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Preparation and Characterization of Potassium Nitrate Controlled-Release Fertilizers Based on Chitosan and Xanthan Layered Tablets

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ABSTRACT: Solid polymeric matrices based on xanthan and chitosan and using KNO_3 as a model agrochemical were prepared by direct compression, with a view to evaluating their potential as controlled-release fertilizers (CRFs). The swelling behavior, surface characteristics, and durability in soil of the tablets were studied. The release data were treated with a power law model in order to understand the delivery kinetics of KNO_3. This proved to be non-Fickian diffusion, with release exponents ranging from 0.80 to 0.88, highlighting the importance of polymer relaxation on drug release. The presence of drug-free surface layers was an important factor in modulating the release. When comparing experiments without and with stirring, the release time ratios between them were as high as 40, predicting a significantly greater release time in soils. In durability experiments in soil, the polymeric matrices lasted longer than 6 weeks. These results show that layered xanthan and xanthan–chitosan matrices perform as a promising system for developing CRFs. © 2013 Wiley Periodicals, Inc. J. Appl. Polym. Sci. 130: 2422–2428, 2013

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INTRODUCTION

Fertilizers are used in agriculture to release the nutrients required for plant growth. However, a significant amount of the applied fertilizer is lost to the environment, mostly through leaching, volatilization, breakdown by microorganisms, and chemical processes such as hydrolysis. These processes have various adverse effects on the environment.[1–3] Nitrate leaching can cause serious health problems: nitrates and nitrites are implicated in many physiological disorders such as methemoglobinemia in babies and diverse cancers. With the objective of limiting these undesirable effects, controlled release technology has been introduced in agriculture applications.[4]

With slow-release fertilizers (SRFs), the nutrient is released at a slower rate than with common fertilizers. Therefore, it requires less frequent applications and improves the acquisition of nutrients by the plants, thereby minimizing losses which could contaminate the groundwater. According to Trenkel,[5] SRF is used to denote nitrogen products decomposable by microbes, such as urea–formaldehyde. However, the rate, pattern and duration of the release are not well-controlled. They may be strongly affected by usage and soil conditions.

The expression controlled-release fertilizer (CRF) is applied to fertilizers in which the factors dominating the release pattern are known and can be controlled during the CRF preparation.[6] CRFs based on polymers minimize water contamination while maintaining an adequate amount of the active agent to meet the specific needs of the crop.[7] Hydrophilic polymers, which form a gel when applied to soil, may provide an adequate release delay and control the availability of the applied nutrient.[8,9] These gel-based matrices are finding application in CRF development.[2,10] Biodegradable matrices are preferred in order to avoid environmental pollution caused by waste polymers that cannot be degraded by soil microorganisms.[4]

Xanthan gum is an anionic linear heteropolysaccharide gum produced commercially by a pure culture fermentation of a carbohydrate with the bacterium *Xanthomonas campestris*. It has a cellulosic backbone of D-glucose linked β-1,4.[11]

Chitosan is derived from chitin, a natural abundant substance found in the skeleton of insects, shells of crustaceans, and fungal cell walls.[12,13] Chitin is composed of $\beta(1 \rightarrow 4)$-D-glucosamine units with a variable degree of *N*-acetylation. When the average degree of *N*-acetylation is lower than approximately 50%, the polymers are called chitosans. They become soluble in

aqueous solutions in the presence of acids such as acetic acid[14] due to protonation of the amino group.

