HYBRID HYDROGELS PRODUCED BY IONIZING RADIATION TECHNIQUE FOR DRUG DELIVERY

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ABSTRACT

Interest in the preparation of biocompatible hydrogels with various properties has increased considerably in recent years due to their versatile applications in biomedicine, biotechnology, pharmacy, agriculture and controlled release of drugs. The use of hydrogels matrices for particular drug-release applications has been investigated with the synthesis of modified polymeric hydrogel of PVAl, PEG and 0.5, 1.0 and 1.5 % nano-clay. They were processed using gamma radiation from Cobalt-60 source at 25 kGy dose. The characterization of the hydrogels was conducted and toxicity was evaluated. The dried hydrogel was analyzed for thermogravimetry analysis (TGA), infrared spectroscopic analysis (FTIR), swelling in solutions of different pH and gel determinations. The membranes have no toxicity and the gel content reveals the reticulation. The nano-clay influences directly the equilibrium swelling.

Keywords: Hydrogel, PVAl, Clay, Drug delivery

1. INTRODUCTION

The current study of the polymeric science considers the biomedicine as one of the most important areas for application of modified polymeric structures as new materials. An example, is the poly(vinyl alcohol) (PVAl), a polymer of great interest due to its specific characteristics for biomedical applications. PVAl is a water-soluble polymer employed in practical applications due to its excellent chemical resistance, processing properties, biodegradability and physical properties [Peppas N. A., 1986; Finch C. A., 1973].

Interest in the polymeric hydrogels started in the 1950 [Guenet J. M., 1992] During the last few decades, the number of papers published on this subject increased exponentially and continued to increase linearly during the last few years. Both synthetically prepared and biologically derived polymers are used for polymeric hydrogels. Biocompatible polymeric hydrogels are extensively used for biomedical/

pharmaceutical applications such as controlled drug release and delivery, tissue engineering, and regenerative medicine [Jagur-Grodzinski J., 2010].

The presence of nanoparticulas inorganic can performs significant change in the overall crystalline structure of the hydrogel [Shubhangi et. al., 2007]. Morphological changes can lead to different performance of the hydrogel and the characteristics of swelling degree and diffusion behavior may change under physiological stimuli [Hassan et. al, 2000] representing an important feature for controlling release of bioactive species.

Therefore, the purpose of this study was to use gamma radiation crosslinking process in which synthesizes and simultaneously sterilize the polymer forming their nano and microstructures. So with the differentiation of micro and nano structure of the new matrix, hydrogels have the ability to alter the drug release according to the need for treatment.

2. MATERIALS AND METHODS

2.1 Materials

Poly(vinyl alcohol) (PVAl) (Mw = 85000, degree of hydrolysis 98,4%) CelvolTM 325 provided by Dermet Agekem. Agar provided by Oxoid and clay laponite RD coding S/11176/10 provided by Buntech.

The formulations prepared for crosslinking were obtained by dissolving PVAl (10% w/v) in water using a hot plate with magnetic stirrer and temperature between 80 and 85 °C for 40 minutes. The clay, after the dissolution was added to the Agar and PVAl solution about agitation and temperature of 85 °C for five minutes. Were placed in Petri dishes and sent to the crosslinking process by gamma irradiation with ^{60}Co source, dose 25 kGy.

2. 2 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.

$$\text{Swelling} = (ms - md)/md.\ 100\ (\%H_2O \text{ per g hydrogel}) \qquad (A)$$

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

2.3 Thermogravimetry (TG)

TG technique was accomplished in a Mettler-Toledo TGA/SDTA 851 thermobalance, using inert atmosphere of N_2 from 25 to 600 °C at heating rate of 10° C min^{-1}.

2.4 Fourier Transforms Infrared Analysis

FTIR analysis was done using a Thermo Nicolet FTIR-6700 Smart Diamond ATR de 4000 a 400 cm^{-1}.

2.5 Cytotoxicity

Tests for biological evaluation "in vitro" were performed according to ISO 10993-5 standards for procedures. In the cytotoxicity test, the samples were tested in culture of mammalian cells. The samples were placed on plates for cell culture and evaluation of cytotoxicity was performed using the method of incorporation of the vital dye neutral red.

3. RESULTS

Swelling das samples

It is observed by the curves of swellings Fig 1 a similar behavior for without clay PVAl hydrogels and hydrogels with 0.5 and 1.0% clay, is more swelling with water and less swelling with to saline. The hydrogel with 1.5% clay showed a significant shift increasing swelling with saline, followed by water and acetic acid.

