Studies in polymer surface functionalization and grafting for biomedical and other applications*

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A simple and inexpensive treatment for surface functionalization and grafting carried out under mild aqueous conditions and suitable for prefabricated medical devices, has been developed. The two stages are performed separately; the first is hydroxylation by a peroxy compound, particularly a peroxydisulfate or peroxymonosulfate, in aqueous solution with strong nitrogen purging; and the second is grafting of a vinyl monomer by the conventional ceric ion technique. Types of polymer studied include polypropylene, polystyrene, polyacrylonitrile, polyurethanes, aliphatic polyesters, nylons, aromatic polyesters and polycarbonates. Surface properties of the substrate polymers may be greatly modified by this treatment. To illustrate possible applications for covalent coupling of bioactive molecules to polymers we have attached the blood-anticoagulants heparin and hirudin to the polyester Ecdel and to polystyrene, respectively. The products were highly bioactive.

(Keywords: surface functionalization; grafting; medical devices)

INTRODUCTION

The processes of polymer functionalization and grafting are becoming increasingly important in advanced materials technology, particularly in medical applications when it is necessary to impart some specific property to the polymer, e.g. to increase its haemocompatibility, or reduce its complement activation. When prefabricated medical devices have to be treated it is generally necessary to use mild conditions and aqueous media as far as possible. In spite of a voluminous literature, processes operating under these conditions and suitable for common polymers such as polypropylene and polystyrene have not been reported. Conventional methods of surface activation include photoinitiation with the aid of a sensitizer such as benzophenone[1-3], ozonization[4], flaming the surface[5], use of high-energy radiation[6] and plasma treatment[7]. Exposure to the discharge through a gas at low pressure from a laboratory Tesla coil is included in the last group. This is a way of generating surface radicals suitable for polymer grafting[8,9]; it has been used for biomedical applications by Iwata *et al.*[10].

Confronted by a problem involving grafting to polypropylene, we thought it worthwhile to re-examine some simple polymer reactions and to explore their use in grafting, both for biomedical and other applications.

The facts that most polymers contain hydrogen atoms which are abstractable by free radicals and that oxygen-centred radicals are most effective in reactions of this type provided obvious starting points. Further, both the literature and experience indicate that functionalization and grafting are separate processes and that 'one-pot' procedures in which the two are combined are likely to lead to the generation of large quantities of unwanted homopolymer. These considerations suggested the use of peroxydisulfates or peroxymonosulfates as radical sources in aqueous solution; both are, of course, well known as initiators of free-radical polymerization and as oxidizing agents. The thermal decomposition of potassium peroxydisulfate was studied by Bartlett and Cotman[11] who proposed the following reactions, in aqueous solution, pH 8, at 80°C:

$$^{-}O_3SO\text{–}OSO_3^{-} \rightarrow 2SO_4^{\cdot -} \quad \text{(a)}$$

$$SO_4^{\cdot -} + H_2O \rightarrow HSO_4^{-} + \dot{O}H \quad \text{(b)}$$

$$2\dot{O}H \rightarrow H_2O + \tfrac{1}{2}O_2 \quad \text{(c)}$$

$$SO_4^{\cdot -} + CH_3OH \rightarrow HSO_4^{-} + \dot{C}H_2OH \quad \text{(d)} \quad (1)$$

Subsequently Kolthoff and Miller[12], using ^{18}O-labelled water, showed that in the pH range 7.2–13, 96–100% of the oxygen generated in the reaction originates from the water, as required by the mechanism of the reactions shown in (1). These reactions appeared to offer the possibility of functionalizing polymers such as polypropylene by hydrogen abstraction by hydroxyl followed by combination of the resulting macroradical with a second hydroxyl radical [reaction (2)]. The hydroxylated polymer thus formed might then be submitted to grafting by the familiar ceric ion technique or otherwise reacted. If successful, this procedure would be a simple two-stage grafting process [reactions (2)

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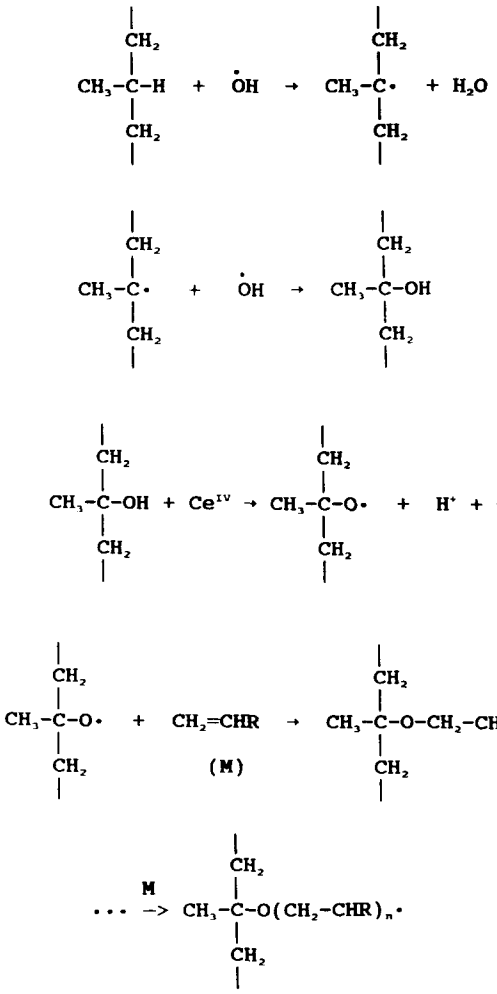
and (3)], operating in aqueous solution:



(2)

(3)

The present paper is an account of some of the possibilities offered by this technique for functionalizing and grafting which we have successfully applied to a number of medical devices including blood oxygenators, blood filters, cannulas and catheters. In the following we refer to the two stages as hydroxylation and grafting, without wishing to imply that the processes are as simple as those shown in reactions (2) and (3). Some comments on the component reactions are presented later.

