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P(HEMA) - APPLICATION IN THE TISSUE ENGINEERING OF THE ARTICULAR CARTILAGE♦

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Abstract: The extent of the osteo-articular diseases carried out, in the last decades, to the development of new surgical and prosthetic techniques of treatment. Many studies focused on polymeric materials with the purpose to replace the articular cartilage or to optimize the articular prostheses. Some of this materials allow the regeneration of the articular cartilage: VAP (polyalcohol vinyl), HEMA (hydroxyethyl metacrilate) etc. The choice of these biomaterials is difficult to make because they must to have the same structure and to reproduce the mechanical and physicochemical properties of the biological tissue, in this case, the articular cartilage. The paper presents the experimental results about mechanical properties of poly(HEMA) hydrogels. The influence of a highly hydrophilic monomer AA (acrylic acid), included by co-polymerization into hydrogels structure, on their mechanical properties were analyzed. The results

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obtained show that poly(HEMA-AA) are promising materials for tissue engineering of cartilage.

Keywords: *acrylic acid, articular cartilage, biomaterial, p(HEMA), tissue engineering*

INTRODUCTION

Articular cartilage is avascular, aneural, sparsely populated by cells, and resides in an extreme mechanical environment. The tissue is highly hydrated, being 75 – 80% water by wet weight. The balance in the tissue is composed of 50 – 75% type II collagen and 15 – 30% proteoglycans. Since it has such a simple composition compared to other tissues in the body, articular cartilage has been studied intensely as a candidate for tissue engineering [1].

There has been an increased interest in recent years in using synthetic compliant materials for articulated surfaces of replacement joints. The idea is to create a more compliant form of synthetic articular cartilage than the polyethylene (UHMWPE) commonly used in partial and total joint replacements, thus reducing contact stresses and encouraging fluid film lubrication mechanisms.

One class of materials receiving attention for this purpose is synthetic hydrogels-essentially cross-linked hydrophilic polymer networks which are water swollen but do not dissolve in water. Hydrogels have been used extensively in various forms (porous sponges, non-porous gels, optically transparent films, coatings) in a variety of medical applications, including electrophoresis cells, cell culture substrates, contact lenses, burn dressings, dentures, and drug delivery systems [2].

Several studies have been made on the possible use of hydrogels as synthetic articular cartilage. The increasing number of biomedical application of hydrogels [3] and in particular of poly(2-hydroxyethyle methacrylate) [p(HEMA)] gels requires efficient control of their structure and properties.

Although, hydrogels based on p(HEMA), in simple form, don't have adequate mechanical properties according as solicitation that are constrained. Hence, it was incorporating a hydrophobic element in the polymeric network, and that carried out at obtained of required biomechanical [4].

MATERIALS AND METHOD

Model of articular cartilage - Choice of the material

The hydrogel p(HEMA) expose heavy polymeric methacrylate chains cross-linked by small hydroxyethyle chains (figure 1), which are hydrophilic through their negative charges HO^-. This structure is similar with those of the articular cartilage which exhibit reticulated collagen fibers cross-linked by proteoglycans assembly (agrecans, figure 2), which are hydrophilic through their negative charges represented by SO_3^- and COO^- groups.

