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Inclusion complexes of α- and γ-cyclodextrins and the herbicide norflurazon: I. Preparation and characterisation. II. Enhanced solubilisation and removal from soils

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Abstract

The interaction of norflurazon with α- and γ-cyclodextrins (CDs) yielded the formation of inclusion complexes at a 1:1 stoichiometric ratio in solution and in the solid state. Apparent stability constants of 50.7 ± 1.6 and 37 ± 1.7 M^{-1} and an increase in herbicide solubility by up to five and fourfold for α- and γ-CD, respectively, were determined from the phase solubility diagrams at 25 °C in water. Three processing methods (kneading, spray-drying and vacuum evaporation) were used to prepare norflurazon–CD solid inclusion complexes, which were characterised by infrared spectroscopy, differential scanning calorimetry and scanning electron microscopy. A high increase in the norflurazon dissolution rate was obtained with all the solid complexes with γ-CD, but when α-CD was used, only the solid system obtained after the vacuum evaporation process showed a higher dissolution rate. This finding is a first step in the development of new, environmentally sound formulations of norflurazon (NFL), due to the capacity for increasing its dissolution rate and hydrosolubility, and thus diminishing the use of organic solvents. On the other hand, the effect of α- and γ-cyclodextrin on the solubility of norflurazon in solution was also considered as a way of modifying its behaviour in the soil environment. Desorption studies of NFL from soils in the presence of α- and γ-cyclodextrin were carried out using a batch equilibration method. The results obtained showed that α- and γ-cyclodextrin greatly increased the removal of norflurazon previously adsorbed, proving the potential use of these CDs for in situ remediation of pesticide-contaminated soils.

Keywords: Norflurazon; α-cyclodextrin; γ-cyclodextrin; Inclusion complex; Removal; Soils

1. Introduction

Cyclodextrins (CDs) are produced by the microbial breakdown of starch and have hydrophobic doughnut-shaped cavities that are able to form inclusion complexes with various guests, both in solution and in the solid

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state. It is sufficient that only a portion of the molecule fits in the cavity to form an inclusion complex (Szejtli, 1998).

Inclusion complexes with CDs are gaining wide use in chemistry, agriculture and the pharmaceutical industry (Uekama, 2002). Many publications confirm the prediction that, in the future, rapid development can be expected in the application of CDs to pesticide formulations, resulting in improvements in their chemical and physical properties, such as enhancement of solubility and bioavailability (Ginés et al., 1996; Pérez-Martínez et al., 1998; Lezcano et al., 2002; Manolikar and Sawant, 2003; Villaverde et al., 2004), increased stability of photodegradable and/or unstable pesticides (Kamiya et al., 2001), catalytic effects on the degradation of pesticides and controlled release (Szente, 1998; Ishiwata and Kamiya, 1999), and influence on pesticide adsorption and leaching in soils (Pérez-Martínez et al., 2000a; Morillo et al., 2001).

Norflurazon (NFL) is a selective pre-emergent herbicide widely used to control germinating annual grasses and broadleaf weeds in fruits, vegetables, nuts, cotton, peanuts and soybeans (Ahrens, 1994). NFL presents problems due to its retention in soils with high organic matter and iron oxide content (Morillo et al., 2004), and therefore it is of concern that NFL may persist in a non-bioavailable form in soil, implying a high risk of long-term contamination.

The principal objectives of the present work were: (a) to investigate the possibility of obtaining inclusion complexes in solution and in the solid state for NFL with α- and γ-CDs; and (b) to increase the aqueous solubility and bioavailability of NFL in soils via complexation with α- and γ-CDs, in order to develop new in situ technology for the removal of organic pollutants from contaminated soils.

2. Experimental

2.1. Materials

Norflurazon (purity 97.8%), 4-chloro-5-methylamino-2-(α,α,α-trifluoro-*m*-tolyl(pyridazin-3-(2*H*)-one, was kindly supplied by Novartis (Barcelona, Spain). The CDs employed were: α-CD from Rindex (Paris, France) and γ-CD from Cyclolab (Budapest, Hungary). Two soils (AL and CR) were employed to carry out the adsorption–desorption experiments. AL is a silt loam soil classified as Typic Eutrochrepts and CR is a loamy sand soil classified as Typic Xeropsamment. They were taken from the superficial horizon (0–20 cm). The main physicochemical properties of both soils were as follows for soils CR and AL, respectively: pH, 8.0 and 7.6; $CaCO_3$, 69 and 0 g kg^{-1}; cationic exchange capacity, 4.8 and 17.2 cmol kg^{-1}; organic carbon, 4.6 and 11.0 g kg^{-1}; sand, 87.6% and 16.4%; silt, 4.0% and 61.0%; and clay, 8.4% and 22.6%.

3. Methods

3.1. Studies in the aqueous phase

Solubility studies were carried out according to the method reported by Higuchi and Connors (1965). NFL (5 mg) was added to aqueous solutions (10 ml) containing various concentrations of one of cyclodextrins (from 0 to 0.1 M). The experiments were carried out in triplicate. Flasks containing the solutions were sealed and shaken at 25 °C for 1 week. This reaction time was chosen after preliminary kinetic studies (data not shown). Suspensions were then filtered using a syringe through a 0.22-μm Millipore cellulose glass fibre membrane filter, and the concentration of NFL in the filtrate was determined by HPLC equipped with a fluorescence detector. α- and γ-CDs cannot be detected using this analytical method, and therefore they did not interfere with the assay. The conditions were as follows: mobile phase, acetonitrile/water (60:40); flow, 0.6 ml min^{-1}; temperature, 30 °C; chromatographic column, Kromasil C18 reverse-phase; fluorescence detector (Shimadzu RF-535), with excitation and emission wavelengths at 310 and 405 nm, respectively.

The apparent stability constant K_c was calculated from the straight line obtained in the phase solubility diagram, following the equation proposed by Higuchi and Connors (1965):

$$K_c = \text{slope}/S_0(1 - \text{slope}) \quad (1)$$

where S_0 is the NFL equilibrium concentration in aqueous solution in the absence of CD, and slope is the slope of the phase solubility diagram.

3.2. Preparation of solid complexes

The 1:1 stoichiometric ratio employed for the preparation of solid complexes was obtained from the phase solubility diagrams of the CDs, and NFL–CD physical mixtures (1:1) were used as references. They were prepared by shaking both components for 45 min. Three different processing methods were employed to prepare the solid complexes.

3.3. Vacuum evaporation method

NFL ethanol solutions 83.2 mg/70 ml and 303.7 mg/120 ml were mixed with α- and γ-CD aqueous solutions 26 mg/100 ml and 1297 mg/110 ml, respectively. The solutions were mixed for 20 min by sonication to obtain clear solutions. Then, the ethanol was evaporated under vacuum for 20 min. Finally, the products were dried at 37 °C for 48 h.