HYDROPHILIC POLYMERS

by

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SUMMARY

The design of polymers for use in both daily and continuous (day and night) wear contact lenses and the correlation of polymer structure with those properties relevant to contact lens wear are described.

Two approaches have been examined:-

a) The surface modification of existing polymers having otherwise attractive properties.

b) The use of copolymerisation to combine some of the desirable properties of the respective homopolymers.

The first approach is restricted to thermoplastic and elastomeric polymers that have potential advantages over the established material, poly (methyl methacrylate), in that they are more flexible and more oxygen permeable. Of the polymers examined, all of which are too hydrophobic for direct use, poly (4-methyl pent-1-ene) proved to be the most readily modified in such a way that its surface became sufficiently wettable to sustain a coherent tear film without reducing its optical properties to an unacceptable level. The successful use of equilibrium advancing water contact angle measurements to provide an 'in vitro' assessment of this behaviour is described.

In an attempt to produce more hydrophilic versions of such other wise acceptable polymers as poly (4-methyl pent-1-ene) copolymerisation of 4-methyl pent-1-ene with hydrophilic monomers (such as 2-hydroxyethyl methacrylate and N-vinyl pyrrolidone) has been attempted with a combined Lewis acid/free radical initiator. The compositions of the resulting polymers are discussed in terms of complex formation between the hydrophilic monomer and the Lewis acid.

A class of polymers possessing several advantages over thermoplastics and elastomers, particularly for continuous wear use, are the synthetic hydrogels. These polymers are conveniently described as "water swollen cross-linked polymers" and may be synthesised from various combinations of hydrophilic and hydrophobic monomers to give polymers possessing a range of properties. In the present work conventional free radical polymerisation techniques have been used in conjunction with monomers having broadly similar radical reactivity ratios.

The equilibrium water contents of the hydrogels produced in this way were examined and found to be governed by a balance of polar and steric effects. Anomalous water contents which were encountered in hydrogels containing methacrylic acid are described in terms of the strong hydrogen bonding ability of methacrylic acid. A similar type of anomalous behaviour was encountered in the measured values of "dissolved" oxygen permeability coefficients. At water contents of less than 30% these were markedly dependent on the molecular structure and possible water binding ability of the hydrogel polymer, although at higher water contents the oxygen permeability showed a simple dependence on the equilibrium water content. On the basis of this work and available information on corneal oxygen consumption rates predictions of oxygen permeability/thickness requirements for continuous wear contact lenses have been made.

In a similar manner initial work has been carried out on the adaption of an 'in vitro' technique for the correlation of the surface hydrophilicity of hydrogels with mucous build up on hydrogel lenses during continuous wear.

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To the Memory of

my Mother

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CHAPTER 1

INTRODUCTION

The capacity of the human body to regenerate components that are lost, damaged, or diseased is much more limited than is the case for many of the lower animals. Consequently man has long endeavoured to find or develop materials that might replace or supplement the tissue and organs of the body. Although metals and ceramics have been used to a limited extent in this way the recent upsurge in the use of biomaterials has closely followed the growth of the polymer industry. Medical researchers have been provided with a wide spectrum of polymers having properties covering the extremes of elastic and rigidity moduli and ranging from hydrophobic to hydrophilic. They were originally developed, however, for uses far removed from biomedical applications and it is only in the last ten years that increasing co-operation between polymer chemists and medical research workers has resulted in the development of new materials specifically designed for biomedical use. One device which has recently benefitted from such co-operation is the contact lens, which is ordinarily used to correct refractive errors of the eye.

Before discussing the development of contact lens materials however, it is important to consider the environment with which the lens interacts in order to ascertain the properties required of material for this type of application.

1.1. ANATOMY AND PHYSIOLOGY OF THE CORNEA

1.1.1. Structure of the Cornea

The cornea is the transparent structure which constitutes the foremost optical component of the eye. It is composed of five layers: epithelium, Bowman's membrane, stroma, Descemet's membrane and endothelium (Fig. 1).

