

## CHARACTERIZATION AND IMPROVEMENT OF PVAI/PVP/PEG HYDROGELS

Maria José A. Oliveira<sup>1</sup>, Duclerc F. Parra<sup>1</sup>, Monise F. Almeida<sup>1,2</sup>, Ademar B. Lugão<sup>1</sup>

<sup>1</sup>Instituto de Pesquisas Energéticas e Nucleares IPEN-CNEN/SP, Centro de Química e Meio Ambiente (CQMA). Av. Prof. Lineu Prestes, 2242, 05508-900, São Paulo, Brazil.

<sup>2</sup>Faculdades Oswaldo Cruz  
Rua Brigadeiro Galvão, 540 - Barra Funda - São Paulo – SP CEP 01151-000  
[mariajhho@yahoo.com.br](mailto:mariajhho@yahoo.com.br) / [dfparra@ipen.br](mailto:dfparra@ipen.br)

### ABSTRACT

The use of hydrogels matrices for particular drug release applications has been investigated with the synthesis of modified polymeric hydrogel of poly (vinyl alcohol) (PVAI), poly (N-vinyl-2-pirrolidone) (PVP) and poly (ethylene glycol). They were processed using gamma radiation from Cobalt-60 source at 25 kGy dose. In this study it was compared the hydrogels reticulation for irradiation gamma O<sub>2</sub> and N<sub>2</sub> atmosphere. The characterization of the hydrogels was conducted and the toxicity was evaluated. The dried hydrogel was analyzed by differential scanning calorimetry (DSC), thermogravimetry (TGA), swelling and gel determinations. The membranes have no toxicity and gel content revealed the crosslinking degree.

### 1. INTRODUCTION

Hydrogels can be defined as a three-dimensional network that swell in contact with water or aqueous solutions without dissolving [1]. Poly(vinyl alcohol)(PVAI) and Poly(N-vinyl-2-pirrolidone) are water-soluble polymer, employed in practical applications because of its easy preparation, excellent chemical resistance and physical properties, other than is completely biodegradable[2].

Nowadays a new class of hydrogels, capable of reacting to various environmental stimuli as temperature, pH, ionic strength, solute concentration, electric field light, is tested for use in the so-called “intelligent biomaterials”. Certainly there is still a big gap between the artificial hydrogels fish that moves by swinging its tail in a laboratory bath (Shiga et. al., 1989) and an implementation of artificial muscles. However, rapid progress in this field, correlated with increasing demands for more effective medical treatment indicates that there is no exaggeration in including these systems in the list of the “materials of XXI century”[3].

Radiation technique, due to the additive-free initiation and easy process control, are very suitable tools for synthesis of hydrogels. In our group, a number of techniques have been elaborated allowing for gels synthesis of various size ranges, forming internally crosslinked individual macromolecules, via nano, microgels to macroscopic hydrogels [4].

Many researchers working into radiation effects on polymers are used with samples sealed under vacuum. However, polymers materials may, in practical applications, be subjected to irradiation in air. The effect of irradiation is usually substantially different in presence of oxygen, with increased scission at the expense of crosslinking, and the formation of other oxygen-containing structures including reactive hidroperoxides.

Diffusion rates control the access of oxygen to radicals produced by the radiation, and at high dose rates, as in electron beam, with thick samples, the behavior may be similar to irradiation in vacuum where reactions occur before reaches access for oxygen. Surface changes may be quite different from bulk due the relative availability of oxygen.

Irradiation of polymers in atmospheres of other gases offers the possibility of a variety of chemical modifications of the polymer molecules, especially at the surface. This may enhance scission or crosslinking, or alter the materials properties [5].

A very important parameter in release behaviors is the water content of the gel. Two extremes can be distinguished:

- The gel is in equilibrium swelling;
- The gel is completely dry.

