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Copolymerization of 2-Hydroxyethyl Methacrylate with Alkyl Methacrylates. Part IV. Mechanical Properties and Biocompatibility

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ABSTRACT

Mechanical properties of copolymers of 2-hydroxyethyl methacrylate with methyl methacrylate, ethyl methacrylate, and n-butyl methacrylate have been investigated using an Instron tensile tester. It was observed that the overall mechanical properties decrease as the ester alkyl group of alkyl methacrylate becomes bulkier. Biocompatibility of the copolymers was also investigated by implanting them subcutaneously in rats.

INTRODUCTION

Curiosity in polymers based on 2-hydroxyethyl methacrylate (HEMA) began with the pioneering work of Wichterle and Lim in 1960 [1, 2]. Since then many publications have cited the high level of biocompatibility of poly(2-hydroxyethyl methacrylate) (PHEMA). Cross-linked gels based on HEMA and ethylene glycol dimethacrylate (EDMA) have been

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used in medicine to replace damaged tissues. This is primarily due to their high chemical stability in living environments.

Although chemical and biological aspects of biomedical polymeric materials are undoubtedly of paramount importance, any individual application requires that the given material be formed into a certain shape having the necessary mechanical properties. The mechanical behavior of PHEMA has been reported in a number of papers [3]. The tensile strength of this polymer is comparatively low. Janacek et al. [4] have reported the stress-strain behavior of PHEMA samples swollen in water. The tensile properties of PHEMA cross-linked with varying weight percents of EDMA have been investigated by Ilavsky et al. [5].

The viscoelastic behavior of HEMA-BMA copolymers in the main transition region has been evaluated by Ilavsky and Kolarik [6]. Viscoelastic and equilibrium characteristics of PHEMA and its copolymers with propyl methacrylate, ethyl methacrylate, and diamino ethylacrylate have been measured in both the main transition and the rubberlike regions at three different ratios of the copolymer components [7]. In the present work the mechanical properties of various copolymers of HEMA with methyl methacrylate (HEMA-MMA), ethyl methacrylate (HEMA-EMA), and butyl methacrylate (HEMA-BMA) have been investigated. The purpose of the present study was to evaluate the biocompatibility of copolymer samples of HEMA-EMA and HEMA-BMA. The different physical forms of the same material can cause different tissue reactions [8-10]. To eliminate this variable from the study, all polymers were used in film form.

EXPERIMENTAL

Copolymerization and Polymer Films Preparation

The copolymerization of HEMA with MMA, EMA, and BMA was carried out in bulk under an nitrogen atmosphere using 0.2% benzoyl peroxide as an initiator at 70 ± 1°C. After 1 to 2 h, when the contents became viscous, the reaction was stopped. The flask was removed from the thermostat, cooled, and to it 0.5 mL DMF + 0.5 mL acetone was added. The contents, after shaking were poured onto a stretched cellophane film tied on one side of a hollow cylindrical glass disk. The disks were placed on a uniform glass plate leveled with the help of spirit level prior to casting of the polymer films. The films were dried for 3 to 4 d by slow evaporation of solvents.

Several copolymer samples were prepared by changing the mole fraction of alkyl methacrylate with respect to HEMA in the initial monomer feed.

Evaluation of Mechanical Properties

The load-elongation curves for the copolymer films of HEMA-EMA and HEMA-BMA were obtained using an Instron tensile tester with the following setting: Gauze length = 2 cm, cross-head speed = 2 cm/min, load = 5/10 kg. Dumbbell-shaped strips of 5.7 cm length and 5 mm width were cut from copolymer films with the help of a die. All the measurements were made at 25°C. The thickness of copolymer films was determined with the help of an "Essdiel thickness gauze." Five specimens were tested for each copolymer sample.

