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Polymeric microparticles for modified release of NPK in agricultural applications

Júnior Olair Chagas^a, José Messias Gomes^a, Isabela Cristina de Matos Cunha^a,
Nathalie Ferreira Silva de Melo^b, Leonardo Fernandes Fraceto^c,
Gilmare Antônia da Silva^a, Fabiana Aparecida Lobo^{a,*}

^a Department of Chemistry, Institute of Exact and Biological Sciences, Federal University of Ouro Preto, Ouro Preto, MG 35400-000, Brazil

^b Department of Immunology and Molecular Biology, Faculty of Dentistry and Center for Dental Research São Leopoldo Mandic, Campinas, SP 13045-755, Brazil

^c Department of Environmental Engineering, State University of São Paulo Júlio de Mesquita Filho, Sorocaba, SP 18087-180, Brazil

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Abstract The aim of this work was to synthesize polymeric microparticles as carriers for nitrogen, phosphorus, and potassium (NPK fertilizer) for agricultural applications, using polyglycerol (PG) to improve the synthesis procedure. Multivariate experimental designs were employed to obtain a satisfactory synthesis. The desirability function identified the best conditions for preparation of the microparticles as being 100.00 mg of poly(ϵ -caprolactone) (PCL), 825.00 mg of PG, 9.25 mL of chloroform, and 0.9% w/v of polyvinyl alcohol (PVA). This resulted in average encapsulation rates of 94.23% for N, 99.80% for P, and 65.00% for K. The profile of release from the microparticles was according to diffusion following Fick's Law. These observations confirmed the capacity of the proposed microparticles to sustain a continuous and prolonged release of NPK for the purpose of plant fertilization.

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1. Introduction

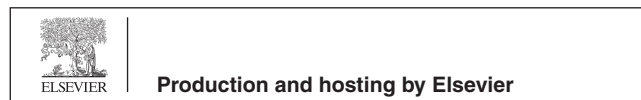
Fertilizers are inorganic or organic chemical compounds, alone or in mixtures, which are produced naturally or synthetically, with the capacity of supplying some of the thirteen essential nutrients necessary for plant development. They are extensively applied in agriculture to improve crop yields (de Urzedo et al., 2013).

Among the principal essential plant nutrients, nitrogen, phosphorus, and potassium (NPK) are required in higher concentrations (mmol/kg dry mass) for plant growth, relative to

* Corresponding author.

E-mail address: fabiana@iceb.ufop.br (F.A. Lobo).

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the other elements. Nitrogen is crucial because it is needed for vigorous plant growth and protein production. Phosphorus is important in cell division and the formation of cellular structures in the plant. It also stimulates healthy root growth, is essential for seed germination, and aids in the conversion of solar energy into chemical energy for photosynthesis. Finally, potassium is necessary for fruit formation, confers resistance against diseases and winter, is essential for photosynthesis, and maintains the hydric levels in plants (Ghormade et al., 2011; Carson and Ozores-Hampton, 2013).

Studies have demonstrated that most of the fertilizers used lose part of their nutrients to the environment, which can lead to environmental contamination. Fertilizers containing nitrates and phosphates can lose these compounds by leaching, generating eutrophication processes in surface waters and groundwater. Furthermore, when fertilizers are not applied correctly, they can cause an imbalance in the ecosystem and increase the number of acute toxicity and carcinogenic sources for humans, especially in the case of sandy soils exposed to high rainfall or intense irrigation (Lezcano et al., 2002; Manolikar and Sawant, 2003; Azeem et al., 2014; Hanafi et al., 2000). Therefore, fertilizer usage is an activity that should take into consideration the economic, environmental, and social sustainability of the agricultural sector.

Over the last few years, controlled/modified nutrient release technology has emerged as an important way to mitigate problems associated with the use of substances such as anesthetics, antibiotics, herbicides, and pesticides, among others (Carson and Ozores-Hampton, 2013; Lezcano et al., 2002; Manolikar and Sawant, 2003; Azeem et al., 2014; Hanafi et al., 2000; Grillo, 2011; Silva de Melo et al., 2010). This technology can be used to modify the physical-chemical properties of fertilizers, assisting in soil management and supplying the nutritional needs of plants.

Several studies reported in the literature describe the development of formulations for the modified release of fertilizers, notably natural or synthetic organic fertilizers and low solubility inorganic compounds (Azeem et al., 2014). However, to the best of our knowledge, there have been no studies involving the association of nitrogen, phosphorus, and potassium in microstructured polymeric systems. The term “controlled microstructured release system” is used for those that present particles in the size range 1–1000 μm and that have the capacity to release the active substance(s) in a continuous and prolonged manner. Due to these properties, such systems present advantages including the ability to reduce the amount of the chemical substance necessary and hence diminish contamination risks; the capacity to reduce energy consumption by reducing the number of applications needed; and the ability to maintain elevated concentrations for longer periods than achieved with conventional applications, this being one of the main goals of new fertilization strategies (Silva de Melo et al., 2010; Grillo et al., 2014; Guo et al., 2014; Assis et al., 2012).

Biodegradable polymers are the materials most widely used in the preparation of modified release systems, since they degrade to carbon dioxide, water, and biomass (organic matter) as a result of the action of enzymes or microorganisms (Martins Franchetti and Marconato, 2006; Schaffazick et al., 2003), avoiding adverse effects in the environment. These polymers have been exhaustively studied for the synthesis of micro- and nanostructures, with aliphatic polyesters being the most attractive, due to their biodegradability, biocompatibility, lack of tox-

ins, and capacity to incorporate a wide range of hydrophobic substances. Poly(ϵ -caprolactone) (PCL) is a biodegradable polymer that is water-insoluble and degrades slowly without damaging the environment, which are the reasons for its selection in the synthesis of carrier systems (Smidsrod and Skjakbraek, 1990; Espevik et al., 1993; Fialho et al., 2008).

Polyglycerol (PG), with properties similar to those of the alginate polymers, is obtained by the polymerization of glycerin, which is generated in abundance during biodiesel production. For this reason, the development of processes for the management of this residue is of great value, especially from the environmental perspective. One way to use PG is to incorporate this polymer in the synthesis of modified release systems, providing a way of using/recycling an industrial waste that would otherwise have few relevant applications (Medeiros et al., 2010; Eliana et al., 2012).

The aim of this study was to develop and characterize PCL/PG microparticles as nutrient transport systems for NPK, in order to produce an alternative fertilizer for agricultural usage. A new formulation is proposed that employs glycerin, an industrial waste that still has few important applications in industrial processes, to produce polyglycerol.

2. Experimental

2.1. Materials

The following reagents were used in the synthesis and characterization of the microparticles: ammonium molybdate, boric acid, copper sulfate, chloroform, ethanol, methyl blue; methyl red, methyl orange, nitric acid, PCL, PVA, NPK standard solution ($999 \pm 4 \text{ mg/L}$), stannous chloride, and sodium hydroxide (all from Sigma-Aldrich); glycerol, sodium carbonate, sulfuric acid, and phenolphthalein (from Synth); and polyglycerol (70% m/m, from Verti Ecotecnologias UFMG).

All solutions were prepared with analytical grade reagents and deionized water from a Milli-Q (Millipore Corporation) system. All glassware was previously soaked for 24 h in baths containing 10% (v/v) HNO_3 (Synth). All the solutions used were stored at 8 $^\circ\text{C}$ for preservation.

