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RADIATION-INDUCED GRAFTING OF 2-HYDROXYETHYL METHACRYLATE ONTO POLYPROPYLENE FOR BIOMEDICAL APPLICATIONS. II. EVALUATION AS ANTIMICROBIAL SUTURE

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ABSTRACT

Antimicrobial sutures were prepared by the radiation grafting of 2-hydroxyethyl methacrylate (HEMA) monomer on polypropylene monofilament. It was found that the inherent characteristics of monofilaments are considerably influenced by the grafting of poly(HEMA). The grafting decreases the crystalline/amorphous ratio in the polymer by the incorporation of amorphous poly(HEMA) grafts. The tensile strength shows slight improvement for a low degree of grafting. However, higher grafting brings about a drastic deterioration in the strength of the sutures. Poly(HEMA) hydrogel grafted sutures were used for the immobilization of 8-hydroxy quinoline as an antimicrobial drug. It was found that modified sutures exert an antimicrobial behavior against *Staphylococcus aureus* bacteria due to the sustained release of the drug into the system.

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INTRODUCTION

The graft copolymerization of hydrophilic monomers offers an attractive way to modify polymers for biomedical applications [1–5]. The resultant material not only retains its original characteristics but also acquires additional properties of the grafted moiety. However, grafting results in a considerable change in the physical properties of the material, and that change determines its ultimate application in a system. Several authors have reported the grafting of hydrogels on the surface of various polymers in order to produce biocompatible materials [6, 7]. The modification of a polypropylene suture surface by the grafting of polyhydroxyethyl methacrylate hydrogels should not only provide a material with better compatibility, but also offer a system where immobilization of certain drugs may be achieved. Therefore, we felt it would be interesting to prepare a suture which would not only retain its inherent properties during clinical trials but would also exert antimicrobial activity for a prolonged period and thus prevent bacterial infections in postoperative wounds. However, grafting may influence the inherent characteristics of the suture material, and that may ultimately be reflected as a prominent factor in determining its surgical application. We have already reported the grafting of 2-hydroxyethyl methacrylate (HEMA) on polypropylene suture by using radiation techniques [8]. The present studies were carried out to evaluate the structural changes in polypropylene sutures induced by hydrogel grafting. The grafted sutures have been evaluated for their antimicrobial nature.

EXPERIMENTAL

Materials

The preparation of poly(HEMA) grafted polypropylene (PP) sutures was reported earlier [8]. Sutures with various poly(HEMA) contents were evaluated for their structure and drug release behavior.

8-Hydroxyquinoline (8-HQ), from E. Merck, India, was used as an antimicrobial drug for the immobilization on modified sutures.

A pure strain of *Staphylococcus aureus* was supplied by the Department of Microbiology, All India Institute of Medical Sciences, New Delhi.

Methods

Characterization

The diameters of sutures were measured by using a Projectina microscope. An average of 20 values was reported for all the samples.

Density measurements were made by using a Davenport density gradient column at 25 ± 2°C.

X-ray diffraction patterns of all the samples (intensity vs diffraction angle plot) were recorded in the range of 2θ, 10–34°, on a Phillips X-ray Diffractometer equipped with a scintillation counter by using the following experimental conditions: Filament current, 30 mA; voltage, 40 kV; scanning speed, 1°/mm; X-ray λ, 1.54 A.

The degree of crystallinity of PP was evaluated from the x-ray diffraction pattern by separating the crystalline and amorphous regions as reported in the literature [9].

The tensile properties of the original and grafted sutures (straight as well as single knotted) were determined by using an Instron tensile tester under the following conditions: Gauge length, 5 cm; cross-head speed, 10 cm/min; chart speed, 10 cm/min; full scale load, 2 kg; temperature, 20 ± 2°C; relative humidity, 65 ± 2%.

Immobilization

8-HQ was converted into its hydrochloride form as reported earlier [5]. The PP sutures were immersed in a 15% aqueous 8-HQ-HCl solution for 24 hours. The samples were removed, washed with distilled water, and dried under vacuum at 40°C for 2 hours. The percent weight add-on of the drug was calculated by:

$$\% \text{ add-on} = \frac{W_d - W_i}{W_i} \times 100$$

where W_d is the weight of the drug immobilized sample and W_i is the weight of the sample before immobilization.

