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Nanocomposite Polymer Clay to Support the Release of Drug

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Abstract: It is estimated that there are about 300,00 products named biomaterials that are used in the area of Health. Although they are widely used they have yet to be optimized for therapeutic use. Hence, the objective of this work was to develop nanocomposites hydrogels with poly (vinyl alcohol) (PVAl), glucantime, chitosan and synthetic clay Laponite RD, processed by gamma irradiation. To compare the behavior of drug release two systems were compared, PVAl / chitosan / clay and PVAl / clay. The morphology of the nanocomposites hydrogel was understood by using characterization techniques: X-ray diffraction, scanning electron microscopy (SEM) and atomic force microscopy (AFM) and gel fraction. The release kinetics was analyzed at 37 °C for period of 48 hours. It was observed that the slower release of the drug occurs in the delivery system composed by PVAl / chitosan / clay with correlation of the crosslink type formed by chitosan.

Introduction

Recently, clay–polymer nanocomposites (NCs) have been the focus of much attention due to their excellent physical properties, such as heat resistance, transparency, and so on. These properties are much superior to those that would be expected by a simple additive rule. This is partially due to the strong interactions at the clay–polymer interface [1].

Exfoliated clay-polymers nanocomposites have attracted attention of researchers in last years due to the combination of organic molecules and inorganic ions, offering new products perspective, with different applications [2]. Among polymeric matrixes, hydrogels are investigated especially as biomaterials and the exfoliated clay shows great interactions with the polymer due to their hydrophilic superficial area. The polymeric hydrogels with dispersed clay is a new class of polymeric composites that combine elasticity and permeability of hydrogels with high capacity of absorbing different substances of clay [3].

The hydrophilic hydrogels are made of water insoluble polymeric materials, since the polymer is crosslinked [4]. The terminally attached polymer chains are flexible and capable of fast changing of their conformation. This feature has been used for increasing the swelling degree and swelling rate of hydrogels [5] and to accelerate the rate of shrinking/swelling of stimuli-sensitive hydrogels in response to changes of external condition (pH, temperature) [6].

The aim of this work was the synthesis of hydrogels nanocomposites from PVAl /chitosan with clay nanoparticles with the objective of feasible controlled liberation of high efficiency systems. Gamma rays reticulation process was used to synthesize and sterilize the hydrogel nanocomposites at once and creating the nano and microstructures.

Experimental

Materials and Methods

X-Ray Diffraction

The analysis is aimed to evaluate the intercalation or exfoliation of clay in polymer nanocomposite films using by employing X-ray diffractometer, PANalytical brand, model X'Pert PRO detector X'Celerator. The analysis parameters were: source of X-rays of Cu, energy 45 kV x 40 mA, angular range from 1.17 to 40 °, 0.03 ° step, time / step 100ms. The basal interplanar

spacing "d" of the clay structures were determined by Bragg Law, according to the equation: 2d sen θ = n λ
where:
n = an integer;
λ = wavelength of the incident radiation; d = the distance or spacing set to "hkl" levels (Miller index) of the crystal structure;
θ = angle of incidence of X-rays (measuring between the incident beam and the crystal plane). Fig. 1 shows the different states of dispersion of the clay in relation to polymer characterization by XRD.

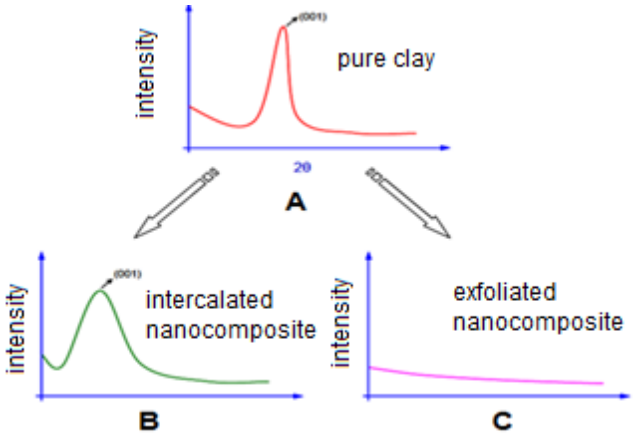

Fig. 1 - The different representations of the dispersion of the clay in relation to the polymer by XRD analysis (A) pure clay (B) in relation to the intercalated clay and the polymer (C) exfoliated clay relative to the polymer.

Scanning electron microscopy with field emission (SEM-EC).

The technique was used for verification of polymeric structures. To obtain high resolution structures of pores in the macro and micro level by using low voltage in the range of 5 kV. The device used was the JSM-6701F.