2.2. Instrumentation

The following instruments were used in this study: Aname Q150R S metalizer, Biospectro ABB Model MB 3000 IV infrared spectroscope, Du Pont SDT2960 thermogravimetric analysis (TGA) system, Excelsa II 206 BL centrifuge, Hidrosan 50–320 $^\circ\text{C}$ heating plate, Hot Lab II Nalgon magnetic agitator, incubator with orbital agitation, JEOL 1200 scanning electron microscope (SEM), Quimis Kjeldahl Macro distillation device, Nova Ética 404/D oven with range 50–200 $^\circ\text{C}$, Pike Technologies Crushir press, SpectrAA 50B atomic absorption spectrophotometer, Thermo Scientific Orion Star A221 pH meter, and Varian 220-2000UV UV-Vis spectrophotometer.

2.3. Multivariate optimization of the preparation of NPK-loaded PCL/PG microparticles

The solvent emulsification/evaporation synthesis method was first described by Fessi (1988) (Silva de Melo et al., 2010; Schaffazick et al., 2003; Eliana et al., 2012; Besheer et al.,

2009; Souto et al., 2012) and involves the interfacial deposition of a polymer after the displacement of a semi-polar solvent, miscible in water, from a lipophilic solution.

For this study, the organic phase contained suitable amounts of the PCL and PG polymers, chloroform, and an aliquot of water for PG dissolution. The aqueous phase was composed of PVA, deionized water, and a 1.00 mL aliquot of NPK standard solution. The solubilization of PVA was performed in water at 70 °C, under constant magnetic agitation. After dissolution of the components of both phases, the organic phase was added to the aqueous phase, using a syringe. The resulting suspension was homogenized under magnetic stirring for 4 h and was then kept at atmospheric pressure for 24 h for complete evaporation of the organic solvent (chloroform). A control formulation was prepared without the nutrients.

The proposed particle synthesis procedure involved several variables that directly influenced the system under investigation. Therefore, it was essential to use statistically designed multivariate experiments to determine the effects of the variables and obtain the optimum conditions for preparation of the particles. The synthesis was performed according to the multivariate experimental approaches presented in [Tables S1 and S2 \(Supplementary Information\)](#).

Definition of the levels at which the variables were studied in the screening was based on preliminary tests in the laboratory and literature reports for similar samples, since there have been no previous studies concerning the specific synthesis presented here. A 2^{5-1} fractional factorial design with resolution V was performed ([Table S1](#)), with triplicate of the central point. The independent variables investigated were PCL mass (m_{PCL}), PG mass (m_{PG}), chloroform volume (V_{Chl}), water volume (V_{H_2O}), and PVA concentration (C_{PVA}).

Electronic spreadsheets were employed ([Teofilo and Ferreira, 2006](#)) to generate the codification of the experiments, taking into consideration the combinations between the proposed levels, and also for the statistical treatment of the results. The response parameter was the percentage rate of NPK nutrient association (NA%) with the microparticles. This was of great importance, because it indicated the degree to which the polymeric particles were able to associate with the target substances for future modified release; particles with poor degrees of association tend to have a short useful life, with the concentration available being insufficient for slow and continuous controlled release ([Grillo, 2011; Silva de Melo et al., 2010; Grillo et al., 2014](#)).

The NPK percentages associated with the microparticles were determined by specific methods for each chemical element. Samples of 100 mL of suspensions of microparticles containing NPK were slowly filtered through Nalgon 3552 blue ribbon quantitative paper filters. The NA% value was then determined by the difference between the quantified nutrient concentration in the filtered solution and the total concentration (100%) of the nutrient present in the microparticle suspension (Eq. (1)) ([Grillo, 2011; Silva de Melo et al., 2010](#)).

$$NA\% = \frac{(X_o - X_f)}{X_o} \times 100\% \quad (1)$$

where X_o is the nutrient concentration in the microparticle suspension and X_f is the quantified nutrient concentration in the filtered solution.

For nitrogen quantification, 100 mL of the sample was digested on a hotplate at 320 °C with 50 mL of a solution con-

taining 134 g/L potassium sulfate, 7.3 g/L copper sulfate, and 134 mL/L sulfuric acid. Following the digestion, addition was made of 300 mL of distilled water and 50 mL of a solution containing sodium hydroxide (50% m/v) and sodium thiosulfate (2.5% m/v). This mixture was filled into a Kjeldahl flask using a dosage cup, followed by traditional Kjeldahl distillation. The product of the reaction was placed in an Erlenmeyer flask containing a boric acid solution. This acidic solution was made with 20 mg of methyl red, 10 mg of methyl blue, and 20 g of boric acid, in an acetic medium. Finally, the distilled solution was titrated with 0.01 mol/L sulfuric acid ([A modified kjeldahl flask for determining soil nitrogen, 1914](#)).

Phosphorus was quantified according to the stannous chloride method ([Davies et al., 1973](#)). The filtrate was diluted 100 times and the diluted sample was digested with 1.00 mL of concentrated sulfuric acid and 5 mL of concentrated nitric acid on a plate heated to 250 °C. After that, 20 mL of distilled water and 0.05 mL of phenolphthalein were added to the filtrate. This solution was neutralized with a solution of 6.0 mol/L sodium hydroxide and was then titrated with a solution obtained by mixing concentrated sulfuric acid with concentrated nitric acid. Finally, addition was made of 4.00 mL of ammonium molybdate solution (35 g of ammonium molybdate and 280 mL of sulfuric acid for one liter of solution) and 0.5 mL of stannous chloride medium (2.5 g of stannous chloride in 100 mL of glycerol). The solution obtained was analyzed using a UV-Vis spectrophotometer, at 690 nm, in a 10 mL glass cuvette. The analytical curve was constructed using serial dilutions of a 100 mg/L phosphorus standard solution.

Quantification of potassium was performed using a flame atomic absorption spectrophotometer. The operational conditions were 5 mA lamp current, air/acetylene flame and air auxiliary gas, oxidizing flame stoichiometry, wavelength of 766.55 nm, and slit width of 1.0 nm. A multivariate study ([Chagas et al., 2016](#)) was performed to determine the ideal conditions for sample preparation, with the most efficient digestion achieved with 5 mL of filtrate and 10 mL of concentrated nitric acid, at 60 °C, under magnetic agitation for 90 min. The resulting solutions were made up to 100 mL in volumetric flasks, prior to subsequent analysis of potassium.

The quantification methods were validated according to the protocol (DOQ-CGCRE-008: Revision 03 – Feb/2010) of the Brazilian National Institute of Metrology, Quality, and Technology (INMETRO).

The conditions that generated the best NA% values were selected and the significant variables and levels were studied using response surface methodology.

A central composite design (CCD) was used for optimization of the synthesis process for the polymeric microparticles loaded with NPK. The variables and levels evaluated in this step are provided in [Table S2](#).

Electronic spreadsheets ([Teofilo and Ferreira, 2006](#)) were used to generate the CCD assays and to treat the data. Quantification of N, P, and K in all the synthesized particles was performed by the Kjeldahl method with titration against phosphoric acid, UV-Vis spectrophotometry, and flame atomic absorption spectrophotometry, respectively. The desirability function was subsequently used for simultaneous NPK association optimization according to the NPK NA% values. All assays generated in the multivariate optimization procedure were performed in a random manner.

