PERGAMON

Radiation Physics and Chemistry 63 (2002) 543–546

Radiation Physics and Chemistry

www.elsevier.com/locate/radphyschem

Rheological behaviour of irradiated wound dressing poly(vinyl pyrrolidone) hydrogels

Ademar B. Lugão*, Sizue O. Rogero, Sônia M. Malmonge

Institute for Energy and Nuclear Research, IPEN, P.O. Box 11049, CEP 05422-970, Sao Paulo, Brazil

Abstract

The use of hydrogels as biomaterials has increased lately. Poly(vinyl pyrrolidone) (PVP) is an example of polymer hydrogels applied for the synthesis of hydrogel to be used in different biomedical applications. This paper describes a study on rheological properties of PVP hydrogels obtained by gamma radiation techniques. PVP hydrogels were obtained by gamma radiation of PVP water solutions with different radiation doses. It was studied the influence of additives such as poly(ethylene glycol) (PEG), poly(ethylene oxide) (PEO) and glycerol on the rheological behaviour of the gel. The rheological behaviour of hydrogel samples was characterized by measuring the shear storage modulus (G') under dynamic shear loading. Besides this, sterility and cytotoxicity tests were performed. The study on rheological behaviour of hydrogels showed that G' of PVP gels change according to the additive used. Glycerol increases the fluidity of the gel. The influence of PEG depends on the amount and on its molecular mass. The increase on PEG amount and molecular mass cause a decrease of G' and an increase in the crosslinking density of PVP hydrogel network. The use of high molecular weight PEO allows the increase of the elasticity of the PVP gels.

Keywords: Hydrogel; Poly(vinyl pyrrolidone); Wound dressing

1. Introduction

The use of hydrogels as biomaterials has increased lately. Since 60's when Wichterle (Wichterle and Lim, 1960) studied poly(2 hydroxy ethyl methacrylate) (PHEMA) hydrogels for using in ophthalmology, the application of these materials have spread in different areas of medicine and dentistry since hydrogels present the ability to hold substantial amount of water, showing soft and rubbery-like consistency and low interfacial tension. The structural feature of these materials dominates its surface properties, permeselectivity and permeability that give to hydrogels their unique and interesting properties (Ratner and Hoffman, 1976).

PVP is an example of polymer applied for the synthesis of hydrogel to be used in different biomedical applications (Rosiak et al., 1995; Lugão et al., 1998). PVP hydrogels can be obtained by gamma irradiation of PVP/water solutions. The physical and mechanical characteristics of the resultant gel depend on the radiation dose as well as the presence of additive in the solution. The irradiation causes crosslinking between the PVP chain and consequently results in the formation of a polymer network. In gel synthesis the presence of chemical substances different of PVP in the starting solution as well as the radiation dose influence the mechanical behaviour of the resultant product since it influences the network crosslinking density. The network crosslinking density is one of the decisive parameters on the mechanical behaviour of the gel.

The knowledge of the chemistry of PVP radiation and the rheological behaviour of resultants gels allow the use of this technique for obtaining PVP hydrogels with physical and chemical characteristics required by different uses, for instance from dressings to drug delivery systems.

*Corresponding author. Tel.: +55-11-3816-9382; fax: +55-11-3816-9325.

E-mail address: ablugao@net.ipen.br (A.B. Lugão).

0969-806X/02/$ - see front matter
PII: S0969-806X(01)00551-5

This paper describes a study on rheological properties of PVP hydrogels obtained by gamma radiation techniques for use as wound dressing.

2. Material and methods

PVP hydrogels with different characteristics were obtained by ionizing radiation of PVP (Povidone K90) water solutions with different irradiation dose (5–15 KGy). The influence of additives such as PEG (MW 600 and MW 6000), PEO (MW 400.000) and glycerol on the rheological behaviour of the gel was tested.

PVP/additive water solution in different concentration was prepared in polyethylene flasks, capped and exposed to irradiation by using a Co^{60} gamma cell. The rheological behaviour of hydrogel samples was characterized by measuring the shear storage modulus (G') under dynamic shear loading by using a NETSZCH DMA-242 equipment. The measurements were performed with a maximum shear dynamic load of 0,5 N, in view to get a maximum of deformation amplitude equal to 120 μm. The DMA tests were performed under 37°C.

