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Focus on:

Polymer-based nanoinsecticides: current developments, environmental risks and future challenges. A review

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Introduction. The rapid development of the nanotechnology industry opens new perspectives for modern crop protection strategies. This review summarizes and discusses the use of polymers as nanocarriers of insecticides. They are expected to ensure a higher level of protection for humans and the environment, while ensuring good efficacy of the active ingredient.
Literature. Some of the synthetic polymers (including polyethylene glycol, polylactic acid, polycaprolactone and polyhydroxybutyrate), which are widely used in pharmaceutical or cosmetic areas, can be employed as insecticide carriers. But natural polymers (including chitosan, alginate, cellulose, starch and cyclodextrins) are receiving increasing attention because of their environment-friendly properties. The polymeric materials can be prepared in various types of tridimensional structures, among which nanocapsule, nanosphere, micelle, nanogel and nanofiber are the most common for the delivery of the active ingredient. The environmental risks of polymer-based nanoinsecticides are highlighted, together with the main challenges that must be solved before future marketing. These challenges include the reduction of their production cost and assessment of their performance, especially at the field level. New protocols for characterizing, detecting and quantifying are also urgently required.
Conclusions. Polymer-based nanoformulations appear to be promising for target release of active ingredients while reducing excess runoff. In order to facilitate the development of new beneficial products, collaboration among countries around the world is required.
Keywords. Pesticides, nanotechnology, pests insects, Aphididae, formulation.

Nanoinsecticides à base de polymères : développements actuels, risques environnementaux et défis futurs (synthèse bibliographique)

Introduction. Le développement rapide de l'industrie des nanotechnologies ouvre de nouvelles perspectives pour les stratégies modernes de protection des cultures. Cette revue de la littérature résume et discute l'utilisation des polymères comme matrice de support aux insecticides. Ces nouvelles matrices doivent assurer un niveau de protection plus élevé pour les humains et l'environnement, tout en assurant une bonne efficacité de la matière active.
Littérature. Certains des polymères synthétiques (y compris le polyéthylène glycol, l'acide polylactique, la polycaprolactone et le polyhydroxybutyrate) qui sont largement utilisés dans les domaines pharmaceutique ou cosmétique, peuvent être utilisés comme matrice de support aux insecticides. Mais les polymères naturels (dont le chitosane, l'alginate, la cellulose, l'amidon et les cyclodextrines) bénéficient d'une attention croissante en raison de leurs propriétés écologiques. Les matériaux polymères peuvent être préparés sous différents types de structures tridimensionnelles, parmi lesquelles les nanocapsules, les nanosphères, les micelles, les nanogels et les nanofibres sont les plus courantes. Les risques environnementaux des nanoinsecticides à base de polymères sont discutés, ainsi que les principaux défis à relever avant leur commercialisation future. Il s'agit notamment de la réduction de leurs couts de production et de l'évaluation de leurs performances, en particulier sur le terrain. De nouveaux protocoles de caractérisation, de détection et de quantification sont également nécessaires de toute urgence.
Conclusions. Les nanoformulations à base de polymères semblent prometteuses pour la libération ciblée de matières actives insecticides tout en réduisant la dérive de ces substances nocives. Afin de faciliter le développement de nouveaux produits bénéfiques, une collaboration entre les pays du monde entier est nécessaire.
Mots-clés. Pesticides, nanotechnologie, insectes nuisibles, pucerons, formulation.

1. INTRODUCTION

Nanotechnology is considered as the fifth revolutionary technology of the last hundred years, after biotechnology (Chhipa, 2017). Nanoscale materials are increasingly used in electronics, energy, medicine and life sciences, which benefit from their small size, chemical composition, surface structure, solubility, shape and aggregation (Nel et al., 2006). In the recent two decades, the knowledge accumulated in these areas is being transferred and adapted in the agricultural sector, facilitating the development of plant protecting agrochemicals (Mattos et al., 2017). In order to avoid the deleterious effects of pesticides, the agrochemical industry looks for new active ingredients (AI), but also develops new pesticide formulations (Villaverde et al., 2017), enhanced by the development of nanotechnology.

