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EFFECT OF GAMMA RADIATION ON POLYVINYLPYRROLIDONE HYDROGELS

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ABSTRACT

Polyvinylpyrrolidone (PVP) hydrogels have been investigated as drug delivery matrices for the treatment of wounds, such as cutaneous leishmaniasis, and matrices with silver nanoparticles for chronic wounds and burns. The preparation of such hydrogels can occur by various cross-linking methods, such as gamma, chemical, physical, among others. The most feasible for wound dressings is gamma irradiation from cobalt-60, because gamma irradiation simultaneously promotes crosslinking and sterilization, leaving the wound dressing ready for use. The objective of this work was to investigate the effect on physico- chemical properties of gamma radiation on PVP hydrogel according to the radiation absorbed dose variation. The PVP hydrogels were irradiated with doses of 5, 15, 25, 35, 45, 55, 65, 75 and 95kGy at dose rate of 5 kGy/h and characterized by swelling, thermogravimetric and mechanical analysis. Results shown a favorable dose range window for processing of these hydrogels related to the application. The results showed that mechanical strength was affected at doses starting at 25 kGy.

1. INTRODUCTION

The PVP belongs to the class of water soluble polymers and it is a polymeric lactam having an internal amide bond. Considering the structure of the monomeric unit, PVP is amphiphilic in character, since it contains a highly polar amide group which confers hydrophilic, polar and non-polar attraction properties, methylene groups on the backbone and the ring, as shown in Fig. 1 [1].

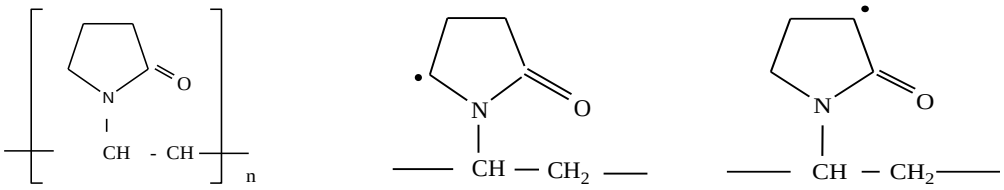

Figure 1: PVP monomer and PVP radical, figure adapted [1]

PVP is biocompatible and can be used in matrices as support for drug release, among other biological applications. Under exposure to gamma irradiation, PVP undergoes crosslinking and forming three-dimensional networks that can be classified as hydrogels, malleable, soft and flexible. However, its mechanical resistance capacity is fragile, limiting its capacity of use. The cobalt-60 source gamma irradiation is recognized as a very suitable tool for the formation of hydrogels [2]. The irradiation process has numerous advantages, such as an easy process control, to prepare the hydrogel and sterilize simultaneously, it is not necessary to add any additives or initiators for the crosslinking reaction. Due to its biocompability, PVP has been used by several researchers in the preparation of hydrogels for dressings of wounds and burns [3-7], among others.

Hydrogels can be differentiated in their physical and chemical interactions according to their crosslinking, being used for drug release, wound treatment and dermatological use [8]. These hydrogels remain in a transition phase of swelling according to the application needs [9], containing 75-82% water [10]. If subjected to swelling, they can increase volume by up to 300% in water or biological fluids, without breaking their structures and without modifying their physicochemical characteristics, they can also be removed without causing trauma to the wound. Swelling is an essential feature for hydrogels, both for use in dry wounds, and for wounds that are difficult to heal with exudate. These hydrogels provide swelling control conditions according to the molecular structure of the polymer and the irradiation dose [11]. The objective of this work was to investigate the effect of gamma irradiation on the physico-chemical properties of PVP hydrogels crosslinked by cobalt-60 source varying the radiation dose, in order to determine the most adequate dose range for obtaining these hydrogels.

2. METHODOLOGY

2.1 Obtaining the hydrogel membrane

The reagents used were Polyvinylpyrrolidone (PVP) *Kollidon* 90F from Basf 8%, 1.5% agar provided by labsynth and 1.5% polyethylene glycol 300 (PEG) labsynth, which were solubilized in 22 ppm silver aqueous solution provided Khemia, using autoclave for 40 min. After that the ready formulation was placed in 13cm x 8cm x 2cm plates, sealed and sent to the crosslinking and sterilization process by ionizing radiation of gamma cobalt-60 source, at doses 5, 15, 25, 35, 45, 55, 65, 75 and 95 kGy. In this way, the hydrogels were obtained as shown in Fig. 2.