The epithelium comprises the outermost 10% of the total corneal thickness and consists of five or six layers of cells that

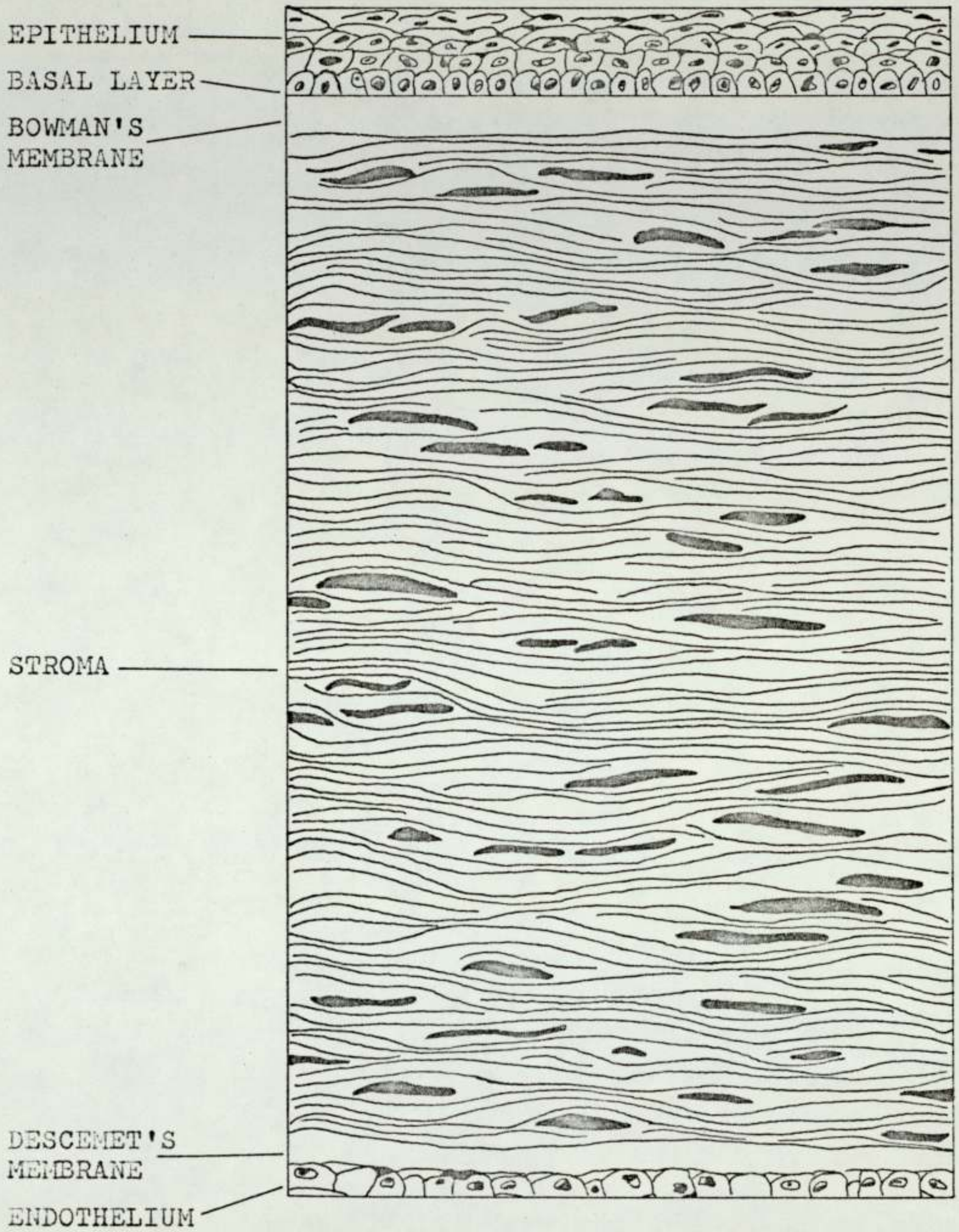


FIGURE 1 Sectional View of the Cornea[1]

can be regenerated rapidly after injury. However, Bowman's membrane which is considered to be a condensed layer of the stroma does not possess such regeneration properties and injury can lead to opacity. Thus, whilst a limited amount of damage by a contact lens to the epithelium can be tolerated, it is important that Bowman's membrane remains undamaged.

