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Preparation and Characterization of Polymeric Microparticles Used for Controlled Release of Ametryn Herbicide

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1. Introduction

There is increasing pressure to improve agricultural productivity, due to rapid population growth, increased consumption and global demand for high quality products. As a result, agricultural chemicals have become essential for the control of weeds, pests and diseases in a wide range of crops. Ametryn (2-ethylamino-4-isopropylamino-6-methylthio-s-2,4,6-triazine) is a selective herbicide belonging to the s-triazine family, whose activity is the result of inhibition of photosynthesis by blocking of electron transport. The ametryn molecule (Figure 1) contains a symmetrical hexameric aromatic ring in its chemical structure, consisting of three carbon atoms and three nitrogen atoms in alternate positions. The herbicide is classified as a methylthiotriazine, due to the presence of the SCH_3 group (Tennant et al., 2001).

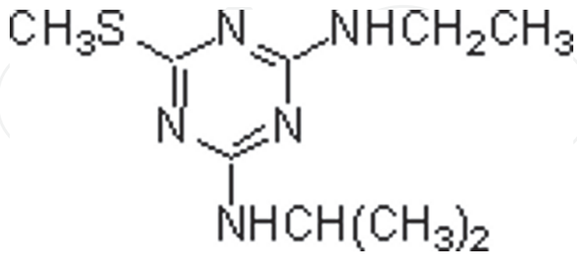


Fig. 1. Structural formula of ametryn.

Ametryn is used for the control of graminaceous and broad-leaved weeds in plantations of annual crops (Tennant et al., 2001). Once in the soil the herbicide may be taken up by plants, absorbed by the soil and plant residues, biodegraded, or undergo chemical transformations that increase its volatilization and photocatalytic decomposition. Studies have shown that prolonged human exposure to triazine herbicides can lead to serious health problems including contact dermatitis, intoxication, hormonal dysfunction and cancers (Friedmann et

al., 2002). It is therefore desirable to develop techniques whereby the physico-chemical properties of these chemicals can be altered and their usage made safer. The goal is to enable the use of soil management strategies that can produce foods at the current high levels of demand, without significant human or environmental risk.

Micro- and nanostructured polymeric materials can be used as transport systems for active chemicals. Advantages of these materials include good physical, chemical and biological stability, simple and reproducible preparation procedures, and applicability to a wide range of chemicals. In use, the active principle is released slowly and continuously, enabling the use of smaller quantities with greater efficiency, which reduces the risk of adverse environmental impacts (Sinha et al., 2004; Sopena et al., 2009).

Controlled release systems have been extensively used in the food and pharmaceutical industries for active substances including nutrients, drugs and aromas (El Bahri & Taverdet, 2007; Grillo et al., 2008; Mello et al., 2008; Moraes et al., 2010), and there has been a recent increase in their application in medicine (Natarajan et al., 2011; Parajo et al., 2010; Vicente et al., 2010).

Amongst the new controlled-release system technologies under development, the use of polymeric micro- and nanoparticles is of special interest in agribusiness. Several studies have investigated controlled-release systems for bioactive compounds in agricultural applications (Ahmadi & Ahmadi, 2007; Bin Hussein et al., 2010; El Bahri & Taverdet, 2005, 2007; Grillo et al., 2010; Hirech et al., 2003; Li et al., 2010; Lobo et al., 2011; Silva et al., 2010; Singh et al., 2008, 2010). Materials that have been used include silica, bentonite and sepiolite clays, and polymeric substances such as alginate, lignin and synthetic polymers. The latter include the poly(hydroxyalkanoates) (PHAs) (Salehizadeh & Loosdrecht, 2004), of which poly(3-hydroxybutyrate) (PHB) and its hydroxyvalerate copolymer (PHBV) have been most widely used (Amass & Tighe, 1998). The advantages of using polymers such as PHB and PHBV are that they are fully biodegradable, inexpensive and easily prepared by bacterial fermentation (Pouton & Akhtarb 1996; Reis et al., 2008). These polymers are isotactic and highly crystalline (55-80 %), so that their degradation rates are relatively slow compared to those of lactate (PLA) and glycolate (PGA) copolymers (Sudesh et al., 2000).

The objective of this work was to develop a novel release system for ametryn, employing microparticles prepared using two different polymers, PHB and PHBV (either individually or as mixtures). It was envisaged that the encapsulation of the herbicide in these microparticles would improve its chemical stability and enable the use of smaller quantities of the chemical, hence reducing the risk of environmental contamination.

2. Experimental

2.1 Materials

Polyvinyl alcohol (PVA), poly(3-hydroxybutyrate) (PHB, MW = 312,000 g mol^{-1}), poly(3-hydroxybutyrate-co-hydroxyvalerate) (PHBV, MW = 238,000 g mol^{-1}) and ametryn (Pestanal®) were purchased from Sigma Chem. Co. The solvents employed in the chromatographic analyses were acetonitrile, HPLC grade methanol (JT Baker) and Milli-Q water. The solutions were filtered using 0.22 μm nylon membranes (Millipore, Belford, USA).

2.2 Methodology

2.2.1 Determination of ametryn

The HPLC analyses were performed using a Varian ProStar instrument fitted with a PS 210 pump, a UV-VIS detector (PS 325), a Metatherm oven and an automatic injector (PS 410). The chromatograms were acquired and processed using Galaxy Workstation software. The eluent used was acetonitrile/water (70:30, v/v), at a flow rate of 1.4 mL min^{-1}, and separation was achieved using a Phenomenex Gemini C_{18} reversed phase column (5 µm, 110 Å, 150 mm x 4.60 mm i.d.). Ametryn was detected at a wavelength of 260 nm. The injection volume was 100 µL, and all samples were previously filtered through 0.22 µm nylon membranes.