Atomic Force Microscopy (AFM)

The AFM technique was used to scan the surfaces of the samples. This technique has been widely spread for the study of polymers, since it allows to obtain new information on the surface of polymers such as morphology, phase distribution in blends and composites, tribological data polymer chain conformations, among other information. Apparatus used in the analysis was the *SOLVER (Scanning Pobre Microscope)* NT-MDT.

Gel fraction

The determination of the gel fraction was obtained from the dried samples, which were weighed and placed in stainless steel cages (500 mesh) and immersed in boiling water into flasks still coupled to reflux for a period of 12 h. The extracted sample was dried at 50 ° C until constant weight. The gel fraction of the material is calculated by the equation 1, the system being adapted to standard (ASTM D 2765). The gel fraction indicates the insoluble part, whose value is assigned to the crosslinked polymer fraction.

$$\text{Gel fraction } (\%) = [(m_i - m_f)/mi] \times 100 \quad (1)$$

where m_i is the mass of the dry sample before extraction and m_f the final mass of the sample after extraction and drying.

Release of Drug

The evaluation of release was taken from a sample of the membrane. Samples of the hydrogel with the concentration of the drug were placed in vials with 40 mL of water. Then placed in a centrifuge at a temperature of 37.0 ° C under stirring at 100 rpm (dynamic mode) for 48 hours

and the periods 3, 6, 9, 12, 24, 36, and 48 h, an aliquot 2 mL was removed for analyze of antimony concentration, which were replaced by 2 ml water at each withdrawal rate. Release in static mode were done without stirring and the same procedure was used for the samples.

Results and Discussion

X-Ray Diffraction

Diffractogram of pure nanoparticle was compared to the of nanoparticule compared. By this technique it was possible to assess the type of clay interactions / polymer intercalated or exfoliated. For the system PVA / clay, nanocomposites diffractogram, in Fig. 2, shows the prevalence of exfoliation of the clay by the disappearance of the signal d_{001}.

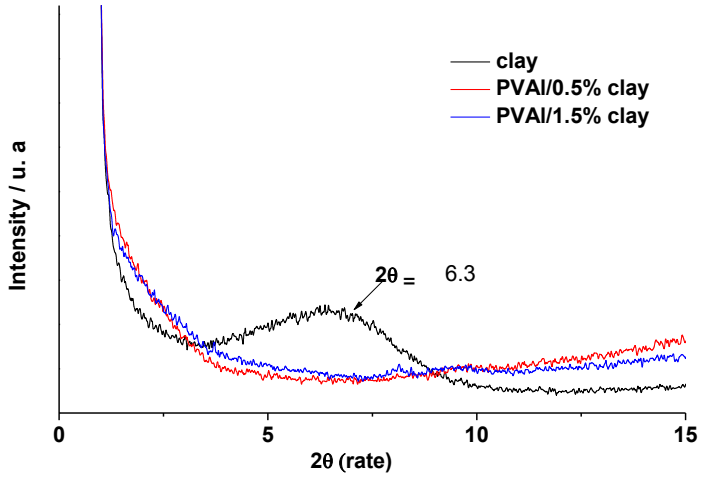

Fig. 2 - XRD curves of hydrogel membranes of PVAL / clay.

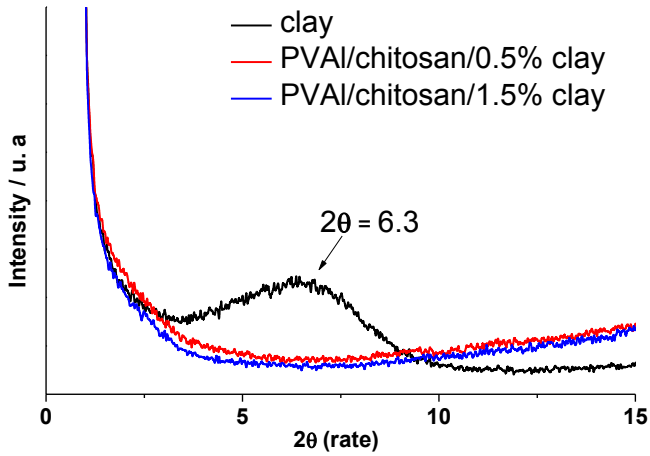

Fig. 3 - XRD curves of hydrogel membranes of PVAL / chitosan / clay.

For PVAl / chitosan / clay system, Fig. 3, is compared XRD patterns of the nanocomposites to clay. It was observed the xfoliation of the clay by the disappearance of the signal d_{001}.

The laponita have properties of cation exchange, intercalation and swelling that make them interesting. The hydrated cations in the interlayer surface can be replaced by others of interest by the method of ion exchange, such as the sodium ion in the structural form: $Na^{+0.7}[(Si_8\ Mg_{5.5}\ Li_{0.3})\ O_{20}\ (OH)_4]^{-0.7}$. And neutral organic molecules such as polymers can be interdispersed between the lamellae of these clays (Silva, 2008).