The stroma which constitutes 90% of the total corneal thickness is structurally composed of cells and of lamellae of collagen fibrils. These lamellae which run parallel to the surface and to each other across the cornea[2, 3] are embedded in a springy mucoid matrix which keeps them apart and prevents their compression[3]. This arrangement allows for the transfer of substances through the tissue for adequate nutrition.

The two posterior layers are Descemet's membrane, a strong structureless layer, and the endothelium, a single layer of flattened cells.

The thickness of the cornea is determined to a great extent by corneal hydration and anything which tends to increase the water content of the cornea will cause an increase in corneal thickness[4]. Von Bahr[5] has found the normal thickness of the cornea to be 0.46 to 0.67 mm.

1.1.2. The Transparency of the Cornea

To maintain its vital function as an optical medium of the eye, the cornea must have a high degree of transparency. There are a number of theories explaining corneal transparency but the most widely accepted is the Lattice Theory proposed by Maurice[6]. He has suggested that the regular arrangement of collagen fibrils in the stroma causes them to behave as a series of diffraction gratings which eliminate the scattered light arising from the difference in refractive indices of the collagen fibrils and the mucoid matrix or ground substance as it is often called. If the collagen fibrils are displaced, for example, during corneal hydration (the stroma is normally in a state of partial hydration), the normal light interference relationship is destroyed and corneal transparency is lost.

1.1.3. The Metabolism of the Cornea

The cornea is maintained in its normally partially hydrated state (deturgescence) by an active transport of water away from the cornea. The energy required for this process is provided by the metabolism of glucose in the presence of oxygen. In the absence of oxygen glucose is broken down increasingly to lactic acid which yields less energy than the oxidation of glucose via the hexosomonophosphate shunt and Krebs cycle[7]. Thus under anaerobic conditions water accumulates in the stroma and swelling of the mucoid matrix occurs. This disrupts the spatial regularity of the collagen fibrils resulting in a decrease in corneal transparency and in a thickening of the cornea. This phenomenon is known as corneal oedema, the onset of which can often be recognised by the formation of coloured halos around point sources of light.

There are four recognised pathways for the transport of oxygen to the cornea[8]:-

a) by air that is dissolved in the tear film which oxygenates the cornea by a continuous bathing process with blinking.

b) by the blood of the conjunctival vessels.

c) by the blood of the limbal vessels.

d) from the aqueous humour.

The exact contributions of these sources are not known. However, Smelser[9] and Langham[10] postulated that oxygen is obtained primarily from the tears and this has now been confirmed by Hill and Fatt[11 - 13]. When the eyes are closed during sleep sufficient oxygen to enable the cornea to continue its normal metabolism is provided by the capillaries in the palprebal conjunctiva. The oxygen tension at the corneal epithelium for the closed eye is 55 mm. Hg. compared with a value of 155 mm. Hg. for the open eye[14]. However, this is more than adequate as Polse and Mandell[15] have established 11 to 19 mm. Hg. as the minimum oxygen tension required at the epithelium for sustaining normal corneal thickness.

By measuring the oxygen uptake from the limited reservoir of a polarographic electrode by the in vivo human cornea, Hill and Fatt[11] have calculated the oxygen flux into the cornea at 155 mm Hg. oxygen tension to be about $4.8\,\mu l\ .\ cm.^{-2}\ hr.^{-1}$ within the range $3.7 - 7.8\,\mu l\ .\ cm.^{-2}\ hr.^{-1}$. The oxygen permeabilities of the stroma[16], epithelium and endothelium[17] have also been measured as 300×10^{-10}, 188×10^{-10} and 53×10^{-10} cc. mm. $(cm.^{2}\ tissue)^{-1}\ sec.^{-1}\ cm.\ Hg.^{-1}$, respectively. These values are for the separate layers of the rabbit cornea as there are obvious experimental difficulties in obtaining values from the human cornea.

1.1.4. The Precorneal Tear Film

The corneal epithelium is covered by a thin aqueous layer--the tear film. Its importance in maintaining the optical properties of the cornea has made it the subject of much investigation and a number of reviews[18 - 21] of its chemistry and function have been published.