2.2.2 Preparation of the polymeric microparticles containing ametryn

Microparticles were prepared with the PHB and PHBV polymers, used either individually or as a mixture, by formation of oil in water emulsions using the emulsification-solvent evaporation technique (Coimbra et al., 2008; Conti et al., 1995; Lionzo et al., 2007; Lobo et al., 2011). 200 mg of polymer (PHB, PHBV or a mixture of the two polymers, as described in Table 1) and 10 mg of herbicide were dissolved in 10 mL of chloroform to form the organic phase. The aqueous phase (200 mL) was prepared using 0.5 % (w/v) polyvinyl alcohol, at 50 ^{o}C. The organic phase was transferred to the aqueous phase (at 50 ^{o}C) with magnetic stirring (1000 rpm for 15 min). The chloroform was then evaporated from the emulsion. The suspension of microparticles formed was stored in an amber flask (to avoid any photodegradation of the herbicide). The final concentration of ametryn was 50 mg L^{-1}.

Formulation	PHBV		PHB	
	(mg)	%	(mg)	%
A	200	*100*	0	*0*
B	150	*75*	50	*25*
C	100	*50*	100	*50*
D	50	*25*	150	*75*
E	0	*0*	200	*100*

Table 1. Proportions of polymers used to prepare the different formulations.

2.2.3 Measurements of encapsulation efficiency

Portions (10 mg) of the different microparticles containing herbicide were dissolved in 50 mL of acetonitrile, and the association rate of the herbicide with the microparticles was determined by the technique described previously, which involves ultrafiltration/ centrifugation and analysis using HPLC (Kilic et al., 2005; Schaffazick et al., 2003). The samples were centrifuged in regenerated cellulose ultrafiltration filters that had a molecular size-exclusion pore size of 30 KDa (Microcon, Millipore), and the filtrate was analyzed using HPLC. The ametryn concentration was obtained from an analytical curve. The association

rate of ametryn was calculated from the difference between the concentration measured in the filtrate and the total concentration (100 %) in the microparticle suspension. The total concentration was measured after diluting the suspension with acetonitrile, which dissolved the polymer and ensured complete release of the herbicide. The measurements were performed in triplicate for each formulation. The encapsulation efficiency (EE, %) was expressed as the ratio:

$$EE(\%) = \frac{W_S}{W_{TOTAL}} x\ 100\% \quad (1)$$

Where, W_s is the quantity of ametryn in the microparticles and W_{total} is the amount of ametryn used in the formulation.

2.2.4 Scanning electron microscopy (SEM)

A scanning electron microscope (Model JSM-6700F, JEOL, Japan) was used to investigate the size distribution and surface morphology of the microparticles. Suspensions of microparticles containing the herbicide were filtered and the particles were then washed with 150 mL of distilled water. The solid residues were dried overnight over Na_2SO_4 in a desiccator. The samples were then attached to metallic supports (stubs) with double-sided tape, and metalized by deposition of a gold layer at a current of 25 mA for 150 s. Images (electron micrographs) of the samples were then generated using the microscope. Particle sizes were measured using the ImageJ 1.42 program, and the size distributions of the different microparticles were obtained using OriginPro 7.0. At least 1000 individual particles of each sample were used for these measurements.

2.2.5 Release of ametryn from the microparticles

The release profiles of ametryn, either free or associated with the microparticles, were investigated using a two-compartment experimental system. A cellulose membrane (Spectrapore, with a molecular exclusion pore size of 1000 Da) separated the donor compartment, containing 4 mL of solution (or suspension) of the herbicide, from the acceptor compartment, which contained 50 mL of deionized water maintained under gentle agitation at ambient temperature (Paavola et al., 1995). The pore size of the membrane only allowed passage of the free herbicide, while the herbicide associated with the microparticles was retained in the donor compartment until the equilibrium was shifted so as to release the ametryn present within the particles. The size of the microparticles prevented their passage through the pores of the membrane. These experiments were conducted under *dilution sink* conditions, whereby the volume of the dissolution medium was sufficiently large that the herbicide concentration never exceeded 10 % of the value of its saturation concentration (Aulton et al., 2002).

Samples were retrieved from the acceptor compartment as a function of time, and analyzed by HPLC at a detector wavelength of 260 nm. During the first hour, samples were collected every 15 min, during the second hour every 30 min, and subsequently at hourly intervals until the peak area stabilized. The peak area values were then converted into the percentage of herbicide released as a function of time (De Araújo et al., 2004).

2.2.5.1 Mathematical modeling of ametryn release

Mathematical modeling is increasingly used to investigate the release profiles of bioactive compounds in polymeric systems, since it can provide important information concerning the release mechanism. Analysis of the mechanism of release of ametryn from the microparticles employed the zero order, first order, Higuchi and Korsmeyer-Peppas models (Colombo et al., 1995, 2005; Costa & Lobo, 2001; Ferrero et al., 2000; Hariharam et al., 1994; Ritger & Peppas, 1987a, 1987b).

3. Results and discussion

The encapsulation efficiency values obtained for the different microparticles are listed in Table 2. Formulation A (100 % PHBV) showed the highest encapsulation efficiency (76.5 %). The efficiency decreased as the proportion of PHBV decreased, and formulation E (100 % PHB) provided the lowest encapsulation efficiency (26.2 %). The values obtained for formulations A and B were fairly high, relative to values that have been reported in the literature for other active principles (Bazzo et al., 2009; Grillo et al., 2010; Lobo et al., 2011; Sendil et al., 1999). Grillo and colleagues (2010) showed that the encapsulation efficiency of the herbicide atrazine in PHBV microparticles was in excess of 30 %. Lobo et al. (2011), using an experimental design optimization procedure, obtained an encapsulation efficiency of 24 % for atrazine in PHBV microparticles.

