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Ethylcellulose and lignin as bearer polymers in controlled release formulations of chloridazon

M. Fernández-Pérez*, M. Villafranca-Sánchez, F. Flores-Céspedes, I. Daza-Fernández

Department of Inorganic Chemistry, University of Almería, La Cañada de San Urbano s/n, 04120 Almería, Spain

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ABSTRACT

Polymeric materials like ethylcellulose and lignin have been used to improve the application of the herbicide chloridazon, preparing controlled release formulations (CRFs). The lignin-based formulations prepared were coated in a Wurster-type fluidized-bed equipment using ethylcellulose and dibutylsebacate.

Chloridazon has been successfully trapped, with values of encapsulation efficiency (EE) higher than 94% in all cases. FT-IR and DSC studies indicate the compatibility between polymers and chloridazon in lignin based CRFs. SEM pictures show a homogeneous film in ethylcellulose coated CRFs.

Using experimental equations, the time taken for 50% of the active ingredient to be released into water (T_{50}) was calculated. From the analysis of the T_{50} values, it can be deduced that the release rate of chloridazon can be mainly controlled either by selecting the granule size of controlled release lignin matrixes, or by changing the thickness of the coating film and modifying its surface properties adding a plasticizer for ethylcellulose coated CRFs.

1. Introduction

Polymeric matrixes have been vastly used in different fields: as drug delivery vehicles, in protection of functional ingredients, as sensing devices, in biomaterials, and for catalysis (Varshosaz, Tavakoli, & Eram, 2006). The polymeric matrix can be made of both synthetic and natural polymers. Natural polymers such as dextrans, gelatin, chitosan, sodium alginate, lignin and cellulose derivate are more interesting than synthetic polymers for food and biomedical applications due to their higher biodegradability and biocompatibility (Beneke, Alvaro, Viljoen, & Hamman, 2009). These polymers can be also used to prepare controlled release formulations (CRFs) of pesticides. The primary objectives of controlled release technology, in crop protection, include improved performance on the desired target and the effectiveness of the agents which protect the crop, allowing a reduction of the environmental problems associated with its implementation.

CRFs regulate the supply of pesticides, allowing a lower and continued concentration of them in soil. Therefore, they reduce the losses caused by leaching and evaporation (Mogul et al., 1996), always maintaining their concentration between the limits of toxicity and the effectiveness. In CRFs, pesticides are trapped, that is, they are integrated into a polymer matrix, where they are dissolved or linked to it physically or chemically. In this way, the active ingredient is released through controlled diffusion processes achieving minimal losses. In this research, new CRFs of chloridazon have been developed using natural biodegradable polymers such as ethylcellulose and lignin.

Chloridazon, 5-amino-4-chloro-2-phenylpyridazin-3(2H)-one, is used as a selective systemic herbicide which inhibits photosynthesis and it is used for general weed control (Flores-Céspedes, Villafranca-Sánchez, Pérez-García, & Fernández-Pérez, 2007). Although results are conflicting, chloridazon appears to be mobile in some soils. Several researches reported the K_{oc} of chloridazon as 89–340 (Tomlin, 2002). According to a classification by Cohen (1990), these K_{oc} values indicate that chloridazon would generally have high mobility in soil. The use of this product in areas where soils are permeable and water tables are shallow could result in leaching to ground water leading to potential pollution. However using polymeric CRFs of chloridazon can reduce this risk.

The lignin polymer is a low-cost waste product in the paper pulp manufacturing process, which is readily available, cheap, and an underutilized resource nowadays. The use of the lignin by-product produced in the pulping of soft wood (kraft lignin) has been reported in other papers (Fernández-Pérez, González-Pradas, Ureña-Amate, Wilkins, & Lindup, 1998; García, Díez, Vallejo, García, & Cartagena, 1996; Zhao & Wilkins, 2003). Polyethylene glycol (PEG) was used in some of the formulations due to its characteristics such as hydrophobicity, low density, lack of reactivity with the other components within the system, suitability for

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* Corresponding author. Tel.: +34 950015961; fax: +34 950015008.
E-mail addresses: mfernand@ual.es (M. Fernández-Pérez), villafra@ual.es (M. Villafranca-Sánchez), frflores@ual.es (F. Flores-Céspedes), idf482@ual.es (I. Daza-Fernández).