If the gel is in equilibrium swelling, there is (ideally) only efflux of drug, and transport occurs according to the normal Fickian laws of diffusion. Unless special adaptations are employed, release is time-dependent. If the gel is swollen, the efflux of drug is accompanied by an influx of water. This influx may proceed according to the so-called case II transport described in swelling controlled devices. This is essentially a time-dependent process, and zero-order release of the drug may be obtained [6].

## 2. MATERIALS AND METHODS

PVAI (Mw = 85000 degree of hydrolysis 98.4%) from Celvol TM 325 Dermet Agekem. PEG 300 from Oxiteno. PVP *Kollidon* 90F from Basf.

PVAI (10% m/v) was prepared by the dissolution in deionized water under reflux at 85 °C for 40 minutes for total dissolution. And PVP (10% m/v) was prepared by the dissolution in deionized water under reflux at 90 °C for 5 minutes for total dissolution.

Formulation were prepared by the addition of PEG 0.5 % in the PVAI / PVP solution and heated for 5 minutes at 85 °C in different atmospheres. Irradiation was processed in <sup>60</sup>Co at 25 kGy.

### 2. 1. Swelling

After synthesis, the samples were immersed in distilled water and weighed in periods of time until 72h and the swelling was calculated according to the equation A.

$$\text{Swelling} = (m_s - m_d)/m_d \cdot 100 (\%H_2O \text{ per g hydrogel}) \quad (\text{A})$$

where:  $m_s$  is the mass of swelled polymer and  $m_d$  is the mass of the hydrogel.

### 2.2. Gel content

The gel fraction was obtained by immersion of the samples in water 100 °C for 10h to proceed the extraction, under stirring. The water was replaced after each 4h. After that the samples were dried in oven (100 °C) and the gel fraction was calculated by the equation B.

$$\text{Gel fraction} = m_f / m_s \cdot 100 \quad (\text{B})$$

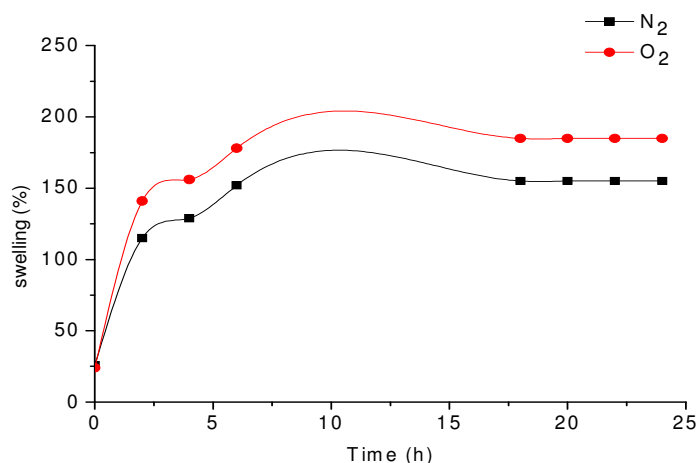
where:  $m_s$  is the mass before extraction and  $m_f$  is the mass of the dried sample after extraction.

### 2.3. Thermogravimetry (TGA)

TGA 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  $10^\circ \text{C min}^{-1}$ .

## 3. RESULTS AND DISCUSSION

It is important observed the conditions of the crosslinking reaction, since they determine and allow the modulation of the crosslinking density, which is the main parameter influencing interesting properties of hydrogels crosslinking, and therefore the crosslinking density, is influenced by various parameters, but mainly by interference of atmosphere. Fig. 1 shows minor swelling to the matrix of crosslinked hydrogel in the presence of  $N_2$ , as compared to reticulate in the presence of  $O_2$ . It was observed that interfere with the  $O_2$  crosslinking, probably the effect of oxidation in aqueous medium.



**Figure 1. Swelling curves of PVAI+PVP+PEG hydrogels**

Oxygen inhibition effects free radical polymerizations by slowing polymerization rates, increasing induction periods, decreasing conversion, decreasing polymer kinetic chain length, the inability of free radical photopolymerizations to overcome oxygen inhibition has limited their applicability and in many cases forced the application of inerting equipment. The synthesis and characterization of patterned hydrogel structures at the micro and nanoscale is

critical for many applications, but currently, limited methods are available for the synthesis and characterization of hydrogels at the micro- and nanoscale. In particular, no methods are available to synthesize the micro patterned hydrogel and simultaneously study the effect of oxygen inhibition during the polymerization and creating tacky surface properties [5].

