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Drug delivery glucantime in PVP/chitosan membranes

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ABSTRACT

The current study of polymer science considers the area of biomedical application very important to establish developments in new polymeric materials. Examples of that are hydrogels for controlled release of drugs. In this work, hydrogels of poly (N-2-vinil-pirrolidone) (PVP) containing chitosan and clay nanoparticles were obtained and characterized to investigate chitosan influence on Glucantime drug delivery. The matrixes were crosslinked by gamma irradiation process with doses of 25 kGy. Hydrogels morphologies were observed by X Ray diffraction (DRX). Atomic Force Microscopy (AFM) and swelling kinetic at 22 °C to study the capacity of water retention and, finally, drug delivery tests were performed "in vitro". The system showed higher gel fraction for the matrix with 1.0% of clay and 0.5% of chitosan. In this case, besides the interactions of clay ions with PVP, there are interactions of chitosan amine group with PVP amide group.

1. INTRODUCTION

The application of polymers for biomedical purposes is of great importance to establish changes in order to obtain new polymeric materials. Such materials are catheters, pacemakers, replacement tissues, cell immobilization, diagnosis and supports for controling of drugs release from hydrogels made of synthetic nanogel and microgel [1; 2]. The use of ionizing radiation as for reticulation process has demonstrated, over the years, progress in hydrogels studies for various applications including the release of drugs [3].
Recently, especially polymeric nanocomposites with natural clays have been reported the interest of many researchers [4]. Nanocomposites represent a rational alternative to conventional polymers that employ a small percentage of clay and result in polymers with improved mechanical properties, good transparency, thermal stability and low gas permeability [5].
The nanoclay hydrogels are a new class of composite materials that combine the elasticity and permeability of the hydrogels with high capacity clays to adsorb different substances [6]. The exfoliated clay nanocomposites have attracting more interest because the increase of the interactions between the polymer and clay [7].

In the present work, hydrogels were formulated from poly (N-2-vinyl-pyrrolidone) (PVP), chitosan and nanostructured clays in order to enable controlled release systems of high efficiency.

2. MATERIALS AND METHODS

2.1 Materials

Poly(N-2-vinyl pyrrolidone) (PVP) *Kollidon* 90F from Basf. Agar provided by Oxoid, clay laponite RD coding S/11176/10 provided by Buntech and chitosan.

2.2 Methods

The formulations prepared for the crosslinking radiation process were obtained by dissolving PVP (10% w/v) in water using a hot plate with magnetic stirrer at temperature of 95 ºC. Chitosan (0.5 g) was dissolved in 100 mL of solution of acetic acid (0.1% v/v). Stirring up to total solution the mixture was performed at room temperature. The clay was added to the PVP solution and heated, at about 85 ºC, for 5 min. The solutions were placed in Petri dishes and with ^{60}Co gamma radiation at 25 kGy dose.

2. 2 X Ray diffraction (DRX).

The analysis evaluated the intercalation or exfoliation of clay in polymer nanocomposite films. Using 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:

$$2d \operatorname{sen} \theta = n \lambda \qquad (A)$$

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).

2.3 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 obtain new information on the surface of polymers such as morphology, phase distribution in blends and composites, tribological data polymer chain conformations, among others. The *SOLVER (Scanning Pobre Microscope)* NT-MDT equipment was used in the analysis

2. 4 Swelling

After synthesis, the samples were immersed in distilled water and weighed in periods of time until 60h and the swelling was calculated according to the equation A.

Swelling = (ms - md)/md. 100 (%H_2O per g hydrogel) (B)

where: ms is the mass of swelled polymer and md is the mass of the hydrogel.

3. RESULTS

X Ray diffraction

The diffraction pattern of pure nanoparticle was obtained to compare the interlayer distance "d001" in the pure nanoparticle and in the composites. By this technique it was possible to evaluate the type of interaction clay/polymer. Fig. 1 shows the shift of d_{001} for the PVP/chitosan/clay nanocomposites. The displacement to lower angle is attributed to intercalation of the clay.