So far as we known no similar work has been reported in the literature, which is rich in patents in this area[13]. Early work with polypropylene, for example, was aimed at introducing peroxide groups; thus it was shown[14] that the powdered polymer in slurry form stabilized by surfactant, when heated at 100°C in aqueous potassium peroxydisulfate in the presence of oxygen under pressure, forms a peroxide if the surfactant is cationic, but not if it is anionic. Graft copolymers could be prepared from this on addition of a metal redox system and a vinyl monomer. In most of the reports we have seen in the literature the monomer to be grafted was present from the start of the reaction.

EXPERIMENTAL

Materials

Sources of supply of the main materials are shown in *Table 1*.

Methods

Functionalization. The polymers were treated with an aqueous solution of the oxidizing agent, generally potassium peroxydisulfate, with nitrogen purging, for periods varying from 10 to 60 min at temperatures in the range 70–100°C. Concentrations of oxidizing agent were

Table 1 Sources of materials

Material	Form	Supplier
Polypropylene	Film, 0.013 mm in thickness	Goodfellow
Polypropylene	Microporous hollow fibres, 200 μm in diameter	Polystan
Polystyrene	Granules: $M_w = 100\,000$	BDH
Polyacrylonitrile	Powder	Aldrich
Aliphatic poly(ether urethane) (Tecoflex)	Granules	Thermomedic
Aliphatic polyester (Ecdel)	Film	Kodak
Poly(ethylene terephthalate)	Granules	Goodfellow
Polycarbonate	Film, 0.075 mm in thickness	Goodfellow
Peroxydisulfates		Aldrich
Potassium peroxymonosulfate (Oxone)		Sigma
Other peroxy salts		Aldrich
Heparin, $M_w = 20\,000$, sodium salt		Fluka
Jeffamine		Fluka
Acrylamide		BDH
Recombinant hirudin		Ciba-Geigy
Ceric ammonium nitrate		BDH
3-Aminopropyl methacrylamide		Kodak
Poly(*p*-vinyl phenol)	Powder: $M_w = 1500$–7000	Polysciences
1,1′-Carbonyl dimiidazole		Aldrich
Chlorosulfonyl isocyanate		Aldrich
Oligo(dT), labelled with ^{32}P		Amersham International

from 5 to 20% (w/v). Polymers were then removed, washed copiously with hot water and dried in vacuum.

Grafting to functionalized polymers. After the above treatment polymers were submitted to grafting reactions in aqueous solution with the aid of the ceric ion technique[15]. Our standard conditions were: ceric ammonium nitrate (2×10^{-3} M) in nitric acid (0.04 N) at 50°C under a stream of nitrogen. Typically, acrylamide, methacrylic acid and 3-aminopropyl methacrylate were used in these experiments.

Characterization. Molecular weights of some polymers were determined before and after treatment with the peroxydisulfate solution to assess degradation. Measurements were made by RAPRA. Tensile properties were measured with the aid of a Nene Universal Mechanical Tester M5. *FT*i.r. spectra of some grafted polymers were also recorded.

RESULTS AND DISCUSSION

The polymers studied included: polypropylene, polystyrene, polyacrylonitrile, an aliphatic polyester (Ecdel), a poly(ether urethane) (Tecoflex), a polycarbonate, poly(ethylene terephthalate) and several polyamides.

Polypropylene hollow fibres

Bundles (18 cm × 4 cm) of microporous hollow fibres were heated under reflux with an aqueous solution of potassium peroxydisulfate under the conditions shown in *Table 2*. Weight- and number-average molecular weights and tensile measurements, before and after hydroxylation, are shown.

According to these data, treatment at 100°C with concentrations of peroxydisulfate up to 10% w/v and reaction times up to 20 min causes no serious degradation or deterioration in properties of the hollow fibres. These results lead us to believe that the degradative effect of our treatment is less severe than that normally encountered with ozonization. Whereas the latter generates polymer peroxides we have been unable to detect any peroxide formation during the peroxydisulfate treatment, either by the potassium iodide test or by addition of aqueous ferrous sulfate and acrylamide in an attempt to set up a redox polymerization.

Acrylamide was grafted to hydroxylated polypropylene hollow fibres prepared as indicated for sample number 4 in *Table 2*. Standard grafting conditions were used; the acrylamide concentration was 20% w/v, the reaction time 3 h, and samples of 0.2 g of hydroxylated polypropylene were immersed in 100 ml solution. Grafted specimens were removed and washed copiously with water to remove ungrafted polymer. The (hydrated) hydrophilic polymer prepared in this way had a surface so slippery that handling was difficult. It was strongly coloured by Trypan Blue whereas the initial polypropylene was unaffected.

Estimates of the extent of grafting were made by direct weighing. Samples were prepared as described, except that the initial hydroxylation was continued for 30 min with a range of grafting times. Grafted samples were washed for prolonged periods (>24 h) with water and dried at 50°C in vacuum. Results are shown in *Table 3*.