The chemical composition of tear fluid is very similar to that of blood plasma; the main exceptions being that it is slightly more dilute (98.2% water) and the protein content is much smaller at about 0.6%. Other dissolved solids present include mucopolysaccharides, lipids, glucose and inorganic salts. Tears are slightly alkaline having a pH in the region of 7.4 to 7.5 and have an osmotic pressure similar to that of plasma being isotonic with a 0.9% salt solution.

Wolff[22] has described the tear film as being composed of three layers: a mucoid layer, an intermediate watery (lachrymal fluid) layer, and an oily (sebaceous) layer on the surface. These three layers are derived from the bulbar conjunctiva, where goblet cells produce the mucous secretion; the accessory lachrymal gland; and the meibomian glands, situated at the tarsus, which produce the sebaceous layer.

The tear film has a number of important functions. An obvious one is its lubricating effect allowing the eyelid to sweep across the cornea and remove any debris whilst ensuring the further distribution of the various secretions. In addition the tears cover microscopic irregularities in the epithelium and thus provide the cornea with an optically smooth surface so essential for the maintenance of its refractive properties. Evaporation of the tears between blinks is reduced by the presence of the sebaceous layer on the surface of the tear film[23]. As previously mentioned the tear film is also the prime source of oxygen for the metabolism of the cornea[9 - 14].

The normal bacterial flora of the tear fluid secretions is controlled by lysozyme in the tears which can kill the common bacteria. Lysozyme is mycolytic and dissolves the bacterial membrane.

One of the most interesting aspects of the tear film is its interaction with the surface of the cornea. The epithelium is covered by a hydrophobic lipid layer[24] and thus difficulty would be expected in maintaining a continuous tear film over the cornea. For the majority of people this is not the case but the reason for the adequate wetting of the cornea by the aqueous tear solution is not readily apparent.

In 1965 Mishima[18] reported that wiping the corneal surface rendered it non-wettable by the tears. This observation was followed up by Holly and his co-workers[24 - 29] who carried out investigations into the wetting of the corneal epithelium by the tear film. They have calculated from measurements of the contact angles of a series of non-hydrogen bonding liquids on enucleated rabbit corneas that the clean epithelial surface is hydrophobic with a critical surface tension of 28 dynes/cm.[27]. Critical surface tension, a characteristic of the solid surface, was first defined by Fox and Zisman[30] and its concept and relationship to wettability will be discussed more fully in Section 1.2.2. It will suffice for the present to state that liquids with a lower surface tension than the critical surface tension of a solid will spread over (or wet) the surface, and liquids with a higher surface tension will form droplets on the surface.

Miller[31] using human subjects has established the surface tension of tears to be 46 dynes/cm. (surface tension of water is 72.8 dynes/cm.) However, the relative nature of the method used and the data of Lemp et al[24] indicate that this value is probably too high. The lower surface tension of tears compared to water results from the effect of the surface activity of the glycoproteins present in the conjunctival mucous[24, 27]. Even when considering that there is hydrogen bonding occurring between the water in the tears and the epithelial surface, it is insufficient to ensure complete wetting[27]. Thus, it has been suggested that the conjunctival glycoproteins not only reduce the surface tension of the tears as conventional wetting agents (or surfactants) would but also adsorb on to the surface of the cornea resulting in a high energy surface and so rendering the cornea wettable.

1.2. THE DEVELOPMENT OF CONTACT LENS MATERIALS

Contact lenses are usually divided into two types:-

1. Corneal contact lens. A contact lens which rests primarily on the cornea rather than the sclera.
2. Scleral (or Haptic) contact lens. A contact lens which fits over both the cornea and the surround-

ing sclera, used with or without an auxiliary fluid to fill the space between the lens and the cornea.

The majority of contact lenses manufactured today are corneal in design and in accordance with accepted practice the term contact lens will refer to a lens of the corneal type unless specifically stated otherwise.

1.2.1. General Development

The precursor to the contact lens was first described by Leonardo da Vinci at the beginning of the 16th Century[32]. Although, it was not until the late 19th Century, nearly 400 years later, that the first successful fitting of a contact lens took place. For sixty years after their introduction glass scleral lenses were the most commonly used type of contact lens. Because of the obvious disadvantage of their weight glass corneal lenses were seldom used. However, in 1947 Tuohy[33] began to manufacture corneal lenses out of poly (methyl methacrylate) (PMMA); a light, transparent, easily processable, non-toxic and readily available material. The next ten years saw little development in the way of materials but many improvements were made in the design of the lens. One such refinement was the micro-corneal lens developed by Sohnges[34]. This lens was much smaller and flatter than earlier corneal lenses and permitted greater tear circulation.