Formulation	PHBV (%)	PHB (%)	EE (%)
A	100	0	76.5
B	75	25	54.7
C	50	50	40.5
D	25	75	29.3
E	0	100	26.2

Table 2. Encapsulation efficiencies (EE, %) of the different microparticles.

The relationship between the percentage of PHBV and the encapsulation efficiency is illustrated in Figure 2. There was a polynomial relationship between the encapsulation efficiency and the PHBV concentration, which was positive for PHBV and negative for PHB. This can probably be explained by the structural differences between the microparticles, due to the different polymer ratios used in their preparation (Table 1).

The morphological characteristics of the microparticles, as well as the influence of the encapsulation of ametryn, were analyzed using the SEM procedure. Electron micrographs of the microparticles containing ametryn are illustrated in Figure 3. All types of microparticle were spherical, although the surface structures were different. Most of the PHB microparticles possessed smooth surfaces with few pores, while most of the PHBV microparticles were rough-surfaced with many cavities and pores, some of which were quite large, as can be clearly seen for formulation A (Figure 3, a1 and a2). Grillo et al. (2010) also found that PHBV microparticles, prepared using the same methodology as that

described here, were rough-surfaced with pores, while PHB microparticles had smooth surfaces and fewer pores.

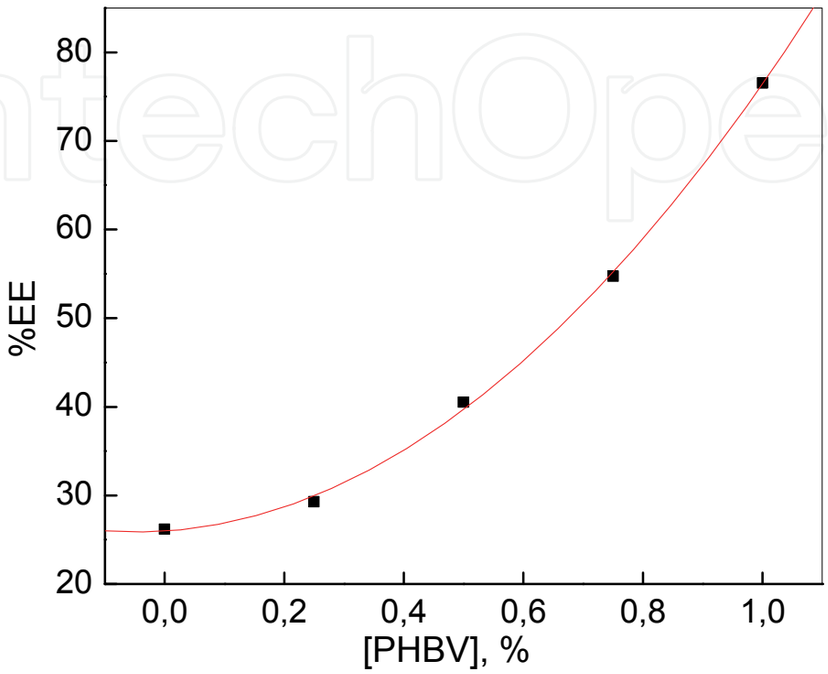


Fig. 2. Encapsulation efficiency according to PHBV content of the microparticles.

A higher encapsulation efficiency of ametryn was therefore related to a greater number of pores in the microparticles, probably due to greater contact (and/or affinity) of the herbicide with the microparticles during the formulation preparation procedure. Ametryn is likely to have greater affinity for the PHBV polymer, since both of these molecules possess alkyl branches, with interaction being further enhanced by the porosity of the PHBV microparticles.

The size distribution profiles (Figure 4) differed between microparticle formulations (it was not possible to measure the size distribution of the formulation D microparticles due to focusing problems). The average size of the microparticles (Table 3) increased as the PHBV concentration decreased and the PHB concentration increased, and was greatest for the PHB microparticles (formulation E). These size differences could be related to the incorporation of the herbicide as well as to associations between the molecules (as discussed above). At higher encapsulation rates, the amount of ametryn present within the microparticle increased, and the potential for reactions and interactions with the polymer therefore also increased. Ametryn is likely to have a higher affinity for PHBV, and as a result of this affinity (and/or reaction) the polymer contracts due to the formation of linkages between the polymer chains. As the proportion of PHBV decreases, the affinity of ametryn for the polymer mixture also diminishes (due to the lower affinity of ametryn for PHB), so that there is less shrinkage.

