable nanoparticles (liposomes, solid lipid, and polymeric nanoparticles) and (3) hybrid (combination of both inorganic and organic components) nanoparticles.

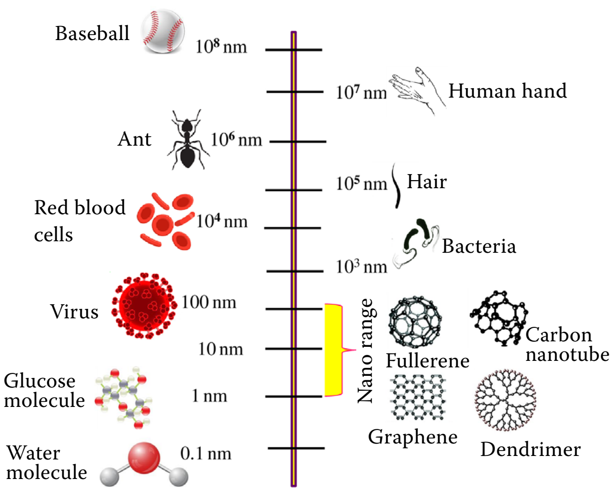

Figure 1. Comparison of the nano-size range to commonly known materials

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ISSUES WITH CONVENTIONAL PESTICIDES

Pesticides are considered one of the important components of crop protection measures and have been used widely in agriculture. Their use during the green revolution era contributed significantly towards increasing the crop yields besides the use of high-yielding crop varieties alone (Popp et al. 2013). However, it is only after the publication of the book "Silent Spring" by Rachel Carson in the early 1960s, the environmental risks associated with their use were first realised (Köhler & Triebskorn 2013). Worldwide, investigations are on-going regarding the hazards associated with pesticide use and their toxicity to humans, animals, and their toxic effects on the ecological balance of life. This area is considered to be one of the most researchable issues nowadays (Laborde 2008). It has been observed that only 0.1% of the pesticides applied by various modes (spray, soil, seed treatment, etc.) reach the target, while the remaining 99.9% leaks into the surrounding environment leading to soil and groundwater pollution, which ultimately hampers the ecological imbalance (Goulson et al. 2015; Kumar et al. 2018). In addition, the use of non-selective pesticides also destroys beneficial natural enemy species, insect pollinators, and birds leading to the proliferation of damaging pest species.

The solubility of pesticides is another limitation in agricultural applications (e.g., Wettable Powders), as the proper dispersion of the active ingredient in the liquid phase is required for spraying. Water is the most convenient medium for pesticide applications due to its low cost, easy availability, and ecological compatibility, but many pesticides are poorly soluble, or even insoluble in water (Whitehouse & Rannard 2010). Therefore, large quantities of organic solvents are required to dissolve them, for their uniform application, and this increases the cost of cultivation, environmental pollution, and increased human exposure (Stackelberg et al. 2001). Additionally, spray efficacy depends upon the stability of the active ingredients in the pesticide formulation because abiotic and biotic factors can degrade pesticides before reaching their target sites. The chemical stability of a pesticide determines its persistence and toxicity to the target organism. Stable compounds are not easily broken down in the environment due to their low water solubility and may end up in aquatic organisms with the run off of the surface water. Most of these pesticides are lipophilic and tend to accumulate in adipose tissues and enter into the food chain. As a result, the pesticide concentration increases at each food chain level known as bioaccumulation, and causes toxic effects on animal and human health. Sometimes, due to the interactions between mixtures of pesticides, phytotoxic effects can also appear which can lead to a complete crop failure (Rizzati et al. 2016).

To overcome the problems associated with the use of conventional pesticides, researchers worldwide started working towards the development of a new pesticide type, i.e., a "nanopesticide", based on nanotechnology principles. Nanotechnology has the potential to mitigate the potential drawbacks associated with conventional pesticide formulations. Reducing the material size to a nano level provides several advantages in terms of the enhanced efficiency, durability, lesser non-target effects, and a reduction in the use of the active ingredients for crop protection which can provide ecological benefits.

BENEFITS OF NANOPESTICIDES

Unlike conventional pesticide formulations, nanoformulations are specially designed to increase the solubility of insoluble or poorly soluble active ingredients and to release the biocide in a controlled and targeted manner (Margulis-Goshen & Magdassi 2013). Therefore, a smaller amount of an active ingredient per area is sufficient for the application and may provide the sustained delivery of the active ingredients which may remain effective for extended periods. Thus, due to the reduced dose, the cost of production, non-target effects, and phytotoxicity are also reduced (Figure 2). Also, it is important for controlled-release formulations that they must remain inactive until the active ingredient is released.

Nanocapsules, nanospheres, nanogels, and micelles are the most frequently synthesised controlled-release formulations and various physical and chemical methods are described for their preparations. Nanoencapsulation with a polymer matrix may enhance the dispersion of hydrophobic active ingredients in aqueous solutions allowing their controlled release with high selectivity and without hindering the biocidal activity (Peteu et al.

