Water Sorption Properties of Poly(Ethyl Acrylate-*co*-Hydroxyethyl Methacrylate) Macroporous Hydrogels

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Summary: Synthetic porous hydrogels are becoming more and more important in the field of biomaterials. Different studies demonstrate that the porous structure promotes the colonisation of living cells and improves the biocompatibility of the implants. The macroporous structure allows not only the control of cellular ingrowth morphology but also the mechanical integration and the regulation of nutrient and hydraulic flow in the hydrogel. In this work poly(ethyl acrylate-*co*-hydroxyethyl methacrylate) (PEA/PHEMA) copolymers were polymerized using 2% of ethylene glycol dimethacrylate as cross-linking agent and azoisobotyronitrile as initiator. Five samples were prepared with the EA/HEMA weight ratios of 75/25, 50/50, 25/75 and pure PEA and PHEMA polymers, obtaining different degrees of hydrophilicity. The macroporous structure was obtained by adding poly(acrylonitrile) fibres to the monomers. After polymerization the fibres were eliminated by dissolution in dimethyl formamide. The holes are cylinders of approximately 40μm diameter and are all, more or less, in the same direction, although they are not uniformly distributed. Water sorption isotherms and diffusion properties of the macroporous samples are compared with the samples without holes.

Keywords: biomaterials; copolymers; poly(ethyl acrylate); poly(hydroxyethyl methacrylate); porous materials; water sorption

Introduction

Poly(2- hydroxyethyl methacrylate), PHEMA, has been used in many biomedical and pharmaceutical fields for a variety of applications including soft contact lenses,[1,2] articular cartilage,[3] and drug delivery devices.[4,5] Different studies demonstrate that the porous structure promotes the colonisation of living cells and improves the biocompatibility of the implants. The macroporous structure improves not only the control of chondrocyte morphology but also the mechanical integration and the regulation of nutrient and hydraulic flow in the hydrogel. Chirila and co-workers have synthesized sponges of PHEMA networks polymerized with a large amount of water. These materials have been proposed to constitute the biointegrable skirt of a keratoprosthesis. The response of the living tissue and the viability

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of cells inside the pores of the sponge have been thoroughly studied.[6,7,8,9] The main problem found with this kind of porous material is its weak mechanical response, mainly when swollen in water. One way to increase the mechanical strength of the hydrogel is to form a composite with a hydrophobic material. In this work poly(ethyl acrylate-*co*-hydroxyethyl methacrylate) (PEA/PHEMA) copolymers were polymerized using 2% by weight of ethylene glycol dimethacrylate, EGDMA, as cross-linking agent and 0.13% by weight of azoisobotyronitrile AZBN as initiator. Five samples were prepared with the EA/HEMA weight ratios of 100/0, 75/25, 50/50, 25/75 and 0/100 obtaining different degrees of hydrophilicity. The macroporous structure was obtained by polymerizing in the presence of poly(acrylonitrile) fibres. After polymerization the fibres were eliminated by dissolution in dimethyl formamide. The holes have the shape of cylinders of approximately 40μm diameter and are all more or less parallel, although they are not uniformly distributed. Chang et al.[10] have studied the influence of the pore configuration on the osteoconduction showing that cylindrical type pores present a similar bone ingrowth to the sponge type porous structure.

Experimental

The cross-linked poly(ethyl acrylate-*co*-hydroxyethyl methacrylate (PEA/PHEMA) was polymerized between glass plates to form sheets approximately 1 mm thick. The monomers (ethyl acrylate, EA, and hydroxyethyl methacrylate, HEMA, from Aldrich, 96% pure) were used without further purification. 2% weight of ethylene glycol dimethacrylate, EGDMA, (Aldrich 98% pure) was used as cross-linking agent and 0.13% weight of azoisobotyronitril, AZBN, was added as initiator. Polymerisation took place between glass plates at 65°C for 24 hours. The low molecular weight substances remaining in the sample after polymerisation were extracted with boiling ethanol for 24 hours and then dried at 80°C in vacuum to constant weight.

