SUPPLEMENTARY INFORMATION

Methods

We describe a method to perform encapsulation of the insecticide, imidacloprid. The first step consists of testing solubility of imidacloprid (Chem Service, cat. no. N-12206-200 MG) in various organic solvents [e.g. Chloroform, Dichloromethane (DCM) and Ethyl acetate]. This step was conducted showing solubility at concentrations higher than 50 mg/mL in DCM and Chloroform. The next step involved encapsulation of imidacloprid using PLGA (50:50 poly (DL-lactic-co-glycolic)-COOH, i.e. 0.15-0.25 g/dL, Lactel Absorbable Polymer, cat. No. B6013-1) by the emulsion-solvent evaporation method. Solvent evaporation is one of the most widely used methods for particle formation and active ingredient encapsulation due to the convenience and scalability of the process. This method consists of three major steps: (1) dissolution of the active ingredient and polymer into an organic solvent; (2) dispersion of the organic solution into a stirred, aqueous solution to form an emulsion; and (3) evaporation of the solvent until particles are formed. Stability of the emulsion was established by using surfactants, including Tween 80 or Tween 20 (Sigma Aldrich, Inc.), which prevents aggregation and precipitation in the emulsion form. In terms of stability for storage, the particles were lyophilized using the aforementioned surfactants in concentrations of less than 4 % in volume, allowing for a stable lyophilized product that can be easily reconstituted using water. Based on this method, 200 mg of PLGA crystals and 50 mg of imidacloprid were added into a 10 mL nominal volume glass vial containing 1 mL of DCM which was then sonicated in an ultrasonic cleaner (FS20H) and vortexed (Vortex Genie 2) until the biopolymer and the active ingredient was dissolved. Additionally, 20 mL of a 0.25 % (w/v) aqueous solution of 80 % hydrolyzed polyvinyl alcohol (PVA, MW 9,000-10,000 Sigma Aldrich, cat. no. 360637-25 MG) was prepared into a 25 mL beaker. The 20 mL of PVA solution was placed

into a 50 mL centrifuge falcon tube and placed into ice allowing it to chill to 4-8 ˚C. A tissue homogenizer (Omni International Tissue Master 125 with 7 mm probe) with clamp was secured to stand over an ice bucket. A falcon tube containing the PVA solution was then placed into the ice bucket and the homogenizer probe was positioned so that the probe was submerged, but not in contact with the bottom of the falcon tube (e.g. 5 mm). The homogenizer was turned to 35,000 rpm (highest speed on a Tissue Master 125). A Pasteur pipette was used to add the PLGA and imidacloprid solution dropwise while homogenizing was taking placed. Homogenization of the mixture was performed for 5 minutes to create a single emulsion. The resultant emulsion was then added again into a 25 mL beaker to complete the solvent evaporation and form solid imidacloprid in polymer particles. The beaker was covered with aluminum foil with small holes and stirred at ambient temperature for 4 hours to remove organic solvent at a speed of 350 rpm using a Corning stir plate (PC-620D, USA). The microsphere suspension was added into a 15 mL polypropylene centrifuge tube (TC1500, USA) and centrifuged using an Eppendorf centrifuge (5810R 15 amp version) at 3000 rpm for 10 minutes at 4 ^{o}C. The microsphere suspension was washed several times with distilled water (pH 7.4) and lyophilized in a freeze-dryer (LANCONCO Freezer dryer, USA) to obtain imidacloprid loaded PLGA microspheres. The resulting microspheres were spherical and had a smooth surface.

Formulation Model

Method drug loading (DL) is defined as the percent of amount of active ingredient encapsulated into PLGA microspheres to the initial total amount of active ingredient-PLGA microspheres under analysis, which is calculated by:

$$DL = \left(1 - \left(\frac{M_d}{M_T}\right)\right) \times 100\% = \left(1 - \left[\frac{(C_d \times V_{Td})}{M_T}\right]\right) \times 100\% \quad (1)$$

M_d is defined as the total amount of active ingredient (~523 μg) found after dissolving the PLGA microsphere in DMSO. M_T is the initial total amount of PLGA-active ingredient microspheres (20 mg); C_d is the drug concentration (0.523 ng/μL) of the outer DMSO phase as determined by HPLC and/or UV spectrophotometric method (absorption wavelength: 270nm); V_{Td} is the total volume of the outer DMSO phase containing active ingredient after dissolving the PLGA microspheres (1 mL). . The approximate payload per particle is therefore calculated as approximately 2.62 %. DMSO was used only for the purpose of determining active ingredient concentration on samples during HPLC assays and was not used for the final preparation of FNDs.