The increasing rate of grafting which sets in after ~3 h points to a proliferating polymerization. We believe this behaviour is connected with the non-uniform nature of hydroxylation, a process by which very polar substituents are introduced into a non-polar substrate. The first few stages of substitution are the most difficult; as the process continues new groups tend to enter in the proximity of those in place, so that clumping occurs. In the regions of high hydroxyl density grafting is relatively fast and chain entanglement becomes important, being favoured by the high propagation coefficient of acrylamide ($\approx 18\,000$ dm^3 mol^{-1} s^{-1} at

Table 3 Extents of polyacrylamide grafting to polypropylene hollow fibres

Grafting time (h)	Weight increase (% w/w)
2	16.0
3	23.3
4	>76.5

In a control experiment with untreated fibres no grafting was obtained in 4 h

Table 2 Properties of polypropylene hollow fibres hydroxylated at 100°C

Sample no.	Concentration of $K_2S_2O_8$ (% w/v)	Reaction time (min)	$10^{-3}M_w$	$10^{-3}M_n$	Stress at peak (MPa)	Strain at peak (%)
1	Control	Control	567	86	36	630
			566	85	42	807
2	5	10	450	80		
			447	80		
3	5	60	259	58	31	545
			258	56	29	498
4	10	10	423	84	49	746
			422	77	42	792
5	10	20			30	747
					33	686
6	10	60	361	64	24	464
			359	63		

25°C), chain transfer and radical combination. Microgel established in this way becomes strained as propagation continues, until ultimately chain rupture takes place with generation of new radicals, which initiate and so give rise to proliferation. These processes are basically similar to those described by Barb[16], who first proposed chain rupture by this mechanism. Experimental evidence was subsequently adduced by Breitenbach[17].

An illustration of this phenomenon is provided by the scanning electron micrographs in *Figure 1*. *Figure 1a* is a control showing the surface of the untreated hollow fibres. *Figure 1b* refers to the surface grafted with polyacrylamide. (Note the numerous small protuberances corresponding to regions of high grafting.) A very large protuberance is evident in *Figure 1c*.

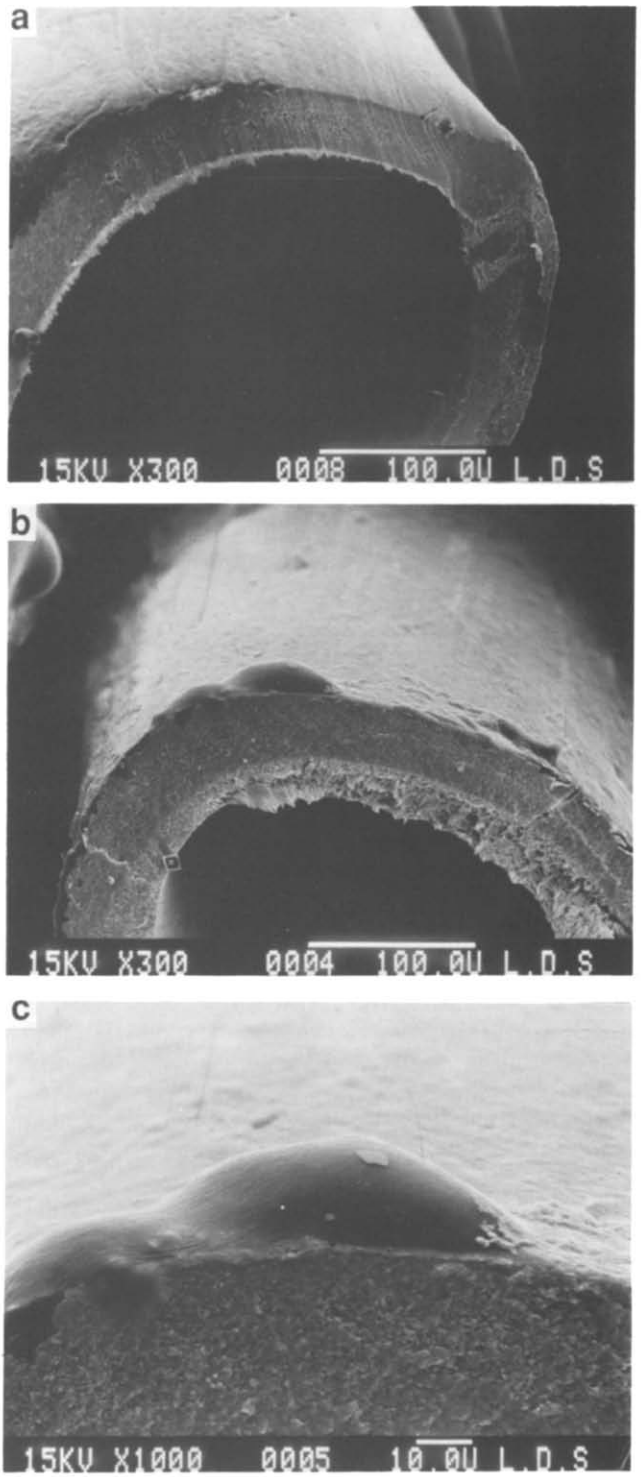


Figure 1 Scanning electron micrographs of polypropylene microporous hollow fibres from blood oxygenators: (a) original; (b) after hydroxylation (3 h) and grafting with polyacrylamide (*Table 3*). Note numerous protuberances; (c) portion of (b) enlarged to show protuberance

Polypropylene films

Films were hydroxylated at 80°C with aqueous potassium peroxydisulfate (10% w/v) for 2 h. After this treatment their mechanical properties were unchanged. Hydroxylated films were grafted with acrylamide as described, then washed copiously with water. The resulting material was extremely hydrophilic and was stained strongly by Trypan Blue. The i.r. spectrum of a grafted film in *Figure 2* shows very strong absorption at 3351, 3199 (amide A) and 1662 cm^{-1} (amide I). No such absorption was observed when an unhydroxylated film was treated in the same way.

To examine possible effects of any additives in the films, untreated specimens were extracted in toluene for 3 days. They were washed with acetone and finally with water, then hydroxylated and grafted. The results were identical with those outlined above, indicating that any material extracted by toluene had no influence on the process.