Five samples were prepared, pure PEA and PHEMA polymers and PEA/PHEMA copolymers with weight ratios of 75/25, 50/50, and 25/75, obtaining different degrees of hydrophilicity. The macroporous structure was obtained by adding poly(acrylonitrile), PAN, fibres of around 40μm diameter to the monomers (Courtelle fibres were graciously provided by FISIPE Barcelona S.A.). After polymerization the fibres were eliminated by dissolution in dimethyl formamide. The holes have the shape of cylinders of approximately 40μm diameter.

Equilibrium water sorption isotherms were measured at 23°C. The samples were allowed to equilibrate to constant weight in a desiccator where the relative humidity (*rh*) was kept

between 0.11 and 0.97 using different saturated salt solutions.[11] The water content was determined by weighing.

The amount of water uptake by the samples was measured as a function of time at 23°C when the samples were immersed in distilled water. Prior to weighing the samples, excess water was removed with absorbent tissue. Some of the porous samples did not allow the water to enter into the channels; in those cases, samples were put under vacuum to allow the water to enter. Only water equilibrium uptake was measured in those cases.

Starting from dry samples, weight was recorded as a function of time, when the sample was maintained at 23°C and 54% (relative humidity). Desorption was performed for the sample in 97% relative humidity atmosphere and for the sample immersed in water; in both cases samples were maintained at 23°C and 15% relative humidity atmosphere in the balance chamber. A Sartorius BP211D balance with a sensitivity of 0.01 mg, with a YDK01 density determination kit, was used in these measurements. To obtain the temperature and humidity conditions, a constant air flow was led through a saturated salt solution before it arrives to the sample chamber. This chamber was surrounded by a water flow maintained at constant temperature.

The specific volume of the dry networks was determined by the weight of each sample in air and immersed in n-octane at 23°C. The same balance was used in these measurements.

DSC thermograms were obtained using a Pyris apparatus. Starting with an annealing temperature of 120°C during 5 minutes to erase the effects of previous thermal history, the cooling rate to –50°C was 40°C/min. Then the heating scan from -50°C to 120°C at a constant rate of 10°C/min was recorded. The glass transition temperature, Tg, was calculated from the heating scan as the fictive temperature in the glassy state, in other words, as the crossing point of the enthalpy lines corresponding to the glass and the liquid state.[12]

Results

The specific volume of the dry samples can be seen in Table 1. It increases monotonically from the PHEMA sample to the PEA sample and is greater in the porous samples. Glass transition temperatures of the copolymers are shown on Table 1; the porous samples have the same glass transition temperature as the non porous ones.

PHEMA and the copolymer 25/75, 50/50 have the glass transition temperature above ambient temperature but when the samples absorb water (due to the plasticizing effect of water) the glass transition temperature decreases.

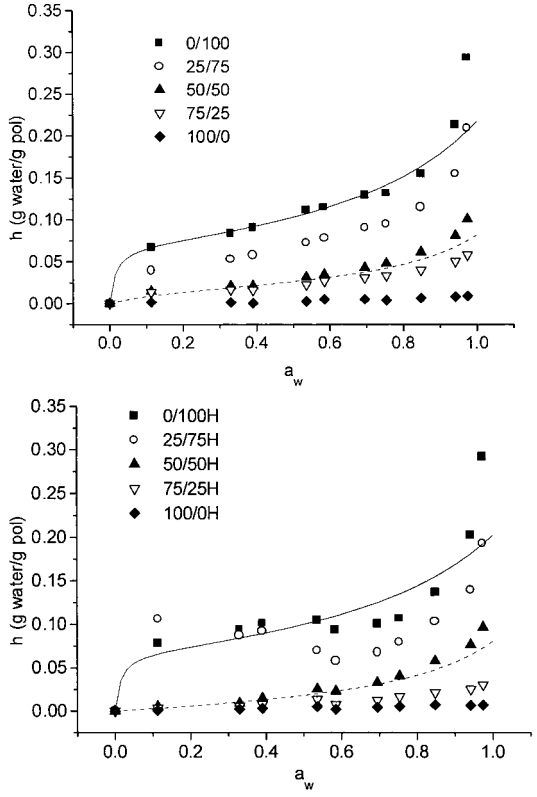

Fig. 1. Equilibrium water sorption isotherms of reference samples (top) and porous samples (bottom). Continuous lines, curves calculated from the GAB equation for the 0/100 samples, dashed lines for the 50/50 samples. Parameters as shown in Table 2.