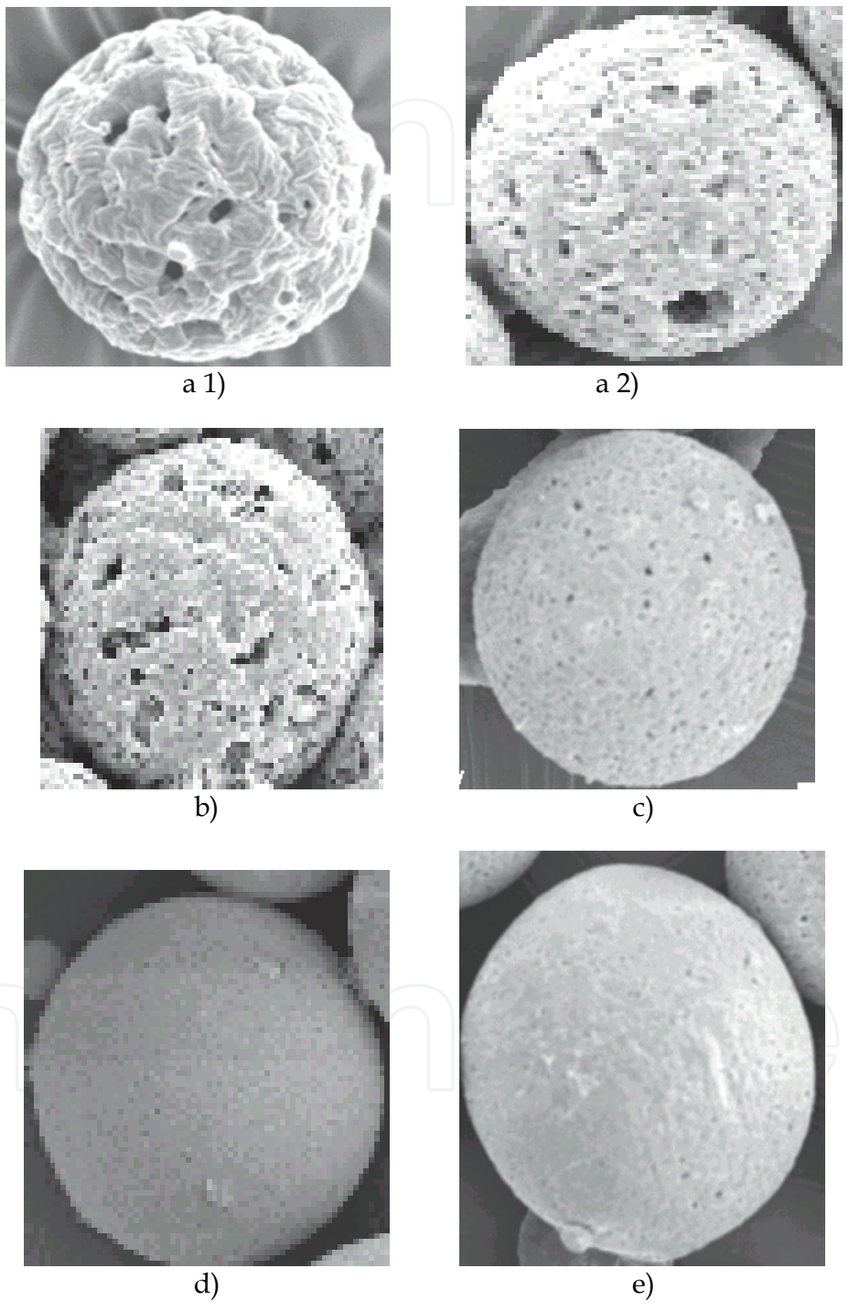


Fig. 3. SEM images of the polymeric microparticles: a) Formulation A; b) Formulation B; c) Formulation C; d) Formulation D; e) Formulation E.

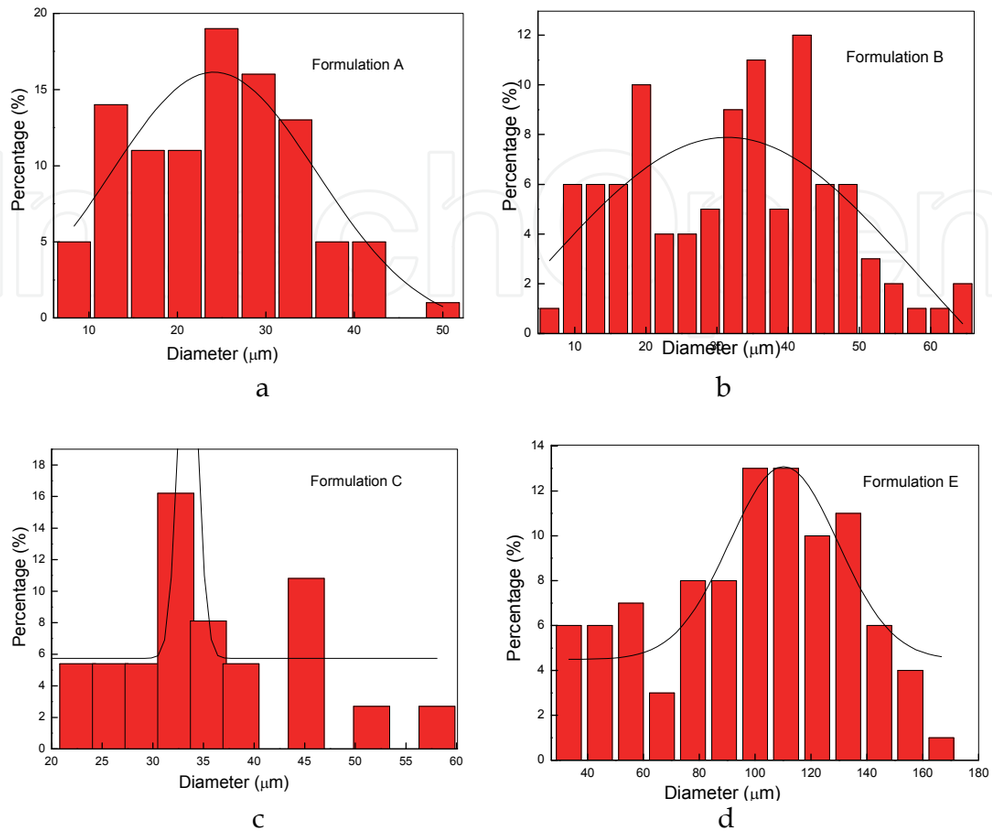


Fig. 4. Size distributions of the polymeric microparticles: a) Formulation A; b) Formulation B; c) Formulation C; d) Formulation E.

Formulation	PHBV (%)	PHB (%)	Average size (μm)
A	100	0	24.14 ± 1.606
B	75	25	31.45 ± 2.797
C	50	50	33.5 ± 3.22
D	25	75	*
E	0	100	110.2 ± 3.881

* Not determined.

Table 3. Average sizes (± SD) of the different microparticles.