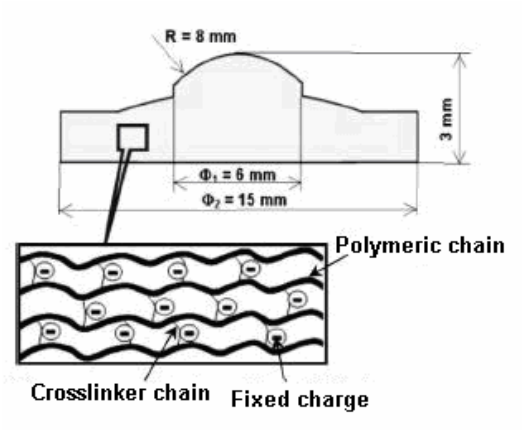


Figure 1. *Model of articular cartilage [p(HEMA)]*

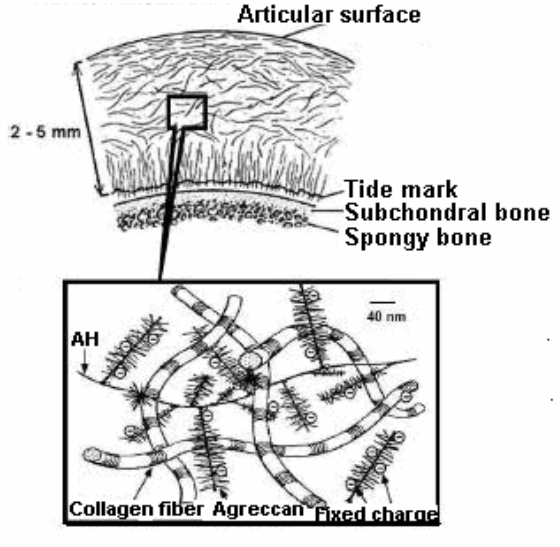


Figure 2. *Structure of articular cartilage[5]*

The bibliographically data (table 1) reveals the similarity between mechanics properties between hydrogel HEMA and articular cartilage.

Table 1*. Properties similarity between p(HEMA) and articular cartilage*

Properties	Hydrogel HEMA [6]	Cartilage [7]
Elasticity modulus in compression (MPa)	0.2 - 0.9	0.5 - 1
Permeability ($m^4.N^{-1}.s^{-1}$) for 1 mm layer of material constrained to a hydrostatic pressure difference of 2 MPa	$\sim 10^{-16}$	10^{-16} - 10^{-15}

The cross-linking of p(HEMA) was realized in presence of acrylic acid (AA), in order to avoid the hydrosolubilisation of the hydrogel the cross-linking agent utilized was tetraethylenglycol diacrylate (TEGDA), ammonium persulfate (APS) which at low temperature active the initiator tetramethyle-ethylendyamine (TEMED).

Sample preparation

- HEMA, AA and TEGDA were purified by passing through the changed ions columns for removing the inhibitors.
- The amount of AA is varied: 5; 10; 15; 20; 25; 30; 35 %.
- It is added 0.5% TEGDA (mo/mol HEMA-AA), 1% initiators TEMED (mol/mol), 5% APS.
- The mixture is homogenized by blending.
- The mixture is casted molded in flask (hip prosthesis) (figure 3) for 24 h at room temperature. The obtained samples are shown in figure 4.

Figure 3. *Mould casting (hip prosthesis)*

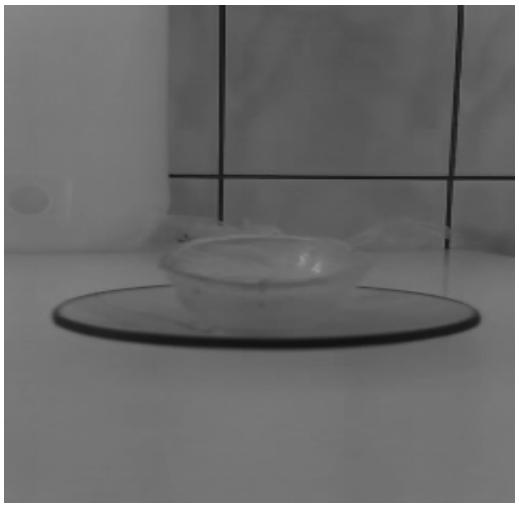


Figure 4. *Obtained samples*

The samples obtained by varying the amount of acrylic acid (5, 10, 15, 20, 25, 30 and 35%) used are depicted in table 2.

Table 2. *Mixing formula for the obtained samples*

Sample	HEMA (mL)	AA (mL)	TEGDA (mL)	APS (mL)	TEMED (mL)
1	10.19	0.525	0.05	3.90	1.80
2	9.65	1.05	0.05	4.10	1.90
3	9.12	1.58	0.05	4.25	1.98
4	8.58	2.10	0.05	4.5	2.06
5	8.04	2.63	0.05	4.60	2.14
6	7.50	3.15	0.05	4.75	2.20
7	6.97	3.68	0.05	4.85	2.25

Biomechanical tests

The obtained samples were constrained at depth shear stress to determinate the subtract wear, utilizing the apparatus from figure 5 which allow the rotation of the prosthesis head in the acetabular cup. In order to simulate the *in vivo* condition we realize an assembly in which a perfusion (figure 6) with physiological serum assures the lubricating condition at the contact level.