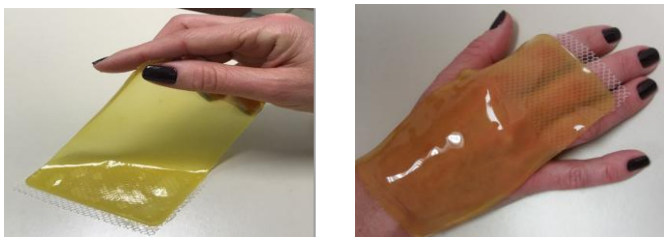

Figure 2: Hydrogel ready for use

2.2 Swelling

After the synthesis, the samples were immersed in distilled water and weighed in periods of time until 48h and the swelling was calculated according to equation 1.

$$\text{Swelling} = (M_s - M_d) / M_d \times 100 \ (\%\ H_2O / g \text{ hydrogel}) \qquad (1)$$

Where: M_s is the mass of swelled polymer and M_d is the mass of the dry hydrogel.

2.3 Infrared spectroscopy analysis

The infrared spectra of the samples were collected to investigate PVP degradation. FTIR analysis was done using a Thermo Nicolet FTIR-6700 Smart Diamond ATR-Attenuation Total Reflectance, in the interval 4000-400 cm^{-1}.

2.4 TGA / DTGA Thermogravimetric

The hydrogels were submitted to thermal characterization tests from TGA / DTGA thermogravimetric analysis in Mettler-Toledo SDTA / 851^{e} apparatus (heating rate: 10 ºC min^{-1} from 25 to 600 ºC, under N_2 flow (10 $mL.min^{-1}$).

2.5 Tensile test

To carry out the tensile test it was used a textured device, the tests followed the standard ASTM D 638-02a - 2003 with adaptation of sample dimensions. Samples of 60mm x 24mm x 3mm where fixed between two claws, model A / TGT and submitted to draw at a speed of 0.8 mm s^{-1} based on the initial distance of 60mm, up to break.

3. RESULTS

Swelling

Note the different swelling behavior between the dose variations shown in Fig. 3. It is noticeable that the hydrogel matrices submitted at doses 5 and 15 kGy present percentages of swelling above 100% and swelling equilibrium after 20h. Compared to hydrogel matrices with doses of 25 to 95 kGy and with swelling below 100% and equilibrium in the period of 8h. The cross-linking of the gamma radiation hydrogels consists of free radicals that corroborate with intramolecular and intermolecular interactions forming a three-dimensional network increasing or limiting this swelling. In general, the swelling equilibrium of the hydrogel depends on the rearrangement of the molecules after crosslinking.

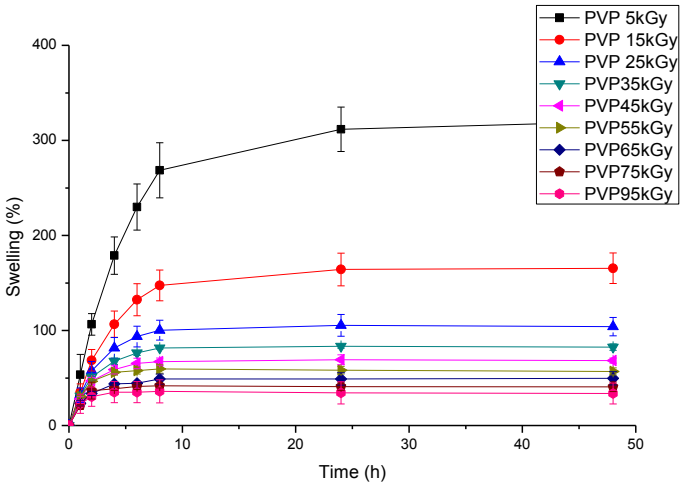

Figure 3: Swelling curves of PVP hydrogel matrices at doses of 5, 15, 25, 35, 45, 55, 65, 75 and 95 kGy

Thermogravimetry (TGA)

Residual water loss is observed for all samples at about 100 °C, Fig 4. It was also observed a decomposition event attributed to the pure PVP without receiving the dose of radiation, the T_{onset} around 460 ºC, while the hydrogel matrix the decomposition event presents in two events the first around 250 ºC that Was associated with loss of mass of PEG and agar and the second around 480 °C which was attributed to PVP.