The release profiles of free ametryn (as the reference) and ametryn encapsulated in the microparticles are illustrated in Figure 5, as a function of time (up to approximately 360 min). In these experiments the herbicide could traverse the pores of the membrane, while the microparticles were retained, so that it was possible to measure the influence of the association of ametryn with the polymeric matrix of the microparticles on its release rate. The release kinetics of free ametryn was faster than that of the encapsulated herbicide, with

almost total release after 360 min. Association with the microparticles resulted in retarded release, with around 70 % (formulations A and B), 30 % (formulation C), 20 % (formulation D) and 40 % (formulation E) being released after 360 min.

The release of other bioactive compounds from systems composed of microstructured polymers has been described in the literature, but usually for only one type of polymer (Grillo et al., 2010; Maqueda et al., 2009; Sendil et al., 1999; Singh et al., 2010; Wang et al., 2007). However, interpretation of release profiles relies to a large extent on knowledge of the composition and structural characteristics of the microparticles concerned, and in this respect studies that use more than one type of microparticle are advantageous. In the present work, the release of ametryn increased in line with the content of PHBV for formulations A-D, indicating that increased porosity aided the exit of ametryn molecules due to increased contact with the solvent. However formulation E was an exception to the rule, since it was composed of PHB alone and showed the fastest release of ametryn. There are two possible explanations for this observation. Firstly, the encapsulation efficiency of this formulation was lower than those achieved using the other formulations, which could have resulted in higher concentrations of ametryn crystals in the solution, and consequently higher release rates. Secondly, it is possible that lengthy refrigerated storage of this sample could have resulted in solubilization of the herbicide, due to increased contact time with the solvent.

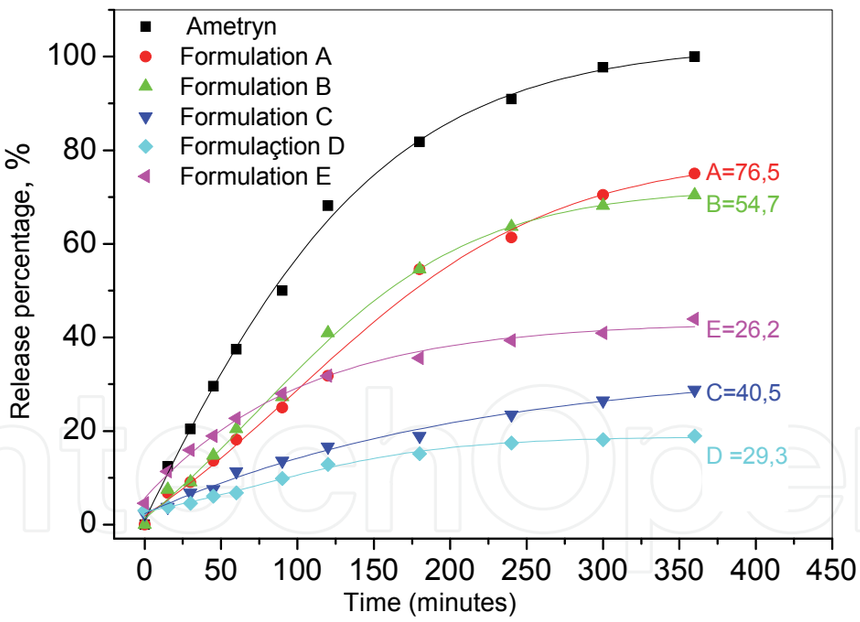


Fig. 5. Results of the release experiments, comparing the kinetic profiles of free ametryn and ametryn associated with the different microparticles (PHB, PHBV and PHBV+PHB), at ambient temperature (n = 3).

Analysis of release curves can provide important information concerning the mechanisms involved in the release of compounds from microparticles (Polakovic et al., 1999). Possible mechanisms include desorption from the surface of the polymeric matrix, diffusion through the pores or wall of the matrix, disintegration of the microparticle with subsequent release

of the active principle, and dissolution and erosion of the matrix or the polymeric wall (Polakovic et al., 1999; Schaffazick et al., 2003).

A number of mathematical models have been extensively used to analyze the characteristics of the release of substances from polymeric systems (Costa & Lobo 2001). Here, the results of the release experiments (Figure 5) were analyzed using the zero order, first order, Higuchi and Korsmeyer-Peppas models (Table 4). For the formulations investigated, the Korsmeyer-Peppas model provided the best explanation of the ametryn release mechanism, according to the correlation coefficient obtained. The curves obtained for each formulation using this model are illustrated in Figure 6.

	Zero order	**First order**	**Higuchi**	**Korsmeyer-Peppas**
Formulation A				
				n = 0,82641
Release constant (k)	4.59184 min^{-1}	0.00667 min^{-1}	4.49925 $min^{-1/2}$	0.00628min^{-n}
Correlation coefficient (r)	0.92307	0.98452	0.97721	0.99364
Formulation B				
				n = 0.79373
Release constant (k)	0.20767 min^{-1}	0.00624 min^{-1}	4.35701 $min^{-1/2}$	0.0072min^{-n}
Correlation coefficient (r)	0.89455	0.96782	0.98115	0.9879
Formulation C				
				n = 0.62532
Release constant (k)	0.07283 min^{-1}	0.00581 min^{-1}	1.52624 $min^{-1/2}$	0.0162 min^{-n}
Correlation coefficient (r)	0.86545	0.97701	0.9893	0.9929
Formulation D				
				n = 0.5671
Release constant (k)	0.048 min^{-1}	0.00495 min^{-1}	1.00913 $min^{-1/2}$	0.0194min^{-n}
Correlation coefficient (r)	0.90337	0.96059	0.97587	0.98839
Formulation E				
				n = 0.42726
Release constant (k)	0.0983 min^{-1}	0.00441 min^{-1}	2.17047 $min^{-1/2}$	0.0429min^{-n}
Correlation coefficient (r)	0.79093	0.92828	0.99035	0.9927

Table 4. Results of the application of four mathematical models to the release curves of ametryn associated with different microparticles.

