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Preparation of Cypermethrin Loaded PLGA/PVA Nanoparticles as Medical Vector Control

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ABSTRACT

In this work, a copoly(lactic/glycolic)/cypermethrin nanoparticles was synthesized. A delivery system of insecticides induces active ingredient having desirable for pest control. The developed cypermethrin nanoparticles were then characterized by a UV-visible spectrophotometer, DLS and transmission electron microscope, proved that the spherical, medium sized (230-340 nm). This nanoparticles may be an efficient candidate as a insecticide for control cockroach after the biological study which is in progress.

KEYWORDS

Nanopesticide, Cypermethrin, Polylactic acid glycolide, Pesticides, Emulsion.

INTRODUCTION

The development of new formulations for plant protection products has long been a very active field of research. Regulatory pressure is now adding to classical drivers such as marketing and product improvement [1]. The application and delivery of active ingredient (pesticide) are therefore being important to enhance pesticide activity, while keeping the environmental pollutions to a minimum. During the past years nanotechnology has been presented as having the potential to impact agricultural production [2]. Suggested applications such as the development of nanoparticles, nanofibers or nanocapsules as vectors for DNA are still in progresses. However, if one calls nanopesticides as any formulation that includes elements in the nanometer size range and novel properties associated with these small size range, it would appear that some nanopesticides have already been on the market. Nanoformulations are already used extensively in pharmaceuticals [3]. In contrast, applications within the agrochemical fields are only just starting and observed a rapid growth in coming years . Up to know, more than 3,000 patent applications have been lodged, 60 peer-reviewed papers published and 25 reports and reviews presented dealing directly with nanopesticides, confirming the intensity of activity in this area. Many nanoformulations combine several surfactants, polymers and metal nanoparticles in the nm size range. The development of economically viable preparation and stabilization

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methods remains the subject of intensive research. Several reviews on the preparation of organic nanoparticles have been published [2]. The aim of nanopesticide formulations are generally similar to those of other pesticide formulations, these being (a) to increase the apparent solubility of poorly soluble active ingredient or (b) to release the active ingredient in a slow/targeted manner and/or protect it against premature degradation. Currently, the most common pesticide formulations for poorly water-soluble active ingredient are emulsifiable concentrates (ECs) and oil-in-water (O/W) emulsions. Emulsifiable concentrates still represented about 28 % of the total number of formulations listed in the Pesticide Manual in 2007 [4].

The development of novel nanoparticle systems with original composition aiming to provide designed properties has been attention exclusively. This impressive progress in nanotechnology inspires the researchers to develop the nanoparticles. The aims of nanoformulations are generally same to other pesticide formulations, these being to increase the solubility of poorly soluble active ingredients, to release the active ingredient in a slow release manner and to protect against premature degradation [5,6].

Biodegradable materials are natural or synthetic polymers are degraded to produce biocompatible safe by-products. The number of such materials that are used in or as adjuncts in controlled drug delivery has increased dramatically over the past decade. The basic category of biomaterials used in drug delivery can be broadly classified as (a) synthetic biodegradable polymers, which includes relatively hydrophobic materials such as the hydroxy acids (includes poly lactic-*co*-glycolic acid, PLGA), polyanhydrides, *etc*. and (b) naturally occurring polymers, such as complex sugars (hyaluronan, chitosan) and inorganic hydroxyapatite [7-9].

A delivery system of insecticides induces active compounds having slow releasing desirable for pest control many research has been focused of pesticides delivery system by biodegradable polymer. Polylactic-*co*-glycolic acid (PLGA) has shown potential as a active ingredient delivery carrier and slow releasing system. Polylactic-*co*-glycolic acid (Fig. 1) is a copolymer of polylactic acid and polyglycolic acid, which more popular because of biodegrable an sustain delivery (Fig. 2). Furthermore, it is possible to control the overall physical properties of

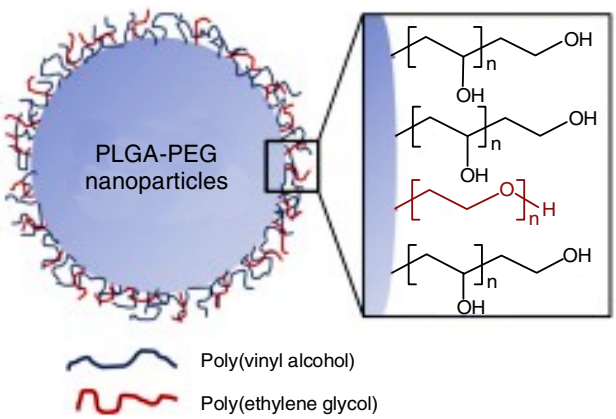

Fig. 1. PLGA/PEG nanoparticles [Ref. 14]

polymer-pesticides matrix by adjusting the relevant parameters such as polymer molecule weight, ratio of lactide to glacolide. Single emulsion process (oil-in-water) methods encapsulate water-insoluble pesticedes.