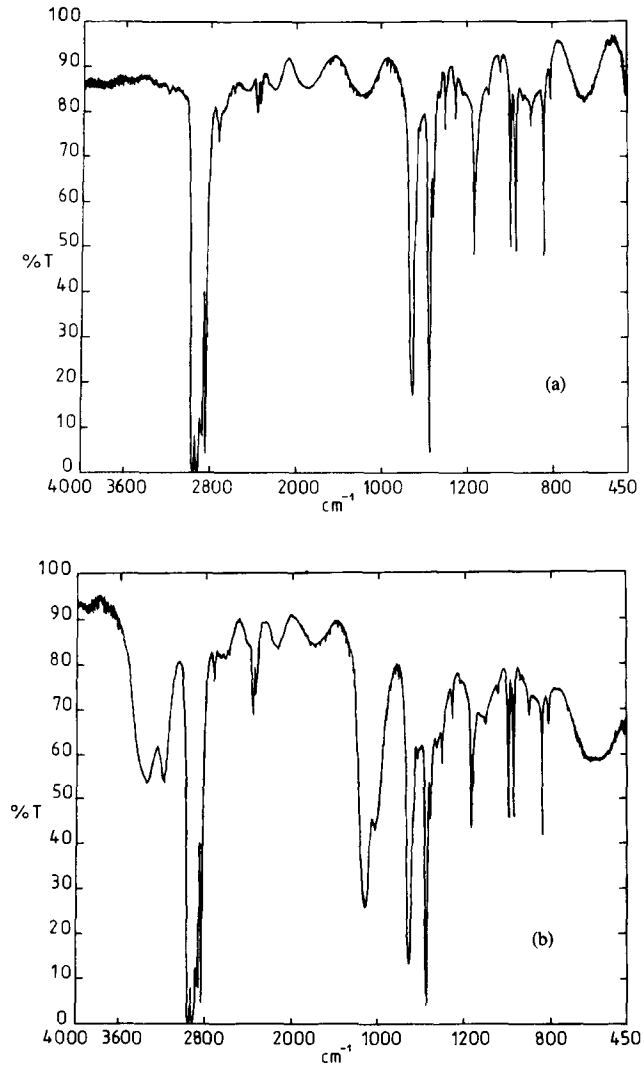
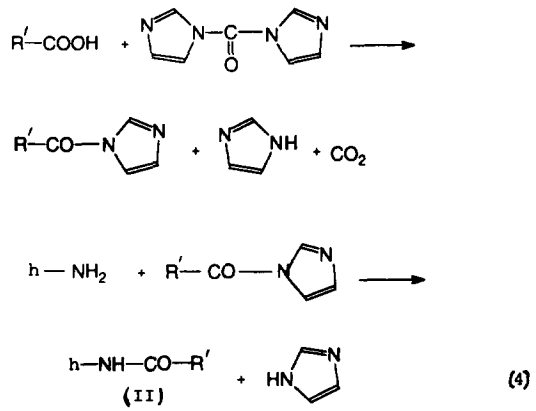


Figure 2 *FT*i.r. spectra of polypropylene films: (a) original; (b) after grafting (3 h) with polyacrylamide

Polystyrene films

Polystyrene is readily functionalized by our method. This would be anticipated in view of the relative stability of the benzyl-type radical formed by abstraction of an α-hydrogen atom. Grafting may subsequently be carried out with the aid of the ceric ion technique as already described. Substitution in aromatic nuclei may also occur following electron abstraction, but is unlikely to lead to grafting (see later).

The haemocompatibility of polystyrene is rather poor, but it may be improved by coupling the polymer to a suitable antithrombotic agent. To illustrate the scope of the present technique we describe the covalent coupling of polystyrene to hirudin, the thrombin-specific inhibitor from the leech. The structure of recombinant hirudin shown in *Figure 3*[18] indicates that the molecule containing 65 amino acid residues has three lysine residues of which the amino groups may be used for coupling. A film of polystyrene cast from toluene solution was dried carefully in vacuum and treated in aqueous potassium peroxydisulfate (10% w/v) at 80°C for 2 h. After grafting with polyacrylamide (3 h) and washing it was heated with 1 N NaOH at 60°C for 15 min to (partially) hydrolyse the polyacrylamide. The product, containing carboxyl groups, gave a positive test with Toluidine Blue[19]. A portion (10 cm^2) of the dry film was activated by reaction with 1,1-carbonyl diimidazole (CDI) by immersion in a solution of 2 g CDI in 50 ml acetonitrile for 4 h at 25°C. It was then washed with acetonitrile and dried in vacuum. The activated film was allowed to stand overnight at ambient temperatures in a solution of 10 mg of recombinant hirudin in 1 ml of sodium borate buffer (pH 8.70). Coupling occurs to amino groups in hirudin as shown in reaction (4) (hirudin = h-NH_2) giving the adduct (II).