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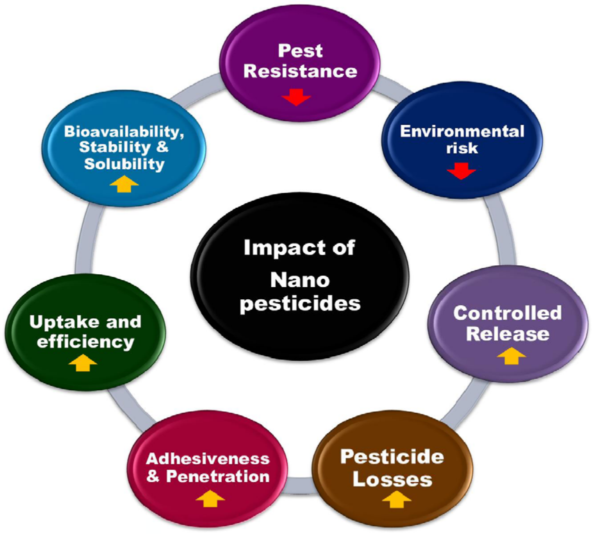

Figure 2. Advantages of nanopesticides in comparison to conventional pesticides

2010). The release profile of an active ingredient is closely connected with the chemical properties of the polymeric matrix, the strength of the chemical bonds, and the size of the biocide molecules. Diffusion or the disassembly of the polymer containing the active ingredient commences after contacting the water and receiving the proper stimuli (Xin et al. 2018).

Encapsulation technologies are widely being used in agricultural applications because, in controlled release formulations prepared using the encapsulation technology, hydrophobic or hydrophilic bioactive compounds can be entrapped, for example, by liposomes formed by lecithin and in micelles (Yang et al. 2014; Demetzos 2015). These can reduce the amount of pesticides used, enhance the stability of the unsteady core materials, suppress the sharp odours of the released chemicals, and secure biocompatibility to carrier systems. Chitosan is predestined to be a valuable carrier for the controlled delivery due to its biodegradability, non-toxicity, and adsorption abilities. A chitosan matrix can function as a protective reservoir for the encapsulated active ingredients, protecting them from the surrounding environment and controlling their release (Kashyap et al. 2015). The benefits of polymer encapsulated nanoformulations in comparison with conventional formulations are the controlled-release (Rudzinski et al. 2002), reduced evaporation, degradation, and leaching losses (Adak et al. 2012), and extended activity of the active ingredients having a short half-life (Bajpai et al. 2007). However, increasing health hazards ranging from inhaling to penetration through the skin are still open for questioning, because nanoformulations have considerably different properties when compared to conventional bulk pesticides (Cao et al. 2015).

CATEGORIES OF NANOPESTICIDES

Nanoformulations of pesticides can be classified according to their intended purpose as (1) formulations that increase the solubility of water-insoluble active ingredients; (2) formulations that slow down the release rate of active ingredients and (3) formulations able to achieve targeted delivery and increased chemical stability (Kah et al. 2013).

Herein, nanoformulations based on the chemical nature of the nanocarriers are reviewed, such as polymer-based formulations, lipid-based formulations, nanosized metals, and metal oxides, clay-based nanomaterials, silica nanoparticles, etc.

Nanoemulsions

Nanoemulsion pesticidal formulations have enhanced bioavailability, improved chemical stability and controlled release mechanisms. Depending upon the quantity and type of surfactant used, nanoemulsions can be further classified as (1) thermodynamically stable and (2) kinetically stable nanoemulsions. Thermodynamically stable nanoemulsions are formed when the non-polar pesticide is partially soluble in the aqueous phase as well as having a strongly repelling surfactant that is present in concentrations higher than critical micelle concentration (CMC). These are highly recommended for commercial formulations due to their chemical characteristics and simple preparation techniques (Tomlin 2009). However, these types of nanoemulsions also have disadvantages, such as the high cost and phytotoxicity due to the requirement of a large quantity of surfactant and limited incorporation into the micelles (Katagi 2008). In contrast, kinetically stable nanoemulsions are formed when the pesticide is almost completely insoluble in the aqueous phase and there is less aggregation of the surfactant molecules into the micelles due to the weakly repelling surfactant (Mason et al. 2006; Song et al. 2009). The main advantage here is that a wider range of surfactants can be utilised (McClements 2012), but the major drawback with such formulations is that the pesticide

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molecules need to be broken up into nanosized droplets before the surfactant is coated for stabilisation purposes. Thus, this approach is inefficient and difficult for commercial pesticide production and on-site preparation on the farmer's level (Anton et al. 2008). Examples of nanoemulsion formulations for the control of pests are described in Table S1 [in electronic supplementary material (ESM); for the supplementary material see the electronic version].