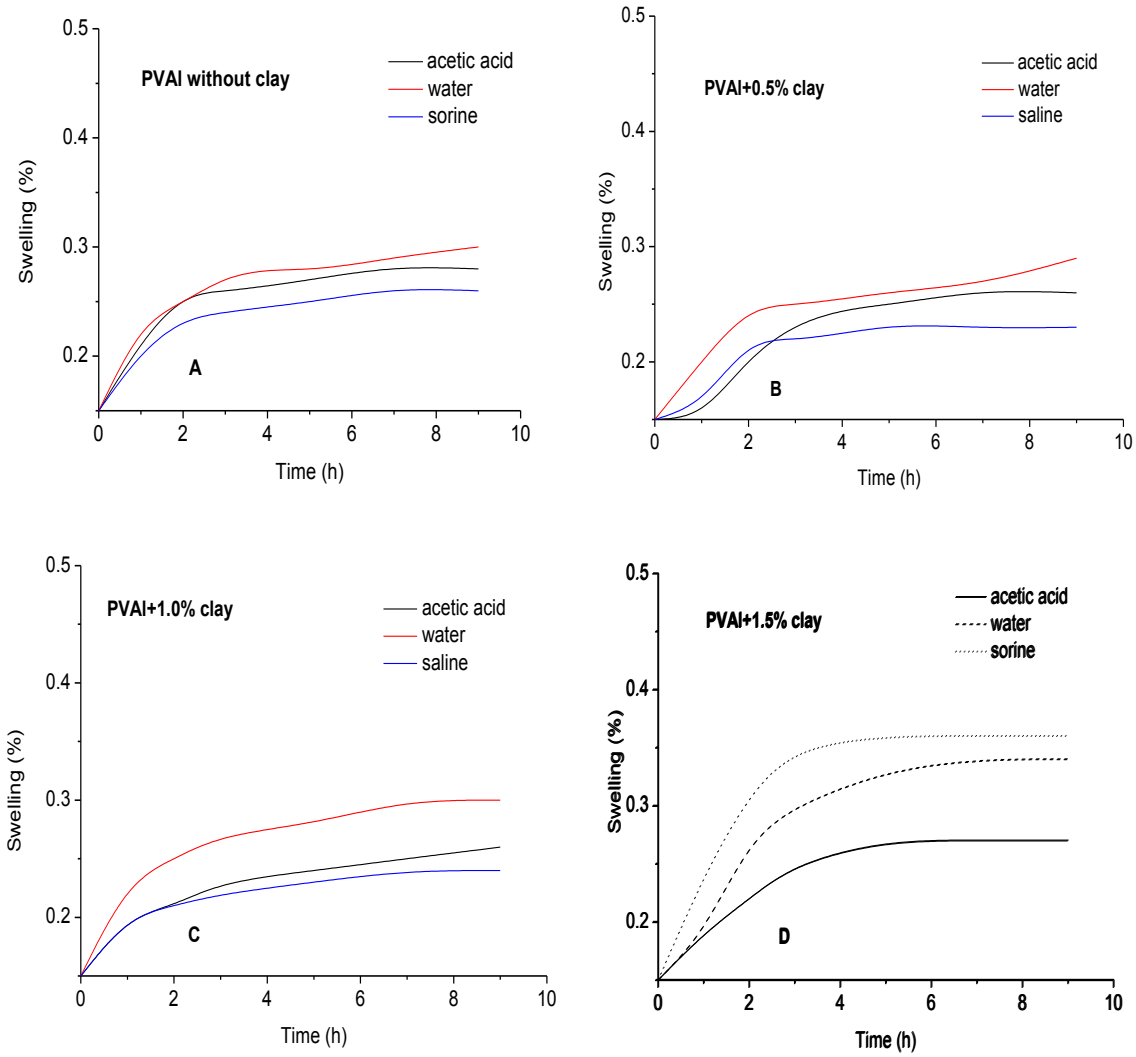

Figure 1 - Swelling behavior of hydrogels PVP and clay laponite RD in acetic acid, water and sorine, (A) PVAl without clay, (B) acetic acid, (C) water and (D) sorine, obtained by gamma irradiation dose 25 kGy.

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The swelling may be associated with hydrogen bonds, this type of secondary links can be favored in both molecules and ionic bonds, [Callister, 2008].

Hydrogels are hydrophilic three-dimensional polymeric networks, which are insoluble in water due to the presence of chemical or physical crosslinks. The reticulated structures are of random nature so it is observed that the swelling is a complex phenomenon involving interactions between the polymer-clay-solvent, [Shubhangi et. al., 2007].