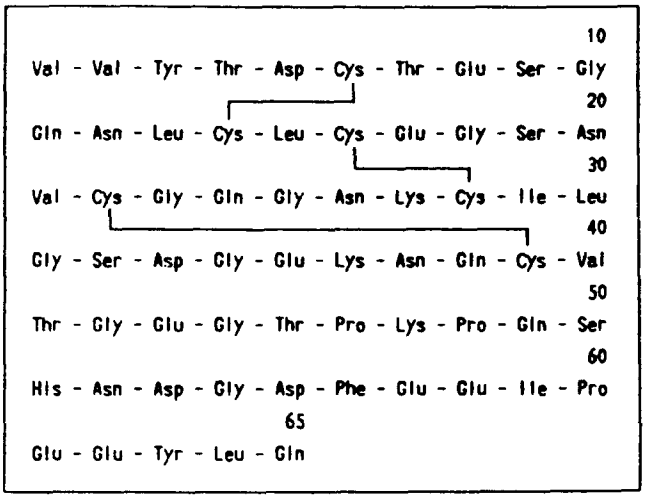


(4)

After prolonged washing with water, the film was submitted to measurements of the partial thromboplastin time (PTT) to assess its bioactivity. Portions of film (1.5 cm × 0.5 cm) were immersed in 200 μl of human blood plasma together with 200 μl of platelet substitute; 200 μl of 25 mM calcium chloride solution were then added. Clotting times were measured from the addition of the calcium chloride, with results presented in *Table 4*. The haemocompatibility of the polymer films has been greatly increased by hirudin coupling.

Ecdel

Ecdel is an aliphatic polyester containing 1,4-cyclohexane dimethanol units in the backbone. Films were hydroxylated



(I)

Figure 3 Sequence of amino acids in recombinant (desulfato) hirudin (h)[18]. This differs from natural hirudin only in the absence of a sulfate group from Tyr 63

Table 4 Blood plasma clotting times for polystyrene films grafted with hirudin

Sample	PTT (s)
Control (activated polystyrene film)	300
Film grafted with hirudin	1300

Table 5 Extents of polyacrylamide grafting to hydroxylated Ecdel at 40°C

Grafting time (h)	Weight increase (% w/w)
1	30.4
2	49.3
3	60.0

Control: unhydroxylated Ecdel, 0.33% (3 h)

at 80°C with aqueous potassium peroxydisulfate (10% w/v) for 2 h, then washed, grafted with acrylamide (20% w/v) at 40°C and washed with water for at least 24 h. Reaction times in one series were in the range 10 min–3 h; grafted films were dried in vacuum after washing. The 10 min film showed very strong absorption in the i.r. region corresponding to the N–H and C=O stretching bands already referred to. Weights of polyacrylamide grafted to three films are given in *Table 5*.

Proliferating polymerization is much less in evidence during grafting in these systems than with polypropylene hollow fibres. This finding is consistent with the mechanism outlined since hydroxylation is probably less heterogeneous with Ecdel and initial microgel formation is less likely.

Hydroxylation is confined to surface layers and would not be expected to cause significant overall degradation of the film. This is confirmed by the data in *Table 6*.

Covalent coupling of Ecdel to the blood anticoagulant heparin has been carried out with the aid of our technique. For this purpose a macromer of heparin carrying reactive methacrylate-type double bonds (III)[20] was used.

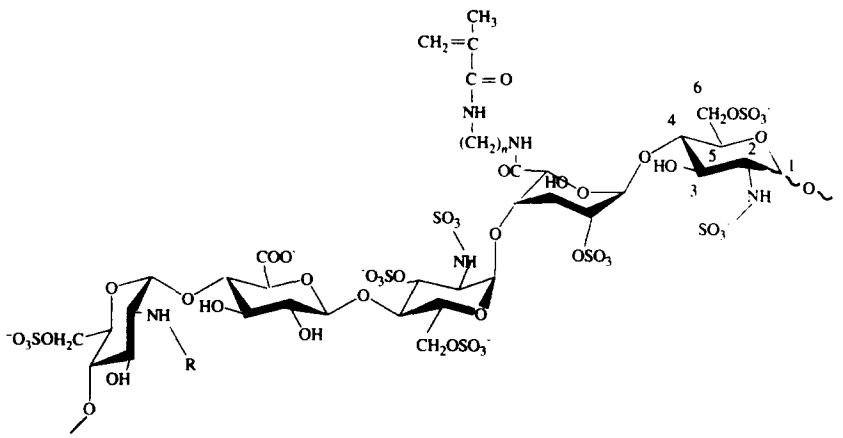
Table 6 Properties of hydroxylated Ecdel films

Sample no.	Concentration of $K_2S_2O_8$ (% w/v)	Reaction time (min)	$10^{-3}M_w$	$10^{-3}M_n$	Stress at peak (MPa)	Strain at peak (%)
1	Control	Control	117	37	31	488
			114	38	32	503
2	5	10	117	36		
			107	41		
3	5	60	112	37		
4	10	10	113	39	26	387
			117	38	32	514
					32	506
5	10	60	118	37	30	509
			188	37	27	427
					30	530

The structure shown includes a short section of the heparin chain (actually an active site for complexation with antithrombin III), coupled through amide bond formation to a basic methacrylate monomer of type $CH_2{=}C(Me)CONH(CH_2)_nNH_2$. The whole molecule will, of course, carry a number of these substituents, depending on the reaction conditions. In the present experiment we used heparin with a molecular weight of $\approx 20\,000$, with 34 double bonds per molecule and $n=3$.

Table 7 Blood plasma clotting time for grafted Ecdel films

Sample	PTT (s)
Ecdel film, untreated	330
Ecdel film grafted with acrylamide	460
Ecdel film cografted with heparin and acrylamide	1400

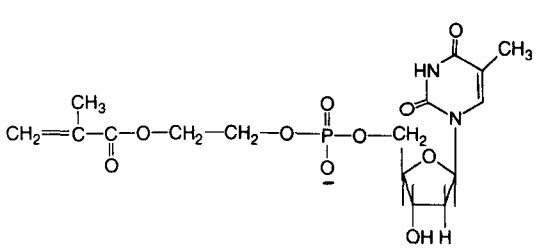


(III)

With a high molecular weight macromer the concentration of double bonds is low (0.085 M in this experiment) and cografting with acrylamide (or other small monomer) promotes propagation. Hydroxylation of an Ecdel film (4 cm × 3 cm) was performed at 100°C in 10% w/v aqueous potassium peroxydisulfate for 4 h. For subsequent cografting 0.1 g acrylamide with 0.3 g heparin macromer and Ce(IV) (2×10^{-3} M) were reacted at 25°C for 2 h in 0.04 M HNO_3, total volume 6 ml. After very copious and prolonged washing of the film, its bioactivity was assessed by the standard PTT test previously mentioned. Two controls were used — untreated Ecdel and Ecdel grafted with acrylamide without heparin. Results are presented in *Table 7* and show that the thrombogenicity of the film has been markedly reduced by the heparin coupling. Note that in this system radicals originating from OH groups in heparin[21] probably play some part in the coupling by interacting with those growing from the hydroxylated Ecdel.