The key motivation to develop nanoformulations is to improve the efficacy of pesticides, while lowering doses and application frequency. Indeed, nanoformulations should allow for regular, precise, long and targeted delivery, which also reduce environmental contamination and exposure to human and other non-target organisms (Khandelwal et al., 2016). Ideally, a pesticide should maintain an adequate AI level for pest control and leave minimum residue in crops and in the environment. This can be achieved by encapsulating pesticide in polymeric controlled release systems, where the polymer properties can be adapted by modifying the molecular weight and basic structure of the polymer, according to actual needs (Roy et al., 2014). Intelligent nanopesticides with precise controlled release modes, that can respond to micro-ecological environmental changes such as humidity sensitivity, light-sensitivity, thermo-sensitivity, soil pH, and enzyme activity, are intensively studied (Huang et al., 2018).

According to the meta-analysis of Kah & Hofmann (2014) conducted on nanopesticides publications (2000-2013), insecticides accounted for 55% of peer-reviewed publications. This high proportion can be explained by the fact that AI of many conventional insecticides have poor water solubility, and are sensitive to the environmental factors as well as easy to evaporate or degrade. In order to decrease the amount of organic solvent put in the environment and prevent the premature degradation of AI, a delivery system is required for the application of insecticides. Polymer-based nanoformulations are suitable for a great number of applications, including slow release of AI, protection against degradation and increased water solubility of AI.

In this review, we focus on the development of the polymer-based nanoinsecticides, including the polymeric materials, the AI formulations and their efficacy. In addition, our attempt is to describe the environmental risks and future challenges of polymer-based nanoinsecticides, which have received a great deal of attention in recent years.

2. CURRENT DEVELOPMENT OF POLYMER-BASED NANOINSECTICIDES

Polymeric nanoparticles are among the most important nanostructured systems used for controlled release of drug formulations. They were recently utilized for pesticide delivery (Nuruzzaman et al., 2016). In general, AI are loaded or entrapped with polymers, which are within the nano-range of 1-1,000 nm, at least for one of their dimensions (Kah et al., 2013; Nuruzzaman et al., 2016). Environment-friendly polymers are more suitable as carrier materials due to their non-toxic degradation of by-products, and they can serve as protective reservoirs of AI, which reduce dosage and usage frequency. Besides, the efficacy of polymer-based formulations can be further increased by precise delivery and adhesive modification (Lowry et al., 2019). The most popular shapes of polymer-based nanoinsecticides are nanocapsule, nanosphere, micelle, nanogel and electrospun nanofibers (Perlatti et al., 2013; Kah & Hofmann, 2014).

2.1. Polymeric materials

A large group of nanoinsecticide-focused research papers explores the applicability of new polymeric materials for plant protection (Kah et al., 2014). With an increasing awareness of environmental protection, more and more polymers of natural or synthetic origins are used as nanocarriers of insecticides. The qualities of these polymeric materials typically include the fact that they degrade most easily, leaving no secondary pollution and are available at low-cost (Perlatti et al., 2013). Various polymer-based nanoinsecticides and their efficacies are listed in **table 1**.

Natural polymers. Natural materials are receiving increasing attention by the manufacturers for all the reasons described above, but also because petroleum resources are diminishing all over the world. Natural polymeric materials and their derivatives are sustainable sources, which are readily available, facilitating their large-scale production. The main natural polymers employed as nanocarriers of insecticides are described below.

Chitosan is industrially produced by partial deacetylation of chitin, which is the primary component of the invertebrates' exoskeleton and of the cell walls of some bacteria and fungi (Campos et al., 2015). Because it is non-toxic, biodegradable and

Table 1. Efficacy of various nanoformulations compared to conventional formulations — *Efficacité de plusieurs nanoformulations et comparaison avec les formulations conventionnelles*.