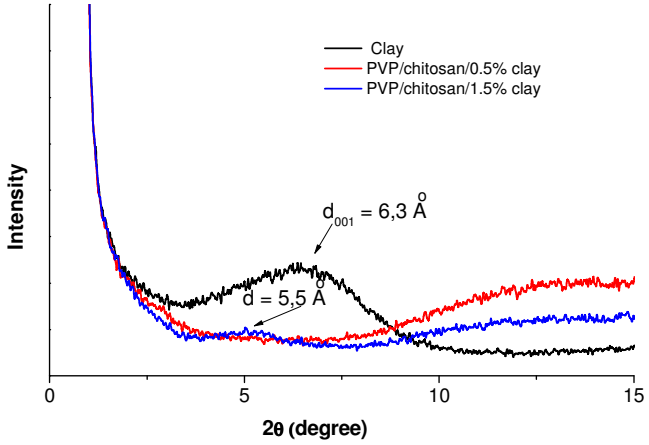

Figure 1 - DRX curves for PVP/chitosan/clay membranes compared to clay.

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Atomic Force Microscopy

The Atomic Force Microscopy shows uniform roughness across the sample surface, Fig. 2. Agglomeration of clay nanoparticles was observed in regions of the sample.

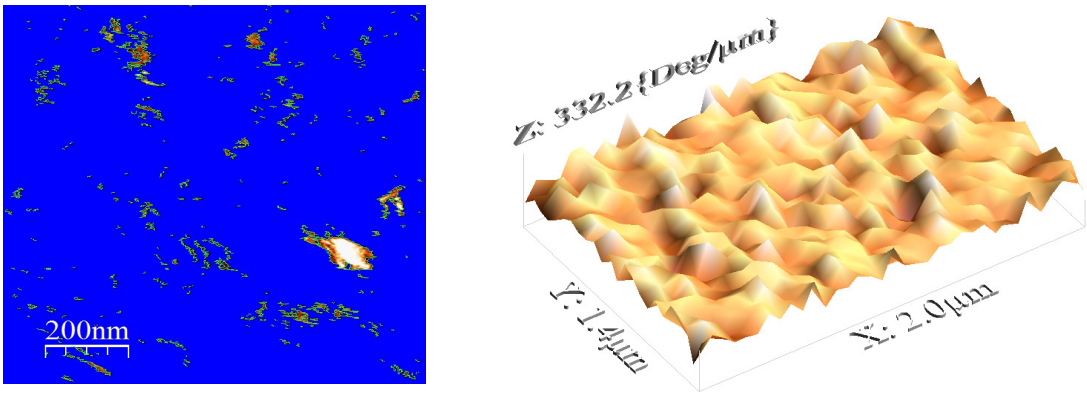

Figure 2 - Images AFM of lyophilized surfaces of PVP / 1.0% clay hydrogels matrices.

Swelling

The rate of swelling was determined by various physical and chemical parameters and the type of porous structure formed by molecular interaction during crosslinking. During the

process, intermolecular between the amino group of chitosan and the hydroxyl PVP occurs as reported previously (Srivastava et. al. 2010). Generally the swelling of hydrogels depends on the rearrangement of the molecules and is related to the functional groups present along the polymer chain. It can be seen from Fig. 3 that swelling of hydrogel decreased in the order: PVP/chitosan/clay< PVP/clay< PVP/chitosan. It showed that clay other than chitosan interferes directly in the swelling.

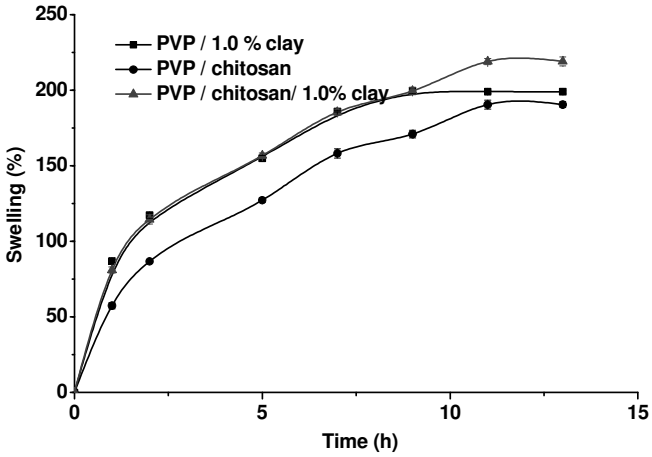

Figure 3 – Swelling Curves of hydrogels PVP / clay, PVP/chitosan/clay and PVP/chitosan.

