Preparation and characteristics of dextran—methyl methacrylate graft copolymer

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A graft polymer of dextran–methyl methacrylate (MMA) has been prepared using ceric nitrate. The solubility, infra-red absorption spectrum and thermal behaviour of the graft copolymer together with those of dextran and PMMA have been studied. It was found that a hot-pressed film of the copolymer not only shows better water wettability and water absorbing power than PMMA but also thromboresistance, and can be shaped into a transparent contact lens having an affinity for tears and blood. High resolution electron scanning microscopy shows that the surface of the contact lens has a microheterogeneous structure, consisting of phase separated grains of about 0.2 μm in size which are distributed uniformly.

INTRODUCTION

Since graft polymerization of acrylamide onto poly(vinyl alcohol) in the presence of Ce^{IV} salts was first reported by Mino and Kaizerman[1], many attempts have been made to graft-polymerize vinyl compounds onto cellulose and starch[2,3]. Most reports in this field have been concerned with water-insoluble polysaccharides, and a few reports concerned with graft polymerization of vinyl compounds onto water-soluble polysaccharides[4]. In particular, papers on the graft polymerization of vinyl compounds onto dextran, a water-soluble neutral polysaccharide, have rarely been published[5].

For the purpose of the development of biocompatible materials, grafting of hydrophobic methyl methacrylate onto dextran, a hydrophilic polysaccharide used as a substitute for blood, has been carried out in the present experiment. Some of the properties of the dextran–MMA graft copolymers, obtained by treating the reaction products with hot water and acetone to remove unreacted dextran and side product PMMA have been studied, especially those material characteristics closely related to the application of the moulded copolymer plate to contact lenses and artificial blood vessels.

EXPERIMENTAL

Grafting of methyl methacrylate onto dextran and separation of grafted poly(methyl methacrylate)

Dextran* (average molecular weight 61 000, Meito Sangyo Co. Ltd) dissolved in distilled water and methyl methacrylate (MMA) were placed in a reaction vessel. After nitrogen was bubbled through the solution, grafting was initiated by ceric ammonium nitrate solution (0.012 mol %) in nitric acid (0.1 N). The mixture was reacted on stirring for a time needed to obtain various grafting compositions, and subsequently an aqueous solution of hydroquinone (0.1%) was added to terminate the reaction. The polymerization product was precipitated in methanol, washed thoroughly with hot water, filtered and dried in vacuum. A purified dextran–MMA copolymer was extracted from the crude copolymer using acetone.

Separation of the grafted PMMA was carried out as follows. The dextran–MMA copolymer was heated at 30°C for 2 h in 72% sulphuric acid, and then boiled for 40 min after the addition of water until the concentration of sulphuric acid became 2%. The undissolved solids (polymer) were filtered, washed with water and dissolved in acetone, reprecipitated with methanol and dried in vacuum.

The molecular weight (M_w) of the grafted PMMA chain obtained above was calculated from the intrinsic viscosity measured in acetone at 25°C using the equation $[\eta] = 0.96 \times 10^{-4} M_w^{0.67}$.

Preparation of plates of dextran–MMA copolymer and side product PMMA

The powder sample was placed in a stainless steel mould, and heated for 6 min maintaining the temperature inside at 200°C; the mould was then pressed for 5 min at 100 kg/cm^2, and cooled gradually using cold water. When the temperature of the mould fell below 50°C, the sample was removed from the press. The plates obtained were cut to the appropriate size, and subjected to material tests as shown in *Table 2*. Plates were also cut into a suitable size and thickness, and polished and processed on a bevel machine to form contact lenses.

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* Dextran 70 described in the pharmacopoeia of Japan, 1971

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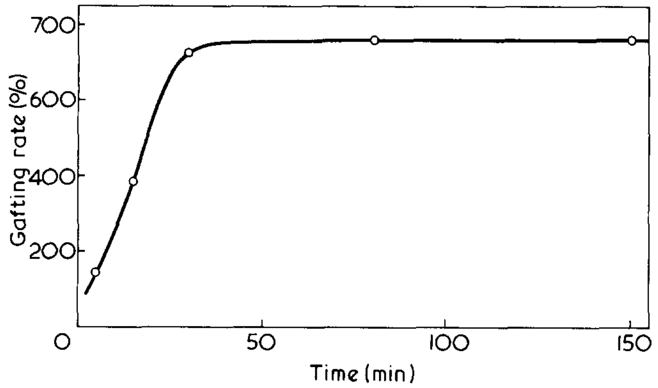