Nanostructure	Polymers	Active ingredients	Particle size	Targets	Efficacy of nanoformulations	Reference
Nanocapsule	Azidobenzaldehyde and carboxymethyl chitosan	Methomyl	98.6 nm	Armyworm larvae	5 days longer control period than unformulated AI	Sun et al., 2014
	Ethyl cellulose	Emamectin benzoate	219.93 nm	*Plutella xylostella*	No significant difference in LC_{50} between the nanocapsules and the unformulated AI	Shoaib et al., 2018
	PLA	Lambda–cyhalothrin	680 nm	*P. xylostella*	Similar efficacy in LC_{50} as a commercial formulation (type not mentioned)	Liu et al., 2016
	PCL, PHB, poly (methyl methacrylate) (PMMA)	Neem extraction and oil (*Azadirachta indica*)	Not mentioned	Fall armyworm	Lower efficacy in mortality than commercial neem oil	Giongo et al., 2016
	PCL	*Rosmarinus officinalis* essential oil	145 nm	*Tribolium castaneum*	Significant increase in fumigant and contact toxicity at different concentration than non-formulated oil	Khoobdel et al., 2017
	Sodium alginate	Pyridalyl	138 nm	Larvae of *Helicoverpa armigera*	As stomach poison, 2.25 and 6.25-fold more effective in LC_{50} than technical grade product and commercial emulsifiable concentrate; as contact poison, 1.88 and 3.13-fold more active in LC_{50} than technical product and commercial formulation	Saini et al., 2014
	PCL	Neem (*A. indica*) oil	4,000 nm (carrier size after dried)	*Bemisia tabaci* Biotype B	Less efficacy in mortality on eggs, first-instar and third-instar nymphs than the commercial neem oil (Organic Neem®)	Carvalho et al., 2012
	Starch	Avermectin	700 nm	--	Favorable to accelerate the avermectin release due to hollow structure, small particle size, and high pesticide content	Li et al., 2016
Nanosphere	Chitosan modified magnetic diatomite	Cypermethrin	Micro-nano sized pores (size not mentioned)	Corn borers	Slow release property controlled by pH of solvent, almost same efficacy in mortality with commercial microemulsion and technical product	Xiang et al., 2017

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Table 1 (continued). Efficacy of various nanoformulations compared to conventional formulations — *Efficacité de plusieurs nanoformulations et comparaison avec les formulations conventionnelles*.

Nanostructure	Polymers	Active ingredients	Particle size	Targets	Efficacy of nanoformulations	Reference
Nanosphere	PEG and chitosan	*Geranium maculatum* and *Citrus bergamia* essential oils	PEG nanoparticles 239-255 nm; Chitosan nanoparticles 439-535 nm	*Culex pipiens*	2.53 and 1.61-fold acute larvicidal activity of geranium chitosan nanoparticles and PEG nanoparticles respectively than essential oil alone 2.11 and 1.13-fold acute larvicidal activity of bergamot chitosan nanoparticles and PEG nanoparticles respectively than essential oil alone	Werdin González et al., 2017
	Sodium alginate	Imidacloprid	150 nm	Jassids/ leafhoppers	Superior effect in control of the leaf hopper population during 15 days	Kumar et al., 2014
	Starch and silver	Dichlorvos; Chlorpyrifo	23-34 nm	--	Highly effective, long-acting, sustained release lasting for 21 days	Ihegwuagu et al., 2016
Nanogel	Chitosan and cashew gum	*Lippia sidoides* essential oil	335-558 nm	Third instar *Aegypti* larvae	Over 90% mortality even at a low concentration (48 ppm); Pure essential oil had LC_{50} of 36 ppm	Abreu et al., 2012
	Low-molecular mass gelators (LMMGs) all-trans tri(p-phenylenevinylene) bis-aldoxime	Pheromone methyl eugenol	100-200 nm	*Bactrocera dorsalis*	A sustained release period of 30 days, compared with free methyl eugenol of 7 days release in field trial	Bhagat et al., 2013
Micelle	PEG	Diethylphenylacetamide	153.74 nm	*Culex tritaeniorhynchus*	80-fold more effective in LC_{50} than technical grade product	Balaji et al., 2015
	Poly(ethylene oxide)-b-poly(caprolactone) (PEO–PCL)	Ricinine	224 nm	*Tetranychus cinnabarinus* (B.)	14.37-fold more effective in LC_{50} than ricinine water solution	Zhang et al., 2017
Electrospun nanofiber	PLA/cellulose nanocrystal	Thiamethoxam	306 nm	Whiteflies	Efficient at 50% of the recommended dosage over 9 days	Xiang et al., 2013
	Cellulose acetate	Avermectin	Not mentioned	No information available	Initially fast and later slow release to achieve the effective utilization of AI	Zhao et al., 2013