During the 1960's there was a tremendous upsurge of interest in the search for new materials for contact lenses, so much so, that virtually every commercially available transparent polymer has now been patented for contact lense use. It was recognised that PMMA was not the ideal contact lens material and improvements in properties were sought in other materials. Flexibility and a high oxygen permeability were two properties not possessed by PMMA that were claimed for silicone rubber (poly (dimethyl siloxane))[35 - 37]. However, the hydrophobic nature of this material meant that it could not be wet, even with the aid of ophthalmic wetting agents, by the tears; so important for ensuring comfort and good vision. Other elastomers have now been patented as contact lens materials; these include ethylene-propylene terpolymers, cis-polyisoprene and cis-polybutadiene[42]. Although they are also hydrophobic it has been suggested that they are capable of being rendered hydrophilic much more easily than silicone rubber.

Plastics have not been neglected in the search for contact lens materials, in fact, in 1969 even polyethylene[43] and poly (vinyl chloride)[44] were patented for contact lens use. More promising though, was poly (4-methyl pent-1-ene)[45, 46] which was claimed to give good optical properties and to have a high oxygen permeability.

It has not just been the readily available materials that have received attention. More exotic polymers, such as a copolymer of perfluoro-2-methylene-4-methyl-1, 3-dioxolane and tetrafluoroethylene and a terpolymer of hexafluoroacetone, tetrafluoroethylene and ethylene have been claimed as suitable for contact lens use[47].

Natural polymers have also received some attention by way of some very interesting research carried out by Soehnges[48, 69] who has reported using protein extracted from animal eyes to produce contact lenses. As little literature is available it is impossible to comment on how successful his approach has been.

1.2.2. Wettability and Contact Lens Wear

The importance of the wetting of contact lenses is now generally accepted and clearly reflected in the number of wetting solutions available, however, there is only a limited amount of published data on the treatment of the surfaces of lenses to increase their wettability. Wettability and its relation to contact lens materials has recently been reviewed by the author[159, 160]. The wetting of contact lenses is important because the adherence of the pre-corneal tear film, in the form of a thin capillary layer, is recognised as being a primary requirement for the physiological compatibility of the lens and the patient[157, 158]. This thin layer of tears on the surface of contact lenses: (a) lubricates between the inner surface of the eyelid and the lens, (b) mechanically supports the lens which floats on the pre-corneal fluid and (c) prevents the accumulation of oily and sebaceous matter on the lens, thus maintaining optical clarity and optimum surface conditions for fluid flow.

By wetting and wettability, we usually mean the adhesion of liquids to solids and the extent to which they spread. Since the tendency for a drop of liquid to spread over a plane solid surface increases as the contact angle, θ, decreases, the contact angle provides a useful inverse measure of wettability. The contact angle is the angle (measured through the liquid) between the liquid-vapour and the liquid-solid interfaces of a drop of the liquid on a solid surface (Fig. 2).

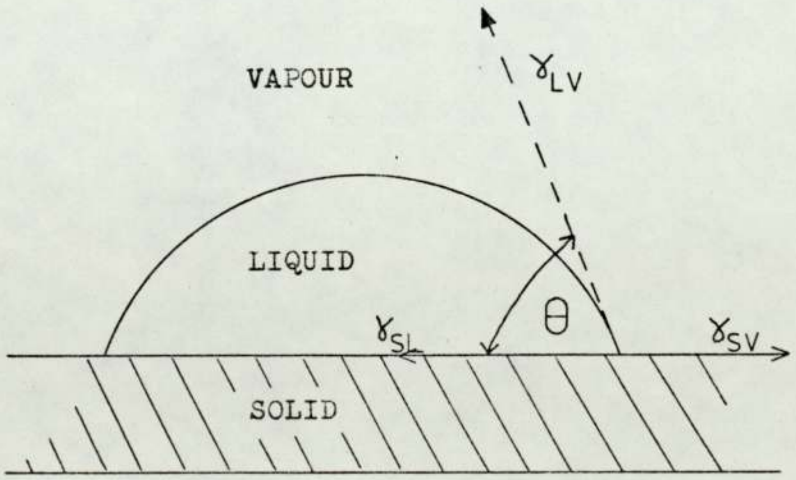


FIGURE 2

Figure 2. Profile of a sessile drop resting on a solid surface, exhibiting the equilibrium contact angle (θ).