When aqueous solutions of xanthan and chitosan are mixed, a complexation reaction takes place as a result of the electrostatic attractions between these two oppositely charged polymers. This leads to the formation of polyelectrolyte hydrogels through the interaction between the macromolecular chains. Structural changes take place in both polymers, creating a water insoluble hydrogel involving the hydrophilic functions (R–COOH in the case of polyanions and R′–NH_2 for the polycations).[15] The polyelectrolyte complexes are of interest in the biotechnology, pharmaceutical, and biomedical fields.[16] They have been investigated for their use as a matrix for enzyme immobilization,[17] and to enhance the dissolution of water-insoluble drugs.[18]

The hydrogel-forming polymers chitosan and xanthan have been widely studied as matrix materials to sustain the release of a diversity of pharmaceutical drugs.[8,19,20]

In agriculture, chitosan has important properties, such as acting as a carbon source for microbes in the soil, thereby assisting the root system of plants to absorb more nutrients from the soil. In addition, the positive charge that chitosan develops in slightly acidic media (pH $<$ 6), due to the protonation of the amino group of each glucosamine unit, gives it biocide properties.[21] Xanthan, for its part, is used in agriculture as a plant growth stimulator.[22]

Besides the properties described above, for applications in agriculture it is noteworthy that residual xanthan and chitosan in the soil are non-toxic substances.

In this study, solid xanthan, chitosan, and potassium nitrate layered matrices are characterized and evaluated for their potential use in controlled release fertilizers. A detailed analysis of the release kinetics of the model fertilizer KNO_3 is presented as a contribution to the knowledge of the mechanism and characteristics of fertilizer delivery for different tablet compositions. The importance of layering the tablets with drug-free polymers is highlighted. The swelling behavior, surface characteristics, and durability in soil of the tablets are also examined. The significant increase in the release time in static experiments when compared with dynamic ones, along with the proven durability of the tablets in soil, show the great potential of these systems for developing CRFs.

EXPERIMENTAL

Materials

Chitosan of medium molecular weight was supplied by Sigma-Aldrich. A deacetylation degree of 83%, defined in terms of the percentage of primary amino groups in the polymer backbone, was determined by conductimetric titration with standardized NaOH of the polymer dissolved in the HCl solution. Deacetylation analyses were made in duplicate. Xanthan was provided by Fluka BioChemika, potassium nitrate and magnesium stearate were analytical grade. Water was purified by means of a Millipore Simplicity System.

Methods

Preparation of Layered Matrix Tablets with Fertilizer. Tablets were manufactured with the different polymers, using KNO_3 as the model drug for release and magnesium stearate as a lubricant. The corresponding compositions are listed in Table I. The polymers were passed through a sieve with a mesh of 420 microns before being processed. The sieving of the polymers and the compression of the components are important procedures that have been kept constant in all formulations as they affect the drug release.

Table I. Composition (% w/w) of Matrix Tablets of KNO_3

Components	A	B	C	D[a]	E
KNO_3	31.2	31.2	12.5	50.0	31.2
Chitosan	-	33.7	43.05	24.5	67.4
Xanthan	67.4	33.7	43.05	24.5	-
Magnesium Stearate	1.4	1.4	1.4	1.0	1.4

[a] Non-layered tablet.

The blend of components was mixed. The percent barrier compositions for the layered matrix tablets are shown in Table II. Layered matrix tablets were prepared by adding the preweighed polymer mixture without drug in the die and slightly compressing for uniform spreading. The preweighed mixture with drug was placed on top of the first layer and again slightly compressed. The other amount of polymer mixture was subsequently placed on top of the middle layer and the three layers were compressed at 6 Tons for 1 min using a manual hydraulic press. The diameter of the tablets was 1.6 cm.

Release Rate of Potassium Nitrate in Water. To study the release behavior of the fertilizer as a function of time for each CRF, a tablet was placed in a stainless steel basket and immersed into a beaker containing 0.500 L of purified water, at (25 ± 2)°C. The release of KNO_3 into the water phase was continuously monitored by conductimetry (conductivity meter Hanna Instruments model HI 9°33 multi Range) and the cumulative concentrations were determined as a function of time using a calibration curve. Three replicates for each experiment were obtained.

The tests were conducted under dynamic and static modes:

(a) Dynamic Experiments. The aqueous phase was magnetically stirred at 250 rpm in all experiments.

(b) Static Experiments. The measurements were performed under unstirred conditions. The conductivity probe was kept in a fixed position relative to the tablet under study.