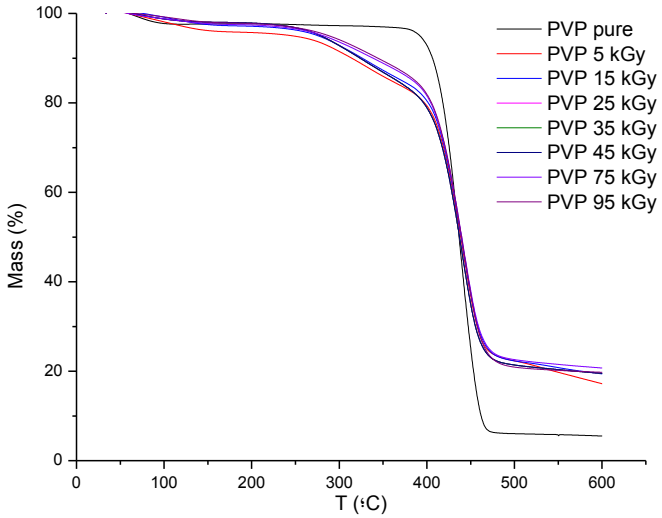

Figure 4: TGA curves of the hydrogels with variations of irradiation doses

Mechanical testing

The tests of the mechanical properties of the hydrogels were carried out in order to correlate the results obtained with their application. The maximum stress at stress rupture (σ) is the resistance offered by the material at the point of rupture, while elongation at strain rupture (ε) gives information on how the material can deform before rupture. In Fig. 5, it is noted that the hydrogels obtained with the 5 and 15 kGy doses present better mechanical performances due to the high deformation presented before the rupture which suggests good flexibility, extensibility and resistance of the hydrogels. The sample with 25 kGy dose presented intermediate elongation, whereas the samples with doses 35 and 45 kGy presented lower elongation due to the fragility caused by excess of crosslinking and eventual degradation of PVP. The mechanical analysis of other samples with doses of 55, 65, 75 and 95 kGy was not possible due to their brittleness.

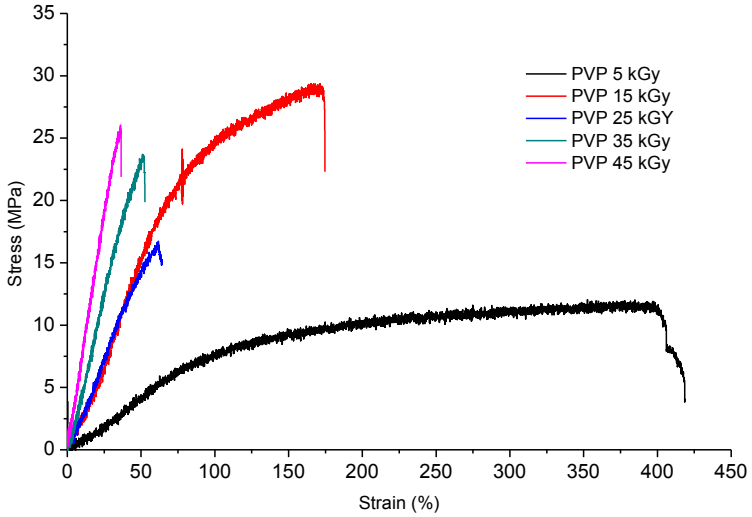

Figure 5: Curves stress x strain of PVP dose 5, 15, 25, 35 and 45 kGy

4. CONCLUSION

The swelling results showed a suitable dose range window for the processing of these hydrogels related to the application. For TGA analysis, the results did not show significant differences. The indicated sterilization for the product is 25 kGy, so the results of the mechanical strength analyses showed that this

dose is within the range unaffected by gamma irradiation. The uncertainty values showed that the dose variation used in the gamma irradiation facility during processing did not interfere with the product properties.

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