Polyacrylonitrile

This polymer may readily be functionalized by the method outlined. We have employed the procedure to couple deoxythymidine-5'-monophosphate (dT) (IV) to a polyacrylonitrile membrane electrostatically — spun as described in reference 22. A portion of the film (3 cm × 2 cm) was functionalized by treatment with 10% aqueous potassium peroxydisulfate at 80°C for 1 h followed by copious washing with hot water. It was then ready for coupling to the monomer (V).



(V)

(V) was synthesized by esterifying (IV) with 2-hydroxyethyl methacrylate (HEMA) in anhydrous pyridine solution with dicyclohexyl carbodiimide as coupling agent. (V) was attached covalently to the functionalized polyacrylonitrile membrane with the aid of the standard grafting procedure. In one experiment a portion of membrane (3 cm × 2 cm) was used with 20 mg (V) and 100 mg acrylamide in 10 ml solution. Grafting was continued for 3 h at 40°C. The membrane was then washed copiously with water and dried in vacuum. The product contained 0.13% phosphorus, corresponding to 1.86% w/w of (V), assessed by radioactivity measurements. In a control experiment, a portion of unfunctionalized membrane incubated in an aqueous solution of labelled (IV) exhibited negligible radioactivity after washing. As in the heparin system, a portion of the coupling probably originates from reactions of hydroxyl groups in the species being coupled to the membrane, in this case 3'OH groups in (IV).

By applying the type of analysis in reference 22 we may estimate the effective area (EA) occupied by each molecule of (V), assuming that only the outer layers of the membrane are involved. The total surface area thus estimated is 1.13×10^5 cm^2 g^{-1} (diameter of individual fibres = 3 μm), so that we find:

EA = (total surface area of membrane)/

(number of molecules coupled) = 44 Å^2

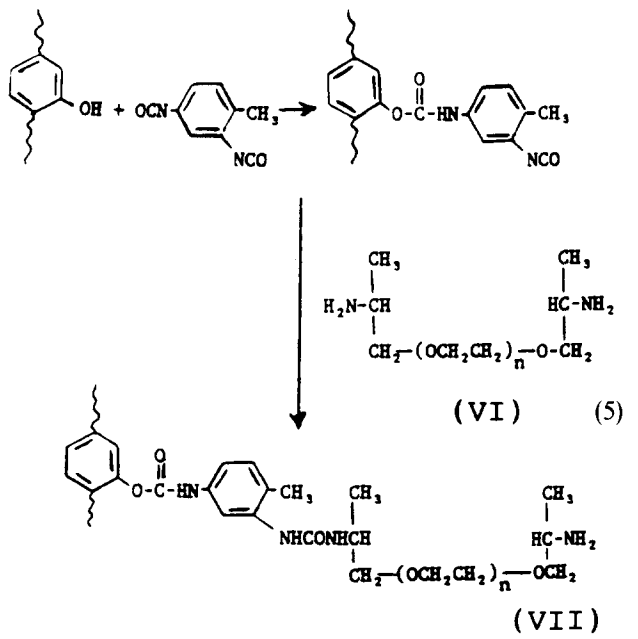
If layers below the surface are involved, obviously the EA per molecule will be larger.

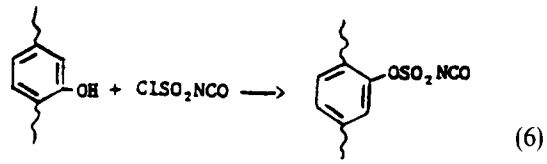
Oligo(dT), with 24 nucleotide residues per molecule, has been coupled similarly. There are no terminal hydroxyls in this compound (which carries terminal phosphate groups) so that only single-point attachment to the membrane can arise. In control experiments radioactivity measurements indicated zero absorption of oligo(dT) by the unfunctionalized membrane.

Aromatic polyesters — polycarbonate and poly(ethylene terephthalate)

These polymers may be functionalized by the method described but subsequent grafting is more difficult and we have had to resort to non-aqueous solutions. This may arise in part from a reluctance of phenolic derivatives to interact readily with the ceric ion according to reaction (3). We have carried out model experiments to examine the possibility of grafting polyacrylamide to poly(*p*-vinyl phenol). A saturated solution of poly(*p*-vinyl phenol) (M_w = 1500–7000) was prepared by shaking 1 g of the polymer with 15 ml water overnight; 5 ml of the filtered solution were mixed with 10 ml water, 1 g acrylamide and ceric ammonium nitrate and nitric acid to give the standard concentrations. No polymerization was observable after heating the degassed mixture for 4 h at 50°C, and the colour arising from the Ce(IV) remained unchanged. These results, particularly the latter, suggest no initiation had occurred; the lack of polymerization could also have been due to inhibition or retardation. Two further tests were performed with 4,4'-azobis(4-cyanovaleric acid) as initiator; one solution contained initiator plus acrylamide plus poly(*p*-vinyl phenol) while the other (control) had only monomer and initiator. The experiments revealed that the polyphenol is a strong retarder of acrylamide polymerization.