Nanosuspensions/nanodispersions

Nanosuspensions, also called nanodispersions, are pesticide formulations having the dispersion of active ingredients, such as crystalline or amorphous solid nanoparticles, in a liquid medium (Kah et al. 2013). These are stabilised by demixing in water in the presence of the adsorbed surfactant molecules on the nanoparticles. Surfactant molecules are arranged in a manner that the polar portion extends into the aqueous solution and the non-polar portion is associated with the solid pesticide nanoparticles (Acosta 2009). In contrast to nanoemulsions, only kinetically stable nanodispersions can be prepared with improved pesticide solubility and stability of a particle size ranging from 50 nm to 200 nm in diameter (Müller & Junghanns 2006). These formulations have enhanced bioavailability, improved chemical stability, and controlled release mechanisms. Nanosuspension formulations of nanopesticides are reviewed in detail in Table S1 in ESM.

Polymer-based nanopesticide formulations

Presently, the main emphasis is being placed on the protection of photo-labile active ingredients, and the development of controlled-release formulations of herbicides, fungicides, and insecticides using polymers for pest management programmes. Like nanoemulsions, a polymer-based delivery system increases the dispersion of the active ingredients in aqueous media, acts as a protective reservoir cover and facilitates the controlled release of the pesticides. The slow-release of the active ingredients depends on the nanocarrier's degradation properties, bonding between the active ingredients and the carrier, and weather factors.

Polymer-based nanoformulations can provide an improved efficiency of the active ingredients with minimised lethal effects on the ecosystem due to the reduced use of organic solvents and surfactants in the formulations (Li et al. 2018). Due to polymer-based controlled formulations, the spatial and temporal doses are reduced, while the stability and effectivity are improved, the losses are minimised because of the reduced runoff (Chen & Yada 2011). They are also attractive to researchers due to their complex delivery systems by incorporating multiple active ingredients with different modes of action, biocompatibility, and biodegradability. The polymers deployed for nanopesticide formulations consist mainly of polysaccharides (e.g., chitosan, alginates, and starch) and polyesters (e.g., poly-ε-caprolactone, and polyethylene glycol). Nowadays, there has been an increasing trend of using eco-friendly and biodegradable natural materials such as beeswax, corn oil, lecithin (Nguyen et al. 2012), and cashew gum (Abreu et al. 2012). Several polymer nanoformulations, such as nanocapsules, nanospheres, nanogels, micelles, nanofibres, and chitosan-based nanoformulations, have recently been developed and are discussed herein (Table S2 in ESM).

Polymer nanoencapsulations. Nanocapsules are tiny reservoir-like nanostructures comprised of an inner central hydrophilic or hydrophobic cavity surrounded by a polymer coating (Soppimath et al. 2001; Balaure & Grumezescu 2014). Pesticide-loaded nanocapsules are developed either from the fabrication of performed polymers or during the polymerisation of suitable monomers. Polymeric nanomaterials are most commonly used for the encapsulation of active ingredients mainly due to their ecologically compatible and biodegradable nature (Kumar et al. 2017; Ramasamy et al. 2017). Nowadays, scientists are actively developing a series of nanocapsule formulations with several synthetic and natural polymers, such as polyethylene glycol (PEG), poly-ε-caprolactone (PCL), cellulose, chitosan, and alginate-gelatin (Rani et al. 2017; Kumar et al. 2018). The release of the active ingredients in water is significantly slower than commercial formulations and the release rates are directly proportional to the molecular weight of the polymer (Shakil et al. 2010). Different polymeric nanoencapsulations have exhibited properties to significantly reduce the consumption of pesticides while maintaining their low cost, selectively toxic, and biodegradable properties.

Nanospheres. Nanospheres are spherical particles that exhibit enhanced size-dependent properties in comparison to larger spheres and have a size range of 10 nm to 200 nm in diameter (Singh

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et al. 2010). These may be amorphous or crystalline and have the capability of protecting the active ingredient from enzymatic and chemical degradation (Lee & Kim 2005; Mohanraj & Chen 2006). They are prepared in the form of colloidal suspensions using the emulsion-solvent diffusion method which relies on the interfacial deposition of the polymer occurring as a consequence of the diffusion of a water-miscible organic solvent from an oily phase into an aqueous phase. By freeze-drying of the colloidal suspension, powder forms have also been prepared which have been shown to protect against the UV degradation of the active ingredient (da Costa et al. 2014).

Micelles. Polymeric micelles are one of the major classes of polymer-based nanopesticides and are generally formed by the self-assembly of the amphiphilic block copolymers (Kataoka et al. 2001). Micelles are amphiphilic block copolymers that aggregate in water to form colloidal particles having a core-shell morphology. Here, the hydrophobic core acts as a reservoir of the pesticide, and the hydrophilic outer shell helps in the stability, aqueous solubility, and inactivation of the active ingredient (Pérez Quiñones et al. 2018). The hydrophilic blocks come together to form a micellar shell that shields the core having active ingredients from degradation, opsonisation, and provides solubilisation in water (Croy & Kwon 2006). Among other polymeric based nanosized delivery systems, micelles have gained considerable attention due to their high loading capacity, solubilisation of the hydrophobic active ingredients, nanoscopic particle sizes, large surface area to mass ratio, and targeted delivery (Xu et al. 2013). Micelles respond to various external stimuli which is an important factor for a sustained and need-based active ingredient release, e.g., photoresponsive properties of micelles (Jiang et al. 2006).