Thermogravimetry (TG and DrTG)

Fig. 2A and 2B shows three events, the first event occurs between 25 - 150 ° C and is associated to the dehydration of water from the nanocomposite PVAl [Shubhangi et. al., 2007] and later then followed by the release of water from the spheres of hydration of exchangeable sodium cations of the clay [Palkova, H., 2009]. The second event, decomposition between 200-380 °C, is related to the loss of PVAl dehydroxilation [Thomas et. al., 2001], in this interval starts the decomposition of polymeric chains. The third event which starts at 380 °C is associated to the polymer decomposition and also to the water loss through the dehydroxilation of structural layers of clay; the loss of structural water is facilitated by the presence of polymers. The PVAl that penetrated is intercalating or exfoliating the clay according to [Shubhangi et. al., 2007].

PVA has a strong tendency to form hydrogen bonding within itself as well as with other species containing highly electronegative groups. Laponite has electronegative oxygen and hydroxyl groups, which can assist the adsorption of PVA onto laponite surface. The adsorption of PVAl onto surface of laponite is presumed to occur through hydrogen bonding. Apart from hydrogen bonding, van der Waals forces between polymer segments and clay surface would also play an important role in the overall adsorption process.

The curves show the amount of waste for PVAl without clay of 9.54% according to the percentage of clay increases the amount of waste reaching 18.30% PVP with 1.5% for the clay. We associate these increases of residue to a possible intercalation of polymer clay or a folding of the polymer chains around the particles of clay.

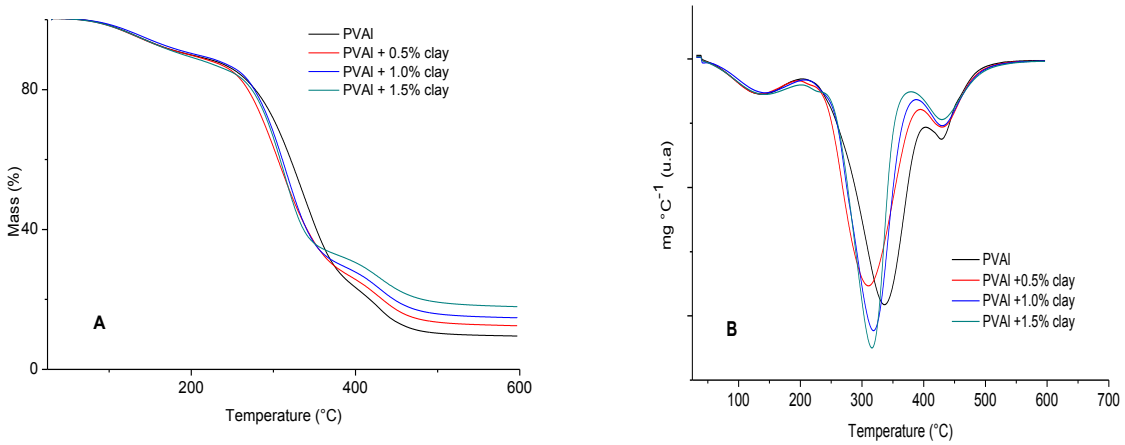

FIGURE 2 – (fig. 2A) TGA and (fig. 2B) DrTG curves of dried hydrogels PVAl and clay laponite RD, obtained by gamma irradiation, 25 kGy.

Fourier Transforms Infrared Analysis

The IR spectra for all samples, including pristine samples used as a point of reference in identifying the peaks of the nanocomposites PVAl and clay, showed broad bands in the region from 3000 to 3500 cm^{-1} Fig. 3, related to stretching of OH present in all samples. Furthermore the nanocomposite, added of 1.5% clay increases the relative intensity of the stretching absorption peaks in the bands 3000-3500 cm^{-1}.

Characteristic bands at 956 and 644 cm^{-1} correspond to the stretching of Si-O-Si. The membrane of hydrogels shows slight shift to 1072 and 813 cm^{-1} of the Si-O-Si stretching when compared to clay. This shift can be attributed to interaction between the polymer PVAl and the clay through Si-OH groups, [Shubhangi et. al., 2007].