Table 1. Characteristic properties of the samples: specific volume, glass transition temperature and water uptake when the sample is immersed in water. The name of the sample indicates its composition and H is added in the corresponding porous sample names.

PEA/PHEMA	ν	T_g	h_{lw}
	cm^3/g	°C	g water/g pol.
0/100	0.798	89	0.48
25/75	0.807	72	0.30
50/50	0.843	47.5	0.12
75/25	0.863	7.5	0.07
100/0	0.894	-10	0.032
0/100H	0.845		0.84
25/75H	0.826		0.5
50/50H	0.862		0.54
75/25H	0.906		0.28
100/0H	0.935		0.19

Figure 1 shows the water uptake by the samples as a function of the water activity, which is identified with the relative humidity, a_w=rh. According to the adsorption isotherm classification[13] they correspond to type II and type III isotherms. Type II isotherms are characteristic for non porous solids: they present an inflection point that is usually related to the completion of the monolayer. This amount of water which can be accommodated in a completely filled single molecular layer is proportional to the specific surface area. In our case, we can ascribe type II isotherms to the PHEMA sample and the copolymers. The data suggest that the monolayer is filled at relatively low water activities, around 0.1. Type III isotherms are characterized by convexity towards the relative pressure axis. It appears in the PEA sample and is related to the weak gas-solid interactions.

Table 2. Fitting parameters of the GAB equation.

PEA/PHEMA	h_m	f	c
0/100	0.069	0.68	96
25/75	0.043	0.77	42
50/50	0.019	0.78	8.3
75/25	0.011	0.79	12
100/0	0.005	0.68	0.46
0/100H	0.068	0.66	106
25/75H	0.052	0.65	250
50/50H	0.022	0.77	1.6
75/25H	0.007	0.80	1.4
100/0H	0.004	0.61	1.6

A quantitative analysis can be reached by application of the Guggengeim-Anderson-De Boer (GAB) equation.[14]

$$\frac{h}{h_m} = \frac{cfa_w}{(1-fa_w)(1+(c-1)fa_w)} \qquad (1)$$

where h is the weight fraction of sorbed water referred to the dry weight of the polymer at a given water activity a_w. The parameter c can be related to entropic and energetic terms, h_m is the monolayer capacity and f, always less than unity, is a parameter that modifies the BET equation.[13] Figure 1 shows the results obtained for the porous and non-porous samples. The fitting parameters c, f and h_m, are shown in Table 2. Although no big differences can be observed, it seems that the porous samples present a plateau for water activities between 0.1 and 0.7. This behaviour has been suggested as characteristic of type I isotherms, or monolayer

Langmuir adsorption. This can be explained by the augmentation of the external surface in the pores. No capillarity seems to be present because the holes are too big for it and no hysteresis appears.

Results of the equilibrium water uptake by the samples immersed in liquid water are shown in Table 1. The water uptake is greater in the porous samples than in the reference ones. Comparing this result with that shown in Figure 1, the difference between porous and non porous samples is much bigger when the sample is immersed in water than when the water is adsorbed from the vapour phase. This could mean that the liquid water fills the cylindrical pores by capillarity, while, in the case of water in the vapour phase, only a layer of superficial water is attached to the polymer.