biocompatible, chitosan is regarded as one of the most promising polymeric materials for the efficient delivery of agrochemicals (Kashyap et al., 2015), especially to build up nanoinsecticides. In the recent decade, research on the preparation of nanogels containing insecticidal essential oils (EO) using chitosan as carrier has become a hot spot (Almeida et al., 2018). Also, due to the functional groups of the polymer chains, it is possible to make some structural modifications and obtain materials with improved properties. Xiang et al. (2017) developed a multifunctional nanopesticide system by coating collectable magnetic diatomite with chitosan, and the pH-responsively system loaded with cypermethrin showed a high adhesion capacity on pests' epidermis, resulting in an improved efficiency against corn borers under lab condition. Sun et al. (2014) encapsulated hydrophilic methomyl in shell cross-linked nanocapsules formed by the self-assembly of photocross-linkable carboxymethyl chitosan. The formulated methomyl showed a longer insecticidal activity in laboratory of seven days on the armyworm larvae while the unformulated methomyl lasted only two days.

Alginate is typically obtained from brown macroalgae and conventionally applied in food industry as emulsion stabilizer, gelling agent, film-forming agent, etc. Alginate polysaccharides are classified as hemocompatible materials and do not accumulate in any organs of the human body (Jerobin et al., 2012). They have been developed as nanocarriers of insecticides *via* an ionotropic gelification process triggered by metal ions (Campos et al., 2015). Saini et al. (2014) prepared pyridalyl-loaded sodium alginate nanocapsules, and compared their efficacy with technical product and commercial formulation by leaf dipping method, concluding that the nanoformulation showed better toxicity to shoot borer (*Helicoverpa armigera*). Kumar et al. (2014) produced imidacloprid-loaded sodium alginate nanoparticles, and carried out field efficacy assays on the leafhopper of okra. Compared to the commercial formulation, the nanoparticles showed improved efficacy and long-lasting properties of controlling pest population. In addition, the cytotoxicity of nanoparticles to Vero cells was lower than conventional formulation. However, it was found that nanocapsules formed only by alginate polymer might have low stability which resulted in loss of encapsulated AI (Kumar et al., 2015). Consequently, sodium alginate was used with other polymeric materials such as chitosan, starch and polyethylene glycol (PEG) for overcoming the limitations associated with swift release of AIs (Jerobin et al., 2012; Kumar et al., 2015).

Cellulose is the most abundant natural polymer in nature. Because of its useful properties including biodegradability, biocompatibility, low toxicity and low-cost, cellulose and its derivatives are intensively used as delivery systems for medical therapy (Gopinath et al., 2018). Since they can be degraded by many naturally occurring bacteria and fungi, these polymers are gradually employed as carriers of agricultural compounds. However, there is only a small portion of research papers focusing on the insecticidal efficacy of nanoinsecticides based on cellulose (and its derivatives). Shoaib et al. (2018) synthesized ethyl cellulose nanocapsules with emamectin benzoate, and tested the insecticidal activity of nanocapsules on *Plutella xylostella* by leaf dipping method. They however found no significant difference in efficacy between ethyl cellulose nanocapsules and unformulated emamectin benzoate, whereas the nanocapsules could effectively protect the insecticide from photolysis. Zhao et al. (2013) prepared ultrafine fiber of cellulose acetate that contained avermectin *via* an electrospinning process, which supplied a continuous release to achieve the effective utilization of avermectin.

Starch is the energy storage molecule of most green plants and is found in grains, roots, legumes and fruits. This polymeric hydrocarbon is made of a large number of glucose units and is easily available at low-cost. Starch and starch-based materials have showed great potential for food, medical and agricultural applications. However, poor water solubility and processability of native starch make it difficult to process under mild conditions. Physical or chemical modifications have been adopted to improve its properties and adequacy as nanoinsecticide formulation: Li et al. (2016) prepared avermectin loaded starch capsules with a diameter range of 0.7-4.8 μm by prexim membrane emulsification method. The capsules with avermectin contents of 16-47% enabled a controlled and consistent release of the insecticide over a two weeks period. Ihegwuagu et al. (2016) assessed that the addition of nanosilver into cassava starch improved the encapsulation efficiency of dichlorvos and chlorpyrifos to 95-98%, which was attributed to the enhanced surface area of the nanoparticles. Moreover, silver nanodichlorvos and nanochlorpyrifos insecticides could achieve highly effective and sustained release lasting for 21 days.