Release of 8-HQ *in vitro*

Release of 8-HQ was studied by following its elution into distilled water. The samples (90 mg) were immersed in 5 mL distilled water, and the supernatent was replaced every day with fresh distilled water. The amount of drug ionomer released into the supernatent was determined by measuring the absorbance of the solution at 310 nm using a Hitachi 160 UV-VIS spectrophotometer.

Infection Studies

The resistance of various sutures to infection against *S. aureus* was studied *in vivo* by using female albino rats in the modified Edlich method [10]. Two different sutures (modified and unmodified) of 2.5 cm length were implanted separately under the skin parallel and equidistant from the vertebral column after shaving the desired area and sterilizing it with 70% alcohol. The designated number of bacteria was injected into the tissues around the middle of each suture. The number of bacteria at the implantation site varied in the range of 10^5–10^6. The sutures were analyzed for infection growth 4 days after implantation.

RESULTS AND DISCUSSION

The grafting of HEMA on polypropylene has been found to alter the inherent physical properties of the suture. The variation of diameter of the suture with the degree of grafting is presented in Fig. 1. The diameter does not show any change for low levels of grafting up to 6%. However, higher grafting is accompanied by an increase in the diameter of the suture. The density, on the other hand, shows a continuous increase with increasing grafting (Fig. 2). The figure shows that density

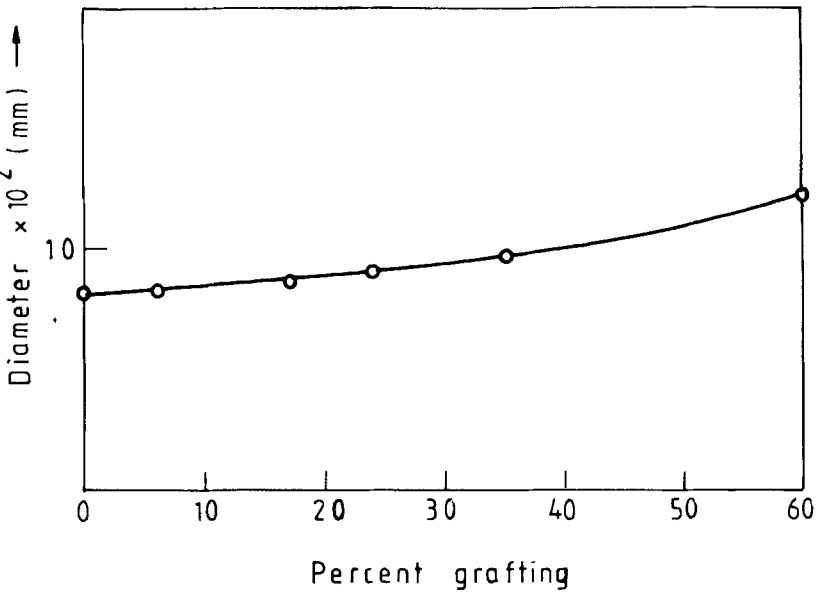

FIG. 1. Variation of diameter of polypropylene suture with percent grafting.

variation is not linear with respect to the graft add-on. Instead, it tends to level off for higher graft levels. The increase in density may be expected due to the higher density of grafted poly(HEMA) moiety. It appears that in the initial stages of grafting, poly(HEMA) fills in the interlamellar regions of the backbone polymer, contributing to the increase in the density of samples without any change in diameter. With the increase in grafting, more poly(HEMA) seems to be incorporated into the interlamellar regions of the polymer which ultimately results in the pushing apart of molecular chains of polypropylene backbone, leading to an increase in the diameter of the samples. The density, therefore, tends to deviate from a linear increase because of the increase in specific volume at higher grafting. Similar observations have been made for the grafting of methacrylic acid on polypropylene fibers [11].