When $\theta = 0$ the liquid will spread spontaneously or completely over the solid surface. A zero contact angle is a necessary condition for spreading. When $\theta \neq 0$ the liquid is considered to be non-spreading. A host of early experiments revealed that every liquid wets every solid to some extent, that is, $\theta < 180^\circ$. In other words there is always some adhesion of any liquid to any solid.

Two terms used to describe those polymers in the context of contact lens usage, and often misleadingly defined, are hydrophobic and hydrophilic. When referring to bulk properties they can simply be used to mean 'water hating' and 'water loving', respectively, for example, a hydrogel forming polymer can be described as being hydrophilic. More often though, the terms are used to describe surface properties and are then more conveniently defined with reference to contact angles. Thus, a hydrophobic solid is one with which water exhibits a contact angle of greater than 0° whereas a hydrophilic solid has a contact angle of zero, i.e. water spreads completely or spontaneously over the solid.

There are a number of methods[159] available for the measurement of contact angles. By far the most common and simplest is by observation of a sessile drop on a plane solid surface. The contact angle is determined by constructing a tangent to the profile of the drop at the point of contact with the solid surface. This can be done on a projected image[161, 162] or photograph of the drop profile[163] or directly using a low power microscope fitted with goniometer eye-piece[30, 164].

Some of the most extensive and significant studies involving the measurement of contact angles to clarify the subject of wetting and spreading of liquids on polymers are those of Zisman and his fellow workers[165 - 167]. They have observed that for liquids on polymers the graph of $\cos\theta$ plotted against the liquid surface tensions resulted in a straight line. The intercept on the surface tension axis at $\cos\theta = 1$ (i.e. $\theta = 0$) was defined as the critical surface tension of wetting, γ_c . In general a rectilinear graph always resulted whenever a homologous series of organic liquids was used. Even when $\cos\theta$ was plotted against the surface tensions of a variety of non-homologous liquids, the graphical points formed a narrow rectilinear band. The intercept at the lower limb of the band at $\cos\theta = 1$ has been defined by Zisman[166] as the critical surface tension, γ_c , of a solid surface. Although this intercept is not as precisely defined as the critical surface tension of a homologous series of liquids it is more useful, in that it is a characteristic of the solid surface only. The measurement of γ_c has enabled a comparison of the wettabilities of a variety of polymers to be made.

For spreading to occur the surface tension of the liquid must be less than γ_c . Thus, nylon 6, 6 which has the highest γ_c (46 dynes/cm) of the more common polymers reported is according to our definition hydrophobic.

The critical surface tension for polymers appear to correlate well with their chemical structures and Zisman[166] has developed a number of qualitative molecular concepts to describe these correlations. Of importance is the fact that contact angles are determined primarily, but not entirely, by the outermost exposed atoms in a molecule. Zisman has called this an extension of Langmuir's "Principle of Independant Surface Action[168, 169]". Shafrin and Zisman have compiled a "wettability spectrum" from which they have concluded that the effectiveness of substitution of individual atomic species in increasing the wettability of organic surfaces is:-

$$F < H < Cl < (Br) < (I) < O < N$$

As the wettability of a surface is determined mainly by the nature of the outermost atoms, it is apparent that by changing the chemical nature of the surface, the wettability of a polymer can be improved. This can be brought about by treating the surface to introduce hydrophilic groups or by coating the polymer with a more hydrophilic substance.