The samples were tested at 10,000 cycles (appreciatively 3 h) and very important was the shape of the sample: the shear phenomena were appeared preceded by breakage if the sample was not fit in the acetabular cup.

Figure 5. *Installation for testing the tribological parameters*

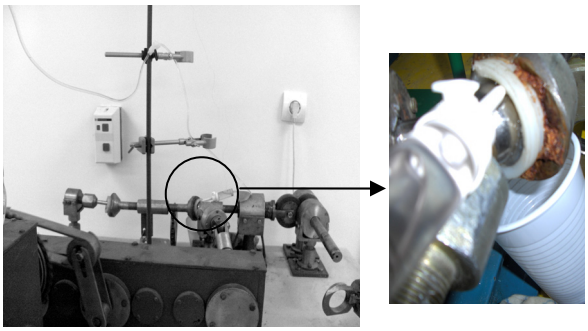
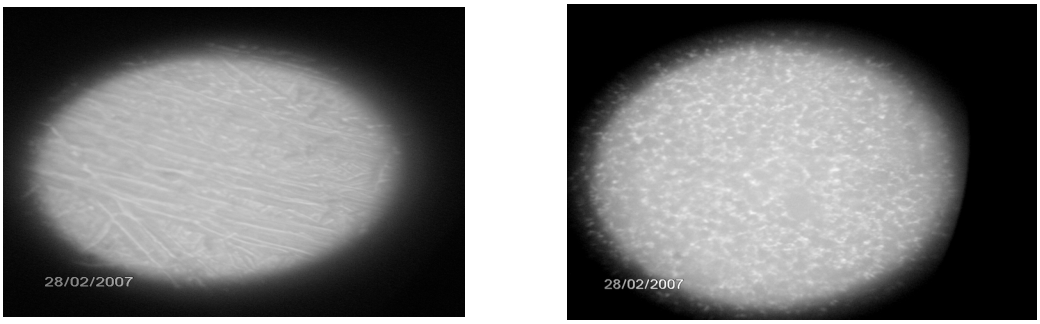


Figure 6. *Control of lubricating*

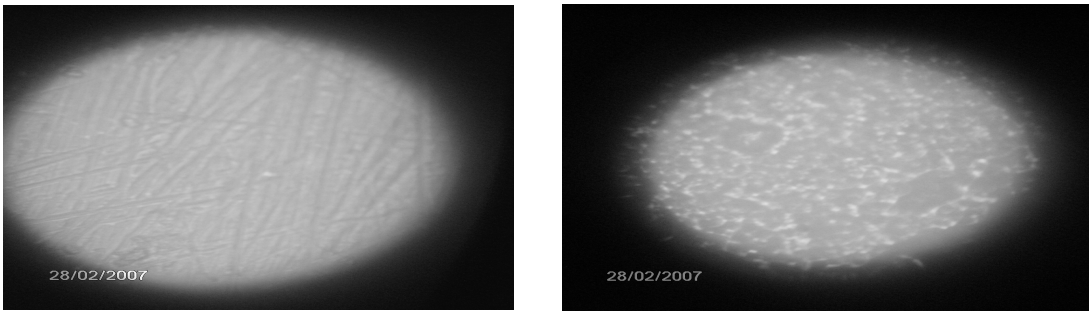
RESULTS AND DISCUSSION

Towards to observe the substrate wear caused by depth shear stress of the tested samples and the references were examined utilizing the optical microscope.
It is obvious from the figures 7 – 12 and table 3, that at samples 5 and 6, with a concentration of acrylic acid of 25 respectively 30%, internal fissures are present. Starting with a concentration of 35% AA the samples present a shape that can't be mechanical tested.