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melting and low cost (Harris, 1992). Ethylcellulose (EC) is one of the most widely-used polymers in film coating because of many advantages it offers as formulator, such as good film formability, excellent physical–chemical stability and minimum toxicity (Rao & Murthy, 2001). Plasticizers are commonly incorporated with the polymeric film, to change flexibility, tensile strength and adhesion properties of the resulting film (Lin, Cheng, & Liang, 2000). Dibutylsebacate (DBS) has been used in previous researches due to its lipophilic character (Lecomte, Siepmann, Walther, MacRae, & Bodmeier, 2004) and also due to a minimum pollution potential for the environment (Pérez-García, Fernández-Pérez, Villafranca-Sánchez, González-Pradas, & Flores-Céspedes, 2007). DBS is an insoluble plasticizer which combined with the ethylcellulose polymer can control the release rate of the herbicide into the CRFs.

The objectives of this study were:

i. To design, prepare and characterize controlled release formulations of chloridazon using biodegradable polymers like ethylcellulose and lignin.
ii. To evaluate chloridazon CRFs in water through kinetic studies.

The lignin-based CR granules were prepared by mixing the herbicide with kraft lignin and polyethylene glycol under melting conditions. The EC coated granules were prepared by coating lignin-based granules in a Wurster-type fluidized-bed equipment.

In order to investigate the physical and chemical compatibility of the materials used in the preparation of the formulations, pure polymers, chloridazon and blends were analyzed by Fourier transformed infrared spectroscopy (FT-IR) and differential scanning calorimetry (DSC).

2. Materials and methods

2.1. Materials

The lignin used in this study was a commercially available pine kraft lignin, Indulin AT (Westvaco Corp., Charleston, SC). To improve the properties of homogeneity of the formulation, polyethylene glycol (PEG) (molecular weight, 1000 g mol^{-1}) was used; the film-forming material of polymer coating was ethylcellulose (EC) (Ethocel®; ethoxy content, 48.0–49.5%; viscosity, 9–11 cP); and the plasticizer selected for the study was dibutylsebacate (DBS) ($\geq$97%, d = 0.936 g mL^{-1}). These products were supplied by FlukaChemie AG (Buchs, Switzerland).

Technical grade chloridazon (94.1%) was kindly supplied by BASF Agro Spain (Barcelona, Spain). Its molecular formula and selected properties are as follows (PPDB, 2009; Tomlin, 2002): molecular formula, $C_{10}H_8ClN_3O$; molecular weight, 221.64 g mol^{-1}; melting point, 206 °C; degradation point, 306 °C; vapor pressure (20 °C), <0.01 mPa; water solubility (20 °C), 0.34 g L^{-1}; octanol/water partitioning ($\log K_{ow}$) (20 °C), 1.19; stable up 50 °C for $\geq$2 years; stable in aqueous media at pH 3–9.

2.2. Lignin based formulations

The CR granules were formed by mixing the lignin (L), polyethylene glycol (PEG) and chloridazon (C) in the optimized ratio [65:20:15 (w/w)] using a glass reactor inserted in a thermostatic bath (model Tectron L by Selecta S.A., Barcelona, Spain) filled with silicone oil. The mixture was heated under melting conditions at 206 °C for 20 min. On cooling, the matrixes were crushed in a hammer mill and then sieved to obtain granules of size between: 0–0.2 mm; 0.2–0.5 mm; 0.5–1 mm; 1–2 mm and 2–3 mm. The resulting products are labelled in the text as CPEL ($0 < d < 0.2$ mm), CPEL (0.2 mm < d < 0.5 mm), CPEL (0.5 mm < d < 1 mm), CPEL (1 mm < d < 2 mm), and CPEL (2 mm < d < 3 mm). The numbers in brackets represent the size range (mm). Additionally, lignin based granules without chloridazon (PEL) were also prepared to evaluate compatibility and interactions through DSC and FT-IR studies.

2.3. Ethylcellulose coated granules

2.3.1. Preparation of coating solutions

Appropriate quantities of ethylcellulose and plasticizer were combined and dissolved in ethanol (Table 1) to obtain the coating solutions with two different polymer levels and, in one case, with a plasticizer. The coating film consists of 10% and 20% ethylcellulose of the weight of the dry granules (20 g) and, for the coating solution containing a plasticizer, the coating film consist of 20% EC and 2.25% DBS of the weight of the dry granules.