Figure 1 Relation between the grafting (%) and the reaction time. Polymerization conditions: dextran (M_w 61 000) 8 g, water 220 ml, initiator concentration 30 x 10^{-4} mol/l, 0.1 HNO_3 60 ml, MMA 60 ml, temperature 25°C

Measurement of infra-red absorption spectra and thermal analysis

I.r. measurements on the copolymer, PMMA and dextran were carried out by the KBr powder method. Differential scanning calorimetry (d.s.c.) was performed on powder samples of ~10 mg which were packed into aluminium sample pans, caulked by a close fitting lid, and heated at 10°C/min. The glass transition temperature was estimated from the point of intersection of a baseline with a tangential line from the anomalous displacement of the baseline toward the endothermic direction in each d.s.c. curve.

Solubility and material test

The solubility of a powdered sample in water and several organic solvents was measured at 25°C. A sheet sample of 1 mm thickness, shaped by the press, was used for the following tests. (a) Tensile strength: the sample used was rectangular (width 12.7 mm) and was examined at 23°C at a test speed of 5 mm/min and with an inter-chuck distance of 50 mm. (b) Bending strength: both ends of a sample 3 cm in width and 10 cm in length were supported in a longitudinal direction on a supporting stand with a span of 5 cm. The load exerted at the centre of the sample at breakage or at maximum load was measured. (c) Contact angle: after 30 sec the contact angle of a water drop (about 0.001 ml, prepared by a microsyringe) with the surface of sample was measured using a contact angle meter. (d) Water absorption: the difference in weight of samples before and after being immersed in distilled water at 37°C for 24 h was measured. (e) Vicat softening point: the measurement was made under a load of 5 kg at heating rate 50°C/h. (f) Rockwell hardness: the measurement was made with the M scale described in ASTM D785-62. (g) Blood clotting tests and scanning electron microscope observations. The blood clotting test was carried out using the method described by Imai and Nose[6], using ACD blood for the contact lenses made of the dextran–MMA copolymer, PMMA and silicate glass; the thrombogeneity of lenses was evaluated from the amount of thrombus formed at an appropriate interval of time after calcium chloride solution (0.1 M) was added to ACD blood placed in contact with the contact lenses.

The surface of the copolymer and of PMMA contact lenses, well-rinsed with methanol and coated with a thin layer of Au–Pd in vacuum to prevent charging of the surface when the electron beam strikes the specimen, were examined with a field emission scanning electron microscope (*FE–SEM*), using a Hitachi S700. Photographs were taken with an accelerating voltage of 15 kV, a beam current of 10^{-12} Å and without tilt.

RESULTS AND DISCUSSION

The relation between the grafting (%)* of dextran–MMA copolymers and the reaction time is shown in *Figure 1*. The grafting increases almost linearly in the range of reaction time less than 30 min and then an equilibrium is reached. At the same time we have found that the grafting increases with decreasing molecular weight of dextran (the backbone polymer).

Table 1 shows the solubility of the dextran–MMA graft copolymer with a grafting of 700% in water, acetone and various other solvents compared with those of the starting material dextran and the side chain PMMA. The graft copolymer was not only insoluble in water, acetone, pyridine, tetrahydrofuran and benzene, but also in dimethylsulphoxide, a common excellent solvent for dextran and PMMA. Furthermore, the copolymer remained unchanged in appearance and insoluble after heating in boiling water for 1 h. From the above facts, it seems reasonable to conclude that the dextran–MMA copolymer is in part crosslinked with graft PMMA.

The plate consisting of dextran–MMA graft copolymer was transparent, whereas that of a polymer blend of dextran and PMMA, moulded in a hot press in same way, became turbid. *Table 2* shows the results of material tests for the dextran–MMA graft copolymer (DM), for which the grafting was 700%, and the chain PMMA (PM). The tensile strength of the graft copolymer decreased about 16% compared with that of PMMA, but there were no significant differences between the graft copolymer and PMMA in the bending strength, the Vicat softening temperature and the Rockwell hardness. Otherwise, the water absorbing capacity of the graft copolymer was four times larger than that of PMMA and the contact angle of the former was fairly small compared with that in the latter.