Cyclodextrins are the products of enzymatic degradation of starch, and consist of a macrocyclic ring of six, seven or eight glucose subunits (α, β, and γ-cyclodextrins, respectively) (Campos et al., 2015). Cyclodextrins have a truncated cone structure, which contain a hydrophobic inner cavity and a hydrophilic, polar outer surface (Campos et al., 2015). Such a structure is expected to enable cyclodextrins to form non-covalent inclusion complexes with various hydrophobic molecules, and impact the biological, chemical and physical properties of the included molecule (Yusoff et al., 2016). Carvalho et al. (2012) studied the efficacy of six neem oil nanoformulations encapsulated in β-cyclodextrins and polycaprolactone (PCL) towards the eggs and nymphs of *Bemisia tabaci* Gennadius. However, none of these six nanoformulations resulted in better efficacy than the commercial neem oil, which might be caused by the slow rupture of the polymer and the gradual release of AI.

2.2. Synthetic polymers

One of the common objectives of developing polymeric nanoinsecticides is to produce environment-friendly products, similar to the biodegradable synthetic polymers used in the pharmaceutical or cosmetic areas. Usually, these synthetic polymeric materials are nontoxic, or can be degraded by microbes, and their decomposition products have low hazard to non-target organisms and the environment. The most common synthetic polymers used as nanocarriers of insecticides are described below.

Polyethylene glycol (PEG) is a linear or branched neutral polyether of a variety of molecular weights, soluble in water and in most organic solvents. Because of its wide range of solubility and safety properties such as lack of toxicity, absence of antigenicity and immunotoxicity, non-interference with conformations of polypeptides and enzymatic activities as well as ease of excretion from living organisms, PEG has been approved by the USFDA and widely used in drugs (D'souza & Shegokar, 2016). PEG-based nanoformulations have great potential in pest control. Balaji et al. (2015) formulated nanomicelles of a poor water-soluble insect repellent, diethylphenylacetamide, by PEG polymerization followed by phase inversion temperature emulsification. The nano-formulated diethylphenylacetamide exerted better bioefficacy on Japanese encephalitis vector *Culex tritaeniorhynchus*, in comparison with its technical grade product, even at minimal exposure concentrations. Werdin González et al. (2017) studied the efficacy of PEG-based EO nanoparticles on mosquitoes *Culex pipiens* pipiens, and the result showed that EO nanoparticles led to higher efficacy than EO alone.

Polylactic acid (PLA) is also a U.S. Food and Drug Administration (FDA)-approved polymeric material, which is widely used as drug or cell carrier in the medical field for its biodegradable and mechanical properties that can be adjustable (Lee et al., 2016). Polylactic acid degrades into lactic acid, and its final metabolized products *in vivo* are carbon dioxide and water. In recent years, research on PLA-based nanoinsecticides has gradually increased. In order to decrease the usage dose and prevent the degradation of lambda-cyhalothrin, Liu et al. (2016) fabricated an aqueous controlled delivery system with PLA as carriers, using the prexim membrane emulsification method. The organic solvent-free lambda-cyhalothrin-loaded nanocapsules showed good water dispersion and stability, which also exhibited a similar biocidal efficacy on *Plutella xylostella* compared to a commercial microcapsule formulation. Yu et al. (2017) developed three types of functionalized abamectin PLA nanoparticles with different adhesive abilities to cucumber leaves. They found no difference among adhesive PLA nanoparticles, commercial water dispersible granules and emulsifiable concentrate in a bioassay performed with cucumber aphids.