Hydroxylated polycarbonate or polyester may be reacted with isocyanates and hence further functionalized as in the following examples. Polycarbonate films (5 cm × 5 cm) were refluxed with aqueous potassium peroxydisulfate for 5 h then washed copiously with water and dried. They were then treated with tolylene 2,4-diisocyanate at 50°C for 24 h. After washing with petroleum ether the product was reacted with excess of bulk jeffamine [*O,O*-bis(2-aminopropyl)ethylene glycol 400] (VI) and formed a basic polymer [(VII), reaction (5)] which was found to dye strongly with Eosin-Y. The original polycarbonate, treated with the isocyanates and jeffamine as above, failed to give any stain with dye. Similar results were obtained with poly(ethylene terephthalate).





In an alternative procedure the hydroxylated polymer was reacted at 90°C for 2 h with excess chlorsulfonyl isocyanate[23] to introduce isocyanate groups by reaction (6). After washing with petroleum ether and reaction with excess jeffamine, the products were again washed with petroleum ether. The final materials dyed strongly with Eosin-Y, whereas unhydroxylated poly(ethylene terephthalate) after treatment could not be dyed in this way.

The overall mechanical properties of the polymers did not appear to be changed by these treatments. We are presently investigating alternatives to avoid use of non-aqueous media. The technique described may, however, be useful in some cases.

Reaction mechanisms

In reaction (2) it is assumed that functionalization of polymers occurs solely through interaction with ȮH radicals. The system is, however, complex and contains three reactive species ȮH, $SO_4^{\cdot}$, $\bar{O}_3S$–O–O–SO_3^-, so that

Table 8 Rate coefficients (k) for hydrogen atom abstraction from alcohols (pH 4.4–4.8)

Alcohol	$10^{-7}k$
CH_3OH	2.5 ± 0.4
CH_3CH_2OH	7.7 ± 2.2
$(CH_3)_2CHOH$	8.5 ± 3.0

it would be surprising if $\dot{O}H$ alone contributed. Bartlett and Cotman[11] reported that if methanol is present in the solution of potassium peroxydisulfate at 80°C, reaction (1b) is suppressed by the competitive process:

$$SO_4^{\cdot-} + CH_3OH \xrightarrow{k} HSO_4^- + \dot{C}H_2OH \qquad (7)$$

Flash photolysis studies by Dogliotti and Hayon[24] on aqueous solutions of potassium peroxydisulfate have provided quantitative information on these competing reactions. The interaction of $SO_4^{\cdot-}$ with water [reaction (1b)] has a pseudo first-order rate coefficient of 10^3–$10^4\ s^{-1}$ in the pH range 9.76–10.41; the rate increases with increasing pH probably on account of the following reaction:

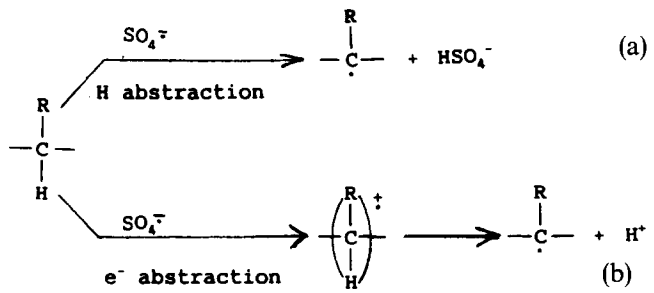
$$SO_4^{\cdot-} + \bar{O}H \rightarrow SO_4^{2-} + \dot{O}H \qquad (8)$$

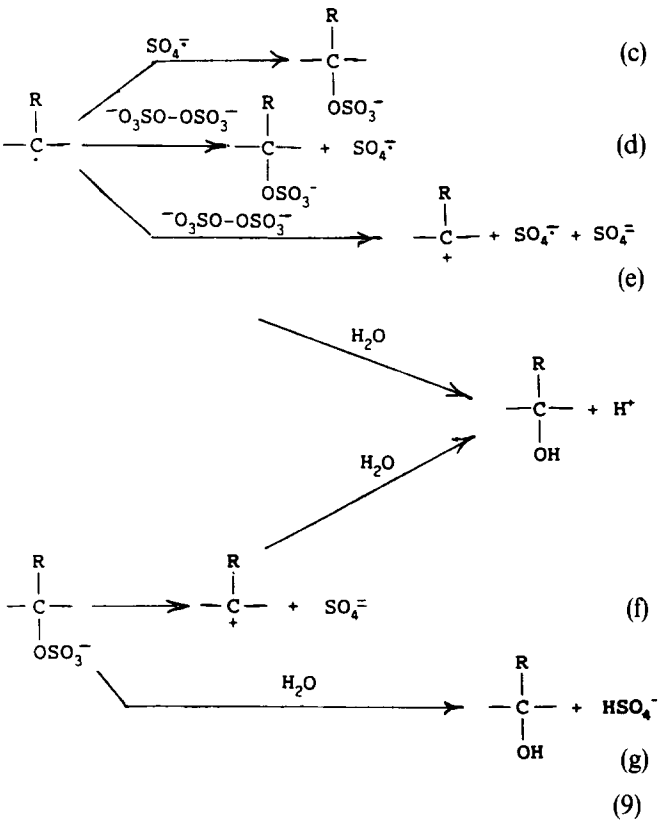
A similar estimate of the rate coefficient of reaction (1b) was made by Pennington and Haim[25] on the basis of published kinetic and flash photolysis studies.