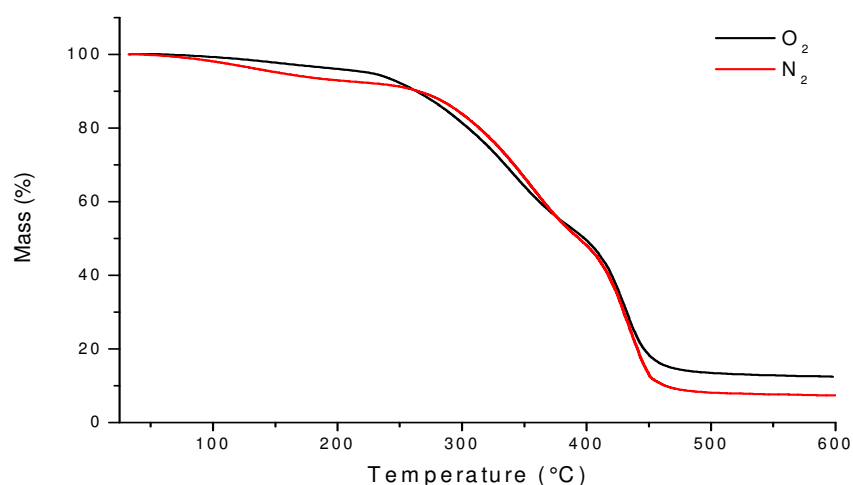
In general an increase in the amount of crosslinker in the gel will diminish its swelling capacity in solvents however, if strong interactions between the solvent and the polymer are present, this effect may be strongly affected.

It was observed that the hydrogels obtained by irradiation of the formulation PVAI + PVP + PEG under O<sub>2</sub> or N<sub>2</sub> atmospheres, have different amounts of gel, Table 1. The evidence is the oxidation caused by O<sub>2</sub> has not contributed to greater reticulation.

**Table 1. Gel fraction (%) of membranes of hydrogels obtained at 25 kGy dose, in different atmosphere of N<sub>2</sub> and O<sub>2</sub>.**

Samples	Gel fraction (%)
PVP+PVAI+PEG N <sub>2</sub>	23.0
PVP+PVAI+PEG O <sub>2</sub>	14.0

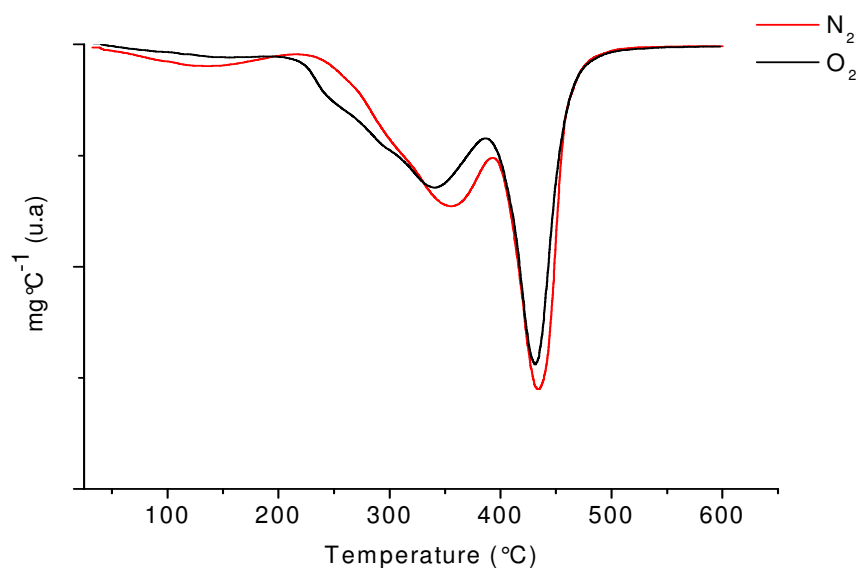
Important emphasize that the membrane of crosslinked hydrogel in the presence of N<sub>2</sub> is increased its thermal stability as observed in fig. 2. One first step was attributed to the residual water loss and an second step to the polymer fraction decomposition, test T<sub>onset</sub> shifted at in the presence of O<sub>2</sub>, the event that the decomposition begins at 213 °C.