The Korsmeyer-Peppas model is based on a semi-empirical equation (Korsmeyer & Peppas, 1991; Korsmeyer et al., 1983) that is widely used when the release mechanism is unknown. When the release exponent (n) is equal to 0.43 the mechanism involved is diffusion. When the value of the exponent is greater than 0.43 but smaller than 0.85, the release occurs due to anomalous transport that does not obey Fick's Law. Values less than 0.43 are indicative of porous systems in which transport occurs by a combination of diffusion through the polymeric matrix and diffusion through the pores. The values obtained (Table 4) differed

according to formulation, as expected considering the different structural characteristics of the microparticles, so that the release mechanisms were not identical. Nonetheless, the values obtained for all formulations were in the range $0.43 < n < 0.85$, indicating that in all cases the release occurred as a result of anomalous transport, involving diffusion and relaxation of the polymeric chains. This information concerning the release mechanism is of vital importance in order to be able to adjust and optimize the release of the active principle according to circumstances.

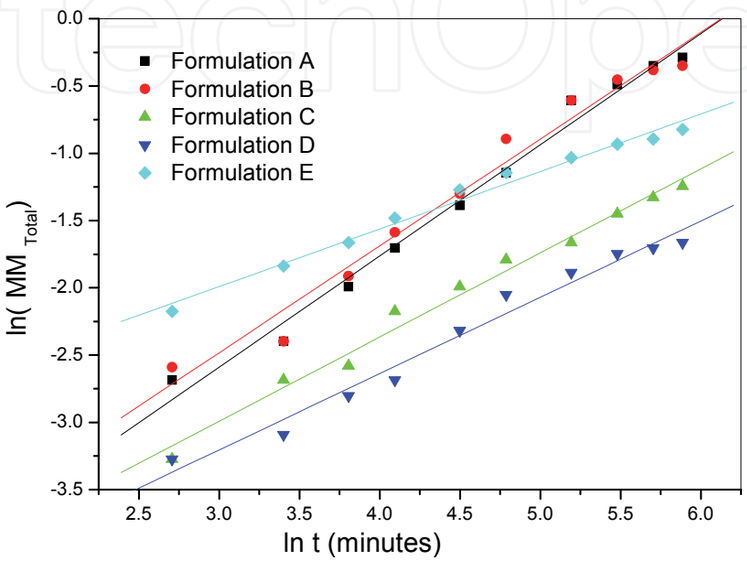


Fig. 6. Results obtained using the Korsmeyer-Peppas model applied to formulations A-E.

4. Conclusions

Ametryn herbicide was efficiently encapsulated in microparticles composed of PHB, PHBV and mixtures of the two polymers. The highest encapsulation efficiencies were achieved when higher proportions of PHBV were used. SEM analysis showed that the microparticles were spherical, although with different surface features (either smooth or rough with pores). The release profile of ametryn was modified when it was encapsulated, with slower and more sustained release compared to the free herbicide. This finding suggests that the use of encapsulated ametryn could help to mitigate adverse impacts on ecosystems and human health. This is particularly important given the increasingly widespread and intensive use of agents such as ametryn in modern agriculture.

5. Acknowledgments

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6. References

Ahmadi, A. & Ahmadi, A. (2007). Preparation and characterization of chemical structure composition of polyurethane's microcapsules pesticides. *Asian Journal of Chemistry*, Vol.19, No.1, pp. 187-194.

Amass, W. & Tighe, B. (1998). A review of biodegradable polymers: uses, current developments in the synthesis and characterization of biodegradable polyesters, blends of biodegradable polymer and recent advances in biodegradation studies. *Polym. Int*., Vol.47, pp. 89-144.

Aulton, M. (2002). Dissolution and Solubility. Pharmaceutics: the science of dosage from design. 2 ed. Edinburgh: Churchill Livingstone, cap. 2, p. 15-32,

Bazzo, G.C.; Lemos-Senna, E. & Pires, A.T.N. (2009). Poly(3-hydroxybutyrate)/chitosan/ ketoprofen or piroxicam composite microparticles: Preparation and controlled drug release evaluation, *Carbohydr. Polym*., Vol.77, pp. 839–844.

Bin Hussein, M.Z.; Hashim, N.; Yahaya, A.H. & Zainal, Z. (2009). Controlled Release Formulation of Agrochemical Pesticide Based on 4-(2,4-dichlorophenoxy)butyrate Nanohybrid. *Journal of nanoscience and nanotechnology,* Vol.9, No. 3, pp. 2140-2147.

Coimbra, P.A.; De Sousa, H.C. & Gil, M.H. (2008). Preparation and characterization of flurbiprofen-loaded poly(3-hydroxybutyrate-co-3- hydroxyvalerate) microspheres. *J Microencapsul* ., Vol. 25; pp.170-178.

Colombo, G.; Padera, R.; Langer, R. & Kohane, D.S. (2005). Prolonged duration anesthesia with lipid-protein-sugar particles containing bupivacaine and dexamethasone. *J Biomed Mater Res Part A* , Vol.75; pp. 458-464.

Colombo, P.; Bettini, R.; Massimo, G.; Catellani, P.L.; Santi, P. & Peppas, N.A. (1995). Drug diffusion front movement is important in drug release control from swellable matrix tablets. *J Biomed Mater Res.,* Vol.84, pp. 991-997.

Conti, B.; Genta, I.; Modena, T. & Pavanetto, F. (1995). Testing of In Vitro Dissolution Behaviour of Microparticulate Drug Delivery Systems. *Drug Dev. Ind. Pharm.,* Vol.21, pp. 1223-1233.

Costa, P. & Lobo, J.M.S. (2001). Modeling and comparison of dissolution profiles. *Eur J Pharm Sci,* Vol.13, pp. 123-133.