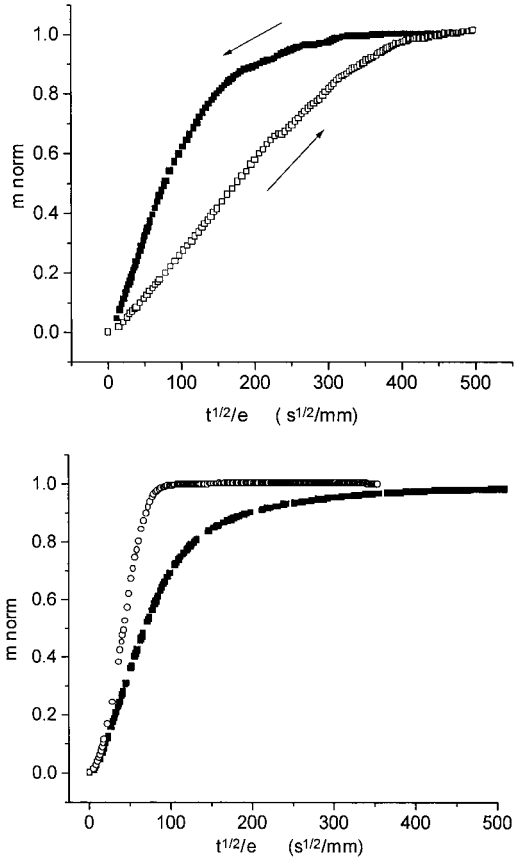

Fig. 2. Top: sorption (open symbols) and desorption (solid symbols) curves for non porous PHEMA sample. Bottom: desorption curves for PHEMA samples previously immersed in water, porous (open symbols), non porous (solid symbols).

Starting from dry samples, weight was recorded as a function of time when the sample was immersed in distilled water. Superficial water was removed prior to weighing. Once the sample had reached equilibrium, it was put in a chamber with controlled temperature and humidity (23°C, 15% *rh*) and its weight was measured periodically. The normalized mass is defined as the water uptake by the sample at a time t divided by the water uptake when the equilibrium is reached.

In all cases hysteresis is present, the desorption process being always more rapid than the adsorption. Results for the PHEMA sample are shown in Figure 2; the porous samples reach the equilibrium water concentration very quickly for all the compositions. This implies that the diffusion coefficient, calculated from the straight part of the normalized curve, supposing Fickian behaviour,[1819,20] is bigger for the porous samples than for the reference ones.

An estimation of the volume fraction of pores in the porous samples can be made by assuming that the swollen polymer consists of a phase formed by a homogeneously swollen polymer network and a phase formed by pure liquid water occupying the volume of the pores V_{pores}. The volume fraction of the pores in the swollen hydrogel is

$$\varphi_{p-s} = \frac{V_{pores}}{V_{swollen\ polymer}} = \frac{\nu_w(h - h_B)}{\nu + \nu_w h} \qquad (2)$$

where ν_w is the specific volume of pure water, ν is the specific volume of the dry polymer, h and h_B are the water uptake by the porous and the reference samples, respectively. The volume fraction of pores lies between 10 and 20%, the same order as was obtained from the SEM microphotographs.

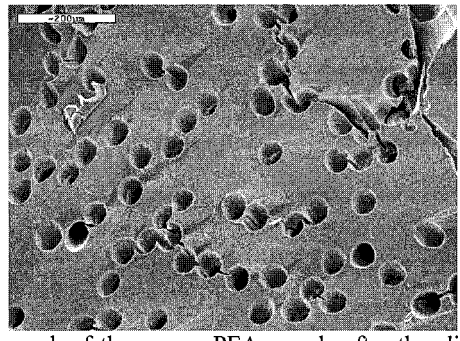

Fig. 3. SEM microphotograph of the porous PEA sample after the elimination of the PAN fibres. Bar 200µm.

Figure 3 shows a microphotograph of porous PEA sample. The pores are cylindrical with a diameter of around 40μm and are all more or less parallel and, as can be seen, they are not uniformly distributed. Similar results were obtained with the rest of the samples. The porosity of the samples can be obtained by dividing the area of pores by the total area. Results in different samples give a volume fraction of pores of around 15%.

Conclusions

Porous polymers have been suggested for many biomedical applications. In general, hydrophilic behaviour and mechanical strength is required. The copolymerization of a hydrophobic and a hydrophilic polymer can achieve this goal. In order to allow the transport of nutrients and the cellular ingrowth we have prepared porous samples by polymerization in the presence of fibres, which are eliminated after polymerization. The holes are cylindrical with a diameter of approximately 40 μm.

The average porosity is 15% and the amount of water uptake when the sample is immersed in water is twice the amount of the non porous one. Dynamic measurements of the sorption and desorption process indicate that the diffusion coefficients are bigger in the porous samples.

Results seem to suggest that the porous samples could be used for cellular ingrowth, but studies in vitro and in vivo would be necessary.

Acknowledgements

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