The hydrogen abstraction reaction, reaction (7), is much more rapid and is not sensitive to pH. Values of second-order rate coefficients for a series of alcohols given in *Table 8* suggest that attack on the polymers in our systems by the sulfate anion-radical may well be important.

Reactions of the sulfate anion-radical have been studied by Norman and his colleagues[26], who used a rapid-flow system with e.s.r. detection. They concluded that $SO_4^{\cdot-}$ can react with organic compounds in at least three ways: (i) by hydrogen abstraction from saturated carbon; (ii) by addition to double bonds or aromatic systems; and (iii) by electron abstraction from compounds with sufficiently low ionization potentials. The anion radical behaves as an electrophilic species (owing to its tendency to form SO_4^{2-}) as indicated by its behaviour in (ii) and (iii).

The reactions shown in (9) are possible reactions leading to hydroxylated polymer, based entirely on sulfate anion-radicals and peroxydisulfate dianions, without intervention of hydroxyl. The relative importance of reactions (9a) and (9b) depends on the nature of the substituent R; if R = CH_3 reaction (9b) would appear very unlikely, whereas with polystyrene (R = Ph) this reaction may contribute, since the benzene ring is able to support the positive charge. Reactions (9c), (9d) and (9e) show possible reactions of the polymer radicals initially formed.





Two features of our systems are important: (i) the systems are heterogeneous, and conditions near the polymer surface differ from those in the bulk solution; and (ii) in spite of vigorous nitrogen purging some oxygen [formed in reaction (1c)] must remain in solution. The formation of peroxy radicals from polymer radicals and oxygen is very fast and would occur in the absence of rapid competitive reactions. Our failure to detect peroxide in the products probably indicates the presence of significant concentrations of reactive species (other than oxygen) near the polymer surface (see following section). Reactions (9d) and (9e) are obviously of interest in this connection and are analogous to the oxidation of the radical $\dot{C}H_2OH$ [formed in reaction (7)] by peroxydisulfate, which has been shown by Norman *et al.*[26] to be very fast (at pH = 1). The rates of reactions (9d) and (9e) depend on the character of the substituent R, presumably increasing with the stability of the carbonium ion product in (9e).

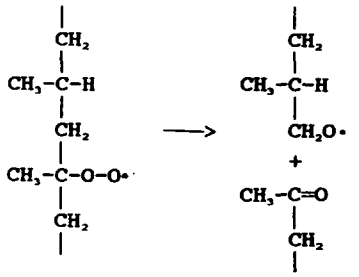
We have examined several types of peroxy salt and found the order of effectiveness in hydroxylating polystyrene as shown:

$$K_2S_2O_8 \approx Na_2S_2O_8$$
$$\approx KHSO_5 > NaClO_4 > NaIO_4 > NaBO_3 4H_2O$$

Fenton's reagent (at 25°C) is also effective, but has a low activity on this scale, just above that of $NaBO_3 4H_2O$. Thus it seems clear that hydroxyl radicals are able to bring about hydroxylation [reaction (2)]; these experiments therefore support the view that in the procedure described in this paper both $SO_4^{\cdot-}$ and OH contribute.

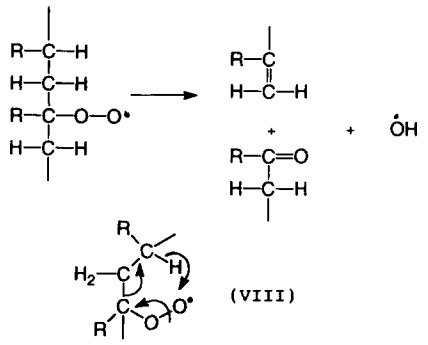
Mention has been made of the degradation observed in polypropylene hollow fibres when hydroxylation is prolonged. It seems likely that this mainly arises from peroxy radicals produced by combination of oxygen with the initial polymer radicals. Many mechanisms for the oxidative degradation of polypropylene have been advanced. That shown in reaction (10) was proposed by

Kaur *et al.*[27] for degradation accompanying high-energy radiation.



(10)

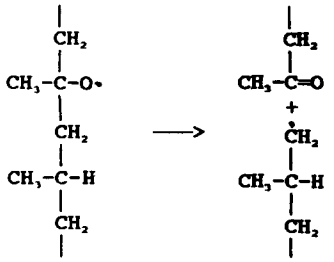
In our opinion reaction (11) represents a likely process which may proceed by the concerted three-bond cleavage indicated in (VIII).



(11)

(VIII)

In the grafting stage [reaction (3)] β-scission is, in principle, a possible source of degradation [reaction (12)]:



(12)

Iwakura and Imai[28] studied grafting of methyl methacrylate on to poly(vinyl alcohol) by the ceric ion method. From intrinsic viscosity measurements they speculated that their polymers may be essentially block-like. This could, of course, arise if β-scission [reaction (12)] were important and would imply that each initiation is accompanied by a degradative step. On the other hand, Odian and Kho[29], in a kinetic study of ceric ion initiated graft copolymerization of vinyl acetate–acrylonitrile mixtures to poly(vinyl alcohol), proposed αC–H bond scission as the radical-generating step so that the possibility of β-scission did not arise.

As a plausible low molecular weight analogue of the polypropyleneoxy radical we may consider t-butyloxy. Griffiths *et al.*[30], in the course of a detailed study of the initiation of methyl methacrylate polymerization by t-butoxy (from the thermolysis at 60°C of di-t-butyl peroxalate), found that only 4% of the total initiation could be attributed to CH_3 arising from β-scission of the radical. In grafting to polypropylene by our procedure significant intervention of β-scission therefore seems improbable.

None of the experiments described in this paper was designed to identify β-scission, but we have not become aware of any effects which would suggest its participation.

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