Biocompatibility Studies

Preparation of Sample for Implants

The polymer chips were sterilized prior to implantation by keeping them at 60°C for 10 to 12 h in a vacuum oven to eliminate traces of benzoyl peroxide initiator which might have been trapped as a trace impurity. They were then hydrated by overnight storage in saline (0.9%).

Complete removal of the monomer was ensured by two saline changes of 4-h each. Finally a washing with fresh saline was given before implantation.

Implantation in Rats

White Indian rats of both sexes weighing approximately 150 g were chosen for the present investigations. They were received and quarantined for a minimum of 1 week prior to surgical procedures. None of the rats showed any evidence of disease and were healthy. The animals were anesthetized with an intramuscular dose of 5 mg/kg thiopentone. The dorsal hair were clipped and the skin was prepped with Savalon (antiseptic solution).

A transverse cut, 1.5 cm long, was made on the dorsolateral side. The hydrated sterilized polymer chips were placed subcutaneously. The incision was closed by stitching with surgical thread. The wound was covered with iodine colloidion. The implants were taken out after 3, 7, and 30 d together with the surrounding tissues and investigated microscopically.

The material was fixed in a 10% formaline solution and, after fixation, the usual histopathology technique was used. Permanent slides were prepared by staining with hematoxylene and eosin.

RESULTS AND DISCUSSION

Effect of HEMA Content on the Mechanical Properties of Copolymers

The stress-strain curves of various HEMA-EMA and HEMA-BMA copolymers are given in Figs. 1 and 2, and the results are summarized in Table 1.

In the case of HEMA-EMA copolymers, the toughness and breaking elongation decreased as the HEMA content was increased in the copolymers. However, in HEMA-BMA copolymers no systematic trend was observed in breaking elongation as a function of copolymer composition. Toughness decreased as the HEMA content was increased in the copolymers of HEMA-BMA.

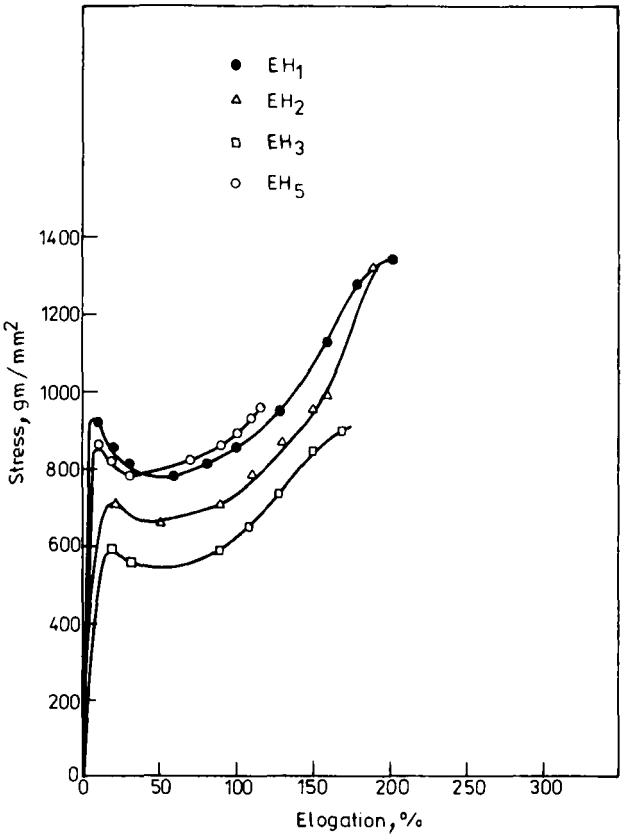

FIG. 1. Stress-strain curves for HEMA-EMA copolymers.