Nanogels. Nanogels are hydrogel compositions nanoscale in size formed by either physically or chemically cross-linked hydrophilic or amphiphilic polymer networks with a high water holding capacity (Soni et al. 2016). Nanogels can be formulated by a variety of natural or synthetic polymers or their combination. Their unique physical properties provide them distinct advantages over other types of nanomaterials for pesticidal applications. Nanogels are superior to nanospheres because (1) they are insoluble in water and, thus, are less prone to swelling or shrinkage with changes in the humidity (Bhagat et al. 2013), and (2) they have improved loading and controlled release capacities (Paula et al. 2011). These are highly biocompatible with a high loading capacity for the active ingredients due to their hydrophilic nature. The active ingredients entrapped in the nanogel formulations are released only after water penetrates the polymeric network to cause swelling and dissolves the pesticides, followed by diffusion to the surface. Thus, the release of pesticides is closely related to the swelling characteristics of the nanogels, which is further dependent upon the chemical composition of the nanogel formulations. Nanogels not only protect the pesticide from degradation, but also possess characteristics like stimuli-responsive behaviour, softness, and swelling to help achieve a controlled and slow release at the target site. Over the last two years, nanogel formulations of pheromones, essential oils, and copper have been used in plant protection chemicals to meet organic farming standards (Oh et al. 2008; Motornov et al. 2010; Mura 2013; Torchilin 2014).

Nanofibres. Nanofibres can be synthesised from a wide variety of polymeric substances. They exhibit many desirable properties for advanced pesticidal applications due to the unique small-sized fibre characteristics, plus the polymers themselves. As a potential controlled delivery formulation, nanofibres have demonstrated many advantages. The main advantage of such nanofibres over nanospheres and nanocapsules lies in their ability to avoid the release bursts that occur when the active ingredients are not homogeneously distributed within the polymeric matrix (Xiang et al. 2013). The release profile can be controlled by modulating the nanofibre morphology, porosity, and composition. Many factors may influence the controlled release performance of nanofibres, such as the type of polymers used, hydrophilicity and hydrophobicity of the active ingredients and polymers, solubility, additives, and the existence of enzyme in the buffer solution. Hellmann et al. (2011) prepared electrospun nanofibres having a size range of 200 nm to 400 nm loaded with the pheromone (*Z*)-9-dodecenyl acetate. These can be applied across the field in a fashion similar to spider webs ensuring the uniform release of pheromones.

Chitosan nanoparticle based formulations. Chitosan is a bioactive polymer, produced by deacetylation of chitin which is one of the most abundant natural polysaccharides (Badawy & Rabea 2011).

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Chitosan has a wide variety of applications in the biomedical industry, agriculture, genetic engineering, the food industry, etc. due to its antimicrobial and insecticidal activity, nontoxicity, ease of modification, and biodegradability (Divya & Jisha 2018). Chitosan is mainly used in the form of nanocarrier systems due to its biocompatibility, high permeability, solubility, non-toxicity, excellent film-forming ability, cationic properties, and cost-effectiveness (Shukla et al. 2013). The enhanced efficiency and improved efficacy of chitosan nanoformulations are due to the higher surface area, smaller particle size, and higher mobility (Sasson et al. 2007; Kah et al. 2013). There have been several studies describing the use of chitosan for biotic and abiotic stress management in agricultural ecosystems (Wang et al. 2015). Chitosan nanoparticles containing active ingredients easily move through the cell membrane, thus, enhancing active ingredients' bioavailability (Rodrigues et al. 2012). Chitosan also gets easily adsorbed onto plant surfaces, prolonging the contact time between plant surface and pesticidal active ingredients (Kashyap et al. 2015).

Lipid-based nanopesticide formulations

Lipid-based nanocarriers are composed of phospholipids which may self-assemble into many bilayers delimiting the aqueous phase (Sala et al. 2018). These are highly efficient nanocarriers for the controlled active ingredient release due to their specific properties, like the physiochemical storage stability, environmental safety, high loading capacity, and target-oriented smart release system (Zheng et al. 2013). The use of lipid nanomaterials in crop protection is a new area of research and only a few studies have demonstrated their use as efficient pesticide nanocarriers for pesticides. As compared to other active ingredient delivery systems, such as nanopolymers, nanoemulsions etc. these lipid-based nanomaterials have several advantages including reduced chemical degradation, incorporation of both hydrophobic and hydrophilic active ingredients, and feasible large-scale commercial production (Wei et al. 2017; Li et al. 2018). Lipid nanocarriers may overcome the photo-degradation of active ingredients without using any of the UV absorbers (Nguyen et al. 2012). The physical state of the nanocarrier matrix significantly affects the biocide penetration into the plant's roots and further transportation to the target pest species is associated with the plant system. A brief review of nanoliposomes and solid lipid nanoparticles is presented in Table S3 in ESM.