The x-ray diffractograms of sutures are shown in Fig. 3. Crystalline reflections for unmodified and grafted polypropylene sutures occur at identical angles. No additional diffraction peak is visible in the diffraction pattern of the grafted samples. Moreover, the diffraction pattern of poly(HEMA) does not show any peak in the above range. These observations suggest that poly(HEMA) is present as an amorphous moiety, and the crystalline contribution to the diffractogram is therefore due to the polypropylene component in the grafted suture. The percent crystallinity calculated from the diffractogram is presented in Table 1. The results show that the crystallinity of the grafted suture decreases with an increase in the degree of grafting. In fact, this decrease in crystallinity may be termed "pseudo" in nature. The visible decrease in crystallinity is due to the relative decrease in the polypropylene component in the grafted suture. The crystallinity may therefore be corrected for the weight fraction of polypropylene in the copolymer according to the following equation:

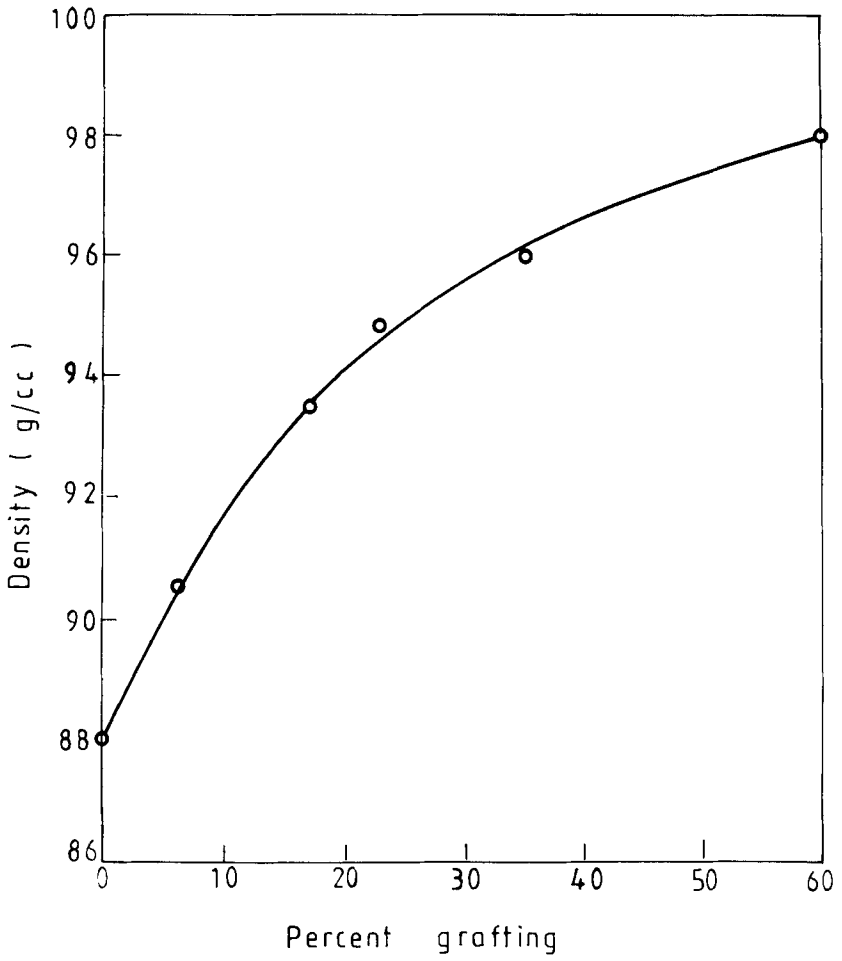

FIG. 2. Variation of density of polypropylene suture with percent grafting.

$$\text{corrected crystallinity } (X_{\text{corr.}}) = \frac{\text{apparent crystallinity}}{1/(1 + G)}$$

where G is the degree of grafting and $1/(1 + G)$ represents the weight fraction of polypropylene in the suture. The corrected crystallinity is plotted against the weight fraction of poly(HEMA) graft in the sample (Fig. 4). The crystallinity does not show any variation in the grafted sample. These observations suggest that the grafting of poly(HEMA) does not influence the inherent crystallinity of the polypropylene suture. The grafting takes place only in the amorphous region without disrupting the crystallites of the original polymer. The visible decrease in the overall crystallinity of various poly(HEMA) grafted sutures is due only to dilution of the crystalline region by the incorporation of amorphous poly(HEMA) in the copolymer.