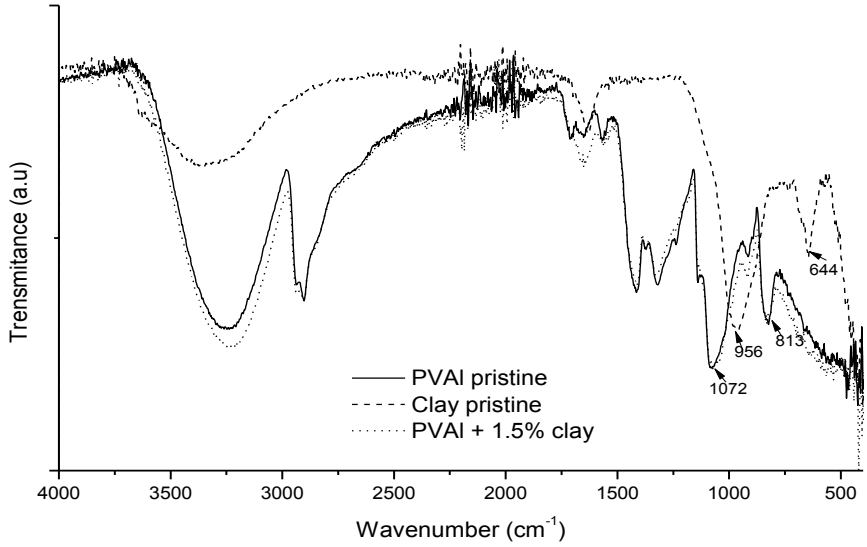

FIGURE 3 – Infrared curves of hydrogels PVAl and clay laponite RD, dried films obtained by irradiation gamma PVAl + 1.5% clay, obtained by gamma irradiation, 25 kGy.

Cytotoxicity

In order to reduce the number of animals used, these standards use a step-wise approach with review and analysis of test results at each stage. Appropriate in vitro investigations can be used for screening prospective biomaterials for estimations of toxic effect. Cytotoxicity in vitro assay is the first test to evaluate the biocompatibility of any material for use in biomedical devices, [Sizue et. al. 2003]. In this work the evaluation of cytotoxicity was performed by using neutral red uptake assay. Positive and negative controls are necessary to confirm the adequate performance of the test procedure and/or to evaluate the results from a new material, as well as to control cell sensitivity. As the test result was not observed toxicity halo around or on samples of cells, and these showed that intact without any morphological alteration, with identical behavior of the negative control curve, Fig.4, then we can say that hydrogels synthesized by crosslinking dose 25 kGy gamma radiation developed in this work do not cause death or injury to the cell population is therefore characterized as non-cytotoxic.

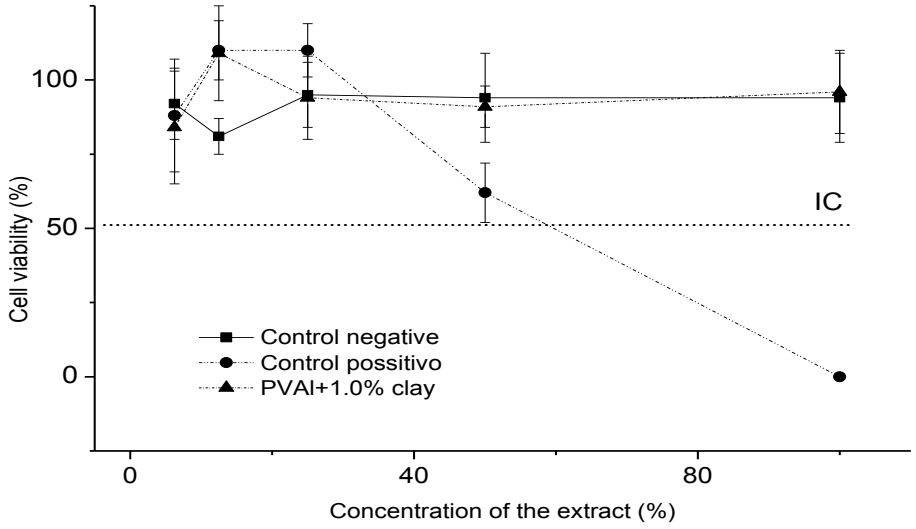

FIGURE 4 - Curve cytotoxicity hydrogels PVAl and clay crosslinked crosslink gamma radiation 25 kGy.

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CONCLUSION

The hydrogels of PVAl with clay present considerable increasing in swelling. At the same dose of irradiation, different concentration of clay and different solutions. FTIR results indicated the displacement of absorption peaks. These shifts can be attributed to interaction between the polymer PVAl and clay through Si-OH groups. This hydrogel can be exploited for drug delivery in biological systems.

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