De Araújo, D.R.; Cereda, C.M.S.; Brunetto, G.B.; Pinto, L.M.A.; Santana, M.H.A. & De Paula, E. (2004). Encapsulation of mepivacaine prolongs the analgesia provided by sciatic nerve blockade in mice. *Can. J. Anesth*., Vol.51, pp. 566-572.

El Bahri, Z. & Tavedert, J.L. (2007). Elaboration and characterisation of microparticles loaded by pesticide model. *Powder Technol*., Vol.172, pp. 30-40.

El Bahri, Z. & Taverdet, J.L. (2005). Optimization of an herbicide release from ethylcellulose Microspheres. *Polymer Bulletin*., Vol.54, pp. 97-103.

Ferrero, C.; Muñoz-Ruiz, A. & Jiménez-Castellanos, M.R. (2000) Fronts movement as a useful tool for hydrophilic matrix release mechanism elucidation. *Int J Pharm*., Vol.202, pp. 21-28.

Friedmann, A.S. (2002) *Atrazine inhibition of testosterone production in rat males following peripubertal exposure.* Johns Hopkins University, Baltimore, MD, USA.

Grillo, R.; Melo, N.F.S.; Lima, R.; Lourenço, R.; Rosa, A.H. & Fraceto, L.F. (2010). Characterization of atrazine-loaded biodegradable poly(hydroxybutyrate-co-hydroxyvalerate) microspheres. *J Polym Environ*., Vol.18, pp. 26-32.

Grillo, R.; Melo, N.F.; Moraes, C.M.; De Lima, R.; Menezes, C.M.; Ferreira, E.I.; Rosa, A.H. & Fraceto, L.F. (2008). Study of the interaction between hydroxymethylnitrofurazone and 2-hydroxypropyl-beta-cyclodextrin. *Pharm Biomed Anal*., Vol. 47, pp. 295-302.

Hariharam, D.; Peppas, N.A.; Bettini, R. & Colombo, P. (1994) Mathematical analysis of drug delivery from swellable systems with parcial physical restrictions or impermeable coatings. *Int J Pharm.,* Vol.112; pp. 47-54.

Hirech, K,; Payan, S.; Carnelle, G.; Brujes, L. & Legrand, J. (2003). Microencapsulation of an insecticide by interfacial polymerization. *Powder Technol*., Vol.130, pp. 324-330.

Kilic, A.C.; Capan, Y.; Vural, I.; Gursoy, R.N.; Dalkara, T.; Cuine, A. & Hincal, A.A. J. (2005). Preparation and characterization of PLGA nanospheres for the targeted delivery of NR2B-specific antisense oligonucleotides to the NMDA receptors in the brain. *Microencap,* Vol. 22, pp. 633–641.

Korsmeyer, R.W. & Peppas, N.A. Macromolecular and modeling aspects of swelling-controlled systems. In: Roseman TJ, Mansdorf SZ (Eds.). Controlled release delivery systems. New York, USA: Marcel Dekker Inc, 1991.

Korsmeyer, R.W.; Gurny, R.; Doelker, E.; Buri, P. & Peppas, N.A. (1983). Mechanisms of Solute Release from Porous Hydrophilic Polymers, *Int. J. Pharm.*, Vol.15, pp. 25-35.

Li, J.Y.; Zu, B.Y.; Zhang, Y.; Guo, X.Z. & Zhang, H.Q. One-Pot Synthesis of Surface-Functionalized Molecularly Imprinted Polymer Microspheres by Iniferter-Induced "Living" Radical Precipitation Polymerization *Journal Of Polymer Science Part A-Polymer Chemistry,* Vol.48, pp. 3217-3228.

Lionzo, M.I.Z.; Ré, M.I., Guterres, S.S. & Pohlmann, A.R. J. (2007). Microparticles prepared with poly(hydroxybutyrate-co-hydroxyvalerate) and poly(ε-caprolactone) blends to control the release of a drug model. *Microencapsulation*, Vol.24, pp. 175-186.

Lobo, F.A.; Aguirre C.L.; Silva, M.S.; Grillo, R.; Melo, N.F.S.; Oliveira, L.K.; Morais, L.C.; Campos, V.; Rosa, A.H. & Fraceto, L.F.; (2011). Poly(hydroxybutyrate-co-hydroxyvalerate) microspheres loaded with atrazine herbicide: screening of conditions for preparation, physico-chemical characterization and *in vitro* release studies. *Polym. Bull.* Vol.67, pp. 479–495.

Maqueda, C.; Villaverde, J.; Sopeña, F.; Undabevtia, T. & Morillo, E. (2009). Effects of soil characteristics on metribuzin dissipation using clay-gel-based formulations. *J. Agric. Food Chem*, Vol.57, pp. 3273-3278.

Melo, N.F.; Grillo, R.; Rosa, A.H&; Fraceto L.F.J (2008). Interaction between nitroheterocyclic compounds with β-cyclodextrins: Phase solubility and HPLC studies. *Pharm Biomed Anal.* , Vol.47, No. 4-5, pp. 865-869.

Moraes, C.M.; De Paula, E.; Rosa, A.H. & Fraceto, L.F. Physicochemical stability of poly(lactide-co-glycolide) nanocapsules containing the local anesthetic Bupivacaine. *Journal of the Brazilian Chemical Society*, v.21, p. 995-1000, 2010.

Natarajan, V.; Krithica, N.; Madhan, B. & Sehgal, P.K. (2011). Formulation and evaluation of quercetin polycaprolactone microspheres for the treatment of rheumatoidaArthritis. *Journal of pharmaceutical sciences*, Vol.100, No.1, pp.195-205.