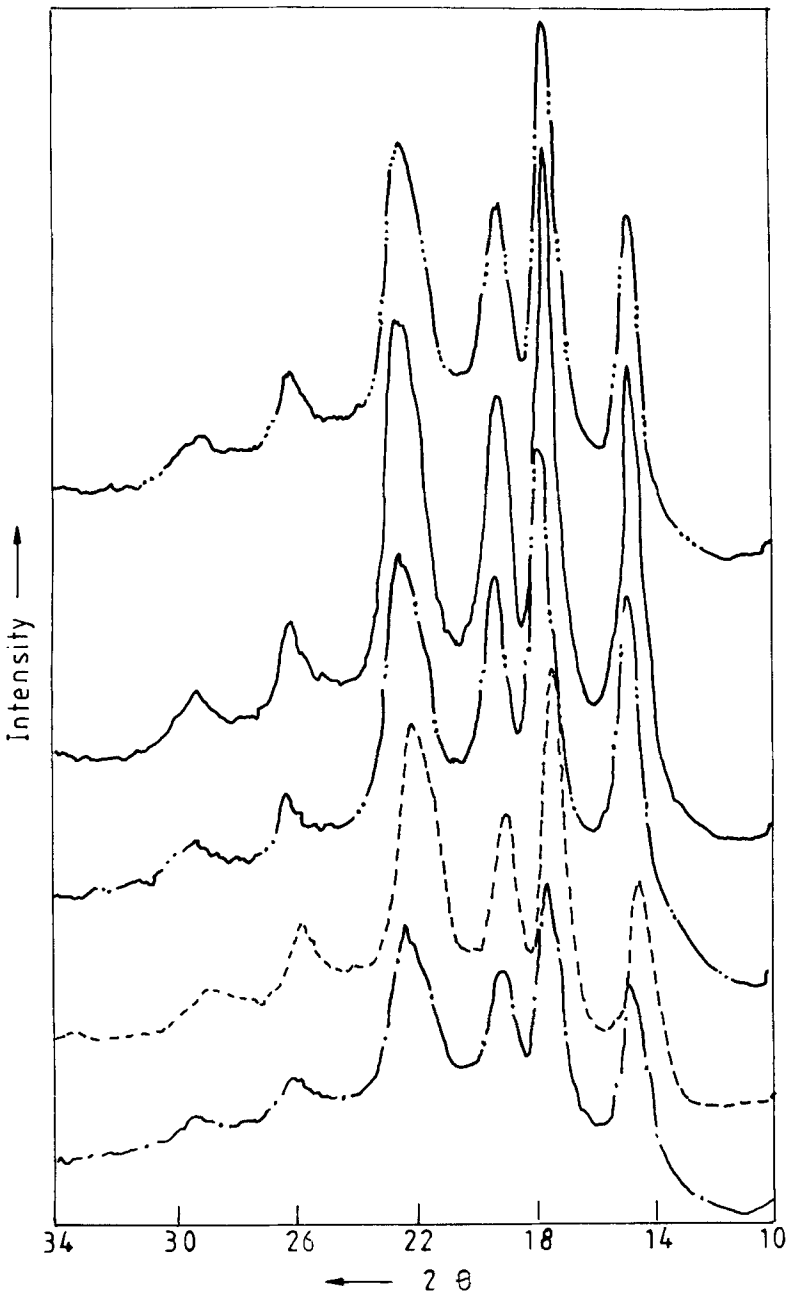

FIG. 3. X-ray diffractograms of unmodified (——) and grafted polypropylene suture with various poly(HEMA) content: (-·-·-) 17%, (-·-·) 35%, (- -) 40%, (-··-) 60%.

TABLE 1. X-Ray Data of Crystallinity of Original and Poly(HEMA) Grafted Polypropylene Sutures

Sample no.	Grafted poly(HEMA), %	Crystallinity, %
1	0 (original PP)	47.2
2	6	45.5
3	17	39.0
4	23	39.2
5	35	36.0
6	60	31.2

The tensile properties of polypropylene sutures were evaluated in straight and knotted forms. The variation of tensile strength and elongation with the degree of grafting is presented in Figs. 5 and 6. The results show that the tensile strength of the original suture is improved for low levels of grafting. A decrease in tensile strength was observed beyond 17% graft add-on. Grafted poly(HEMA) microstructures are dispersed in the amorphous region of polypropylene. It seems that these microstructures act as filler in the grafted sample and exert a reinforcing effect in