Micrograph (SEM-EC).

System Micrographs of fracture surfaces of PVAl / clay the nanocomposites showed images of morphology PVAL / clay 1.0% porous shape, some regions with larger macropores, while PVAl / 1.5% clay shows homogeneous regions with agglomeration points of clay on the original surface, Fig. 4 (A and B).

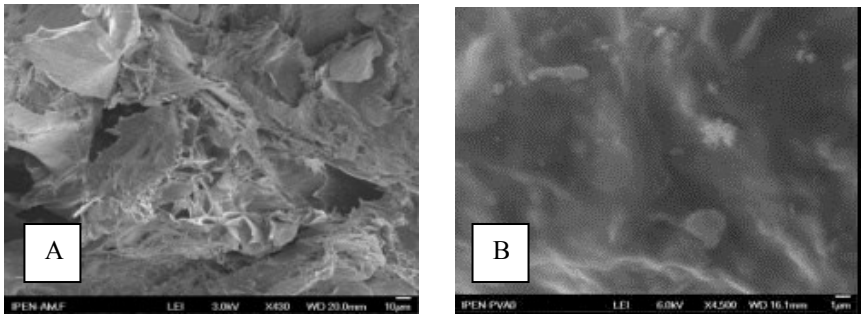

Fig. 4 - SEM micrographs of lyophilized hydrogels (A) PVAl / 1.0% clay and (B) PVAl / 1.5% clay.

Samples PVAl / chitosan / clay 1.0% has irregular morphology in layers Fig A. And when he increased the percentage of clay to 1.5% Fig. B, there is a reduction in pore size.

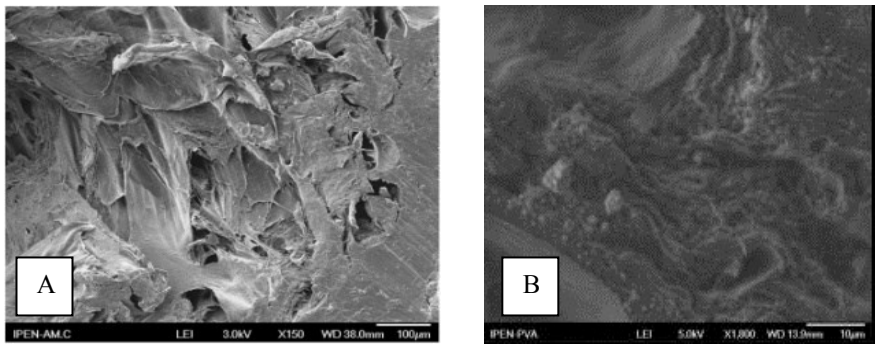

Fig. 5 - SEM micrographs field emission (SEM-EC) of lyophilized hydrogels (A) PVAl/chitosan/1.0% clay and (B) PVAl/chitosan/1. 5% clay.

After removing the water by freeze-drying there is the organization and format of these pores according to the percentage of clay, formed during the rearrangement of the molecules in crosslinking.

Atomic Force Microscopy (AFM)

It was observed in PVAl / chitosan / clay that chitosan has little influence on the dispersion of clay nanoparticles on the surface of the sample system, comparing the PVAl / clay system Fig. A. Were Nanoparticles are dispersed clays with few agglomerations.

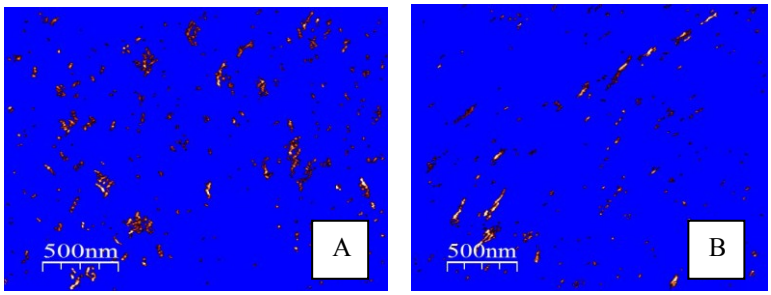

Fig. 6 - AFM obtained from the sample surface lyophilized hydrogels (A) PVAl / / 1.0% clay and (B) PVAl/chitosan/1 0% clay.

Gel fraction

It was observed that chitosan contributed with higher gel fraction comparing with PVAl / clay system, the proportion of crosslinking is important for increasing the gel fraction of samples factors presented in Table 1. PVAl / clay / gel fraction increases gradually with the percentage of clay.