2.4. Size measurements

Size measurements of the microparticles synthesized under the optimum conditions was performed using 100 mL of suspension completed with a volume of 200 mL of deionized water, with half of the suspension being filtered through a JP 40 white quantitative filter paper. The material retained on the paper filter was stored in a desiccator. After drying completely, a 10 mg portion of the sample was placed on a carbon strip. The samples were metalized by the deposition of gold (100–200 nm) under vacuum, followed by morphological analysis using a scanning electron microscope (SEM). The size distributions were measured and expressed as the average of three determinations.

2.5. Chemical stability measurements

The chemical stability of the optimized formulation was evaluated by measuring the pH of the suspension of PCL/PG microparticles loaded with NPK, as a function of time, since a change in pH can be indicative of particle degradation. The pH measurements were made during a period of 90 days, using a potentiometer calibrated with standard buffer solutions (pH 4.01, 7.00, and 10.01). Measurements were also made of particle size and NA% during the same period, in order to evaluate degradation of the microparticles.

2.6. NPK release experiments

The profile of release of the NPK from the microparticles was performed under *sink* conditions, using a modified methodology described by Asrar et al. (2004) and Ramos Campos et al. (2015). The assays were performed with a system of tubes, where the microparticle formulations were placed in contact with deionized water in order to release the nutrients. A volume of 400 mL of microparticle suspension was prepared, with 10 mL aliquots being transferred to Falcon tubes that were closed and shaken at 150 rpm, at room temperature. The samples were collected at times of 0, 10, 15, 30, 60, 120, 240, 480, 960, and 1440 min. At each time, three tubes were removed from the shaker and centrifuged in order to sediment the microparticles. The supernatant was filtered through quantitative filter paper and the nutrients were analyzed. The concentrations obtained were converted into released nutrient percentages, using a solution of free nutrients as a standard.

Analysis of the mechanism of NPK release from the PCL/PG microparticles employed the theoretical models proposed by Higuchi and Korsmeyer-Peppas, with determination of the kinetic parameters (Grillo, 2011; Silva de Melo et al., 2010; Schaffazick et al., 2003; Ramos Campos et al., 2015; Lobo et al., 2011).

2.7. Characterization using infrared spectroscopy

The KBr tablet method was used for analysis of the samples by infrared spectroscopy. Approximately 100 mg portions of the PVA and PCL polymers, microparticles without associated NPK (controls), and microparticles loaded with NPK were dried in an oven for 15 min at 85 °C. Approximately 2.0 mg of the polymers and microparticles were macerated separately using a quartz mortar and pestle, followed by compressing in

an 8-ton press. Fourier transform infrared spectroscopy (FTIR) analyses were then performed in the range from 4000 to 400 cm^{-1} , at 4 cm^{-1} resolution, with 32 scans of each sample.

2.8. Characterization by thermogravimetric analysis

Thermogravimetric analysis (TGA) enabled evaluation of the release of water, using a heating rate of 20 °C/min from 0 to 600 °C. Masses of approximately 10 mg were uniformly distributed in aluminum crucibles to ensure fine and homogeneous layers. The analyses of PCL and PVA were performed in an atmosphere of synthetic air at a flow rate of 100 mL/min, while an atmosphere of nitrogen at a flow rate of 100 mL/min was used for PG and the microparticles.

3. Results and discussion

3.1. Multivariate optimization of the synthesis of microparticles loaded with NPK

Preparation of the PCL/PG microparticles was performed according to Fessi's method, involving the mixing of an organic phase into an aqueous phase, with some modifications (Besheer et al., 2009; Souto et al., 2012). This method is advantageous, compared to other synthesis methods with pre-formed polymers, since it is easy and fast, with no need for high energy homogenization (Schaffazick et al., 2003).

For the variables m_{PCL} and m_{PG} , the principle adopted was that the greater the polymer mass, the greater the NA% of NPK, since it is known that the higher the polymer concentration, the higher is the adsorption/association of the active agent (Silva de Melo et al., 2010; Lobo et al., 2011; Grillo et al., 2012). In addition, combinations of masses of PCL and PG were defined that were able to provide formation of the microparticles. In preliminary tests, it was observed that for masses below 100 mg of PCL and 300 mg of PG, precipitation of the particles was inefficient (with a lack of opacity of the suspension indicating that negligible quantities of particles had been formed), even after 6 h of mechanical agitation. This effect was even more pronounced when the system was kept at temperatures higher than room temperature (60–80 °C).

Due to the insolubility of PG in chloroform, a water-chloroform mixture was added during preparation of the organic phase, resulting in increased efficiency of the precipitation process after 4 h. Since the literature does not describe the presence of water in the organic phase, only small water volumes were used in the mixtures (Silva de Melo et al., 2010; Souto et al., 2012; Grillo et al., 2012).

For C_{PVA} , different concentrations were tested in order to define the levels at which this variable should be investigated. It was found that the precipitation process was hindered when the PVA concentration was below 0.3% m/v, resulting in an absence of particles. Therefore, the PVA concentration was set at 0.3% m/v for the lowest level (–1) of the factorial design in the screening phase.

A 2^{5-1} fractional factorial design with resolution V was performed to identify the variables that presented significant effects on the system, and to determine the levels at which they should be studied in more detail using response surface methodology. All the assays were performed using the

methods described in Section 2.3, and the results obtained are presented in Table 1.

The NA% results for N (Table 1) showed that all five studied variables had significant effects on the system (Table 2), with m_{PCL} having the greatest influence, followed by m_{PG} , $V_{\text{H}_2\text{O}}$, V_{Chl} , and C_{PVA} . For the NA% of P (Table 2), only m_{PG} did not have a significant effect on the system, while the variable with the greatest influence was V_{Chl} , followed by $V_{\text{H}_2\text{O}}$, m_{PCL} , and C_{PVA} . For the NA% of K (Table 2), all the variables had significant effects on the system, with the most

influential being C_{PVA} , followed by m_{PG} , $V_{\text{H}_2\text{O}}$, m_{PCL} , and V_{Chl} . The errors associated with each effect were evaluated using the t test ($\alpha = 0.05$).

Analysis of the influence of the PCL mass showed that this variable had a significant effect on the NA% of NPK, with the best results obtained at 100 mg. Due to its high molar mass, PCL precipitates more rapidly, compared to the polymers with low molar mass, when the internal phase is added to the external phase, leading to increased incorporation of the active agents. Given the requirement for smaller particles, a suitable

Table 1 Results (NA% values for nitrogen, phosphorus, and potassium) of the 2^{5-1} fractional factorial design with resolution V, including three replicates at the central point (assays 17–19), for optimization of the experimental conditions for synthesis of the microparticles loaded with NPK. The values in parentheses represent the decoded levels. m_{PCL} (g) = poly(ϵ -caprolactone) mass; m_{PG} (g) = polyglycerol mass; V_{Chl} (mL) = chloroform volume; $V_{\text{H}_2\text{O}}$ (mL) = water volume; C_{PVA} (% m/v) = polyvinyl alcohol solution concentration.