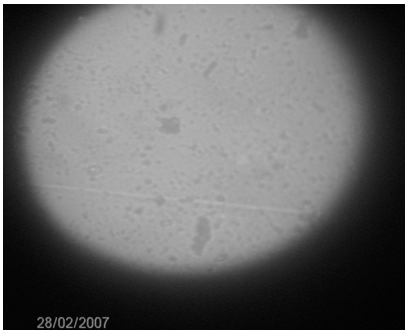
Tested sample *Reference sample*

Figure 7. *Sample 1 (5% AA)*



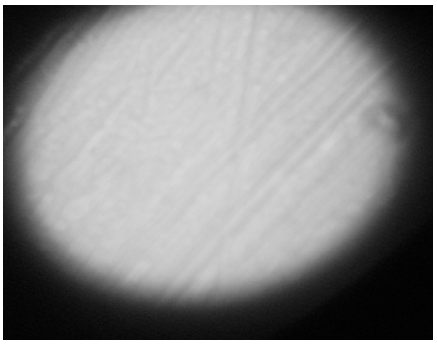
Tested sample *Reference sample*

Figure 8. *Sample 2 (10% AA)*



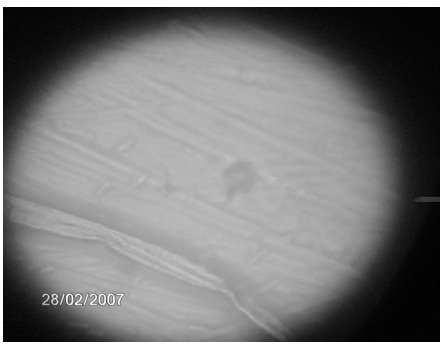
Tested sample *Reference sample*

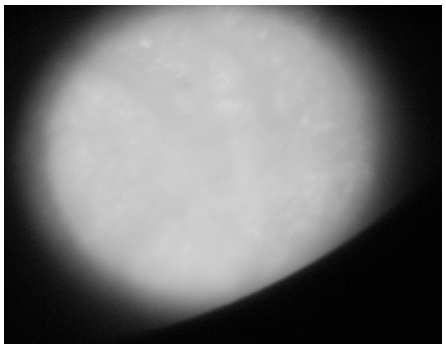
Figure 9. *Sample 3 (15% AA)*




Tested sample *Reference sample*

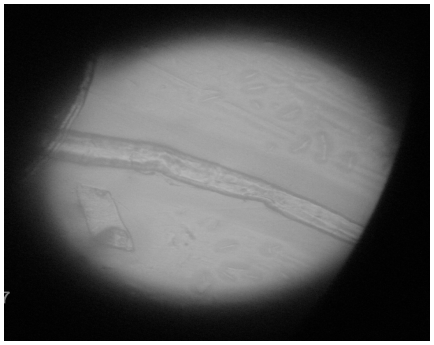
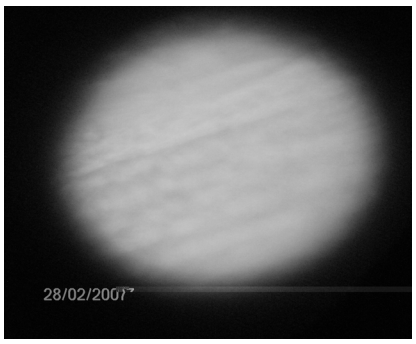
Figure 10. *Sample 4 (20% AA)*





Tested sample *Reference sample*

Figure 11. *Sample 5 (25% AA)*

Tested sample *Reference sample*

Figure 12. *Sample 6 (30% AA)*

Table 3. *The mechanical test results*

Sample no.	AA content (%)	3,000 cycles (1 h)	6,000 cycles (2 h)	10,000 cycles (3 h)
1	5	resistant	resistant	resistant
2	10	resistant	resistant	resistant
3	15	resistant	resistant	resistant
4	20	resistant	resistant	resistant
5	25	resistant	resistant	resistant
6	30	fissures	fissures	fissures
7	35	fissures	fissures	fissures

CONCLUSIONS

The proposed model utilizes a material based on hydrogel p(HEMA), which enable when is hydrated in physiological serum, to reproduce the mechanical and physical-chemical properties of the articular cartilage. It is notable that, the mechanical and tribological properties of hydrogel HEMA are modified as a function of the variation of physical-chemical properties.
The modification of hydrophilic character of HEMA using the acrylic acid demonstrates a good mechanical behavior, but up to 25% AA.
On the side of biomechanics, the hydrogels based on p(HEMA) demonstrate adequate visco-elasticity characteristics.

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