Certain polymers which possess properties advantageous to contact lens wear, e.g. high oxygen permeability, but which are of a hydrophobic nature such that they are not wet by the tears, have been surface treated to improve their wettability. A number of methods for rendering silicone rubber lenses more hydrophilic have been developed. These include the treatment of the lens with an alkyl titanate, preferably tetraisopropyl titanate;[38] with titanium tetra-alkoxide;[39] with chlorosulphonic acid followed by a base;[40] or with a solution containing phosphoric acid and oxides of chromium[41]. Unfortunately the success of these treatments in providing a permanent hydrophilic surface seems to be in some doubt. Similarly the wettability of poly (methyl methacrylate) lenses has been improved by Gesser[171, 172] who used free radicals to interact with the surface in order to produce hydrophilic groups. A large reduction in the contact angle with water was found using this treatment. Similar reductions in the contact angle have been obtained by the formation of a coating of silica or titanium dioxide on the surfaces of PMMA lenses[173 - 176].

1.2.3. The Development of Hydrogel Contact Lenses

In 1960 two Czechoslovakians, Wichterle and Lim, reported the use of covalently cross-linked glycol methacrylates as surgical implants[49 - 51]. They called them hydrogels because of their ability to imbibe large amounts of water without dissolution. Because of their flexibility, biocompatibility and transparency they were immediately recognised as promising materials for contact lens use.

The first hydrogel to be introduced as a potential contact lens material was water-swollen, cross-linked poly (2-hydroxyethyl methacrylate) (PHEMA).

Development of the Czech material has led to the manufacture of PHEMA lenses under the name "Soflens" in the U.S.A. by Bausch and Lomb Inc. and under the name "Hydron" in Europe by Hydron Lens Ltd.

Although PHEMA lenses represent an improvement in certain properties on PMMA lenses they, are a long way from being ideal and thus attention has recently been focused on the improvement of the properties, relevant to contact lens use, of PHEMA through copolymerisation. Comonomers used have included diethylene glycol methacrylate,[52] alkyl acrylates and methacrylates[53], and N-vinyl pyrrolidone[54]. Interest has also been shown in water-swellable cross-linked polymers other than glycol acrylates and methacrylates. Hydrogels from copolymers of N-vinyl lactams and alkyl methacrylates[55], methyl methacrylate and acrylic acid[56, 57] and graft copolymers of poly (vinyl lactams) and 2-hydroxyethyl methacrylate[58 - 60] have all recently been patented.

In order to combine the best properties of hard and soft lenses, contact lenses have been proposed in which the central portion is made from a hydrophobic polymer e.g. PMMA and the peripheral portion is made from a hydrogel e.g. PHEMA. It is, however, doubtful whether the problems involved in manufacture would be overcome.

The hydrogels discussed so far have all been covalently cross-linked. However, ionically cross-linked polyelectrolyte complexes prepared by reacting poly (vinyl benzyl trimethylammonium chloride) with sodium polystyrene sulphonate are also water swellable, transparent and claimed to have high oxygen and water permeability. They have, therefore, been suggested as possible contact lens

TABLE 1 Hydrogel Contact Lenses Available in the UK[199]

Name of Contact Lens	Manufacturer	Chemical Constitution	Mode of Manufacture	Water Content
Soflens	Bausch & Lamb Inc.	Poly (2-hydroxyethyl methacrylate)	Spin cast	38.6% in 0.9% saline
Hydron	Hydron Lens Ltd.	Poly (2-hydroxyethyl methacrylate)	Lathe cut	38% in 0.9% saline
Bionite Naturalens	Frigidtronics Ltd.	2-hydroxyethyl methacrylate----N-vinyl pyrrolidone graft copolymer	Lathe cut	58%
Sauflon	Contact Lens Manufacturing	Copolymer of N-vinyl pyrrolidone and methyl methacrylate	Lathe cut	68%
Permalens	Global Vision	Not known	Lathe cut	> 60%

materials[63, 64] but very little literature is available on their application to contact lenses.

1.2.4 Contact Lens Manufacture

As expected the nature of the raw material determines the method of processing a contact lens. Generally, the conventional forming techniques used in the polymer industry are applicable to contact lens manufacture. Novel manufacturing processes have, however, been developed especially for hydrogel materials.

(1) Thermoplastic Contact Lenses

Thermoplastics could be formed into contact lenses by (a) injection moulding, (b) compression moulding from powder, (c) pressing from a blank, and (d) lathe-cutting of a blank obtained from a rod of the material. Of these (c) and (d) are currently used in the contact lens manufacture.