Figure 2 shows the infra-red absorption spectra of dextran–MMA copolymer, the starting material dextran and side chain

Table 1 Solubility of dextran–MMA graft copolymer, dextran and PMMA

Solvent	Copolymer	Dextran	PMMA
Water	Insoluble	Soluble	Insoluble
Acetone	Swelling	Insoluble	Soluble
Pyridine	Insoluble	Swelling	Insoluble
Benzene	Insoluble	Insoluble	Soluble
Tetrahydrofuran	Insoluble	Insoluble	Soluble
Methanol	Insoluble	Insoluble	Insoluble
Dimethyl sulphoxide	Insoluble	Soluble	Soluble

Table 2 Material tests for dextran–MMA graft copolymer (DM) and PMMA

	Sample	
	DM	PMMA
Tensile strength (kg/cm^2)	420	500
Bonding strength (kg/mm^2)	10.1	8.6
Vicat softening temperature (°C)	99	92
Water absorbing capacity (%)	0.8	0.2
Contact angle (°)	61	71
Rockwell hardness	81	83

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* Grafting (%) = (weight of MMA graft-polymerized/weight of dextran in the copolymer x 100

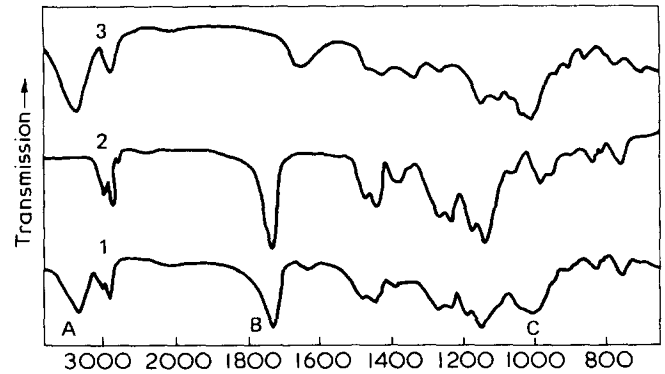

Figure 2 Infra-red absorption spectra. 1, dextran–MMA copolymer; 2, PMMA and 3, dextran

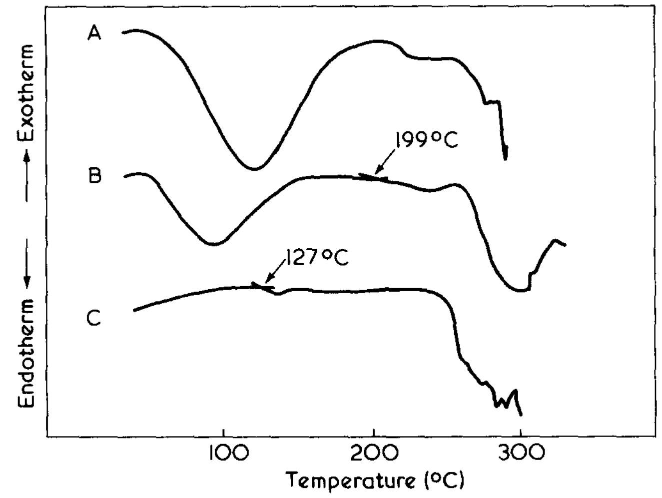

Figure 3 D.s.c. curves for dextran, dextran–MMA copolymer and PMMA. A, Dextran; B, copolymer; C, PMMA

PMMA. The spectrum of the copolymer has some characteristic absorption bands, e.g. the bands at around 3410 cm^{-1} (A), at 1725 cm^{-1} (B) and at 1000 to 1150 cm^{-1} (C) are attributed to O–H stretching vibrations of dextran, the carbonyl group of PMMA and the pyranose ring of dextran, respectively. Comparison of this spectrum with those of dextran and of PMMA shows that the spectrum of dextran alone has no absorption band at 1720 cm^{-1} due to the stretching vibration of C=O, and that the spectrum of PMMA alone has no absorption band at 3410 cm^{-1}.