Data Treatment for the Dynamic Experiments. The temporal behavior of fertilizer concentration during the release process

Table II. Composition (% w/w) of the Upper and Lower Layers of the Tablets

Components	A	B, C	E
Chitosan	-	18.4	36.8
Xanthan	36.8	18.4	-
Magnesium Stearate	0.75	0.75	0.75

(the first 60% of the fractional release curve) was adjusted by a power-law type relationship:[23,24]

$$C_t/C_\infty = k\,t^n \quad (1)$$

wherein C_t/C_∞ (C, molar concentration of KNO_3 in the water phase) is the fractional drug release up to time t, k is a constant depending on kinetic features and experimental conditions, and n is an exponent related to the release mechanism. The n value is utilized to characterize different release mechanisms. Equation (1) can be seen as an expression that involves two independent mechanisms of drug transport, Fickian diffusion and Case II transport. In the last case, the relaxation process of the macromolecules occurring upon water absorption by the system is the rate-determining mechanism.

In our study, the CRFs are tablets with cylindrical geometry. For this case, the power law of *eq.* (1) has two proposed physical meanings for $n = 0.45$ (diffusion-controlled drug release) and $n = 0.89$ (swelling-controlled drug release or Case II transport). Values of n between 0.45 and 0.89 are described as anomalous or non-Fickian diffusion and can be regarded as a superposition of the two mechanisms described above.[25] For cylinders with axial and radial release and pure Case II drug transport, Kosmidis et al.[26] found an n value of 0.89.

The percentages of released fertilizer were calculated and plotted as a function of time. Equation (2) was used to fit the data:

$$KNO_3\ \text{release}\ (\%) = k'\,t^n \quad (2)$$

where the constant k' includes k, C_∞, 0.500 L (volume of the water receptor phase), the molar mass of KNO_3 and the initial mass of this drug in the tablet.

Statistical Considerations. For the drug-release data treatment, a non-linear least-squares data fitting was used. A 95% confidence interval of the nonlinear least-squares estimation was reported for all parameters (Matlab version 8.0, TheMathWorks, Natick, MA, 2012).

Swelling Measurements. The tablets prepared without KNO_3 were swollen in purified water at (25 ± 2)°C, inside glass beakers. During the swelling experiment, the morphological changes (which did not significantly alter the cylindrical shape) were recorded photographically. The volume of the tablet at time t, V_t, was estimated from the measurement of the diameter d_t and the thickness e_t:

$$V_t = (\pi/4)\,d_t^2\,e_t \quad (3)$$

The volumetric swelling degree, Q_v, was calculated using:[27,28]

$$Q_v = V_t/V_0 \quad (4)$$

where V_o is the initial volume of the tablet.

The percentage of volumetric swelling (ratio between the incorporated solvent and polymer volumes) was calculated as:

$$\text{Swelling}\ (\%) = (Q_v - 1) \times 100 \quad (5)$$

Durability of the Polymer Tablets in Soil. In order to estimate the disintegration time of these biodegradable polymers when exposed to a natural environment, the durability of the compressed polymers was tested in soil, a Mollisol from Buenos Aires, Argentina.

Three types of tablets prepared with xanthan, chitosan, and xanthan : chitosan (1 : 1), with the addition of magnesium stearate in each case, were used to contrast their durability. Samples of 1000 g of moist soil were weighed in glass beakers covered with plastic films with small perforations. The tablets were positioned between the soil and the lateral wall of the beaker. The beakers were weighed twice a week and the evaporated water was refilled. In each case, the change in the area of the tablet in contact with the glass was measured as a function of time.

Scanning Electron Microscopy (SEM). The surface characterization of the tablets was performed by SEM (Zeiss Supra 40, Carl Zeiss, Germany). The preparation of the sample was accomplished by placing the tablet on a specimen holder. The samples were coated with gold using a vacuum evaporator. SEM images were obtained at an acceleration voltage of 5 kV. EDX analysis as an extension of SEM (EDS-detector, Oxford Instruments, UK) was used to detect the X-rays emitted in the 0–10 keV range. EDX analysis was used in a semiquantitative detection mode, with an acceleration voltage of 20 kV.

