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Synthesis and characterization of imidacloprid microspheres for controlled drug release study

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ABSTRACT

Polypropylene carbonate (PPC) was synthesized by the alternating copolymerization of carbon dioxide with propylene oxide (PO). Imidacloprid microspheres were prepared by emulsion solvent evaporation, PPC as the drug-carrier material. The effect of the reaction conditions on drug loading (DL) and entrapment efficiency (EE) was examined. High DL of 45.03% was achieved at the methylene chloride and water volume ratio of 1:1, polyvinyl alcohol (PVA)-1788 concentration of 1%, imidacloprid and PPC mass ratio of 1:3, and shear rate of 10,000 r/min. When imidacloprid and PPC mass ratio was 2:3, high EE of 77.91% was obtained. Through the scanning electronic microscopy (SEM) the hollow structure of the microspheres was studied. The effects of shear rate on the diameter and morphology of microspheres were studied by the SEM. The perfect microspheres were obtained at the 10,000 r/min shear rate. The release behavior of imidacloprid encapsulated in the microspheres was studied. The experimental results indicated that the microspheres had a property of sustained drug release.

1. Introduction

Chemical pesticide plays an important role in preventing and temporarily protecting plant diseases and insect pests. However, most pests have had resistance with the long-term and large-scale use. Chemical pesticide also has caused serious environmental pollution [1]. On the other hand, development of a new pesticide not only needs the longer time period but also has to pay much of the development costs. Microencapsulation technology has been widely used in many fields, such as drug delivery, cosmetics, dyes, *etc.* [2]. Microcapsules offer benefits such as improved efficacy, reduced toxicity, and improved patient compliance and convenience. Several approaches have been developed for the preparation of microcapsules, including coacervation [3], emulsion solvent evaporation method [4], interfacial polymerization [5], self-assembly method [6], spray drying [7] and so on. Microencapsulation is an important technology of production in pesticide formulations [8]. In agriculture, the technique of microencapsulation will be widely applied in highly toxic pesticide. Imidacloprid is a neonicotinoid pesticides and has a 5-membered ring Structure. It exhibits a high degree of selectivity for insect nicotinic acetylcholine receptors (nAChRs) [9]. Imidacloprid generally was believed to have low toxicity to mammals and humans, but growing evidence clearly demonstrated that exposure of imidacloprid may be related with the enriched production of dark consequences in animals and particularly humans [10]. Study on microencapsulation has been widely reported at home and abroad. However, there is few works on imidacloprid microspheres. When the imidacloprid microspheres are to be built, suitable drug-carrier material must be chosen for the parts. The delivery carrier can be made of either synthetic or natural polymers.

Poly (propylene carbonate) (PPC) is the copolymer of CO_2 with propylene oxide (PO), which is environmentally benign and have several biomedical and pharmaceutical applications [11]. It has the desirable properties of both biodegradable and cheaper, which makes it a promising delivery carrier for pesticide in particular and will have a good development prospects. PPC had been successfully synthesized in our previous experiment. The basic molecular of PPC is a completely alternating structure. Biodegradable material as a drug-carrier material possesses a vast range of application prospect. However, research about PPC as a drug-carrier material have been reported less in the last few years.

In this work, imidacloprid microspheres were prepared by emulsion solvent evaporation, PPC as the drug-carrier material. The optimum operation conditions of imidacloprid microspheres were obtained by intercross experimental method. The influence of the drug loading (DL) and entrapment efficiency (EE) variables like the ratio of oil phase and the continuous phase, Polyvinyl alcohol (PVA)-1788 concentration, the ratio of imidacloprid and PPC, shear rate was discussed in detail. In addition, its release kinetics in water was studied.

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2. Experimental

2.1. Materials

Imidacloprid was purchased from Qingdao Hailier Pharmaceutical Company and used without further purification. PVA-1788 and dichloromethane were used as received from Aldrich. All other solvents and reagents were purchased from Acros Organics.

2.2. Characterization

Nuclear magnetic resonance spectra were recorded on a Bruker AV 500 M instrument in $CDCl_3$ at room temperature. Chemical-shifts were given in parts per million from tetramethylsilane. IR spectra were recorded on a Perkin-Elmer 2000 FTIR spectrometer. The shape of imidacloprid microspheres were observed by scanning electron microscopy (SEM). Before measurement, the samples were dispersed onto polished aluminum SEM stubs. The samples were coated with a thin layer of gold and observed under HITACHI S-480 SEM (Japan). Particle size was determined by a BT - 9300H type laser particle size instrument (Dandong city Baxter instrument co., LTD). The amount of imidacloprid in the solution was determined by TU-1901 double beam UV visible spectrophotometer (Beijing Purkinje General Instrument Co., public) at 270 nm.