Nanoliposomes. Nanoliposomes are nanoscale vesicular structures having a phospholipid bilayer enclosing an aqueous phase cavity. These nanoliposomes have an average nanoparticle size of 71–350 nm with enhanced physical stability and low polydispersity. The stability of the active ingredients strongly depends on the resistance of the nanocarriers against diffusion through the degrading agents. Nanoliposomes can be produced by mechanical or non-mechanical methods. Mechanical methods include sonication, high-pressure homogenisation, extrusion, microfluidisation, colloid mill, etc. The prime non-mechanical methods are reversed-phase evaporation and depletion of mixed detergent–lipid micelles (Nuruzzaman et al. 2016). The long-term storage of these nanocarriers is not recommended due to the physical and chemical instabilities of liposomes in aqueous dispersions. Lyophilisation is the most commonly used method to prolong the shelf-life of these nanoliposomes (Chen et al. 2010). Bang et al. (2009) firstly described the preparation of nanoliposomes for the controlled release of pesticides. Kang et al. (2012) proposed that the simultaneous application of conventional and nanoformulated active ingredients can reduce the frequency of the application and, thus, the cost of production.

Solid lipid nanoparticles. Solid lipid nanoparticles (SLNs) are one of the novel potential nanocarriers which are composed of a lipid matrix with high melting point and spherical morphology, dispersed in water or in an aqueous solution. They also have many advantages over other nanoformulations, such as physical stability, good biocompatibility, low toxicity and better delivery of the lipophilic active ingredients. There are several techniques that are employed for the production of SLNs including high-pressure homogenisation, emulsification-sonication, solvent emulsification-evaporation, solvent diffusion, solvent injection, and double emulsion, which is particularly suited for the production of hydrophilic active ingredient loaded SLNs (Das & Chaudhury 2011). Solid lipid nanoparticles are being developed on a large scale as an alternative to polymer-based nanoformulations for the delivery of agrochemicals (Pardeshi et al. 2012). Nguyen et al. (2012) developed second-generation solid lipid nanoparticles incorporating liquid lipids in the solid matrix to increase the pay-

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load and to avoid the rapid photodegradation and leakage of the active ingredients.

Clay based nanopesticide formulations

Nanoclays or clay-based nanoformulations are the thin sheets of silicate materials, such as montmorillonite clays commonly found in volcanic ash having a 1 nm thickness and a 70–150 nm width (Hakamy et al. 2015; Saba et al. 2016). These have been designed to enhance the adsorption and controlled delivery of neutral and hydrophobic active ingredients. They are considered potential nanocarriers in agricultural applications because of their economic viability and biocompatibility. Clay-based materials have been proven as an innovative approach for eco-friendly active ingredient delivery systems. Choudhary et al. (2006) investigated the use of three clay materials, namely bentonite, kaolinite, and Fuller's earth in combination with carboxymethylcellulose in a controlled release system. Enormous efforts have been aimed at developing stimuli-responsive silica nanocapsules to obtain a smart and controlled active ingredient release (Chen et al. 2017). Silica nanoparticles offered enhanced pesticide loading due to their charged nature. The modification of clay with organic cations improved their affinity for the adsorption of hydrophobic active ingredients (Rodrigues et al. 2013). Clay-based nanocarriers are also useful for the slow and controlled release of active ingredients due to their dimensional and thermochemical stability (Rani et al. 2014). Recently, research has been focused on the development of renewable and biodegradable clay nanocarriers of plant origin (Mattos et al. 2017). Despite these advancements, there are also certain limitations, such as the presence of crystalline impurities in clay nanocarriers and lack of synthesis procedures and suitable surface modification techniques. A brief review of formulated clay-based nanoformulations is discussed in Table S4 in ESM.

Porous silica based nanopesticide formulations

Silica-based nanoformulations are new to the agricultural sector, but are widely used in the biomedical sector because of their easy and inexpensive commercial production. They are highly efficient delivery systems having specific surface properties, porosity, biocompatibility, higher loading capacity, and are safer for the ecosystem (Liu et al. 2014; Vaculikova et al. 2015). Porous silica-based nanoformulations are mechanically more stable and structurally flexible systems than polymeric materials which makes them more appropriate in agricultural applications (Lou et al. 2008). A plant's tolerance to abiotic and biotic stresses may be enhanced with the use of silicon nanoparticles (Barik et al. 2008). Surface-charged hydrophobic silica nanoparticles have successfully been used to control a variety of agriculturally important pests (Ulrichs et al. 2006). They have also successfully been applied as a thin coating on seeds to decrease fungal infections. Monodispersed mesoporous silica nanoparticles with interconnected pores of 3 nm diameter did not exhibit any negative impact on the seed germination (Robinson & Salejova-Zadrazilova 2010). These nanoparticles were transported to different plant organs via symplastic and apoplastic pathways and can be used as a new delivery system for the transportation of pesticides of different sizes into plant systems (Sun et al. 2014). Also, the application of nanoparticles on the leaf and stem tissues did not alter the photosynthesis and respiration capabilities of several crop and horticultural plants. Thus, it could be concluded that silica-based nanoparticle formulations can be applied as a safer pest management technique. A summary of the work undertaken on silica-based pesticide nanoformulations is presented in Table S5 in ESM.

