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TA OF PVAL HYDROGEL CROSS-LINKED BY CHEMICAL AND EB IRRADIATION PROCESS
Used as artificial articular cartilage

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Abstract

Hydrogels, in general, can be used as a compliant surface in prosthesis of human synovial joints due to their biocompatible characteristics. In this work, different hydrogels were prepared from two aqueous solutions of PVAL (15 and 20 *mass*/*mass*%) by chemical reactions using citric acid as a cross-linking agent and by electron beam (EB) irradiation with doses from 25 to 100 kGy. The hydrogels were evaluated by their mechanical properties through indentation creep test, thermal properties by differential scanning calorimetry (DSC), and also equilibrium water content (EWC).

Keywords: artificial articular cartilage, DSC, electron beam, EWC, mechanical properties, PVAL hydrogels, thermogravimetry

Introduction

Problems concerning the repair of damaged synovial joints are frequently traumatic to a great number of patients. In the artificial joint, the bone part is usually substituted for a metallic component with high corrosion resistance and strength, while the articular cartilage is replaced by a polymer [1]. Among the polymeric materials, the ultra-high molecular mass polyethylene (UHMWPE) is practically the only option for using in prosthesis of human synovial joints today. However, the wear of UHMWPE bearing surfaces and the cytotoxic effects associated with wear particles is considered to play a significant role in the mechanical failure of artificial joint prosthesis. The use of a thin layer of a compliant material, acting as an artificial articular cartilage in human replacement joints, has recently arisen considerable interest since a layer of a compliant material between the surfaces can produce a lubrication film, minimizing the wear friction at the joint. Polymeric hydrogels are very promising materials to be

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used as an artificial articular cartilage in artificial joints. Hydrogels are three-dimensional networks of hydrophilic polymers held together by covalent bonds and weaker cohesive forces, such as hydrogen or ionic bonds. These networks are able to retain a large quantity of water within their structure, without dissolving. Hydrogels can be used as soft tissue prosthesis due to their biocompatibility, high permeability to small molecules, high hydrophilicity and soft consistency. Therefore, a polymeric hydrogel, used as an artificial articular cartilage, should be capable of exercising important mechanical functions of the natural articular cartilage. One of these functions is to limit the stresses applied to the bone surfaces, because hydrogels have the ability to deform and thereby to distribute the applied load homogeneously; another function is to provide a low-friction bearing surface, increasing the resistance to wear [2, 3, 6, 7]. Some studies have shown that hydrogels physical properties are strongly correlated and controlled by several factors such as, the type of polymeric base (i.e. hydrophobic or hydrophilic component), the cross-linking process, thermal treatment, blends or copolymers obtained, cross-linking density and the amount of absorbed water by the polymeric network [4–13]. These last two factors can be modified by changing the type and/or the concentration of the cross-linking agent, the cross-linking process and by the incorporation of monomers or hydrophilic polymers.

Thermal analysis of hydrogels using thermomechanical analysis for other type of hydrogels has been reported by Iijima *et al.* [14, 15]. Differential scanning calorimetry (DSC) was applied to study the alterations of the tissue elements that build up the hyaline cartilage in osteoarthritis [16] and in the invertebral disc [17]. In the present work, the thermal properties of the PVAL hydrogels were characterized by DSC, and their mechanical properties were appraised by indentation creep tests. Also the equilibrium water content (EWC) was evaluated. Hydrogel samples were obtained by chemical process, using citric acid as a cross-linking agent, and by irradiation with electron beam (EB).

Experimental

Materials

The PVAL (M_w 89000–98000 g mol^{-1} and degree of hydrolysis of 99%) and the citric acid (PM 210.14 g mol^{-1}) used in this study were commercial products of Aldrich, Milwaukee, USA. Hydrochloric acid 37%, sulphuric acid and anhydrous sodium sulphate used were commercial products supplied by Merck.

Preparation and irradiation PVAL sheets

Aqueous solutions of PVAL at concentrations of 15 and 20 *mass*/*mass*% were prepared. The solutions were then poured into flat glass moulds with 10 cm diameter and left at room temperature for 7 days. The PVAL sheets were acetalized by immersion in a bath containing formaldehyde (30 g), sulphuric acid (25 g), anhydrous sodium sulphate (150 g) and water (500 mL) at 60°C to obtain poly(vinyl formal). The unreacted formaldehyde was eliminated by thoroughly washing the film with water [5]. The acetalized samples were immersed into water at room temperature for 24 h. After that, the PVAL samples were put into hermetic metallic gadgets, where nitrogen gas was introduced, prior to irradiation, to obtain an inert atmosphere. The samples were irradiated with electron beam from a Dynamitron Accelerator (E=1.5 MeV) with applied doses of 25, 50, 75 and 100 kGy.