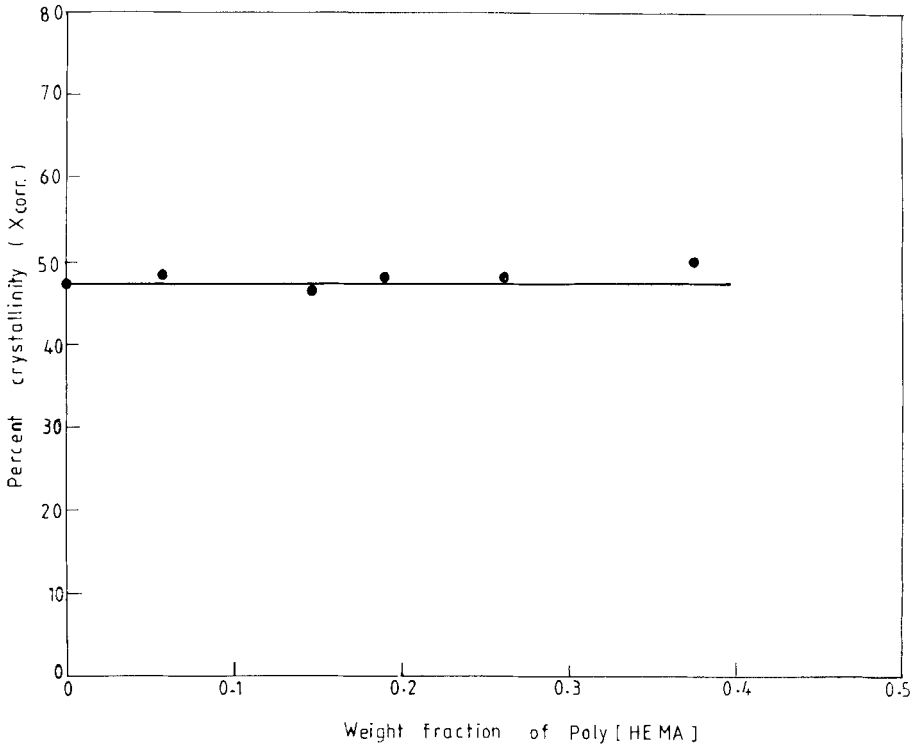

FIG. 4. Variation of crystallinity of polypropylene suture with weight fraction of poly(HEMA).

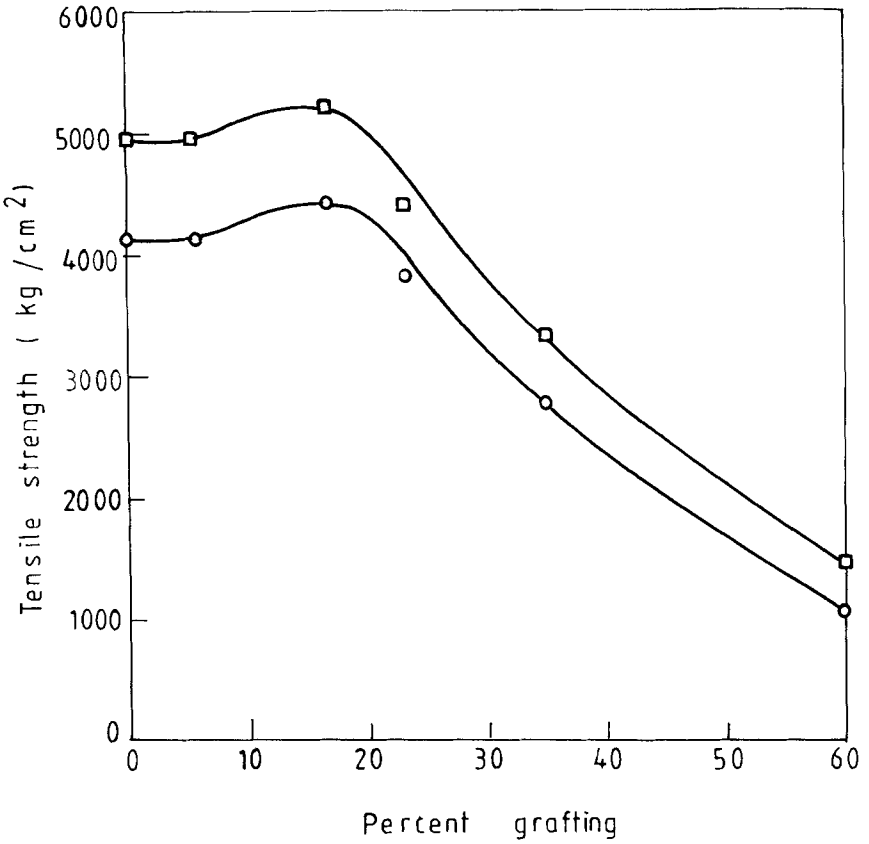

FIG. 5. Variation of tensile strength of polypropylene suture with percent grafting: (□) straight and (○) knotted.