RESULTS AND DISCUSSION

Release of Potassium Nitrate in Water

Dynamic tests. Dynamic tests were undertaken to contrast the release behavior of the different matrices. While the release profiles obtained with this type of test do not reflect the release behavior of the fertilizer in soil, the dynamic experiments provide the necessary data to compare the profiles for different CRF tablets in order to select the polymer matrices with the longest release period.[29,30]

Mechanism of drug release. The kinetics of KNO_3 release from the CRF tablets was analyzed as described in the "Methods" section with the results shown in Figure 1 and Table III. Tablet **E,**

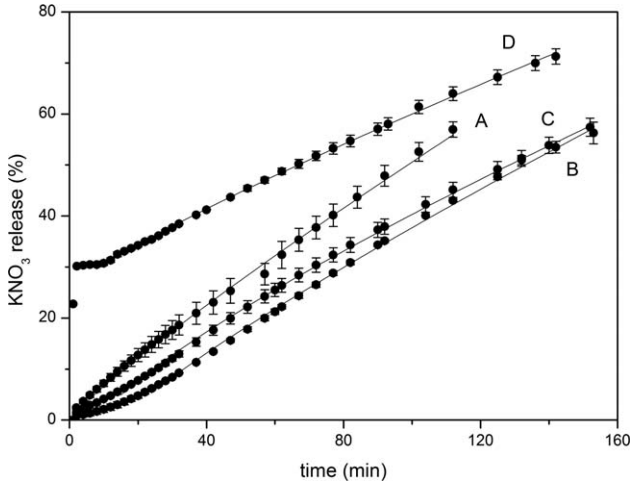

Figure 1. Cumulative KNO_3 Release (%) in dynamic experiments, as a function of time for tablets **A, B, C,** and **D** (Table I). Lines represent the calculated release values from *eq.* (2). Best fit parameters of *eq.* (2) were taken from Table III. Error bars correspond to mean ± standard error of the mean.

Table III. KNO_3-Release Kinetic Parameters in Dynamic Experiments

Tablet (Table I)	n[a]	k'[a] (min^{-1})	R^2
A	0.88 ± 0.02	0.87 ± 0.08	0.9961
B	0.86 ± 0.05	0.83 ± 0.20	0.9961
C	0.80 ± 0.04	1.1 ± 0.2	0.9945
D[b]	0.86 ± 0.03	0.66 ± 0.11	0.9992

Kinetic parameters were obtained by fitting the data through *eq.* (2). Mean and confidence intervals are informed. Statistical treatment of results is mentioned in the "Methods" section.

[a] All parameters are within the 95% confidence interval of the nonlinear least square estimate.

[b] Burst release[29] accounts for the initial 26% of drug released.

with only chitosan in the matrix, quickly disintegrated in the distilled water (pH close to 6) and therefore could not be adequately studied as a delivery system.

For tablets **B** and **C,** we observed that initial points (up to about 15 and 8 min in Figure 1**,** curves B and C, respectively) deviate from the behavior predicted by the power law. Therefore, these points were not taken into account for fitting to *eq.* (2). For fitting purposes, time values were corrected by taking the difference between measured time and the initial time that was determined for each curve. The fact that some points initially deviate from the behavior predicted by the power law suggests the existence of an initial delay before a consistent kinetic behavior is achieved. The polymer layer in contact with the aqueous phase may undergo structural changes in adapting to the contact with the liquid receptor. This lag time is observed when xanthan and chitosan are present but is not detected for xanthan matrices (Figure 1 Curve A). It has been reported that when a mixture of xanthan and chitosan is placed in an aqueous solution, polyelectrolyte hydrogels are formed as a result of the electrostatic attractions between these two oppositely charged polymers.[15,31] Complexation occurring between cationic chitosan and anionic xanthan could account for the observed initial delay.