Assay	m_{PCL}	m_{PG}	V_{Chl}	$V_{\text{H}_2\text{O}}$	C_{PVA}	NA% N	NA% P	NA% K
1	-1 (0.1)	-1 (0.3)	-1 (9.0)	-1 (3.0)	+1 (0.7)	79.28	70.87	56.66
2	+1 (0.5)	-1 (0.3)	-1 (9.0)	-1 (3.0)	-1 (0.3)	47.06	69.34	53.73
3	-1 (0.1)	+1 (0.9)	-1 (9.0)	-1 (3.0)	-1 (0.3)	79.65	63.91	48.26
4	+1 (0.5)	+1 (0.9)	-1 (9.0)	-1 (3.0)	+1 (0.7)	88.07	69.13	55.46
5	-1 (0.1)	-1 (0.3)	+1 (15.0)	-1 (3.0)	-1 (0.3)	45.07	87.82	53.00
6	+1 (0.5)	-1 (0.3)	+1 (15.0)	-1 (3.0)	+1 (0.7)	36.79	77.61	85.73
7	-1 (0.1)	+1 (0.9)	+1 (15.0)	-1 (3.0)	+1 (0.7)	36.03	79.78	48.80
8	+1 (0.5)	+1 (0.9)	+1 (15.0)	-1 (3.0)	-1 (0.3)	72.36	86.08	-10.33
9	-1 (0.1)	-1 (0.3)	-1 (9.0)	+1 (9.0)	-1 (0.3)	56.09	76.74	53.73
10	+1 (0.5)	-1 (0.3)	-1 (9.0)	+1 (9.0)	+1 (0.7)	20.05	82.17	46.06
11	-1 (0.1)	+1 (0.9)	-1 (9.0)	+1 (9.0)	+1 (0.7)	70.50	74.78	53.00
12	+1 (0.5)	+1 (0.9)	-1 (9.0)	+1 (9.0)	-1 (0.3)	34.84	74.34	60.80
13	-1 (0.1)	-1 (0.3)	+1 (15.0)	+1 (9.0)	+1 (0.7)	90.68	72.60	59.26
14	+1 (0.5)	-1 (0.3)	+1 (15.0)	+1 (9.0)	-1 (0.3)	1.78	70.43	52.73
15	-1 (0.1)	+1 (0.9)	+1 (15.0)	+1 (9.0)	-1 (0.3)	88.45	68.26	57.13
16	+1 (0.5)	+1 (0.9)	+1 (15.0)	+1 (9.0)	+1 (0.7)	47.06	73.91	61.00
17	0 (0.3)	0 (0.6)	0 (12.0)	0 (6.0)	0 (0.5)	82.44	71.95	49.26
18	0 (0.3)	0 (0.6)	0 (12.0)	0 (6.0)	0 (0.5)	82.29	70.87	49.80
19	0 (0.3)	0 (0.6)	0 (12.0)	0 (6.0)	0 (0.5)	83.03	73.04	50.73

Table 2 Effect values for the 2^{5-1} fractional factorial design with resolution V, for the association rates (NA%) of N, P, and K in the investigation of the synthesis of microparticles loaded with the nutrients. The values in bold are those found to be significant according to the value of p ($\alpha = 0.05$). 1 = m_{PCL} , 2 = m_{PG} , 3 = V_{Chl} , 4 = $V_{\text{H}_2\text{O}}$, 5 = C_{PVA} .

Variable	NA% N		NA% P		NA% K	
	Effect	p	Effect	p	Effect	p
Average	61.236	7.63×10^{-9}	74.116	3.05×10^{-10}	51.835	1.07×10^{-5}
1	-24.719	1.29×10^{-6}	1.031	8.53×10^{-2}	-3.083	1.41×10^{-2}
2	17.520	3.64×10^{-6}	-2.173	8.69×10^{-3}	-10.850	1.16×10^{-3}
3	-7.164	5.31×10^{-5}	4.401	6.31×10^{-4}	-2.550	2.05×10^{-2}
4	-9.355	2.38×10^{-5}	-1.413	3.56×10^{-2}	6.550	3.19×10^{-3}
5	5.395	1.24×10^{-4}	0.491	3.39×10^{-1}	12.116	9.37×10^{-4}
1 × 2	16.642	4.25×10^{-6}	3.151	2.25×10^{-3}	-6.983	2.81×10^{-3}
1 × 3	-0.842	2.68×10^{-2}	-1.138	6.60×10^{-2}	-4.183	7.78×10^{-3}
1 × 4	-25.780	1.14×10^{-6}	1.086	7.47×10^{-2}	2.450	2.22×10^{-2}
1 × 5	3.5842	4.20×10^{-4}	0.166	7.32×10^{-1}	10.716	1.19×10^{-3}
2 × 3	-0.128	5.79×10^{-1}	2.066	1.03×10^{-2}	-12.683	8.55×10^{-4}
2 × 4	8.000	7.98×10^{-2}	8.000	3.42×10^{-1}	8.000	5.45×10^{-4}
2 × 5	-13.803	7.44×10^{-6}	0.761	1.68×10^{-1}	3.483	1.11×10^{-2}
3 × 4	18.787	2.95×10^{-6}	-10.108	2.40×10^{-5}	6.683	3.07×10^{-3}
3 × 5	-4.670	1.91×10^{-4}	-2.663	4.19×10^{-3}	13.450	7.60×10^{-4}
4 × 5	6.3866	7.49×10^{-5}	2.931	2.95×10^{-3}	-13.383	7.68×10^{-4}

polymer concentration is necessary to enable rapid solvent diffusion, reducing the average size of the drops of the resulting dispersion and leading to smaller particles with greater NA% values (Eliana et al., 2012). It could therefore be inferred that the increase of NA% observed during the screening was directly related to the PCL concentration during the process of formation of the microparticles.

As a rule, the solvent emulsification/evaporation method is used to prepare nano/microspheres containing lipophilic active principles. The hydrophilic active principles considered here (NPK) have lower affinity for the PCL, generating nano/microspheres with a low rate of encapsulation, since these types of active compounds tend to disperse from the internal phase to the external one during the process of spontaneous emulsification (Eliana et al., 2012; Besheer et al., 2009). Hence, it is necessary to diminish the diffusion using other strategies. Here, a hydrocarbon chain (PG) was used, as justified by the fact that the PG mass was significant for the association rates of N and K, since it decreased the tendency of the nutrients to disperse to the external phase, consequently increasing the NA% values.

Considering the effects of the chloroform and water volumes, it was observed that these variables were significant for all the NA% values (15.00 mL (+1) for V_{Chl} and 3.00 mL (-1) for $V_{\text{H}_2\text{O}}$). This was due to the polar/non-polar (water/chloroform) co-solvents system used, with an increase of the organic solvent volume creating microspheres with smaller dimensions, consequently hindering the incorporation of the active agents (Eliana et al., 2012; Lobo et al., 2011; Grillo et al., 2012). Therefore, in this study, the use of greater volumes of organic solvent led to reduced NA% values.

Finally, it was observed that an increase of C_{PVA} generally favored the NA% of NPK, since it altered the interfacial energy so that it did not remain constant and, consequently, there was the formation of ideally sized particles for incorporation of the three active nutrients (Besheer et al., 2009). In other words, the highest C_{PVA} values studied led to a reduction of the interfacial energy for formation of the particles.

After the initial screening, all the influences investigated were subjected to evaluation using response surface methodology. However, for the systems that used chloroform and water as co-solvents, higher water volume values hindered interaction of the nutrients (NPK) with PCL, leading to low NA% values (Eliana et al., 2012; Besheer et al., 2009). Therefore, due to the significance of the $V_{\text{H}_2\text{O}}$ variable, it was set at the lowest level studied (3.00 mL, negative effect; Table 2) for the response surface (Hanafi et al., 2000; Grillo, 2011; Silva de Melo et al., 2010; Ramos Campos et al., 2015; Fialho et al., 2008), since the preliminary tests showed that values below 3 mL were unfavorable for the precipitation process.