Preparation of PVAL hydrogels with citric acid as a cross-linking agent

The hydrogel sheets were prepared adding 5 or 10% of citric acid as a cross-linking agent to aqueous solutions with 15 and 20% of PVAL. The final ratios (*mass*/*mass*) PVAL:citric acid in the solutions were 100:25, 100:33.3, 100:50 and 100:66.6. Hydrochloric acid was used as a catalyst. The liquid samples were heated in a thermal bath at 80°C and stirred for 10 min. After that, the solutions were poured into flat glass moulds to obtain 3 mm thick sheets, and left at room temperature for 7 days. The hydrogel sheets were then thoroughly washed with distilled water for removing the residual cross-linking agent and catalyst.

Thermogravimetry (TG)

Thermogravimetric measurements were performed using a TGA-50 thermobalance from Shimadzu Corporation. The samples were heated from room temperature to 900°C at a heating rate of 20°C min^{-1} under N_2 atmosphere. All the hydrogels samples were previously heated at 80°C for 12 h.

Differential scanning calorimetry (DSC)

The glass transitions temperature (T_g) of the samples previously dried at 80°C for 12 h were measured using a Shimadzu Corporation's DSC-50. About 10 mg of each sample were submitted to four consecutive heating runs at 20°C min^{-1}, starting at –20ºC. The final temperature of the consecutive heating runs were 150, 180, 200 and again 200ºC. The aim of the T_g measurements was to investigate the plasticizing effect of the water present in the PVAL networks. The T_g values – named T_g (1), T_g (2), T_g (3) and T_g (4) – were taken as the midpoint temperatures corresponding to the point of half the heat flow difference between the extrapolated onset and extrapolated end on the DSC curve of 1st, 2nd, 3rd and 4th heating run, respectively.

Equilibrium water content (EWC)

The hydrogel water absorption capacity was obtained using the equation:

$$\text{EWC (\%)} = [\text{swollen gel mass} - \text{dry gel mass})/\text{swollen gel mass}]\cdot 100 \qquad (1)$$

The swollen gel mass was measured with the hydrogels that reached equilibrium state in distilled water, which was indicated by the constant final mass of the sample.

Indentation creep test

The natural articular cartilage compression properties can be conveniently investigated by means of indentation creep tests [6, 7]. The indentation creep modulus (*E*) was determined using a Material Test System (MTS-Teststar II). The determination of *E* was carried out on samples immersed in distilled water using a spherical tip of 3.2 mm diameter and an applied load of 0.5 kgf, during 180 s. The indentation creep was measured 5 s after load application. The values of *E* were calculated using the equation given by Kempson [6]:

$$E=\frac{9{\cdot}10^4\,p}{16\sqrt{r}}\left[\frac{1-\exp(-0.42e/a)}{h}\right]^{3/2} \tag{2}$$

where E is the creep modulus [kgf m^{-2}], p is the applied load [kgf], r is the indenter radius [cm], e is the sample thickness [cm], h is indentation height [cm], and a is $\sqrt{(2rh-h^2)}$ [cm].

Results and discussion

Thermogravimetric curves were recorded to evaluate the thermal stability of the studied hydrogels. All hydrogels prepared by electron beam irradiation process presented a similar thermal behavior under heating in the thermobalance. The same was observed for all the hydrogels obtained by chemical cross-linking. In Fig. 1, the representative curves of the thermal behavior of the two groups of hydrogels considered – a – EB irradiated and b – chemically cross-linked for the samples previously heated at 80ºC, for 12 h, are given.

Curve a corresponds to the hydrogels cross-linked by irradiation process and shows two main steps of mass loss. The first one, from about 100 to 200ºC, can be associated to the volatilization of trapped water among the cross-linked polymer chains.

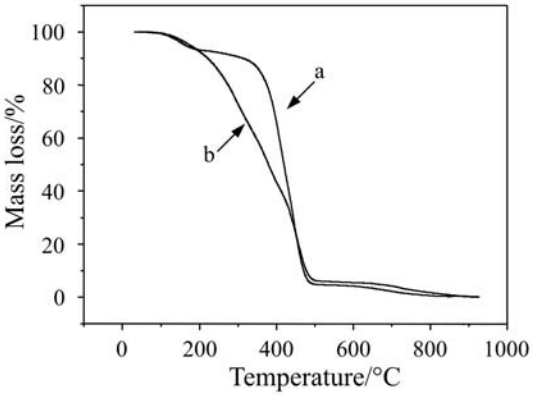

Fig. 1 TG representative curves of a – EB irradiated hydrogels and b – chemically cross-linked hydrogels of PVAL

The second step, from about 250 to 500ºC can be attributed to the thermal decomposition of the polymeric network producing fragments of the original components. On the other hand, curve b shows only one step of mass loss in the range of temperature from about 100 to 500ºC. This behavior can be correlated to dehydration of the sample followed by thermal degradation of the polymer. It can be observed that the irradiation process leads to a more thermal stable cross-linked polymeric network than the chemical process. In this behavior, it must be considered also that the chemical compositions of the two kinds of hydrogels are different due to the presence of citric acid in the non-irradiated samples.

The experimental data of glass transition temperature, EWC and indentation creep modulus (*E*) from the hydrogel samples cross-linked by EB radiation and chemical reaction with citric acid are given in Tables 1 and 2, respectively.