Polycaprolactone (PCL) is a biodegradable polyester, intensively used as controlled release drug carrier and tissue engineering due to its biocompatibility and miscibility with a large range of other polymers (Dash et al., 2012). Khoobdel et al. (2017) prepared *Rosmarinus officinalis* L. EO-loaded PCL nanocapsules, which had a higher toxicity against red flour beetle (*Tribolium castaneum*) than the non-formulated EO. Zhang et al. (2017) used an amphiphilic block copolymer, polyethylene oxide-b-poly(caprolactone) (PEO–PCL), to make ricinine nanomicelles, which were easy to wash-off from the trial leaves and meanwhile enhanced the protection against *Tetranychus cinnabarinus* (B.) during field trials.

Polyhydroxybutyrate (PHB) is a biocompatible and biodegradable material that can be obtained from renewable sources, though its cost is higher than other synthetic polymers (Dos Santos et al., 2017). Publications related to PHB nanoinsecticide formulations are scarce. Giongo et al. (2016) developed nanoformulations of neem (*Azadirachta indica* A.Juss) including colloidal suspension and powder containing PHB, in capsules or spheres. Bioassay results on fall armyworm larvae showed that PHB neither caused adverse effects on insects, nor interfered with the action of neem. In comparison to commercial neem oil, PHB nanoformulations were as efficient in reducing larval weight, though the mortality was relatively low.

Because of the modification and miscibility of these materials, carriers based on polymers, such as copolymers, inorganic carriers mixed polymers and surface modified functionalized polymers are developed. In one word, polymer-based nanoformulations have a great potential for further development and practical crop protection applications (Kah & Hofmann, 2014).

3. STRUCTURES OF POLYMER-BASED NANOINSECTICIDES

The polymeric materials can be prepared in various types of tridimensional structures, among which nanocapsules, nanosphere, micelle, nanogel and nanofiber are the most common for AI delivery (**Figure 1**).

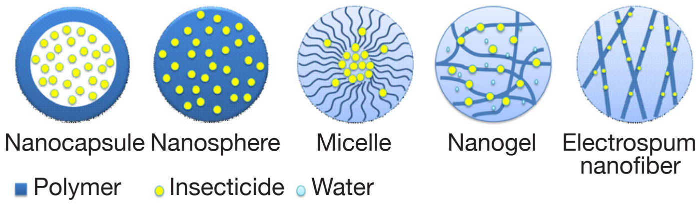

Figure 1. Different structures of polymeric nanopesticides — *Différentes structures de nanopesticides polymériques*.

3.1. Nanocapsules

The AI is concentrated near the solid or liquid inner core that is lined with a protective shell of polymeric materials. Nuruzzaman et al. (2016) have generalized the methods to produce nanocapsules. Owing to the homogeneous distribution, nanocapsules may be more stable for spraying, increase the utilization rate of AI and reduce the phytotoxicity. Controlled release studies indicated that nanocapsules exhibited a higher release rate than the microcapsules because specimen with smaller size possesses larger surface areas being exposed to the surroundings (Li et al., 2016; Liu et al., 2016). However, it is still a challenge to design nanoscale capsules with high AI loading rate.

3.2. Nanospheres

The AI is uniformly distributed and embedded in the polymeric matrix. If the distribution of AI within so-called capsules or core/shell nanoparticles is uncertain, these formulations should be considered as nanospheres (Kah et al., 2013). Although the synthesis process of nanospheres is very similar to that of nanocapsules, the technique of polymerization is still very important. The size, dispersity, and loading efficiency of the nanospheres always change when a different type of surfactants is used. Therefore, selection of suitable materials is critical (Khandelwal et al., 2016). Nanospheres can serve as protective reservoirs and controlled release carriers, which bring about a longer protection and a reduction of leaching losses (Iavicoli et al., 2017).

3.3. Micelles

Core-shell structured micellar systems are self-aggregated in aqueous solutions by copolymers containing hydrophilic and hydrophobic moieties above the critical micellar concentration (CMC). Because of the large amount of interaction points of polymer chains, polymeric micelles show lower CMC values than surfactant micelles, which indicate better thermodynamic stability (Chen et al., 2014). Micelles are mainly used to deliver water-insoluble agrochemicals (Balaji et al., 2015).