the system, thereby enhancing the tensile strength of the suture. However, it appears that beyond 17% graft add-on, the compactness of chains in the suture is affected due to the pushing apart of molecular chains in the amorphous region as is evident from density and diameter studies. As a result, the mechanical strength decreases in spite of the reinforcement provided by the grafted microstructures. These studies are in good agreement with the studies of Osipenko et al. on the polyethylene-acrylic acid system [12]. Percent elongation, on the other hand, showed a continuous decrease with an increase in grafting in the suture. The generation of poly(HEMA) grafts over the polypropylene backbone results in a decrease in the mobility of molecular chains in the amorphous region. The net result is reflected in a continuous decrease in the percent elongation of the samples.

The results of immobilization of 8-HQ on various sutures are presented in Table 2. It is evident from the results that percent immobilization of drug increases with an increase in poly(HEMA) content in the suture. It seems that it is the polar interaction between the drug and the poly(HEMA) grafted suture that determines the degree of immobilization of drug in the sample. Grafting of HEMA imparts hydrophilicity to the suture by introducing polar hydroxyl groups, and this is re-

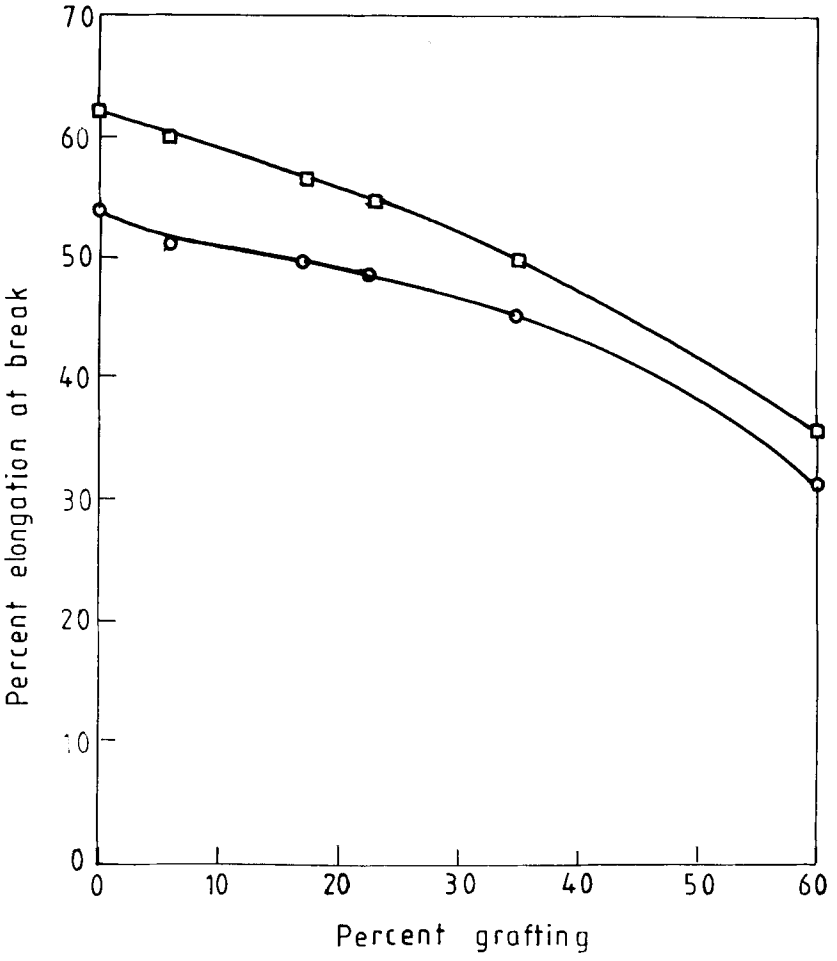

FIG. 6. Variation of percent elongation of polypropylene suture with percent grafting: (□) straight and (○) knotted.