Drug delivery

According to (Ikada et. al. 1994), the area available for diffusion of the solute is the free space that exists between the macromolecular chains. When flow of water or biological fluids reaches the swelling equilibrium, drug will diffuse out of the hydrogel matrix. In Fig. 4 is observed that after 10h the release is equilibrated in PVP/chitosan/clay hydrogel. The value is lower when compared to the PVP/clay system. Between PVP/clay and PVP/chitosan/clay an increase in crosslinking is observed and probably the clay reduces the interaction between polymeric chains and the hybrid material of hydrogel nanocomposites.

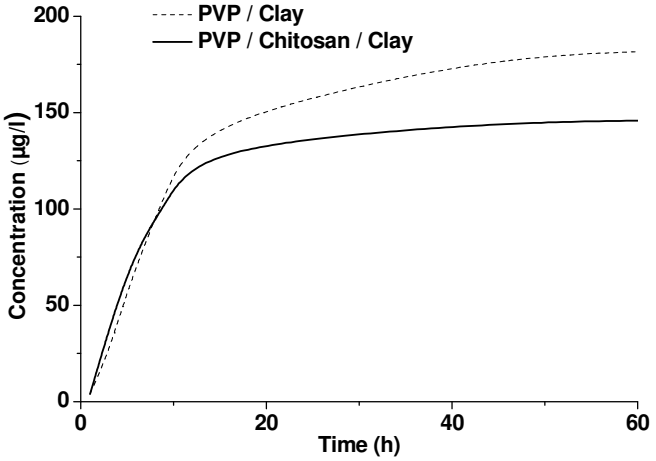

Figure 4 - Drug release of glucantime of hydrogels PVP/clay and PVP/chitosan/clay.

4. CONCLUSIONS

As shown by swelling the highest crosslinking occurred for PVP/chitosan/1.0% clay. It was assumed that the drug release in the PVP/clay system and PVP/chitosan/clay depends on the swelling. Therefore, minor release is presented by PVP/chitosan/clay, which is associated to the crosslinking between PVP and chitosan. The results obtained were satisfactory according to the intended purpose of the research, suggesting further studies for future applications as matrix for drug delivery into skin wounds leishmaniasis

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REFERENCES

1. T. DANIEL, et. al., *Synthesis of Poly(vinyl acetate) Nanogels by Xanthate-Mediated Radical Crosslinking Copolymerization*, Macromol. Rapid Commum, 29, 1965-1972, (2008).
2. P. ULANSKI*, et al., Nano-micro and macroscopic hydrogels synthesized by radiation technique,* Nuclear Instruments and Methods in Physics Research *B*, 208, 325-330, (2003).
3. J. JAGUR-GRODZINSKI, *Polymeric gels and hydrogels for biomedical and pharmaceutical applications,* Review, Polymers Advanced Technologies, (2010).
4. J. H. LEE, et. al., *Poly(Acrylamide/Laponite) Nanocomposite Hydrogels: Swelling and Cationic Dye Adsorption Properties*, Journal of Applied Polymer Science, Vol. 111, 1786– 1798, (2009).
5. Y. TAKEOKA, et. al., *Recent advances in hydrogels in terms of fast stimuli responsiveness and superior mechanical performance*, Polymer Journal, Vol. 42, 839–851, (2010).
6. N. H. NORMA, et al*., Silylation of laponite clay particles with monofunctional and trifunctional vinyl alkoxysilanes*, J. Mater. Chem., 15, 863–871, 863, (2005).
7. K. A. CARRADO, *Polymer-clay Nanocomposites*, Advanced Polymeric Materials-structure Property Relationships, chapter 10, (2003).