With the purpose of obtaining the greatest NPK encapsulation rate of the microparticles after the synthesis, a central composite design (CCD) was performed as part of the response surface evaluation stage. A CCD is a set of technical and mathematical statistics used for the development, improvement, and optimization of chemical, physical, and biological processes, among others (Teofilo and Ferreira, 2006; Silva, 2007; Ferreira et al., 1999). This technique evaluates the significant variables in more detail, because it presents a greater number of levels and allows the evaluation of modeling using higher orders, such as in the case of quadratic models (Teofilo and Ferreira, 2006).

For the microparticles synthesis presented here, a model was established correlating the association rates for N, P, and K with the variables PCL and PG masses, chloroform volume, and PVA concentration in the solution.

All the synthesized particles were analyzed using the methods described in Section 2.3. The results (Table 3) confirmed the significance of the variables m_{PG} , V_{Chl} , and C_{PVA} for the NA% of N, with a greater encapsulation rate (assay 24) observed at the m_{PG} central point of 450 mg, the V_{Chl} central point of 15.5 mL, and a C_{PVA} level of 1.05% (m/v). It was also observed that the system presented nonlinear behavior, since the quadratic interactions of all the variables were significant Table 3.

For the NA% of P (Table 3), the results of the CCD demonstrated that none of the variables significantly affected the system. The highest association rate of the microparticles (assay 6) was observed at the second lowest level studied for m_{PCL} (100 mg, negative effect), at the second highest level for m_{PG} (600 mg, positive effect), at the second lowest level for V_{Chl} (13.00 mL, negative effect), and at the second highest level for C_{PVA} (0.90% m/v, positive effect).

For the NA% of K (Table 3), the CCD results confirmed the significance of the variables m_{PG} and V_{Chl} , with the highest microparticle encapsulation rate observed at the highest level studied for m_{PG} (750 mg, positive effect) and the central point for V_{Chl} (15.5 mL). It was also noted that the system exhibited nonlinear behavior, since the quadratic interactions of the variables 1 (m_{PCL}) and 2 (m_{PG}) were significant.

The errors associated with each coefficient were evaluated using the *t* test ($\alpha = 0.05$). Table 4 presents the effect of each variable on the nutrient association rate.

Analysis of variance was applied to the models in order to determine the statistical significance of the coefficients (Teofilo and Ferreira, 2006; Silva, 2007; Rodrigues and Sanson, 2014) related to the parameters m_{PCL} , m_{PG} , V_{Chl} , and C_{PVA} . ANOVA calculations were used to examine the overall significance of each term in the model, compared to the residual error (Teofilo and Ferreira, 2006; Rodrigues and Sanson, 2014). Terms with *p* below 0.05 were considered significant ($\alpha = 0.05$).

For all the nutrients, the ANOVA coefficients were statistically valid (at the 95% confidence level), although most of them showed lack of fit at the same confidence level. Although the models had not been fitted ($p = 0.0066$, 0.0012, and 0.0139, for N, P, and K, respectively), it was possible to find regions indicative of the optimum experimental conditions.

Fig. 1 compares the results of the screening experiments, performed according to the 2^{5-1} fractional factorial experimental design, with those for the CCD, under the operational conditions that provided highest NA% for NPK. The comparison showed that there were improvements in most of the NA% values when the response surface methodology was used. Although the NA% of K was lower when this procedure was used, relative to the response obtained in the screening, the values for the other elements increased, reflecting improved optimization. Furthermore, the NA% value achieved for K was sufficient for subsequent satisfactory release.

In 2014, Rodrigues and Sanson (2014) optimized an analytical procedure for the simultaneous identification and quantification, by high performance liquid chromatography, of 21 contaminants in water samples retrieved from the Rio Doce (Minas Gerais State, Brazil). In the optimization process, a

Table 3 NA% results for nitrogen, phosphorus, and potassium from the experiments of the central composite design with three replicates at the central point (assays 25–27) used for synthesis of the microparticles loaded with NPK. The values in parentheses represent the decoded levels. m_{PCL} (g) = poly(ϵ -caprolactone) mass; m_{PG} (g) = polyglycerol mass; V_{Chl} (mL) = chloroform volume; $V_{\text{H}_2\text{O}}$ (mL) = water volume; C_{PVA} (% m/v) = polyvinyl alcohol solution concentration.

Assay	m_{PCL}	m_{PG}	V_{Chl}	C_{PVA}	NA% N	NA% P	NA% K
1	-1 (0.10)	-1 (0.30)	-1 (13.0)	-1 (0.60)	88.74	96.80	35.00
2	-1 (0.10)	-1 (0.30)	-1 (13.0)	+1 (0.90)	71.18	97.80	26.80
3	-1 (0.10)	-1 (0.30)	+1 (18.0)	-1 (0.60)	83.80	77.80	48.60
4	-1 (0.10)	-1 (0.30)	+1 (18.0)	+1 (0.90)	65.69	78.00	26.40
5	-1 (0.10)	+1 (0.60)	-1 (13.0)	-1 (0.60)	93.68	77.60	27.80
6	-1 (0.10)	+1 (0.60)	-1 (13.0)	+1 (0.90)	64.59	99.80	35.60
7	-1 (0.10)	+1 (0.60)	+1 (18.0)	-1 (0.60)	87.64	99.20	43.00
8	-1 (0.10)	+1 (0.60)	+1 (18.0)	+1 (0.90)	59.10	99.40	39.80
9	+1 (0.30)	-1 (0.30)	-1 (13.0)	-1 (0.60)	93.68	80.20	50.20
10	+1 (0.30)	-1 (0.30)	-1 (13.0)	+1 (0.90)	70.08	80.60	29.40
11	+1 (0.30)	-1 (0.30)	+1 (18.0)	-1 (0.60)	76.66	78.40	26.80
12	+1 (0.30)	-1 (0.30)	+1 (18.0)	+1 (0.90)	77.21	97.60	38.60
13	+1 (0.30)	+1 (0.60)	-1 (13.0)	-1 (0.60)	47.58	91.60	45.20
14	+1 (0.30)	+1 (0.60)	-1 (13.0)	+1 (0.90)	59.10	99.20	47.80
15	+1 (0.30)	+1 (0.60)	+1 (18.0)	-1 (0.60)	78.31	95.60	33.00
16	+1 (0.30)	+1 (0.60)	+1 (18.0)	+1 (0.90)	61.85	81.00	34.60
17	-2 (0.05)	0 (0.45)	0 (15.5)	0 (0.75)	36.60	82.80	42.60
18	+2 (0.25)	0 (0.45)	0 (15.5)	0 (0.75)	71.72	94.20	24.80
19	0 (0.15)	-2 (0.15)	0 (15.5)	0 (0.75)	77.21	80.80	33.00
20	0 (0.15)	+2 (0.75)	0 (15.5)	0 (0.75)	75.57	81.80	52.00
21	0 (0.15)	0 (0.45)	-2 (10.5)	0 (0.75)	78.31	96.20	36.20
22	0 (0.15)	0 (0.45)	+2 (20.5)	0 (0.75)	60.20	75.80	21.20
23	0 (0.15)	0 (0.45)	0 (15.5)	-2 (0.45)	92.58	73.00	21.00
24	0 (0.15)	0 (0.45)	0 (15.5)	+2 (1.05)	94.23	73.60	35.60
25	0 (0.15)	0 (0.45)	0 (15.5)	0 (0.75)	81.60	85.20	30.80
26	0 (0.15)	0 (0.45)	0 (15.5)	0 (0.75)	82.80	85.40	30.20
27	0 (0.15)	0 (0.45)	0 (15.5)	0 (0.75)	83.00	86.00	32.40

Table 4 Coefficient and p values ($\alpha = 0.05$) of the spherical central composite design for the NA% of nitrogen, phosphorus, and potassium in the study of the synthesis of the PCL/PG microparticles. The values in bold are those that showed significance, according to the value of p . 1 = PCL mass; 2 = PG mass; 3 = chloroform volume; 4 = PVA solution concentration.