Table III shows the values of *n,* related to the release mechanism, ranging from 0.80 to 0.88. These values indicate an anomalous (non-Fickian) diffusion transport, quite near to pure Case II.[25] Our results are close to those of Kosmidis et al.[26] who found an n value of 0.89 in the case of drug release controlled by polymer relaxation (Case II transport) for cylindrical geometry. Accordingly, the relaxation process of the macromolecules occurring upon water absorption by the system appears to be the rate-determining step. In agreement with this interpretation, by comparing the graphs in Figure 1, Curves B and C we can observe that the different drug loadings in tablets **B** and **C** (31.2 and 12.5% KNO_3 w/w, respectively) did not produce a significant difference in the drug release pattern. This result may be taken as an indication that the access of the aqueous phase into the matrix was not significantly modified by the drug loading as the water penetration is mainly dependent on the polymeric matrix.

Tablet **D,** a core tablet without the upper and lower layers of polymer and devoid of fertilizer, was assayed in order to emphasize the influence of such coatings on the release behavior. We observed that the immersion of this tablet in the receptor liquid leads to an initially large amount of drug being released before the release rate reaches a definite curve. This behavior is referred to as a burst release[32] and reduces the effective lifetime of the CRF. Tablet **D** behaves in agreement with the analysis of Huang and Brazel[32] and presents about 26% of burst release followed by a non-Fickian behavior, as shown in Table III. In Figure 1, Curve D, the initial burst release and also the existence of the above-mentioned initial lag time are observed, probably related to the polyelectrolyte complex formation. This result highlights the convenience of layering the tablets with polymeric matrix.

Static Tests. Table IV shows a comparison of the times required for a certain amount of drug to be delivered to the aqueous phase, under static and dynamic release experiments (see "Methods" section). The static tests are closer to a soil application than the dynamic ones, since there is no agitation of the surrounding medium. For polymeric matrices of xanthan (tablet **A**) or xanthan : chitosan (tablet **B**) we observed a significant increase, up to 40 times, in the delivery time of the fertilizer when comparing static versus dynamic tests. However, the total immersion of the tablet in water is still an extreme condition when compared to soil. Therefore it can be expected that the release time would be much higher in soil due to the reduced

Table IV. Comparison of the Times Required for a Certain % of KNO_3 Delivered Under Static or Dynamic Release Experiments (see "Methods" section)

Tablet A			Tablet B		
% KNO_3 released	t_{static} (h)	$t_{dynamic}$ (h)	% KNO_3 released	t_{static} (h)	$t_{dynamic}$ (h)
20.7	20.8	0.6	18.0	20.8	0.9
38.0	47.9	1.2	40.5	47.9	1.7
48.7	71.5	1.5	53.3	71.5	2.4
62.1	94.7	2.1	63.7	94.8	3.0
$(t_{static}/t_{dynamic})^a$ = 42 ± 6			$(t_{static}/t_{dynamic})^a$ = 28 ± 4		

[a] Mean ± standard deviation is informed.

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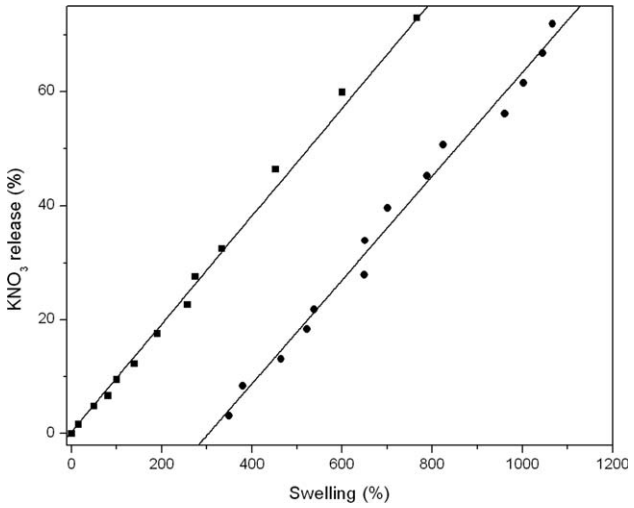

Figure 2. Relationship between KNO_3 release (%) and Swelling (%) for xanthan (■) and xanthan: chitosan (•).