Polylactic-*co*-glycolic acid a naturally occurring polymer has been extensively investigated as a natural cationic biopolymer with excellent biocompatibility, biodegradability, non-toxicity, bioactivity, interesting structural and functional properties, cationic exchange and hydrogen bonding ability, high hydrophilicity and other interesting chemical properties due to the presence of amino and hydroxyl groups [10,11].

Cypermethrin is a synthetic pyrethroid used as pesticide agricultural applications as well as in consumer products for domestic purposes (Fig. 3). It behaves as a fast-acting neurotoxin in insects. It is easily degraded on soil and plants but can be effective for weeks when applied to indoor inert surfaces. Exposure to sunlight, water and oxygen will accelerate it decomposition. For this highly degradable properties, synthesizing the nanoparticles that embedded in polymers of PLGA/PVA prevent decomposition [12,13].

In this study, an efficient one-step synthesis of nanopesticide was performed to prepare a stable aqueous colloids a copoly-(lactic/glycolic)/cypermethrin nanoparticles. A delivery system of insecticides induces active ingredient having desirable for pest control. The nanocparticles were prepared by reaction of PLA and PEG to obtain PLGA copolymer, which can encapsulated

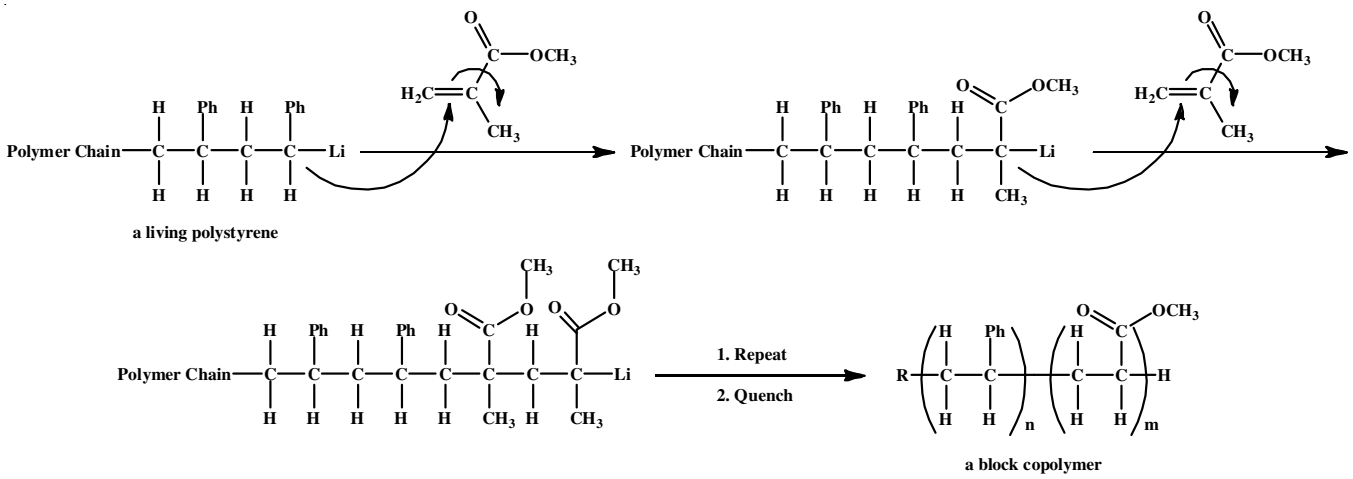

Fig. 2. A block copolymer production

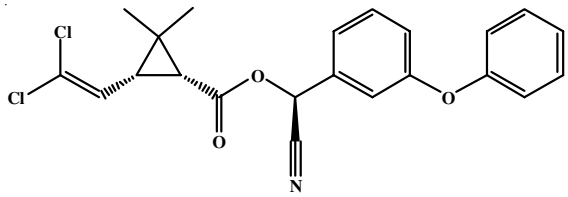

Fig. 3. Structure of cypermethrin

cypermrthrin in neutral condition [10,14,15]. This study would be useful to develop a practical controlling method for termites which is a serious pest of wooden structures and agricultural crops.