Besides this, sterility and cytotoxicity tests were performed. The cytotoxicity assay was carried out with the exposure of NCTC clone 929 cell culture to the eluate obtained from samples which stayed in contact for 24 h with culture medium MEM (minimun Eagle's medium) at 37°C. The cytotoxic effect was quantitatively assessed by measuring the uptake of neutral red by the viable cells, according to Ciapetti et al. (1996) and International Standard Organization (ISO) (1992). The percentage of viability was calculated in relation to cell control and plotted in a graphic to obtain cytotoxicity index, $IC_{50\%}$, the concentration of extract that cause damage or death of 50% of cell population (Rogero et al., 2000).

3. Results

The study on rheological behaviour of hydrogels showed that the shear storage modulus (G') of PVP gels change depends on the additive used in the gel formulation. Table 1 shows the values of the gel shear storage modulus (G') obtained in case of different chemical substances used as additives for PVP gel.

As we can see, the presence of these additives influences the physical and rheological behaviour of PVP gels obtained by ionizing irradiation. The radicals generated by water ionization with gamma radiation are responsible for the PVP crosslinking. Glycerol acts as a radical scavenger suppressing the action of the hydroxyl radical. Consequently ionizing radiation on PVP/water in the presence of glycerol decreases the crosslinking density of the PVP network.

The PEO used as additive in this case probably cause a decrease in the crosslinking density of PVP network, but due to the high molecular weight of PEO chains. The PEO chains remain entangled on the PVP chains, acting as physical crosslinking resulting in the formation of fluid gels with high elasticity.

PEG is an additive typically used in case of PVP hydrogels for biomedical applications since present non-toxicity and allow to changing the rheological characteristics of the hydrogels. The presence of PEG normally increase the elasticity of the gel due to the plasticising effect, that is, the PEG chain remains between the PVP chain, avoiding the crosslinking and additionally causing a decrease in the physical interactions between PVP chains. The rheological behaviour of PVP gels containing PEG is dependent on the molecular weight and amount of PEG present on it.

Fig. 1 shows the influence of PEG amount and PEG molecular weight present in the PVP water solution exposed to gamma irradiation. It can be observed a decrease on the gel G' when PEG molecular weight increases from 600 to 6000.

Additionally, it was verified the changing of G' with shear frequency and with the time elapsed from starting of the test. The Fig. 2 shows typical curves of G' versus shearing frequency in the case of different times of shearing loading.

It can be observed an increase of G' with the shearing time, probably due to the loss of the water contained inside the gel. But, independent of the shearing time it can be observed a maximum G' at frequencies around

Table 1
Shear storage modulus values (G') and physical characteristics of hydrogels obtained from ionizing radiation in case of different additives used in the starting PVP/water solutions

Starting solution	Irradiation dose (Kg)	G' (MPa)	Physical characteristics
PVP 6.0%	5.0	~0	Transparent fluid gel
PVP 6.0%	25.0	0.0025	Transparent solid gel
PVP 6.0% Glycerol 3.0%	25.0	~0	Transparent fluid gel
PVP 6.0% PEG 6000 3.0%	25.0	~0	Transparent fluid gel
PVP 6.0% PEO 3.0%	25.0	0.033	Transparent fluid gel with high elasticity

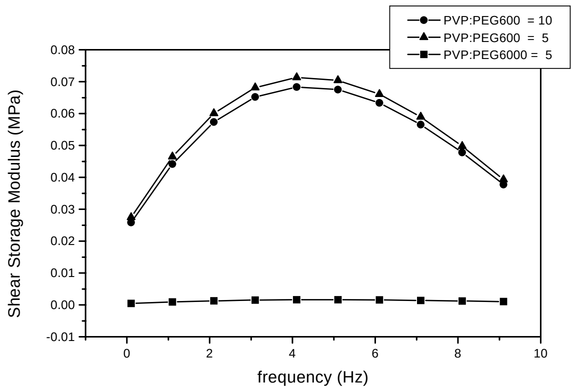

Fig. 1. Shear storage modulus versus frequency measured for hydrogels containing different PVP:PEG solutions.