Metal nanoparticles as active ingredients and their nanoformulations

Metal and metal oxide nanoparticles have wide areas of application in medicine, environmental protection, and agricultural applications due to their capability and versatility. These nanoparticles have a very high surface-to-volume ratio, high pore volumes, flexible pore size, effective surface properties, and high thermal stability when compared to other conventional formulations and microparticles (Vellingiri et al. 2017; Nehra et al. 2019). These could alleviate the toxic and harmful effects of conventional formulations, such as non-target action, poor solubility, and ecosystem toxicity (He et al. 2011; Pinto et al. 2017). There are three proposed modes of biocidal action by metal and metal oxide nanoparticles: (1) antimicrobial activity via photocatalysis due to release of superoxide radicals destroying the molecular structures of microorganisms, (2) membrane rupturing due to the accumulation of metal nanoparticles in the cell membrane and

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(3) the uptake of metallic ions into cells followed by disruption of the DNA replication (Chatterjee et al. 2014).

These nanoparticles either act as active ingredients alone or can be formulated with conventional pesticides in an environmentally safe manner. These nanoformulations have enhanced ion exchange capabilities, high adsorption capacity, and excellent electronic properties which offer multiple active sites for active ingredient delivery (Masoomi et al. 2016). A brief account of major metal and metal oxide nanoparticles used for pesticidal applications in agricultural ecosystems is given in Table S6 in ESM.

Silver. Silver nanoparticles (AgNPs) are considered as one of most effective nanomaterials in pest management programmes and have effectively been utilised for the site-targeted delivery of important agrochemical products and as diagnostic tools for early detection of plant pathogens (Kim et al. 2012; Kashyap et al. 2016). They have strong pesticidal, antifungal, antiviral, and bactericidal effects (Chen & Schluesener 2008) and have been found to be very promising against phytopathogens. Silver possesses multiple modes of inhibitory action against microorganisms and they are more effective compared to synthetic fungicides (Aziz et al. 2016). Moreover, AgNP based pesticide formulations deposit higher doses of active ingredients to the target species when compared to conventional formulations (Ragaei & Sabry 2014). At effective dose levels, these nanoformulations have reduced human toxicity, lower pest resistance problems, and a lower cost of production when compared to conventional synthetic pesticides (Jo et al. 2009; Jung et al. 2010). Higher doses are required for them to disrupt biological functions of mammals and freshwater and marine organisms. So, such silver micromolar concentrations have no harmful effects on humans. On the other hand, the use of nano-sized silver particles as antimicrobial agents has become more common as technological advances make their production more economical. However, till now, their ultimate fate in the soil is unknown and may have effects on non-target organisms after continuous accumulation. A high initial cost of development, uncertainties associated with its non-target toxicity, regulatory frameworks, and negative public perceptions have discouraged their development and their further use in open field applications.

Titanium dioxide. Titanium dioxide (TiO_2) is a natural oxide of the element titanium having low toxicity and negligible non-target biological effects. These are extensively used in food products and as ingredients in a wide range of pharmaceutical products and cosmetics, such as sunscreens and toothpaste. The antimicrobial activity of TiO_2NPs is well recognised and several studies have demonstrated that applying titanium dioxide to crops led to the suppression of bacterial and fungal pathogens (Norman & Chen 2011). Nanoscale titanium dioxide was tested, either alone or doped with silver or zinc, against bacterial pathogens in tomatoes (Paret et al. 2013a) and roses (Paret et al. 2013b) and proved to be effective. The efficiency of these nanomaterials strongly depends upon the chemical and physical characteristics including the size, crystal structure, and photo-activation. The main mechanism of action involves reactive oxygen species production, resulting in oxidative stress, genotoxicity, and metabolic change. The main advantage of titanium dioxide formulations is their potential to lower the ecological and toxicological non-target risks as compared to the currently used silver and copper-based treatments. However, human exposure may occur through ingestion, dermal penetration or inhalation during manufacturing and use, while the biological effects and cellular response mechanisms are still not completely elucidated upon. Thus, a deep understanding of the toxicological profile of TiO_2NPs is required.