EXPERIMENTAL

Silver nitrate (98 %) and poly(ethylene glycol) was from Merck. Other chemicals were analytical grade supplied from Aldrich-Sigma, Merck and Acros and used as received. High-purity deionized water was obtained from milli-Q. Cypermethrin as an oil was taken from Aldrich-Sigma as technical 98 %.

The FT-IR spectra of nanoparticles were analyzed by using a Shimadzu IR prestige-21 FT-IR. Size distributions of the nanoparticles were determined by dynamic light scattering (DLS). Using Malvern Zetasizer Nano ZS (Malvern Instrument Ltd., UK) at a scattering angle of 173º and a temperature of 25 ºC. Samples were diluted by a factor of 100 prior to the measurements to avoid multiple scatteringe effects. UV-visible spectra were acquired with Perkin Elmer Lambada 28 and visible absorption spectra were collected over a wavelength range of 300 to 500 nm. Transmission electron morphology of the nanoparticles was characterized by depositing the suspension (2 µL) onto Formvar-coated copper grids and excess water was evaporated. The obtained samples were left to dry under ambient air, andthen visualized *via* TEM (Zeiss-EM10C-100 KV). Nanoparticle size was analyzed using iTEM software (version 3.2, Soft Imaging SystemGmbH) equipped with the TEM. Structure of Ag/PEG/cypermrthrin nanoparticles was determined using selected area electron diffraction (SAED) technique *via* high-resolution.

Preparation of PLGA was performed according to reported method described elsewhere [7], In brief, 70 mg of DL-lactide was placed in a three-necked flask fitted with a stirrer, thermometer, distillation head plus condenser and flask was purged with argon gas (Fig. 4). The DL-was heated in an oil bath under argon stream at 130 ºC. The reaction flask was maintained at this tempreture and Dowex 50w 8 (0.6 g) was added and refluxed the reaction for 3 h. The extra produced water was collected under reduce pressure at 5 mmHg. Again 0.6 g of Dowex was added and heated at 130 ºC fo 1 h under high vacuum to obtain high-brown solid. The solid was dissolved in CH_2Cl_2 (300 mL) and the product was reprecipitated by addition of hexane and after evaporation of solvents (hexane and CH_2Cl_2), the copolymer was collected as amorphous white solid.

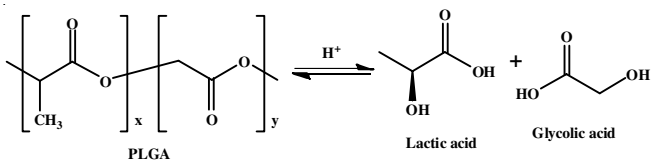

Fig. 4. PLGA formation

250 mg of PLGA, CH_2Cl_2 (2.5 mL) and technical cypermethrin (20 mg) were mixed and stirred to dissolve the compounds completly. Aqueous solution of PVA (0.5 %) was added to emulsify the solution at 15 ºC and raise the temperature to 40 ºC in order to evaporate the solvent. The nanocypermethrin as white suspension was collected. The precipitate was centrifuged three times and washed with distilled water and EtOAc to remove unabsorbed cypermethrin. The obtained white precipitate PLGA/NCs cypemethrin were used for characterization.

RESULTS AND DISCUSSION

The nanocparticles were prepared by reaction of PLA and PEG to obtain PLGA copolymer, which can encapsulated cypermrthrin in a neutral condition. DL-Lactic acid and glycolic acid reacted together in presence of exchange resin of Dowex 50w was heated at 130, 150 and 185 ºC, separately and removed formed water under reduced pressure. The high-brown solid was dissolved in dichloromethane solvent and filtered to remove Dowex and evaporated the solvent gave an amorphous solid which was collected and dried at reduced pressure. Then an appropriate amount of cypermethrin is dissolved in dichlromethane containing sufficient amount of PLGA, followed water was added to form W/O emulsion by high sheering. The water-in-oil primary emulsion is added aqueous alchohol solution of poly(vinyl acetate). Stirring the emulsion at 15 ºC for 45 min and the increased the temperature to form nanocapsule of cypermethrin.

Characterization of cypermethrin nanocapsules: The mean size of β-cypermethrin nanocapsules is 250-300 nm. Fig. 5 shows that cypermethrin nanocapsules also have regular core-shell structure. Cypermethrin is distributed in the interior of nanocapsules PLGA and has well covered by PVA polymer and encapsulation efficiency, which the formation of PLGA/cypermethrin nanoparticles in the nanocomposite was also confirmed by TEM (Fig. 5). The product PLGA nanoparticles was not aggregated during incubation and the colloidal stability was confirmed by the absence of precipitate after centrifugation. Similar research by Zhu *et al.* [16] also reported the preparation of composite hydrogels of polymer chitosan (CS) and silver nanoparticles to encapsulate the gentamycin as model small chemical drugs, for a sustained manner releasing and indeed, *in vitro* test, the results showed CS/MSN composite hydrogels performed much better activity.