2.3. Preparation of imidacloprid microspheres

Microparticles were prepared by the emulsion solvent evaporation method. PPC and imidacloprid were dissolved in methylene chloride. The solution was poured into a certain concentration of PVA watery solution. The mixture was emulsified at a preset speed level by Digital dispersion machine (IKA German). Then the mixture was stirred by using magnetic stirrer until methylene chloride was volatilized completely. The solid particles were filtered from the solution. The solid particles were washed with distilled water several times and freeze-dried to constant weight.

2.4. Calculation of drug loading and encapsulation efficiency

DL is the weight percentage of the actually encapsulated amount of imidacloprid over the total microspheres. EE is the weight percentage of the actually encapsulated amount of imidacloprid over that in feeding. The imidacloprid microspheres with dry weigh W_0 was dissolved in methylene chloride. The imidacloprid content (ΔW) in the methylene chloride was detected by UV–Vis spectrophotometer. The DL was calculated according to the following Eq. (1) [12]:

$$\mathrm{DL}\ (\%) = \Delta W / W_0 \times 100 \tag{1}$$

The EE was calculated according to the following Eq. (2):

$$\mathrm{EE}\ (\%) = \Delta W / (W_0 \times C) \times 100 \tag{2}$$

where C is the imidacloprid content of the microspheres sample calculated from the feed composition.

2.5. Release behavior of imidacloprid from the imidacloprid microspheres in water

To study the release behavior of imidacloprid from the imidacloprid microspheres in water, the following experiment was carried out: the dry imidacloprid microspheres sample (0.5 g) was immersed in 200 mL distilled water in a glass beaker properly covered at 25 °C. A quantity of 3.0 mL of solution was taken out to estimate for the contents of imidacloprid after a certain interval, and then the same volume of fresh water was replenished. According Ehrlich reaction, the amount of released imidacloprid from the imidacloprid microspheres samples were measured at 270 nm by UV–VIS spectrophotometer. All the release experiments were done in duplicate, and their results were averaged. According to the absorbance of different time, the accumulation release quantity of imidacloprid can be obtained through the following Eq. (3) [13].

$$Q = C_n \times V_t + V_s \sum C_{n-1} \tag{3}$$

Q: cumulative release (mg)
C_n: concentration of the release medium (mg/mL) at time t
V_t: volume of the release medium, $V_t = 200$ mL
V_s: volume of solution obtained from the release medium for testing, $V_s = 3$ mL.

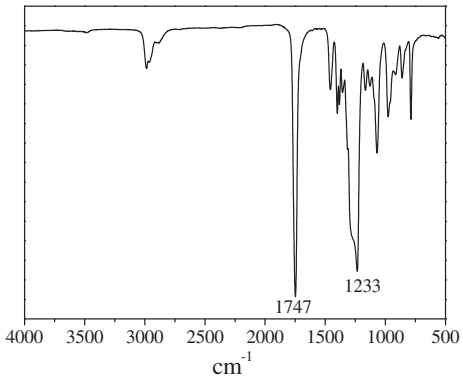

Fig. 1. IR spectrum of the copolymer.

3. Results and discussions

3.1. The synthesis and characterization of the polypropylene carbonate

PPC was synthesized by the alternating copolymerization of carbon dioxide with propylene oxide (PO) in the presence of SalenCo^{III} 2,4-dinitrophenol (Salen = (1*R*,2*R*)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamino)/1,10-Phenanthroline monohydrate (PHEN) catalyst system [14]. These reaction was performed in a 100 mL autoclave (PO = 7 mL; [PO]:[PHEN]:[Co] = 1000:0.25:1, molar ratio) at 50 °C, 2.8 MPa CO_2 pressure, and with 12 h. Under these conditions, PPC was generated in 91% yield. The average molecular weight and molecular weight distribution of the polymer were determined by gel permeation chromatography (GPC). The average molecular weight and molecular weight distribution were 2.45×10^4 and 1.12, respectively. The IR spectrum of the obtained copolymer is shown in Fig. 1. The bands at

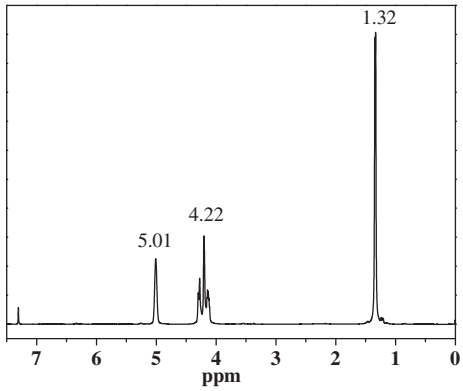

Fig. 2. ^{1}H NMR spectrum of the copolymer.