Copper and copper oxides. Copper nanoparticles (CuNPs) are copper-based small particles in size ranging from 1 nm to 100 nm and can be formulated using natural processes or chemical synthesis (Heiligtag & Niederberger 2013). These nanoparticles have drawn huge scientific attention due to their historical application as colouring agents and modern-day biomedical and agricultural applications as nanosensors (Kashyap et al. 2017). The total cost of the cultivation is an important factor for the selection of plant protection measures and CuNP based pesticides remain inexpensive and efficient relative to modern conventional biocides. These can also be applied frequently or rotated with conventional formulations without any possibilities of resistance development in pest species (Timmer et al. 2008). However, there are certain ecotoxicological concerns over their deliberate use in the agricultural ecosystem because they may enter into terrestrial environments, such

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as soil and plant systems, which will ultimately affect the consumers. The uncontrolled release and inefficient metabolism of the reactive oxygen species are the major consequences of CuNP applications (Anjum et al. 2015). The cupric ions released by CuNPs do not form complexes with other molecules and may cause phytotoxic effects in crop plants (Kurnik et al. 2012).

Other metals and metal oxides. Nanostructured alumina dust or aluminium nanoparticles have been found to protect stored grains from pests. Preliminary experiments showed that the insecticidal activity of aluminium nanoparticles was higher when compared to commercially available insecticidal dust (Stadler et al. 2010). Stadler et al. (2012) compared the pesticidal activity of nanoalumina to the most effective diatomaceous earth formulation in the market and found that nanoalumina was more effective when compared to others. Nanoalumina may, thus, be a good alternative to harmful dust formulations based on diatomaceous earth. However, the detailed mode of action of nanoalumina has yet to be elucidated upon and further research is required to access its effects on the ecosystem.

Zinc oxide nanoparticles (ZnONPs) are nanoparticles of zinc oxide (ZnO) having a size less than 100 nm. These are suitable for application in agriculture due to the easy availability and low price of the chemical. However, phytotoxic effects are associated with the use of ZnONPs, such as effects on the physiological level (inhibition of root growth, delay of plant development), as well as on the cell level (disruption of chlorophyll synthesis, cell membrane damage, or chromosomal aberration), which are often influenced by their size range. A great deal of research has been carried out over the past few decades into inorganic engineered nanoparticles and their ecotoxicological aspects are still being analysed. Further research is required to study their biocompatibility, fate in soil and water bodies, and the impact they cause on biodiversity.

ENVIRONMENTAL CONSIDERATION REGARDING NANOPESTICIDES

One of the considerations favouring nanopesticides over conventional pesticides is that these lessen the environmental contamination through the reduction in pesticide application rates and reduced losses (Jasrotia et al. 2018). Conversely, these may pose a new contamination problem to water bodies and soils due to the enhanced transport, longer persistence, and higher toxicity. Nanoparticles can be prone to rapid sunlight degradation due to the large surface area resulting in the poorer efficacy of active ingredients. Similarly, small droplet sizes may also lead to early evaporation of the nanodroplets before reaching the target. The interaction of nanoformulations with microorganisms, plants, and other animals on different trophic levels is another major area requiring investigation. Moreover, the environmental fate of pesticide nanoformulations on the soil, groundwater, and non-target organisms is unknown. The properties of the nanocarriers and the dispersion of the active ingredients within the nanoformulation matrix determine the release of the active ingredients into the environment. It has been reported that delayed release of nanoparticles over an extended period may affect non-target organisms (Kah et al. 2013).

The nanocarriers mostly used in nanoformulations are either natural polymers or polysaccharides or lipids, which degrade easily; however, very little concern has been raised towards the use of non-biodegradable nanocarriers, such as metal and metal oxides (Kah et al. 2018). Moreover, most of the synthesised nanocarriers are for controlled release which causes human body exposure to nanoformulations in a restricted manner, thus, lowering the health risks in comparison to non-encapsulated pesticides. It can be observed that the majority of studies on determining the impact of nanoformulations on the environment have been carried out at a laboratory level and comprehensive studies on the evaluation of the environmental impacts of nanoformulations under field conditions are lacking (Kah et al. 2018). Phytotoxicity effects of nanoparticles on different plant systems have also been reported. Seed germination and seedling growth decreased in rice crops (Thuesombat et al. 2014), while a significant decrease in the root elongation was observed in tomatoes (Song et al. 2013) with the application of AgNPs. TiO_2NPs inhibited the root hydraulic conductivity, leaf growth and transpiration in maize seedlings (Asli & Neumann 2009). Cvjetko et al. (2018) reported the potential phytotoxicity of silver nanoparticles on tobacco (*Nicotiana tabacum*) plants. The mechanisms and

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effects of the nanoparticle's interactions with plants are only partially understood and more research is required to provide a more complete analysis of the potential risks of nanoparticles on crop plants.