Figure 3 shows d.s.c. curves for the dextran–MMA copolymer, having grafting of 230%, and for the starting material dextran and the side chain PMMA. The glass transition temperature (T_g) which appears as a step or a small kink in the d.s.c. curve is observed near 199° and 127°C for the copolymer and PMMA, respectively, and whereas for dextran the broad and strong endothermic peak (similar to the thermal features of starch having α linkages[7]) is observed in the range 50° to 200°C (peak temperature at 120°C) and complicated decomposition of the dextran occurs at temperatures above 220°C. For the copolymer the endothermic peak relating to the molecular constitution of dextran appears in the range 50° to 160°C (peak 94°C). *Figure 4* shows the value of T_g obtained for copolymers having different percentages of grafting, where the molecular weight of the dextran used was constant (M_w 61 000). T_g values decreased linearly with an increase in the grafting, which corresponds to increase in the molecular weight of side chain, PMMA, and that of the sample having grafting of 1050% is close to the value of T_g (115°C) for isotactic poly(methyl methacrylate)[8]. This fact indicates that the reaction product consisting of dextran and MMA is not an aggregate mixture of dextran and PMMA, but a copolymer of dextran and PMMA. In the preparation of plates or vessels made of the graft copolymer by a hot press moulded technique, it should clearly be preferable to change the moulding temperature according to the grafting.

Figure 5 shows the comparison of thrombus formation curves for DM lens (A), silicate glass (B) and PMMA lens (C) in a blood clotting test, where the percentage of thrombus formed is normalized so that the saturated values for glass, which has been used as a standard material, become 100%. In the case of the DM lens, a firm clot of blood was rarely formed in tests up to 10 min after calcium chloride solution was added to ACD blood, and in addition the maximum amount of thrombus formed is about 6/10 as large as that for PMMA. It also becomes evident that the PMMA lens enhances the coagulation of ACD blood. It can therefore be said from this experiment that the DM lens has an antithrombogenic character whereas the PMMA lens exhibits a promotive thrombogenic one.

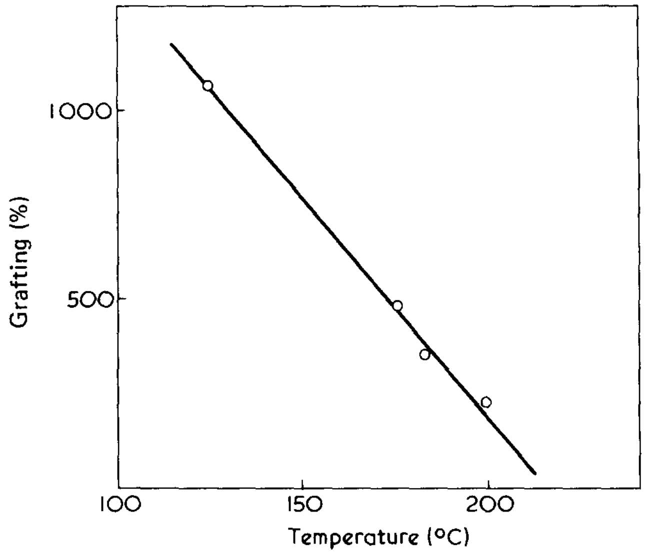

Figure 4 Relation between grafting (%) and the glass transition temperature in dextran–MMA copolymers having different grafting rate

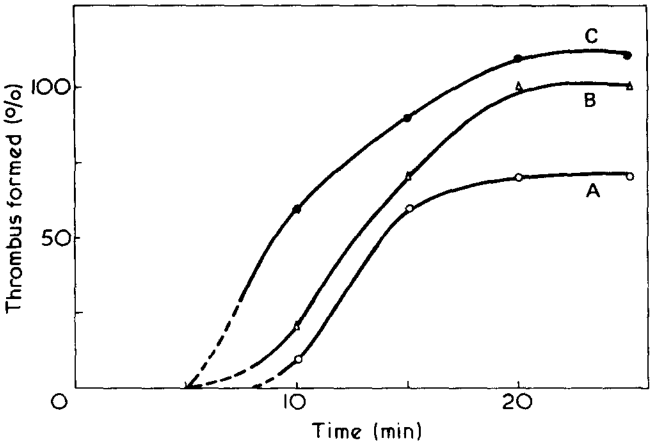

Figure 5 Thrombus formation curves. A, Dextran–MMA graft copolymer lens; B, glass; and C, PMMA. Storage time of blood: 19 days