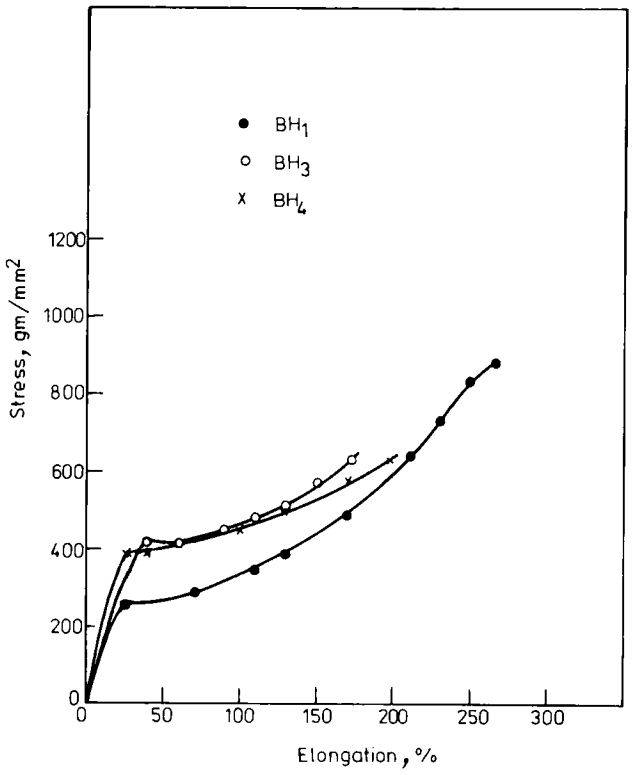

FIG. 2. Stress-strain curves for HEMA-BMA copolymers.

In the case of HEMA-MMA copolymers, such parameters as breaking elongation, toughness, yield stress, and initial modulus could not be calculated because of negligible elongation at break. This may be due to rigidity and better packing of polymer chains in these copolymers.

Effect of Alkyl Methacrylate on the Mechanical Properties of Copolymers

In the case of HEMA-EMA and HEMA-BMA copolymers, the breaking elongation is more but the breaking stress is less as compared to HEMA-MMA copolymers. This could be due to flexibility of the polymer chains of EMA and BMA copolymers. The glass transition temperatures of these copolymers [11] were found to be lower than those of HEMA-MMA copolymers.

From a comparison of breaking stress of HEMA-alkyl methacrylate copolymers, it is evident that mechanical properties decrease as the

TABLE 1. Mechanical Properties of HEMA-MMA, HEMA-EMA, and HEMA-BMA Copolymer Films

Sample	Mole fraction of HEMA in monomer feed (M_1)	Breaking stress (g/mm^2)	Yield stress (g/mm^2)	Breaking elongation (%)	Initial modulus (g/mm^2)	Toughness (g-cm/g)
MH_1	0.0887	1,693	-	-	-	-
MH_2	0.1796	2,500	-	-	-	-
MH_3	0.3689	3,478	-	-	-	-
MH_4	0.4669	3,600	-	-	-	-
MH_5	0.5676	754	-	-	-	-
EH_1	0.1028	1,341	841	203	7,139	45,419
EH_2	0.0048	1,343	885	188	3,267	45,161
EH_3	0.3065	903	933	170	3,858	33,700
EH_4	0.4072	1,304	1,543	87	17,391	26,008
EH_5	0.5080	959	950	113	7,142	30,666
BH_1	0.1287	893	314	266	2,980	31,266
BH_2	0.2497	1,018	1,170	115	11,095	29,577
BH_3	0.3617	635	472	171	4,470	28,194
BH_4	0.4693	624	343	198	3,109	31,594

ester alkyl group becomes bulkier in these copolymers. BMA copolymers have a lower breaking strength compared to EMA copolymers, and a similar trend is obtained for the tougness of these copolymer films.

A comparison of the data of the breaking stress of MMA/EMA/BMA copolymers with HEMA having a similar mole fraction of HEMA in the feed (sample MH_1, EH_1, and BH_1) reveals that the breaking stress value is a maximum (1693 g/mm^2) for HEMA-MMA, while for HEMA-EMA it is 1341 g/mm^2 and decreases to 893 g/mm^2 for HEMA-BMA copolymers. The above data indicate rigidity in the HEMA-MMA copolymer system compared to the HEMA-EMA and HEMA-BMA copolymer systems.