3.4. Nanogels

Hydrophilic polymers are cross-linked by van der Waals forces or covalent bonds, which can absorb high volumes of water. Nanogels are not likely to swell or shrink with changes in humidity due to the insoluble properties and they can improve the loading and release profiles of AIs (Kah & Hofmann, 2014). They have been intensively studied as the carrier of pheromones and EOs (Abreu et al., 2012; Bhagat et al., 2013).

3.5. Electrospun nanofibers

Polymer injection produced by the metal capillary forms nanofibers under the action of an electric field and gathered by a collector (Noruzi, 2016). Though still in the early stage of agricultural application, electrospun nanofibers own potential advantages on avoiding the release bursts, which facilitates the field application of pheromones and EOs.

4. ENVIRONMENTAL RISKS OF POLYMER-BASED NANOINSECTICIDES

Though nanopesticides may offer a range of benefits, they are still in the early developmental stage. Several companies have deposited patents comprising numerous protocols for production and application of nanopesticides, the validation of such products for market deployment is at the very early stages (Kah et al., 2019). During the last two decades, a great number of articles related to environmental health and safety of engineered nanoparticle have been published. However, research on evaluation of environmental safety of polymer-based nanopesticides is scarce, which results from the lack of standard approaches to assess the environmental risk of nanopesticides for regulatory purposes. Walker et al. (2017) described an approach to problem formulation using a case study involving a hypothetical polymer-based nanopesticide, and it helped to understand how a practical assessment strategy would be developed using principles adapted from the ecological risk assessment of conventional pesticide products.

It is usually assumed that ecotoxicity of conventional pesticide is related to AI mass concentration. Environmental fate studies are usually undertaken only with AI or a representative formulation, all of whose ingredients have been approved (Amenta et al., 2015). However, as to nanopesticides, other parameters such as particle number concentration, particle size distribution (PSD), and the ratio of "free" and nanoparticle-bound AI, may be important in evaluating bioavailability and toxicity of pesticide (Kookana et al., 2014). Besides, it may also be very important to characterize these parameters at different stages in the environmental life cycle and throughout fate and effect studies. Nanopesticides will often undergo changes in their degree of dispersion or agglomeration over time, which depend on the concentration of the nanopesticides and environmental factors (Kookana et al., 2014). That is to say, nanopesticides containing approved AI could be considered as a different pesticide product, which would require a separate risk assessment and authorization.

Polymer-based nanopesticides could reduce AI concentration, which may result in better environmental safety properties owing to lower environmental exposure and residues. On the other hand, however, slow release of AI may imply longer duration and consequently higher risk for non-target organisms and potentially greater amount of residues on harvest (Alia & Servin, 2016). De Oliveira et al. (2014) suggested that the effects of nanocarriers on soil microorganisms, pollinators, beneficial insects and other non-targeted organisms, together with the uptake and accumulation of nanoparticles in crop plants and their translocation to edible plant parts, should be studied in detail. However, only one research was found on the biosafety evaluation of nanocarriers of insecticides on different targets (Xiang et al., 2017): the study was conducted on weed (*Cynodon dactylon* [L.] Pers.), pest (cotton bollworms), cell (HaCaT cells), bacteria (*Escherichia coli*), concluding that the nanocarrier possessed a high biosafety with all concentrations. But the biosafety evaluation of nanoformulation on these targets was not elucidated. Some research focused on cytotoxicity of different cells, such as Vero cell line (Kumar et al., 2014) or lymphocyte cells (Jerobin et al., 2012), which is the common method for evaluating the biosafety of nanomedicine. Pasquoto-Stigliani et al. (2017) not only assessed the cytotoxicity of neem oil-loaded PCL nanocapsules on different cell lines, but also performed molecular analysis of the soil nitrogen cycle microbiota after treatment with nanocapsules, concluding that nanocapsules did not affect the soil microbiota during 300 days of exposure. Saini et al. (2015) evaluated the residue, dissipation and safety of sodium alginate-based pyridalyl nanoformulation on tomato, and results indicated that residues of nanopyridalyl did not persist much longer than conventional formulation, which implied a negligible risk to the humans. Meredith et al. (2016) determined how the capsule size of one commercial lambda-cyhalothrin capsule suspension influenced toxicity on embryonic zebrafish, *Danio rerio*, and the results showed that capsule size did not influence the occurrence of sublethal impacts or mortality, but the presence or absence of capsules influenced the toxic response of the entrapped lambda-cyhalothrin.