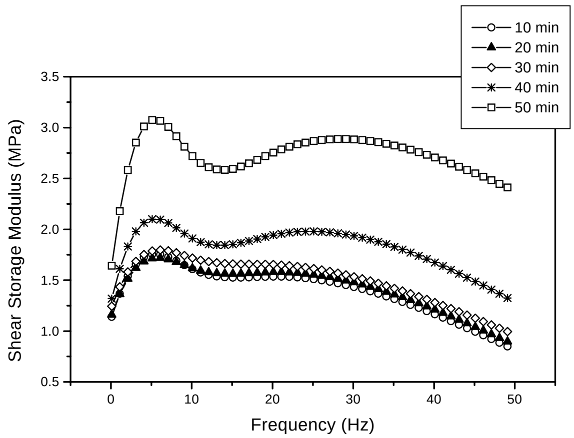

Fig. 2. Shear storage modulus versus frequency for different times after starting the experiment, in the case of PVP:PEG600 (5 gel samples).

5 Hz. Since it is expected the increase of G' with the frequency increase, these maximum may denote a partial disruption of the polymer network as a result of shearing load.

PVP/PEG gels showed to be sterile and non-cytotoxic. In the cytotoxicity assay all the tested samples showed similar behavior of negative control extract, no cytotoxic effect when in contact with cell culture. Only positive control showed to be toxic ($IC_{50(\%)} = 12$), as shown in Fig. 3.

4. Conclusion

The radiation technique shows advantages for PVP hydrogels synthesis since allow an easy control of the hydrogel characteristics by choosing an adequate combination of the starting solution composition and radiation dose rate in view to obtain an hydrogel with the behavior required for different situations such as wound dressing or soft tissue replacement/repair. Additionally the technique allows performing the hydrogel synthesis and sterilization in a same step in lab or industrial scale.

Different chemical substances can be used as PVP gel additives in view to change the gel characteristics. Glycerol increases the fluidity of the gel. The influence of PEG depends on the amount and on its molecular weight. The increase on PEG amount and molecular weight cause a decrease on G' and an increase in the crosslinking density of PVP hydrogel network. The use of high molecular weight PEO allows obtaining PVP gels with higher elasticity.

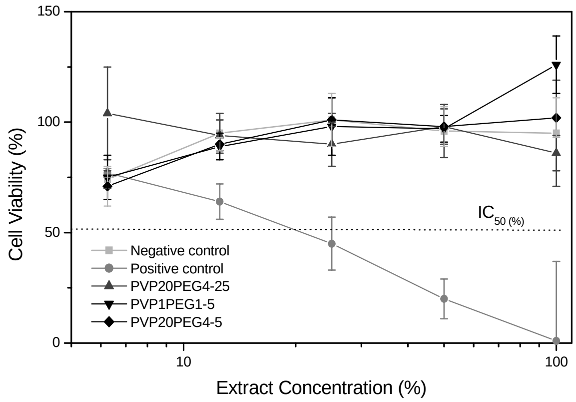

Fig. 3. Cell viability curves of different PVP/PEG hydrogels samples in the neutral red uptake cytotoxicity assay.

Acknowledgements

To CNPq/RHAE, FAPESP and BIOLAB for financial support.

References

Ciapetti, G., Granchi, D., Verri, E., Savarino, L., Cavedagna, D., Pizzoferrato, A., 1996. Application of a combination of neutral red and amido black staining for rapid, reliable cytotoxicity testing of biomaterials. Biomaterials 17 (13), 1259–1264.

ISO document 10993, 1992. Biological Evaluation of Medical Devices. Part 5: Tests for cytotoxicity: in vitro methods.

Lugão, A.B., Machado, L.D.B., Miranda, L.F., Alvarez, M.R., Rosiak, J.M., 1998. Study of wound dressing structure and hydration/dehydration properties. Radiat. Phys. Chem. 52 (1–6), 319.

Ratner, B.D., Hoffman, A., 1976. ACS Symp. Ser. 31, 1–36.

Rogero, S.O., Higa, O.Z., Saiki, M., Correa, O.V., Costa, I., 2000. Cytotoxicity due to corrosion of ear piercing studs. Toxicol. in vitro 14, 497–504.

Rosiak, J.M., Ulanski, P., Pajensky, L.A., Yoshii, F., Makuuchi, K., 1995. Radiation formation of hydrogels for biomedical purpose. Some remarks and comments. Radiat. Phys. Chem. 46 (2), 161–168.

Wichterle, O., Lim, D., 1960. Nature 185, 117–118.