TABLE 2. Amount of Immobilized 8-HQ Drug on Polypropylene Sutures

Sample no.	Grafted poly(HEMA), %	Amount of drug, %
A	0 (unmodified PP)	0
B	17	2.5
C	35	4.6
D	65	7.5

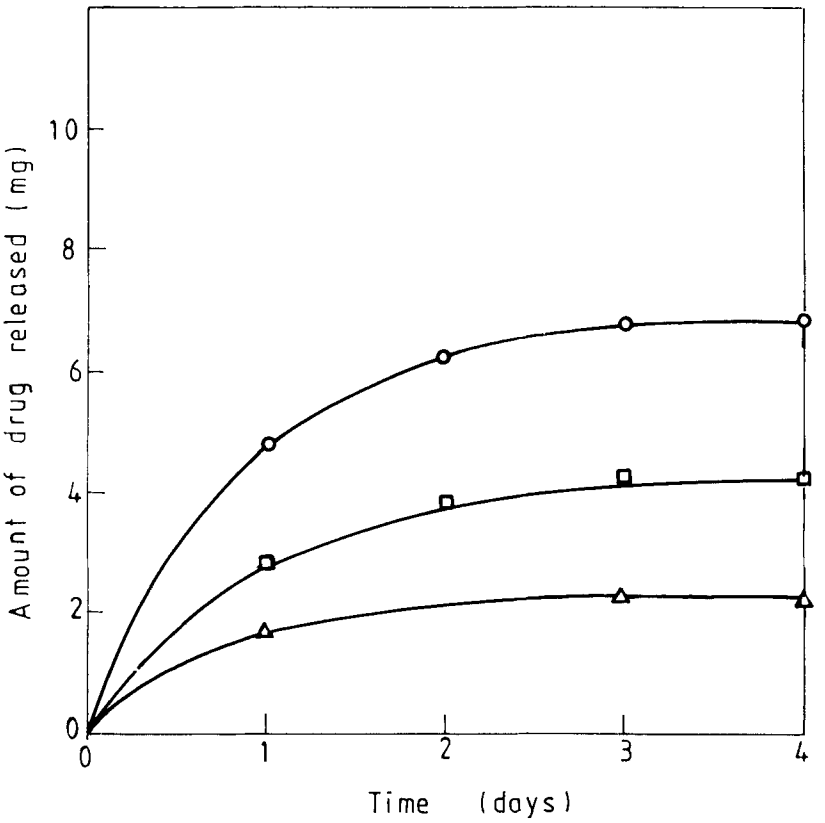

FIG. 7. Cumulative release of drug from various poly(HEMA)-grafted polypropylene sutures. Samples from Table 2: (△) B, (□) C, (○) D.

flected in the higher degree of drug immobilization with increasing graft levels. No drug immobilization was observed on an unmodified PP suture. This is essentially due to the lack of any polar site in the material upon which the drug could interact. The release behavior of all the samples is shown in Fig. 7. The sutures show a sustained release for a period of 4–5 days. However, the rate of release is faster in the initial periods for all the samples. This may be due to the release of an apprecia-

TABLE 3. Infection Studies on Poly(HEMA) Grafted Polypropylene Sutures Against *S. aureus*

Sample no.	Sample	Grafted poly-(HEMA), %	Degree of suppuration
1	Unmodified PP	0	Moderate infection
2	PP-*g*-poly(HEMA)	25	Moderate infection
3	PP-*g*-poly(HEMA)-8HQ	25	No infection

ble amount of drug adsorbed on the surface of the samples. The suture with the higher degree of immobilization showed a higher amount of drug released in the system. These studies suggest that a short-term release of drug may be achieved from hydrogel-grafted PP sutures.

The results on the infection studies against *S. aureus* are presented in Table 3. Polypropylene as well as poly(HEMA)-modified PP sutures show moderate infection. However, 8-HQ immobilized sutures did not cause any infection in the system as no suppuration was found surrounding the suture after the 4th day of implantation. These observations show that 8-HQ-modified sutures are antimicrobial in nature. It appears that the sutures allow sustained release of 8-HQ for a period of 4 days, which in turn inhibits the growth of bacteria in the system.

CONCLUSION

Surface modification of polypropylene sutures may be achieved by the grafting of poly(HEMA) through the use of a radiation technique. The overall properties of the suture are drastically influenced by the presence of poly(HEMA) grafts. In general, a lower level of grafting provides improvement in the tensile behavior along with the maximum retention of inherent properties. The hydrogel modified surface of the suture provides an excellent site for the immobilization of an antimicrobial drug.

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