Variable	NA% N		NA% P		NA% K	
	Coefficient	p	Coefficient	p	Coefficient	p
Average	82.800	0.0001	85.533	0.0000	31.133	0.0004
1	0.845	0.0653	0.025	0.9913	-0.541	0.1448
2	-3.269	0.0048	2.425	0.3040	2.625	0.0077
3	-1.441	0.0240	-2.391	0.3104	-1.541	0.0219
4	-4.916	0.0021	1.558	0.5033	-0.058	0.8251
5	-7.096	0.0012	1.931	0.4357	1.223	0.0382
1 × 1	-1.539	0.0237	0.131	0.9572	3.422	0.0051
2 × 2	-3.323	0.0052	1.306	0.5955	-0.027	0.9225
3 × 3	2.714	0.0078	-1.868	0.4504	-0.127	0.6572
4 × 4	-4.149	0.0045	0.312	0.9119	0.387	0.3061
1 × 2	2.846	0.0094	1.162	0.6817	-4.512	0.0039
1 × 3	4.081	0.0046	-0.687	0.8079	1.312	0.0439
1 × 4	2.641	0.0109	1.912	0.5024	-0.312	0.3863
2 × 3	-0.240	0.4785	-0.337	0.9049	3.012	0.0088
2 × 4	-0.239	0.4805	-1.637	0.5648	0.412	0.2839
3 × 4	82.800	0.0001	85.533	0.0000	31.133	0.0004

2^{4-1} fractional design was used, followed by a Doehlert design. No significant regressions were obtained in the response surfaces constructed for almost all the contaminants, although significant improvements were observed in terms of increased

chromatographic peak areas of the analytes. In the present case, the optimization procedure could be considered highly successful, since it was possible to achieve enhanced nutrient association rates.

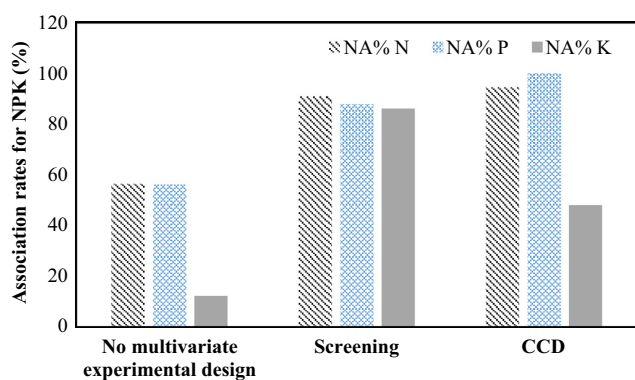


Fig. 1 Comparison of the association rates (NA%) for nitrogen, phosphorus, and potassium, without application of any experimental design, under the best conditions of the screening step, and under the optimized conditions obtained using the central composite design.

Overall, in the approach used for construction of the response surface, the variables behaved in a similar manner to the results of the screening. However, the effect of m_{PG} deserves special attention. According to the results obtained

in the screening, the use of higher PG mass values improved the NA% of N and K, with this effect being directly related to decreased diffusion of the nutrients from the organic phase to the aqueous phase (Besheer et al., 2009; Teofilo and Ferreira, 2006). A similar effect was evidenced in the response surface analysis, although evaluation of the variables at a greater number of levels indicated that PG mass values lower than those tested could provide the system with conditions for the formation of microparticles.

Evaluation of the effects of the variables in the CCD for the NA% of NPK revealed that the polyglycerol mass had a greater influence on the NA% of P and K, compared to the other variables (Table 4). This demonstrated that the presence of polyglycerol was crucial for increasing the encapsulation of the nutrients in these microparticles. In commercial terms, it would therefore be strategically important to consider the use of polyglycerol in the production of microparticles loaded with NPK. As far as is known, there are currently no systems using this polymer available for the release of NPK in agricultural applications.

From the NPK NA% results (Table 4), the desirability function (Fig. 2) was used to simultaneously obtain the responses for the elements studied and identify the optimal synthesis conditions.