Paavola, A.; Yliruusi, J.; Kajimoto, Y.; Kalso, E.; Wahlström, T. & Rosenberg, P. (1995). Controlled release of lidocaine from injectable gels and efficacy in rat sciatic nerve block. *Pharm. Res.,* Vol.12, pp. 1997-2002.

Parajo, Y.; d'Angelo, I.; Horvath, A.; Vantus, T.; Gyorgy, K.; Welle, A.; Garcia-Fuentes, M. & Alonso, M.J. (2010). PLGA:poloxamer blend micro- and nanoparticles as controlled release systems for synthetic proangiogenic factors. *European Journal of Pharmaceutical Sciences*, Vol.41 No.5, pp.644-649.

Polakovic, M.; Gorner, T.; Gref, R. & Dellacherie, E. (1999) Lidocaine loaded biodegradable nanospheres II: Modelling of drug release. *J. Controlled Release*, Vol.60, pp. 169-177.

Pouton, C.W. & Akhtarb S. (1996). Biosynthetic polyhydroxyalkanoates and their potential in drug delivery. *Advanced Drug Delivery Reviews*, Vol. 18, pp. 133-162.

Reis, C.P.; Neufeld, R.J.; Ribeiro, A.J. & Veiga, F. (2006). Nanoencapsulation I: Methods preparation of drug-loaded polymeric nanoparticles. *Nanomedicine*, Vol.2, pp. 8-21.

Ritger, P.L. & Peppas, N.A. J. (1987a). A simple equation for description of solute release II. Fickian and anomalous release from swellable devices. *Control. Release*, Vol.5, pp. 37–42.

Ritger, P.L. & Peppas, N.A. J. (1987b). A simple equation for description of solute release I. Fickian and non-fickian release from non-swellable devices in the form of slabs, spheres, cylinders or discs. *Control. Release*, Vol.5, pp. 23–36;

Salehizadeh, H. & Van Loosdrecht, M.C.M. (2004). Production of polyhydroxyalkanoates by mixed culture: recent trends and biotechnological importance. *Biotechnol. Adv.*, Vol.22, pp. 261-279.

Schaffazick, S. R.; Guterres S. S.; Freitas, L. L. & Pohlmann, A. R. (2003). Caracterização e estabilidade físico-química de sistemas poliméricos nanoparticulados para administração de fármacos *Quim. Nova*, Vol.26, pp. 726-737.

Sendil, D.; Gursel. I.; Wise, D.L. & Hasircia, V. (1999) Antibiotic release from biodegradable PHBV microparticles, *J. Controlled Release*, Vol.59, pp. 207– 217.

Silva, M.D.; Cocenza, D.S.; de Melo, N.F.S.; Grillo, R.; Rosa, A.H. & Fraceto, L.F. (2010). Alginate nanoparticles as a controlled release system for clomazone herbicide. *Quimica Nova,* Vol.33, pp. 1868-1873.

Singh, B.; Sharma, D.K. & Gupta, A. J. (2008). In vitro release dynamics of thiram fungicide from starch and poly(methacrylic acid)-based hydrogels. *Hazardous Materials,* Vol.154, pp.278-286.

Singh, B.; Sharma, D.K.; Kumar, R. & Gupta, A. J. (2010). Development of a new controlled pesticide delivery system based on neem leaf powder. *Hazardous Materials*, Vol.177, pp. 290–299.

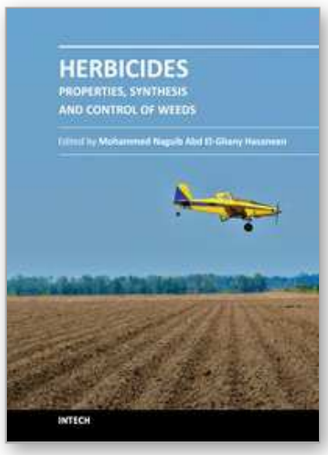
Sinha, V.R.; Bansal, K.; Kaushik, R.; Kumria, R. & Trehan, A. (2004). Poly-ε-caprolactone microspheres and nanospheres: an overview. *Int. J. Pharm.*, Vol.278, pp. 1–23.

Sopeña F.; Maqueda, C. & Morillo E. (2009). Controlled release formulations of herbicides based on micro- encapsulation. *Cien. Inv. Agr*. Vol.35, No.1, pp. 27-42.

Sudesh, K.; Abe H.& Y. Doi. (2000). Synthesis, structure and properties of polyhydro-xyalkanoates: biological polyesters. *Prog. Polym. Sci.* Vol.25, pp.1503-1555.

Tennant, A.H.; Peng, P. & Kligerman, A.D. (2001). Genotoxicity studies of three triazine herbicides: in vivo studies using the alkaline single cell gel (SCG) assay. *Mutation Research* , Vol.493, No.1-2, pp. 1–10.

Wang, Y.; Wang, X.; Wei, K.; Zhao, N.; Zhang, S. & Chen, (2007). Fabrication, characterization and long-term in vitro release of hydrophilic drug using PHBV/HA composite microspheres. *J. Materials Letters*, Vol.61, pp. 1071–1076.



Herbicides - Properties, Synthesis and Control of Weeds
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This book is divided into two sections namely: synthesis and properties of herbicides and herbicidal control of weeds. Chapters 1 to 11 deal with the study of different synthetic pathways of certain herbicides and the physical and chemical properties of other synthesized herbicides. The other 14 chapters (12-25) discussed the different methods by which each herbicide controls specific weed population. The overall purpose of the book, is to show properties and characterization of herbicides, the physical and chemical properties of selected types of herbicides, and the influence of certain herbicides on soil physical and chemical properties on microflora. In addition, an evaluation of the degree of contamination of either soils and/or crops by herbicides is discussed alongside an investigation into the performance and photochemistry of herbicides and the fate of excess herbicides in soils and field crops.

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