**Figure 2. TGA curves of PVAI+PVP+PEG hydrogels obtained under N<sub>2</sub> and O<sub>2</sub> atmosphere.**

DTGA curves show the increase of thermal stability, by displacement of the maximum decomposition temperature, of the hydrogel prepared under N<sub>2</sub> atmosphere. The water loss is

observed at around 100 ° C and a small event at around 200 ° C refers to the PEG loss. As can be seen observed in fig.3.



**Figure 3. DTGA curves of PVAI+PVP+PEG hydrogels obtained under N<sub>2</sub> and O<sub>2</sub> atmospheres.**

Table 2 indicates the temperature of fusion ( $T_f$ ) determined by DSC, that is a function of the reticulation density. According Peppas, the area obtained in the curve for the heat of fusion is greater the higher the degree of crystallinity [7]. For the present samples was observed a tendency to decrease the fusion temperature and crystalline phase in the hydrogel membrane obtained under O<sub>2</sub> atmosphere.

**Table 2.  $T_f$  and enthalpy values for PVAI + PVP + PEG membranes**

Samples	T (°C)	$\Delta H$ mJ/kg <sup>-1</sup>
PVAI+PVP+PEG N <sub>2</sub>	253	- 873
PVAI+PVP+PEG O <sub>2</sub>	208	- 163

#### 4. CONCLUSIONS

Different atmospheres interfere in the amount of gel content and in consequence in the crosslinking density. The hydrogel formed in the presence of O<sub>2</sub> showed lower reticulation compared to that in presence of N<sub>2</sub>. Oxygen inhibition effects free radical polymerizations by slowing polymerization rates, increasing induction periods. Irradiation in presence of N<sub>2</sub> confers to the network an increased thermal stability.

## ACKNOWLEDGMENTS

Thanks to FAPESP 06/53634-3 for grant scholarship

## REFERENCES

1. J. O. Karlsson and P. Gatenholm. “*Surface Mobility of Grafted Hydrogels*”, *Macromolecules*, Volume 32, pp.7594-7598, (1999).
2. A. M. Atta; M. Ashraf; H. Elsayed and I. Shafy. “Uses of Electron-Beam Irradiation to Prepare pH- and Temperature-Sensitive Hydrogels from Reactive Poly(vinyl alcohol) Grafts”, *Journal of Applied Polymer Science*, **108**, pp. 1706–1715 (2008).
3. J. M. Rosiak; P. Ulanski. “*Synthesis of hydrogels by irradiation of polymers in aqueous solution, Radiation Physics and Chemistry*”, Volume 55, pp. 139-151, (1999).
4. J. M. Rosiak; et. al. “*Nono-, micro- and macroscopic hydrogels synthesized by radiation technique*”, *Nuclear Instruments and Methods in Physics Research B* 208 325-330, (2003).
5. J. H. O'Donnell. *Radiation Chemistry of Polymers*. American Chemical Society, pp. 10, (1989).
6. A. N. Peppas; L. Serra. “*Doménech. J. Drug transport mechanisms and release kinetics from molecularly designed poly(acrylic acid-g-ethylene glycol) hydrogels*” *Biomaterials*, pp 5440-5451, (2006).
7. N. A. Peppas; E. W. Merrill. “Differential Scanning Calorimetry of Crystallized PVAI Hydrogels” *Journal of Applied Polymer Science*, **20**, pp 1457-1465, Published Online, (2003).