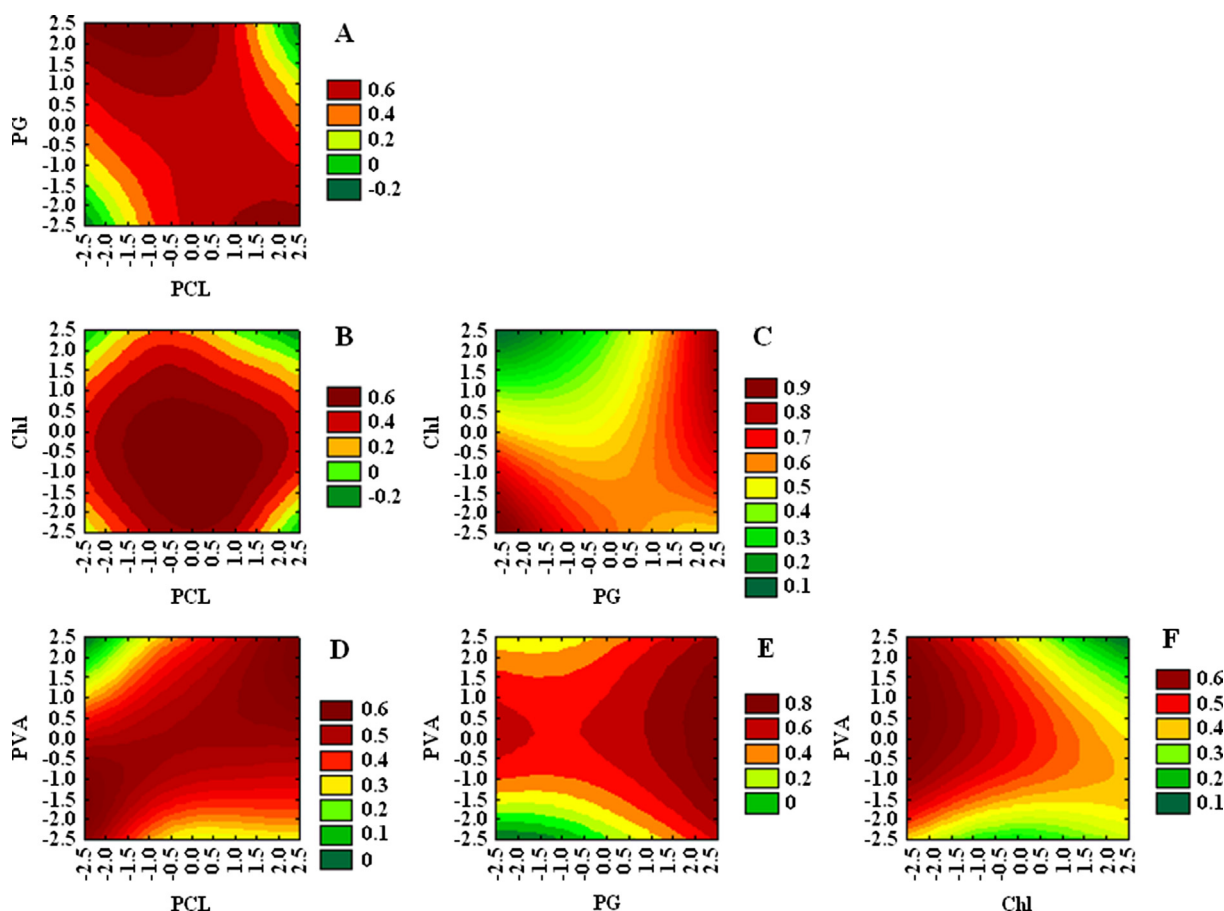


Fig. 2 Desirability graphs for obtaining the simultaneous optimum association rates of the NPK nutrients in the poly(ϵ -caprolactone)/polyglycerol microparticles. NA% for the interactions: (A) m_{PG} with m_{PCL} ; (B) V_{Chl} with m_{PCL} ; (C) V_{Chl} with m_{PG} ; (D) C_{PVA} with m_{PG} ; (E) C_{PVA} with m_{PG} ; (F) C_{PVA} with V_{Chl} . m_{PCL} (g) = poly(ϵ -caprolactone) mass; m_{PG} (g) = polyglycerol mass; V_{Chl} (mL) = chloroform volume; C_{PVA} (% m/v) = polyvinyl alcohol solution concentration.

By simultaneous analysis of the results for the NPK nutrient association rates (Fig. 2, where the intense red regions indicate the highest nutrient encapsulation rates), it was possible to obtain the optimum condition for the synthesis of the PCL/PG microparticles loaded with NPK, which was as follows: 100.00 mg of PCL, 825.00 mg of PG, 9.25 mL of chloroform, and 0.9% w/v of PVA. This condition resulted in encapsulation rates of 94.23% (N), 99.80% (P), and 65.00% (K), corresponding to increases of NA% of 59.68% for N, 50.00% for P, and 18.64% for K. These values could be considered satisfactory, especially since there have been no previous reports in the literature concerning the evaluation of NA% for nutrient substances in formulations produced based on the use of glycerol. On average, the values obtained were generally similar to those reported in the literature for other substances (Table S3).

Use of the experimental multivariate methodologies and the desirability function enabled the simultaneous achievement of satisfactory encapsulation rates for the three nutrient elements, especially considering that in the preliminary tests, the NA% values obtained were 60.00% for N, 66.66% for P, and 12.11% for K. The higher values for the encapsulation of N and P in the PCL/PG microparticles could be attributed to the fact that these nutrients present high solubility in water, which enhances the interaction with PG. A possible reason for the lower encapsulation rate of K, relative to the other nutrients, could have been related to competitive interactions among the nutrients.

3.2. Microparticle size measurement and chemical and physical stability

Fig. 3 shows the morphology of the surfaces of PCL/PG microparticles loaded with NPK, obtained by SEM analysis.

The SEM images (Fig. 3) showed that the methodology adopted for the synthesis was effective, with the formation of slightly rough spherical microparticles with diameters between 5 and 60 μm . The particles could be classified as microspheres, because there was no presence of oil in the organic phase employed for their formation (Eliana et al., 2012; Souto et al., 2012).

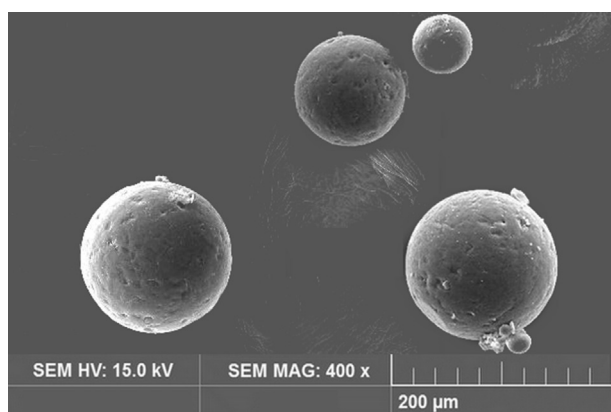


Fig. 3 Scanning electron microscope images of the poly(ϵ -caprolactone)/polyglycerol microparticles containing the nutrients nitrogen, phosphorus, and potassium, at 400 \times magnification. SEM HV = Scanning Electron Microscope High Vacuum; MAG = Magnification.

Evaluation of the chemical stability of the PCL present in the microparticles was performed by monitoring the pH of the suspensions, as a function of time (Fig. S1). This analysis provides an important means of determining the chemical stability of this polymer, since a change in the pH can indicate its degradation in the solution (Grillo, 2011; Silva de Melo et al., 2010). The results (Fig. S1) showed that the microparticle formulation containing NPK had an initial pH of 2.18 and that there was no significant pH change during 60 days (a deviation of 0.02 could be attributed to the variability of the instrumental response). It has been found that changes in the pH of carrier particles can be explained by the presence of oil in the organic phase, with polymer aggregation leading to the concomitant release of the oil into the surrounding medium (Eliana et al., 2012). However, this did not occur in the present study, because the microparticles produced did not contain oil. Therefore, it could be concluded from the pH measurements that the particles developed in this study presented good stability.

The morphological features of the microparticles and the nutrient encapsulation rates were also evaluated (Figs. S2 and S3), concomitant to the pH study. The initial average size of the microparticles containing NPK was $8.00 \pm 0.15 \mu\text{m}$, while the initial NA% values were $96.27 \pm 0.40\%$ for N, $96.58 \pm 0.50\%$ for P, and $59.62 \pm 0.53\%$ for K. During the course of 60 days, both the microparticle size and the NA% values for the three nutrients decreased, for which a possible explanation was the release of nutrients to the external medium.

3.3. Release experiments

The release experiments enabled observation of the effects of the association of NPK with the PCL/PG microparticles on the release profiles of these nutrients. In these assays, the free nutrients (control) and the microparticles loaded with NPK were placed in direct contact with deionized water, enabling determination of the effect of the association on the release kinetics of the nutrients. Fig. 4 shows the release percentage curves for free NPK and for the nutrients associated with the microparticles, as a function of time.

It can be seen from Fig. 4 that compared to the free forms of the nutrients, the associated K and P presented slower and more continuous release during the period up to approximately 800 min, while faster release was observed for N, with a maximum reached after around 500 min. The results con-

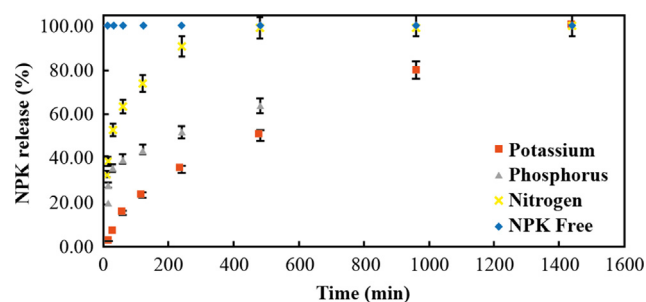


Fig. 4 Cumulative release (%) of nitrogen, phosphorus, and potassium, free and loaded into poly(ϵ -caprolactone)/polyglycerol microparticles ($n = 3$).

firmed that the association of NPK with the microparticles modified the release profiles of these nutrients, relative to the free forms.

In order to obtain information about the possible mechanisms involved in NPK release from the PCL/PG microspheres, linearization of the release curves was performed using the Korsmeyer-Peppas and Higuchi mathematical models (Silva de Melo et al., 2010; Schaffazick et al., 2003). The possible mechanisms include desorption from the surface, diffusion through the pores of the matrix or polymeric wall, and disintegration or erosion (Eliana et al., 2012; da Costa, 2002). The model that provided the best fit (correlation coefficient > 0.9) to the profile of N release from the PCL/PG microparticles developed here was the Korsmeyer-Peppas model, while the Higuchi model provided the best fits to the P and K release profiles.