2.3.2. Preparation of coated granules

To prepare coated granules, 20 g of CPEL formulation, granules of size between 0.2 mm < d < 1 mm were loaded into a fluidized-bed coater (Mini-Glatt, Glatt AG, Pratteln l, Switzerland) assembled with a Wurster insert. The bed temperature was adjusted to 60 ± 2 °C. The granules were preheated at this temperature for 10 min. The coating solution was delivered with a peristaltic pump (Watson-Marlow, Model 1B-1003/R) and sprayed into the fluidized-bed via spray nozzle at the atomizing pressure of 1.2 bar. The coating solutions were pumped with a flow rate of 2.5 mL min^{-1} to prepare CPEL + EC_{10} and a flow rate of 5 mL min^{-1} for both CPEL + EC_{20} and CPEL + EC_{20} + DBS granules. The total spraying time was 40 min. The coated granules were then dried in the same device at 60 °C for 10 min and sieved, selecting the granules of size between 0.2 mm < d < 1 mm.

2.4. Granules characterization

2.4.1. Determination of chloridazon content in the CRFs

The actual concentration of chloridazon in the granules was determined by dissolving 20 mg of the granules in 50 mL of methanol in an ultrasound bath for 15 min, which led to the complete disintegration of the granules. The volume was made up to 100 mL with ultra-pure water. This solution was placed in stoppered conical flasks and shaken in a thermostatic bath at 25 °C ± 0.1 °C for 24 h, then the resulting extract was filtered using nylon filters (0.20 μm). The concentration of chloridazon in the solution was determined by high-performance liquid chromatography (HPLC) using a Beckman Coulter Inc, System Gold HPLC (Fullerton, CA, USA) equipped with a diode-array detector and 32 Karat data station.

The HPLC operating conditions to analyze chloridazon were described previously by other authors (Carabias-Martínez, Rodríguez-González, Fernández-Laespada, & Sánchez-San Román, 2000; Traub-Eberhard, Kördel, & Klein, 1994). The mobile phase used was an acetonitrile–water (purity suitable for HPLC) mixture 35:65 at a flow rate of 1 mL min^{-1}, chloridazon was analyzed at its wavelength of maximum absorption, 229 nm, by injecting a volume of 20 μL. Separation by isocratic elution was performed on a 150 mm × 3.6 mm NOVA PACK C18 column, supplied by Waters Assoc. Three replications were carried out for each formulation.

2.4.2. Particle mean size

The average diameter of CR granules was determined using a Stereoscopic Zoom Microscope from Nikon, model SMZ1000, provided with a camera PixelLINK (*Megapixel FireWire Camera*) model PL-A662. Each measure was taken through the analysis of a basis of two hundred particles using the software *Image Pro-Plus* 6.0.

2.4.3. Differential scanning calorimetry

DSC scans of chloridazon, lignin, polyethylene glycol, PEL and CPEL were taken with a DSC from *TA Instruments*, model *DSC Q20*. The samples (6 mg) were preheated to 120 °C for water evaporation. The heat evolved during the heating process (10 °C/min) from room temperature to 300 °C was recorded as a function of temperature. Nitrogen atmosphere was used at a steam of 20 mL/min.

Table 1
Coating solutions composition for the preparation of CR granules containing chloridazon.

CR granules	Weight of CPEL granules (g)	Coating solution composition				
		EC (g)	DBS (g)	Ethanol (mL)	EC (%)[a]	DBS (%)[b]
CPEL + EC_{10}	20	2	–	100	10	–
CPEL + EC_{20}	20	4	–	200	20	–
CPEL + EC_{20} + DBS	20	4	0.45	200	20	2.25

CPEL + EC_{10}: chloridazon–polyethylene glycol–lignin–ethylcellulose 10%.
CPEL + EC_{20}: chloridazon–polyethylene glycol–lignin–ethylcellulose 20%.
CPEL + EC_{20} + DBS: chloridazon–polyethylene glycol–lignin–ethylcellulose 20%–dibutyl sebacate 2.25%.

[a] EC (%) = (EC (g)/weight of CPEL granules (g)) × 100.

[b] DBS (%) = (DBS (g)/weight of CPEL granules (g)) × 100.