Though guiding principles for evaluating environmental risks of nanopesticides have been suggested (Kookana et al., 2014), there is still no comprehensive study currently in the literature that evaluates environmental impact of nanopesticides under field conditions (Kah et al., 2018). Since direct measurements are not easy to perform, indirect approaches, such as sorption and degradation that can be carried out in laboratory, are valuable for assessing the fate and behavior of a nanopesticide. Kah et al. (2016) compared the sorption and degradation of three polymer-based bifenthrin nanoformulations (type of polymer not mentioned) with a commercial formulation and the pure AI in different types of soil. Results showed that commercial formulation and pure AI had similar sorption. Significant differences in sorption were observed between the nanoformulations and the pure AI, which depended on the type of soil and type of nanoformulations. In addition, nanoformulations could prolong the persistence of bifenthrin as well. With the data obtained in the soil degradation experiment, soil persistence concentration and ground water concentration of nanopesticide could be predicted by simulation with a pesticide leaching model (FOCUS, 2012).

5. FUTURE CHALLENGES OF POLYMER-BASED NANOINSECTICIDES

Although polymer-based nanoinsecticides are at an early stage of development, it is still expected that this technology will improve the efficiency of pesticide and reduce environmental pollution. Therefore, more studies are required to solve the challenges faced by polymeric nanoformulations.

The main challenge associated with polymeric nanopesticides is to demonstrate that they could compete with existing formulations in both cost and performance, especially at field level. At present, nearly all polymeric nanocarriers listed in literature are synthesized in laboratory in very small amount, so it is necessary to establish common procedures for a particular group of pesticide, which could be scaled up for commercial level (Nuruzzaman et al., 2016).

New analytical approaches are needed to fill the knowledge gap of the characterization of nanopesticides. Characterization data are extremely important to connect novel qualities of the products with their physicochemical properties, to understand the relevant mechanisms, and to evaluate if the benefits can be preserved across a range of agronomic conditions (Kah et al., 2018). Consisting of organic ingredient, the various forms of polymeric nanopesticides usually make their characterization difficult.

New experimental protocols for detecting and quantifying nanopesticides are necessary to understand their fate and to carry out the environmental impact assessment. At present, it is impossible to detect or quantify polymer nanocarriers in the soil matrix, because of the similarity of the elemental composition. Also, release rates of nanopesticides are most often measured in the laboratory with a dialysis method that is at considerable high concentration levels, and over relatively short periods of time, which is far from the real scene of pesticide application. Besides, modeling tools are also required to predict the transportation and relocation of nanopesticides.

Improvement in regulation for nanopesticides is urgently required. Establishing clear guidelines can facilitate the development of nanotechnology in agriculture sector. European union (along with Switzerland) is the only world region where nano-specific materials have been incorporated in legislation, including specific information requirements for risk assessment of nanomaterials, and the obligation to label or report the presence of nanomaterials in products (Amenta et al., 2015). Recently, European Food Safety Authority (EFSA) proposed guidance on risk assessment of the application of nanotechnologies in the food and feed chain (Hardy et al., 2018), and Organization for Economic Co-operation and Development (OECD) also proposed guidance for testing dispersion stability and toxicity of nanomaterials (OECD, 2017; OECD, 2018a; OECD, 2018b). In order to advance nanosafety research as well as support the development and implementation of guidelines for risk assessment, it is still necessary to develop transdisciplinary risk governance frameworks based on clear understanding of nanotechnology risk, management practices and societal perceptions.

6. CONCLUSIONS

Nanotechnology is one of the strategies that aim to maximize crop yields and minimize the input of pesticides. Polymer-based nanoformulations have received great attention recently because they appear to be promising for target release of AI while reducing excess runoff. However, it is still notable that the uptake, bioavailability and toxicity of nanoformulations are quite different from the conventional pesticides. Therefore, development of new methodologies is needed to understand the process. The environmental behavior and effects may also differ with their conventional analogues, and refined approaches for risk assessment are needed. In order to ensure a high level of protection for humans and the environment, while not hindering the development of new beneficial products, collaboration among countries around the world is required.

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