A complex interaction of nanoparticles exists with the microbes in the soil, which play a significant role in determining the environmental fate of nanoparticles. Beneficial microbes present in soil help in the soil organic matter decomposition, nutrient recycling, disease suppression, and growth enhancement. It has been reported that the application of nanoformulations can negatively impact the soil microbial community, which can ultimately deteriorate the soil quality and agricultural sustainability. Sweet and Singleton (2015) reported a reduction in fine root development and shoot biomass of pine trees after application of AgNPs in the soil. The reason was the absence of ectomycorrhizal fungi in the AgNP treated roots that were present in the control samples. The soil type also influences the interaction of nanoparticles with microbes in the soil. It was found the application of AgNPs in a sandy soil was toxic to the beneficial soil bacterium, *Pseudomonas chlororaphis*, whereas no cell death was observed in a loamy soil (Calder et al. 2012). Therefore, application of these nanoparticles as agrochemicals in the soil may have serious consequences on the soil microbial population and can hamper the symbiotic nitrogen-fixation in major legumes.

Given these points, pesticide active ingredients or nanoformulations must be evaluated before registration and commercialisation based on standardised testing guidelines by the Organization for Economic Co-operation and Development (OECD) to understand their efficacy, physicochemical properties, behaviour, environmental fate, and toxicity. Also, a comparison of nanopesticides with their conventional analogues, in all aspects, is necessary to guide future research regarding the environmental risks of nanopesticides. Field experiments require more investigations including long-term sampling following applications, to assess the behaviour and risk of nanopesticides on the ecosystem. There is growing concern in the scientific community about the toxicity and impact of nanopesticide formulations on the ecosystem due to their widespread applications, which requires more investigation and research in these areas.

Therefore, efforts should be made to develop smarter nanoformulations. Smart nanoformulations will reduce the risk of any toxic active ingredient dispersions in the surrounding environment due to the control release profiles and will also have increased efficacy at a reduced dosage of active ingredients as compared to conventional synthetic pesticides. The use of harmful organic solvents in developing pesticide nanoformulations is minimal when compared to conventional formulations as these solvents are highly toxic to the environment (Novikov et al. 2010).

CONCLUSIONS AND FUTURE DIRECTIONS

The development of agro-nanotechnology along with biotechnology could revolutionise agriculture, feed a rapidly growing world population, and improve the living standards in the developing world (Watson et al. 2011). Numerous scientific publications have shown very strong findings in the field of nanopesticides and have provided confidence that nanopesticide based formulations have a bright future and potential for developing safer and efficient chemical pesticide delivery systems for sustainable agriculture. Nowadays, the improvement of conventional pesticide formulations, development of new nanoparticle delivery systems, and use of solid nanoparticles as active pesticidal agents are promising strategies for the development of novel nanoformulations. In this review, we summarised the application of various nanotechnologies for pest management, different types of nanoformulations, and their environmental and non-target impacts. Nanoparticles can alter the physical and chemical properties in comparison with their bulk analogues and have superior application strategies for pharmaceutical, medical, industrial, and agricultural products. The development of polymer-based nanoencapsulations is expected to promote the controlled delivery of active ingredients while reducing their premature degradation due to environmental factors. Moreover, the use of nanoparticles as active ingredients and biopesticides will also eliminate some practical problems like water solubility and plant resistance. In short, there are several advantages of nanoparticle-based formulations including the (1) increased water solubility, (2) protection of active ingredients from premature degradation, (3) extended pesticide delivery, (4) enhanced up-

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take by target organisms, (5) small dosages due to controlled release on receiving proper stimuli, (6) improved surface properties, such as leaf adhesion and penetration, (7) reduced pesticide losses through leaching and runoff and (8) auto decomposition of pesticide nanocarriers after active ingredient delivery.

However, most of the research is oriented towards the development of nanodelivery systems for pharmaceutical drugs and very few papers deal with the use of nanoparticles as pesticide nanocarriers. So, there is a huge potential for the application of nanoparticles in plant protection and these new delivery systems could provide the development of safer and greener pesticides. Also, despite the several advantages nanoparticles can also have, some drawbacks exist, such as low selective toxicity, low biodegradability of inorganic nanoparticles, and development of pesticide resistance in target and non-target organisms due to their indiscriminate use. Moreover, the data concerning the environmental fate of these nanoparticles and their possible negative impact on non-target organisms is scarce and there is a lack of knowledge in this regard. So, increased attention must be paid towards the possible impact and adverse effects of nanoparticles on the environment, non-target organisms, and the development of ecologically safer nanopesticides.

Keeping all these points in view, the future research should be focused on (1) the development of smart nanopesticide formulations to combat the limitations of conventional formulations, (2) development of environmentally sustainable nanopesticide developing technologies using green chemistry, (3) development of technologies for reducing the cost of production of nanopesticides, (4) activity comparison of nanoformulations with conventional analogues at field level to determine their practical utility, (5) ecotoxicological assessment of nanopesticides, and (6) establishment of a legislative and regulatory framework for the safe introduction of nanopesticides in agriculture and in other spheres.

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