Table 1 EWC, indentation creep modulus (*E*) data and glass transition temperatures for the hydrogels cross-linked by EB irradiation previously heated at 80ºC for 12 h

PVA in aqueous solution/%	Radiation dose/ kGy	EWC/ %	*E*/ MPa	T_g (1)/ °C[a]	T_g (2)/ °C[b]	T_g (3)/ °C[c]	T_g (4)/ °C[d]
15	25	36	3.1	47	98	97	98
15	50	33	3.1	55	100	100	98
15	75	34	3.7	51	97	102	104
15	100	32	3.7	56	98	104	102
20	25	36	3.0	46	94	99	101
20	50	32	3.3	52	97	100	102
20	75	34	3.4	48	95	97	99
20	100	33	3.7	50	98	99	100

[a]1st run – after heating at 80°C, [b]2nd run – after heating at 150°C, [c]3rd run – after heating at 180°C, [d]4th run – after heating at 200°C

Table 2 EWC, indentation creep modulus (*E*) data and glass transition temperatures for the hydrogels obtained by chemical cross-linking previously heated at 80ºC for 12 h

PVAL: citric acid ratio/ (*mass*/*mass*%)	EWC/ %	*E*/ MPa	T_g (1)/ °C[a]	T_g (2)/ °C[b]	T_g (3)/ °C[c]	T_g (4)/ °C[d]
100:25.0	49	1.1	33	52	66	86
100:33.3	54	1.3	30	55	87	116
100:50.0	49	2.0	29	53	86	116
100:66.6	52	2.3	32	65	92	no detected

[a]1st run – after heating at 80°C, [b]2nd run – after heating at 150°C, [c]3rd run – after heating at 180°C, [d]4th run – after heating at 200°C

Data in Table 1 show that the heating of the samples up to 150ºC in the DSC measurements is enough to eliminate the water plasticizing effect on the T_g of the EB irradiated PVAL. In addition, variations of T_g values as a function of radiation dose or PVAL concentration in the matrix solution were not observed. Then, the glass transition temperatures for all irradiated samples after heating at 150ºC (2nd, 3rd and 4th heating run in DSC) have values of around 100ºC, in the range of experimental errors.

On the other hand, in Table 2 it is observed that the T_g of the hydrogels chemically cross-linked increases continuously with temperature. This fact can be related to two effects. The first one is due to the progressive reduction of the plasticizing effect of water, which is gradually eliminated. The second effect is due to the thermal activation of the chemical reactions between PVAL and the residual cross-linking agent beyond the hydrogel production temperature at 80ºC. This effect is confirmed by the non-detected T_g for the sample obtained from the 100:66.6 (*mass*/*mass*) PVAL:citric acid ratio solution and heated at 200ºC, probably due to the high degree of cross-linking in this sample.

Comparing the T_g (1) values of Tables 1 and 2, it can be seen that they are higher for the irradiated samples than those from the chemically cross-linked samples. This comparison is possible considering that all samples were previously submitted to the same thermal treatment at 80ºC during 12 h. This also indicates that the irradiation process produces a greater degree of cross-linking than the applied chemical process.

The indentation creep test evaluation has shown that the value of the indentation modulus E of the irradiated samples (Table 1) increase from 3.1 to 3.7 MPa with a dose in the range of 25 to 100 kGy. Also, this behavior is independent of the PVAL concentration present in the hydrogel formulation, in the range investigated (15 and 20%). On the other hand, in the hydrogels cross-linked with citric acid E increases with the concentration of the cross-linking agent, reaching values from 1.1 to 2.3 MPa in the range of the citric acid used (Table 2). From these results, the indentation values obtained from irradiated samples are greater than those E values from the samples chemically cross-linked. Therefore, it is possible to conclude that, under the present experimental conditions, the EB irradiation process produces hydrogels with more adequate mechanical strength to be used as artificial articular cartilage.

The water absorption capacity of hydrogels is closely related to the cross-linking density, the presence or absence of hydrophilic groups and the percentage of amorphous regions in the polymeric structure [18]. Furthermore, the increase of the cross-linking density causes reduction of the distances among the cross-linking points, demanding higher force to deform the polymeric chain. Consequently, systems with high cross-linking degree present low degrees of swelling. Finally, if the free volume of the polymeric structure is sufficiently low, the amount of water that will penetrate in the polymeric network will be smaller.

Conclusions

The main effort of the present work was the development of a new material to be used as artificial articular cartilage.

From the obtained experimental results, it can be concluded that the PVAL hydrogels produced by irradiation cross-linking process have lower water absorption capacity, better mechanical properties and higher thermal stability when compared with hydrogels obtained through a chemical cross-linking process with citric acid. Furthermore, it was found that radiation doses above 25 kGy did not produce drastic changes on the mechanical and thermal properties of the irradiated PVAL hydrogels. It is worth mentioning that the radiation process cross-links and sterilizes the hydrogels simultaneously.

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