Table 1 - Gel fraction of hydrogels PVAl / clay and PVAl / chitosan / clay.

Membranes	Gel fraction (%) Mean+standard deviation	Membranes	Gel fraction (%) Mean+standard deviation
PVAl	53.0 ± 2	PVAl/chitosan	63.8 ± 2
PVAl/0.5% clay	58.0 ± 1	PVAl/chitosan/ 0.5% clay	61.5 ± 1
PVAl/1.0% clay	57.0 ± 1	PVAl/chitosan/ 1.0% clay	66.1 ± 1
PVAl/1.5% clay	68.9 ± 1	PVAl/chitosan/ 1.5% clay	71 ± 1

Drug delivery

Observe the behavior of drug release glucantime, by quantifying the antimoniate of PVAl / clay and PVAl / chitosan / clay systems Fig 6 and Fig. 7.

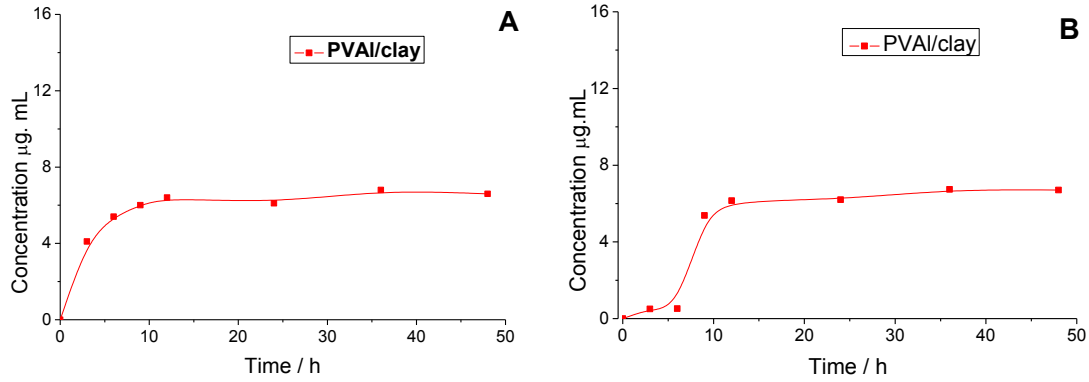

Fig. 7- Dynamic curves of the release kinetics of hydrogels glucantime (A) PVAl / 1.5% clay and (B) PVAl/quitosana/1 5% clay.argila.

It was evident that the slower release of the drug is represented by PVAl / chitosan / clay system where equilibrium release occurs 9h, with a relatively slower release. In the static test for the sample with chitosan, greater concentration of the drug is released from the beginning 9h.

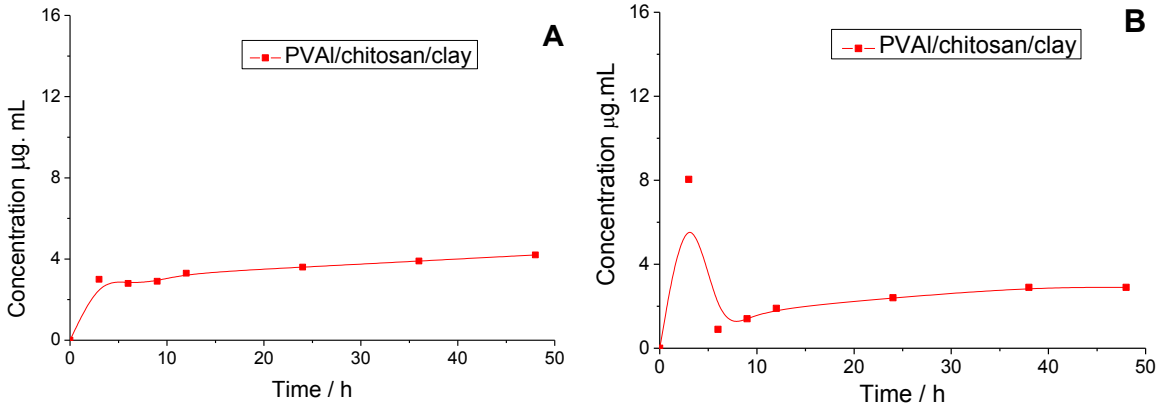

Fig. 8 - Static curves of the kinetics of release of glucantime hydrogels (A) PVAl / 1.5% clay and (B) PVAl/chitosan/1. 5% clay.

Conclusion

It is assumed that the release of glucantime hydrogels occurred by diffusion from a concentration gradient of the samples in the two systems studied, with stirring and without stirring. And as chitosan results suggest, crosslinking of the membrane, interferes with the gel fraction and the release of the drug according was expected in this study.

Acknowledgments

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