The Higuchi model is a semi-empirical model that describes the release of a substance according to a diffusion mechanism based on Fick's Law (f_t) (Silva de Melo et al., 2010; Schaffazick et al., 2003; da Costa, 2002), and can be used to evaluate the modified release from polymeric materials (Silva de Melo et al., 2010; Grillo et al., 2014). According to this model (Eq. (2)), the results showed that the nutrients P and K were released by diffusion based on Fick's Law.

For N, the slope n (linear coefficient, B) obtained by fitting using the Korsmeyer-Peppas model was determined by the natural logarithm of the release rate as a function of the natural logarithm of the release time. Fitting of the data using the Korsmeyer-Peppas model resulted in a release exponent value of $n = 0.49$, indicating that N was released by diffusion based on Fick's law.

The results showed that the mechanism controlling the release of NPK from the PCL/PG particles was diffusion according to Fick's Law. This is a process whereby the material is transported from one place to another in the interior of the system itself, with random molecular movements that occur within short distances. Therefore, the release of NPK from the PCL/PG particles occurred in the following manner: water diffused into the polymeric matrix of the particles, the nutrients dissolved, and they were then transported out of the matrix (Souza et al., 2007).

3.4. Characterization by FTIR and TGA

The FTIR analysis provided important structural information, including the chemical composition and the conformational and configurational features. Fig. 5 presents the IR spectra for PG, PVA, PCL, and the microparticles. The PCL spectrum showed main absorption bands at 1150–1200 cm^{-1} (O—C—O symmetric vibration), 1240 cm^{-1} (C—O—C asymmetric vibration), and 1700–1760 cm^{-1} (carbonyl vibration). The PVA spectrum presented bands at 3440 cm^{-1} (stretching of the OH group), 2900 cm^{-1} (asymmetric vibration of the OH group), 1375 cm^{-1} (coupling between the OH groups), and 1420 cm^{-1} (CH vibration). The polyglycerol presented bands characteristic of the glycerol groups, at 3386 cm^{-1} (OH stretching), 1215 cm^{-1} (secondary alcohol C—O bond symmetric stretching), and 1045 cm^{-1} (primary alcohol C—O bond stretching).

The microparticles developed in this study presented bands characteristic of PCL and PVA, indicating that there was no

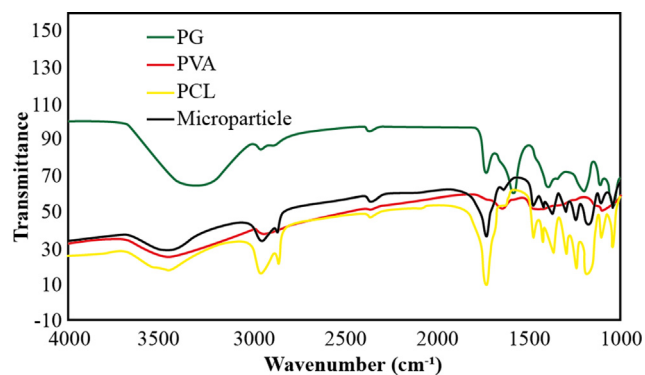


Fig. 5 Infrared spectra of polyglycerol (PG), polyvinyl alcohol (PVA), poly(ϵ -caprolactone) (PCL), and the PCL/PG microparticles.

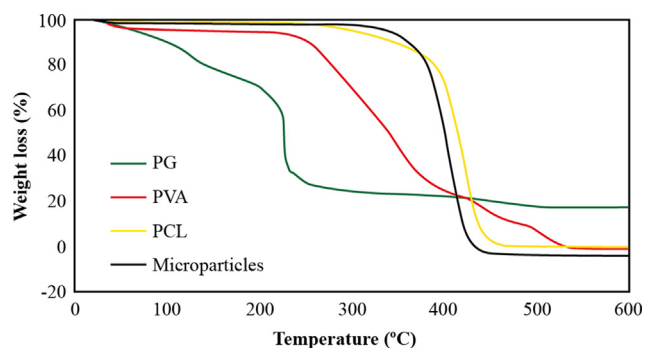


Fig. 6 Thermogravimetric analysis plots of the masses of polyglycerol (PG), polyvinyl alcohol (PVA), poly(ϵ -caprolactone) (PCL), and the NPK-loaded PCL/PG microparticles.

chemical interaction between these polymers and the polyglycerol; in other words, the NPK carrier microparticles were composed only of PCL. However, the polyglycerol was very important in the synthesis of the particles, as observed in the multivariate optimization. The presence of this polymer hindered diffusion of the NPK nutrients towards the aqueous phase (polyvinyl alcohol) during the synthesis procedure, as previously discussed, and in doing so, significantly increased the NA%.

Fig. 6 presents the curves obtained in the thermogravimetric analyses of PCL, PG, PVA, and the microparticles synthesized in this study.

During heating up to 100 °C, there were continuous initial mass losses of 0.28% for PCL, 9.91% for PG, 4.78% for PVA, and 0.92% for the microparticles, which could be attributed to the loss of absorbed water. The main thermal event for polyglycerol, with a maximum mass loss rate at approximately 220 °C, could be attributed to decomposition of the compound. At 600 °C, almost 80% of the total polyglycerol sample mass had been lost.

PCL showed a maximum rate of mass loss at around 405 °C, with the degradation starting at approximately 250 °C. This process resulted in complete degradation and loss of the poly(ϵ -caprolactone).

The thermogravimetric curve for the NPK-loaded PCL/PG microparticles presented a mass loss profile similar to that

obtained for PCL. This similarity in thermal behaviors indicated that the carrier microparticles were composed only of PCL, in agreement with the infrared spectra (Fig. 5) and the statistical results for optimization of the synthesis of the NPK-loaded microparticles.

Emphasis should be given to the importance of polyglycerol in the microparticle synthesis, since it reduced the tendency of the nutrients to disperse to the external phase and consequently increased the NA% values for the nutrients. The use of polyglycerol was crucial for achieving the high encapsulation values and the modified nutrient release profiles, which were the main goals of this work.

4. Conclusions

Optimization of an emulsification/evaporation technique was achieved using chemometric approaches (fractional and central composite designs, and desirability function) to study the influence of the different variables in the system and define the conditions that led to the greatest response in terms of the simultaneous NA% values for nitrogen, phosphorus, and potassium present in the PCL/PG polymeric microparticles. The multivariate experimental designs and the desirability function enabled identification of a suitable experimental condition that led to high nutrient associations in the microparticles. The NA% values were sufficiently high to ensure the controlled and continuous release of NPK from the microparticles. In addition, the PCL/PG microparticles containing NPK presented high chemical stability (little pH variation), as well as small changes in particle size and nutrient association rates during a 60-day period. Analysis of the release profiles using the Higuchi and Korsmeyer-Peppas models showed that NPK was released from the PCL/PG microparticles by diffusion according to Fick's Law. This study provides support for further investigations of the use of the new formulation for encapsulating NPK in microparticles, and also indicates possible research directions involving the administration of this formulation to the soil. In addition, this study has considerable environmental relevance, since it demonstrates a possible application for the glycerin wastes that are produced in very large quantities worldwide.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.arabjc.2018.03.007>.

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