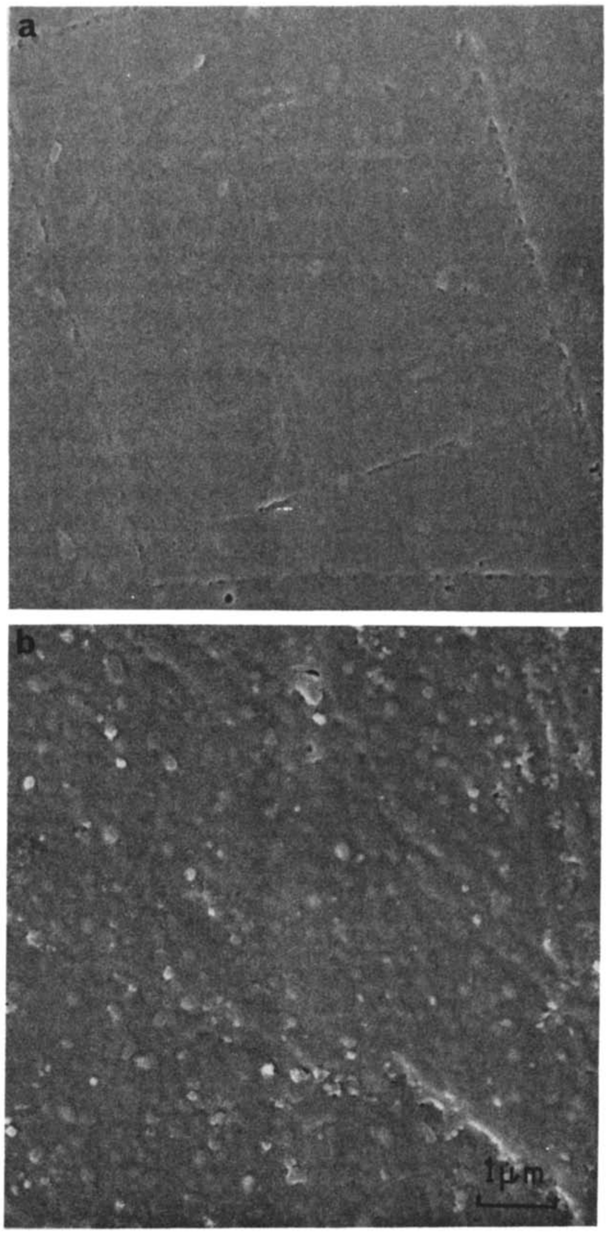

Figure 6 Scanning electron micrographs showing the surface appearance of contact lenses. (a) Lens produced with PMMA and (b) dextran–MMA graft copolymer. Micro-phase-separated structure appears for (b)

When considering the compositional similarity of tears and plasma, the above results and the physical characters of the graft copolymers (given in *Table 2*) suggest that the graft copolymer provides a contact lens which may be worn by persons who suffer from discomforts such as bloodshot eyes, burning feelings in the eyes and blurred vision when provided with conventional contact lenses, mainly produced with methyl methacrylate resin. It was confirmed that contact lenses produced with the graft copolymer of dextran and MMA gave no irritation to the eye.

High resolution scanning electron micrographs of the surfaces of contact lens produced with PMMA (a) and the dextran–MMA graft copolymer (b) are shown in *Figure 6*. There are remarkable differences in the microstructure although polished traces (slanting stripes) can be seen to be present on the surfaces and are especially clear for the sample of (a). The PMMA lens appears to be continuous with a smooth surface, whereas dextran–MMA graft copolymer lenses give rise to coarse surfaces and have a microphase separated structure, similar to phase separated structure in oxide glasses[9]. Since the microphase grains (average size $\sim$0.2 μm) in the micrograph (b) are dissolved in acetone, it is presumed that they consist mainly of PMMA components.

It is known that the surface uneveness of samples and/or their microheterogeneity (0.1–2.0 μm) bring satisfactory results for the application of graft copolymers such as poly(vinyl alcohol) PVA–MMA and PVA–acrylonitrile to as biocompatible materials[10,11]. The DM lens has a good affinity for tears as well as blood compared with the PMMA contact lens. Therefore, it is clear that the surface microheterogeneous structure of the DM lens as well as the water-soluble properties of dextran play a major role in the compatibility for tears and blood.

It seems reasonable to conclude from the present study that the graft copolymer of dextran and MMA is a biological plastic having biocompatibility.

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