Biocompatibility Investigations. The HEMA:EMA (EH_3) sample was chosen for implantation. On Day 7 the polymer (Fig. 3) showed an inflammatory response to tissues. This was indicated by the presence of a large number of polymorphonuclear cells. Mononuclear cells were absent, thereby showing the nonimmunogenic nature of the polymer. Fibroblast cells were also present. On Day 30 the polymer showed reduced tissue inflammation, polymorphonuclear cells were absent, and the polymer was surrounded predominantly by fibroblast cells. A few giant cells were present. Distended capillaries with red cells and few mononuclear cells were also present (Fig. 4). These

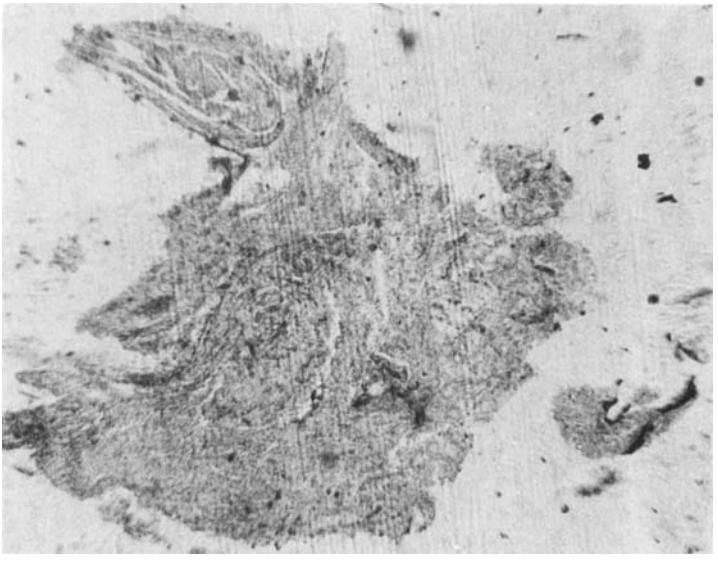

FIG. 3. Biological reaction of subcutaneous implantation (after 7 days) of HEMA-alkyl methacrylate copolymer.

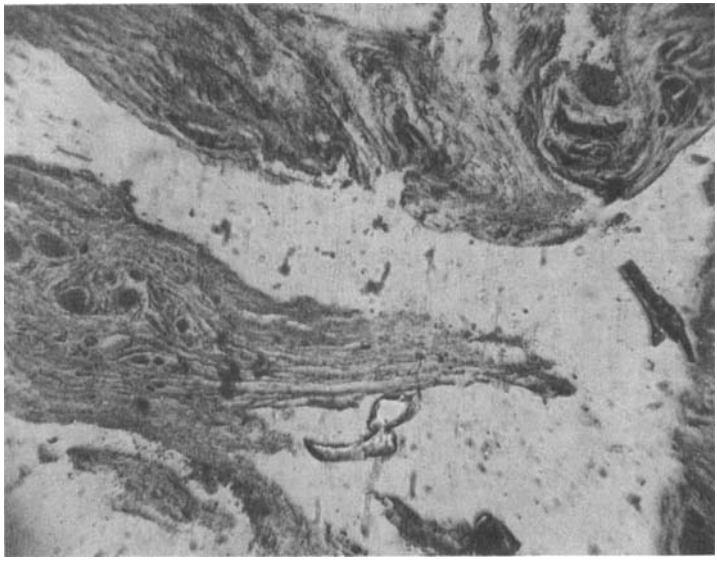

FIG. 4. Biological reaction of subcutaneous implantation (after 30 days) of HEMA-alkyl methacrylate copolymer.

results indicate the potential biocompatibility of HEMA-EMA and HEMA-BMA copolymers.

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