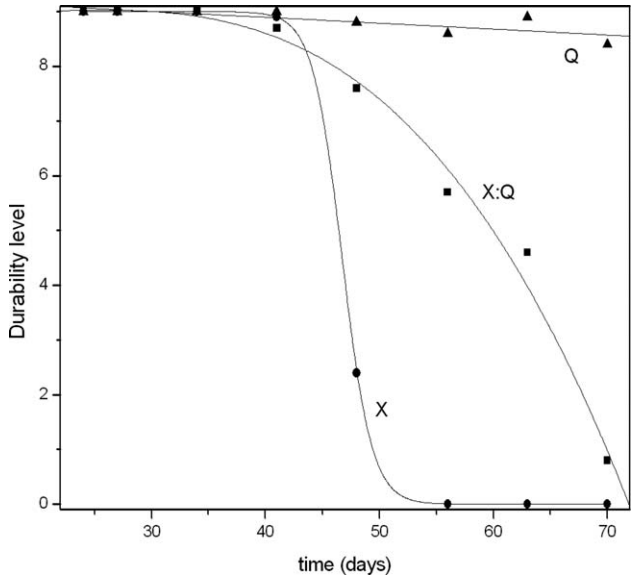

Figure 3. Durability level in soil for chitosan (Q), xanthan (X), and xanthan : chitosan (1 : 1) (X : Q).

availability of a water phase. This is an auspicious result with regard to achieving a sufficiently extended release time to meet the requirements of a crop.

Swelling

Figure 2 shows the relationship between the percentage of fertilizer released from xanthan and xanthan : chitosan (1 : 1) tablets and the percentage of volumetric swelling for each polymeric matrix. The linear correlation obtained during the tests brings out the important role of the swelling process, occurring concurrently with the polymer relaxation, in controlling the drug release mechanism. This is in agreement with the *n* values shown in Table III, as discussed above.

Moreover, it is important to note in Figure 2 that for the xanthan–chitosan matrix a certain percentage of swelling is required to start the release of the drug. In particular, 300% of swelling was reached at 14 min (data not shown) from the beginning of the swelling experiment. This time is comparable with the initial lag time observed for xanthan-chitosan matrices in Figure 1, Curves B and C to establish the release of the drug (15 and 8 min, respectively).

Durability of Polymer Tablets in Soil

The longevity of a polymer in soil may affect its usefulness as a device for the delayed release of a fertilizer. Many natural polymers contain chemical bonds that may be broken through enzymatic hydrolysis in soil. The rate of polymer degradation may be retarded by the addition of small amounts of a microbicide, or by the use of polymers with a well-known antimicrobial effect, such as chitosan.[21]

For the three tablets assayed (see "Methods" section) the area of the tablet was measured as a function of time. The durability of a tablet was ranked on a scale from 0 to 9, taking into account the % of initial area at a given time.[33] Durability level 0 represents a tablet maintaining 0–9% of its initial area and durability level 9 corresponds to a tablet retaining 90–100% of its original area.

Figure 3 shows the durability results in soil for tablets of xanthan, chitosan, and xanthan : chitosan (1 : 1), with added magnesium stearate. In all cases, the tablets remain virtually unchanged until about 6 weeks. Beyond this period, xanthan is quickly degraded, chitosan remains fairly constant until at least 10 weeks, while xanthan : chitosan (1 : 1) has an intermediate durability.

Surface Characterization by SEM

Figure 4 shows the surface of the upper layer of tablets containing chitosan, xanthan or the mixture chitosan : xanthan (1 : 1). It was reported that chitosan has a noticeable tendency to plastic deformation.[34] Figure 4 emphasizes the effect of the presence of chitosan, which exhibits a plastic deformation under compression. In the case of xanthan, the surface proves to be more porous and less deformable by compression than that of chitosan, in agreement with the results of Eftaiha et al.[35] who also found that the weight ratio 1 : 1 represents the maximum interaction between chitosan and xanthan.