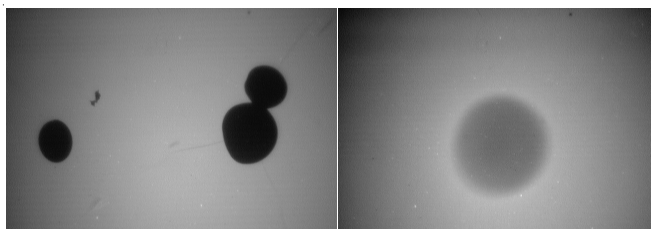

Fig. 5. TEM of carrier nanocapsules

In similar study, the silver-impregnated chitosan films prepared from silver nitrate and chitosan as stabilizer and ascorbic acid as reducing agent *via* thermal reaction [17,18]. In the process of synthesizing nanoparticles, a stabilizer is used to control the formation and dispersion stability of metal nano-

particles. For this purpose, polymers PLGA have been widely used as a particle stabilizer to control the particle growth, stabilize the metal dispersions and limit the oxidation of particle [19,20]. Due to its excellent biocompatibility, biodegradability, non-toxicity and bioactivity properties, PLGA has gained much attention. The fact that it is a potential polymer resource makes its use preferable [21].

Dynamic light scattering (DLS) of PLGA/cypermrthrin nanoparticles image revealed the spherical particles of average size range 230 nm (Fig. 6) and majority of spheres are in this size range. It is obvious that these nanoparticles are monodisperse. UV-visible spectroscopy of the obtained nano-insecticide, a broad peak at 315-330 nm, which strongly suggest that PLGA/Cypermrthrin nanoparticles were spherical, in addition, the cypermethrin absorption bands was at 220 nm, which proved it incubated onto PLGA/PVA nanoparticles. Shameli *et al*. [22] and Sharma *et al*. [23] reported that the spherical nanoparticles contribute to the absorption bands around 400 nm in the UV-visible spectrum .

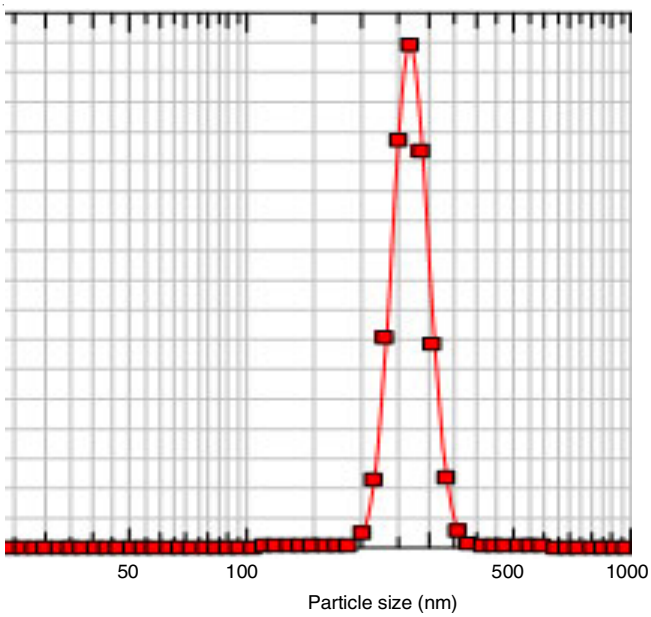

Fig. 6. Size and distribution of nanocapsules

The PLGA/PVA/cypermrthrin nanoparticles had a shape size distribution and a mean diameter of 240 nm, this was due to the fact that big large particles distribution corresponds (Fig. 6). In FT-IR spectrum of nanoparticles, the peaks at 3418, 1634 and 1077 cm^{-1} were due to ester bond, 1436 and 1385 cm^{-1} were due to C-H bending, 1335 cm^{-1} as due to the appearance of medium peak at 1707 cm^{-1}, which was due to the complexation between PLGA/PVA and cypermethrin to form nanoparticles [24].

Conclusion

In conclusion, the encapsulation of cypermethrin in biocompatible PLGA polymer using single emulsion method is successfully demonstrated. The results indicated that cypermethrin was capsulated effectively in the oil core of PLGA/PVA as nanoparticle. This cypermethrin capsule can be used as controlling insect vectors.

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