CONCLUSIONS

The release behavior of the fertilizer was able to be modulated by selecting the composition of the polymer matrix and by the use of an upper and lower drug-free layer in the tablets. The delivery kinetics of KNO_3 resulted in non-Fickian diffusion, being the polymer relaxation essential in the drug release mechanism. Consistent with this kinetic result, the linear relationship observed between the release fraction of the fertilizer and the percentage of swelling indicates that the release process is controlled by the swelling property of the compressed polymers. Soil experiments showed that the durability of these polymeric matrices was longer than 6 weeks. These results show that

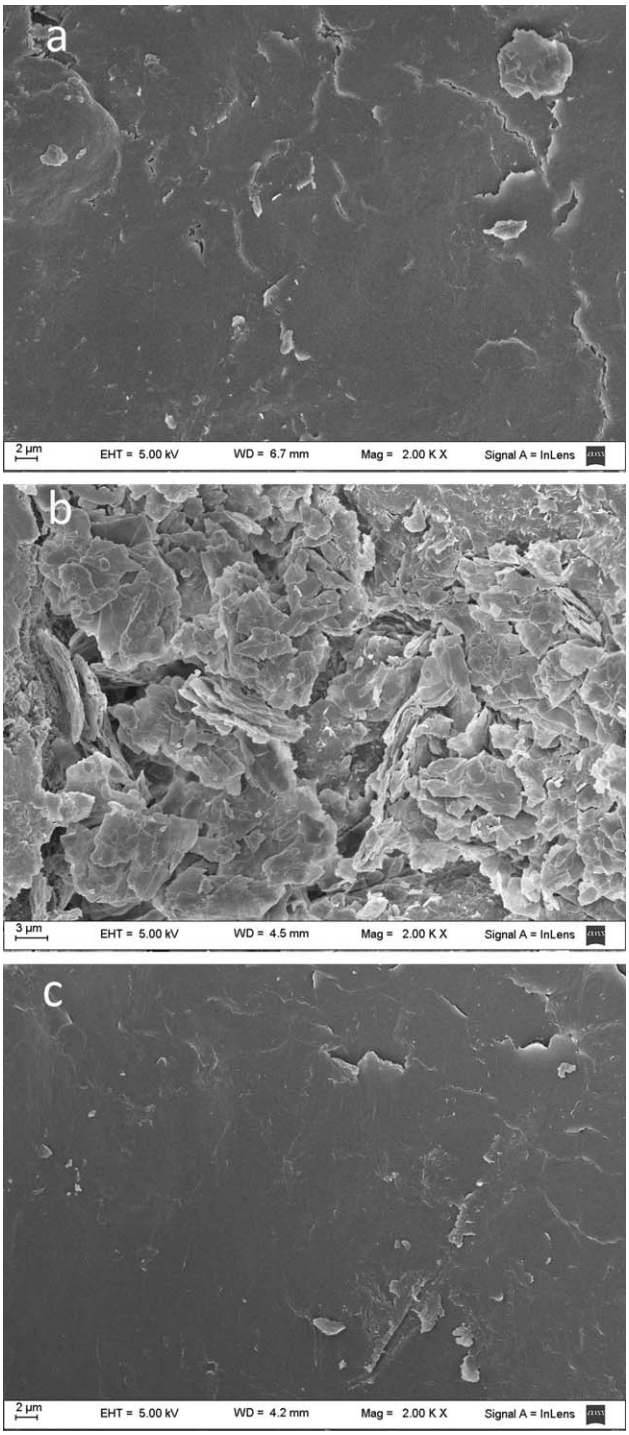

Figure 4. Scanning electron micrographies on the upper surface of (a) chitosan, (b) xanthan, and (c) chitosan : xanthan (1 : 1) subjected to compression (see "Methods" section).

layered xanthan and xanthan-chitosan matrices are promising systems for the development of CRFs.

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