(2) Elastomeric Contact Lenses

Elastomers can be processed by conventional techniques which involve compression moulding in the presence of a cross-linking agent in a contact lens mould under conditions of heat and pressure[42, 65].

(3) Hydrogel Contact Lenses

When cross-linking in hydrogels accompanies the polmerisation conventional moulding techniques are not applicable. At present there are only two methods available for the commercial production of contact lenses from hydrogels: (a) lathe-cutting from a blank of the dehydrated material and (b) spin-casting of the polymerising monomer mixture, containing cross-linking agent, in a contact lens mould in the presence[66] or absence[52, 67] of a suitable solvent.

1.3. THE PHYSIOLOGICAL EFFECT OF CONTACT LENS WEAR

Most of the clinical work has been carried out on just three types of lenses: PMMA, PHEMA and silicone rubber. For this reason the following discussion will be necessarily restricted to observations of the physiological effect of these three lenses.

1.3.1 Effect on the Metabolism of the Cornea

Interference by contact lenses with the normal metabolic processes of the cornea has been a cause of concern since their introduction. This interference often results in corneal oedema and early laboratory and clinical studies indicated that its primary cause was insufficiency of oxygen reaching the cornea[9].

Investigations into the deprivation of oxygen by contact lenses have been carried out by Hill and Fatt[70] who found that in the absence of blinking a tight fitting PMMA lens forms a barrier to oxygen from the atmosphere such that the epithelium cannot respire at its accustomed rate. Calculation of the steady state distribution of oxygen in the vivo cornea covered by a tight fitting PMMA lens[71] has shown that although oxygen is supplied to the cornea from the aqueous humour, the stroma has severely restricted oxygen tension and the epithelium is almost anoxic.

When PHEMA was first introduced as a contact lens material it was claimed that one of its main advantages was a high oxygen permeability. Since then a number of reports, often contradictory, have been published concerning the oxygen permeability of a PHEMA lens and its effect on corneal respiration.

A comparison of the effect of contact lenses made from PHEMA (Geltakt: original Czech lens), silicone rubber and PMMA, on the lactic acid level in rabbit corneas was made by Praus et al[72]. After 8 hours wear PMMA lenses caused an increase in the lactic acid level of 115% of the control whereas the rise was only 30% with PHEMA

TABLE 2

A Comparison of the Properties of PMMA, PHEMA and Silicone Rubber Contact Lenses.

Property	PMMA Lens	PHEMA Lens	Silicone Rubber Lens
Hydrophilicity	Hydrophobic (but just wet by tears)	Hydrophilic	Hydrophobic
Hardness	Hard	Soft	Soft
Rigidity	Rigid	Flexible	Flexible
Permeability to Oxygen	Impermeable	More permeable than PMMA but less than silicone rubber	Very permeable (most permeable polymer known)
Corneal Oedema	Quite frequent	Occasional	Very rarely
Fitting	Straightforward	Simpler than PMMA	Straightforward
Adaptation Time	About 3 weeks	Less than 1 week	About 1 week
Comfort	Not very comfortable	Very comfortable	Moderately comfortable
Visual Acuity	Very good	Not as good as PMMA	Not as good as PMMA
Correction for Astigmatism	For high astigmatism	For low astigmatism	For low astigmatism
Sterilisation Technique	Simple	Complex	Simple
Storage Between Use	Recommended storage solution	In saline solution	Recommended storage solution
Resistance to Mishandling	Good	Poor	Good
Life Span of Lens	About 2 years	$1\frac{1}{2}$ to 2 years	About 2 years

and silicone rubber lenses. As deprivation of atmospheric oxygen to the cornea causes an increase in lactic acid concentration due to anaerobic glycolysis they concluded that PHEMA lenses caused less oxygen deficiency than PMMA lenses and rather surprisingly differed little from silicone rubber lenses in allowing oxygen to diffuse through to the cornea. Their results appear to be consistent with the earlier clinical observations[73] of other Czech workers.

However, from their studies of the effect of three types of contact lenses on the respiration of rabbit and human corneas, Hill and his co-workers[74 - 76] have obtained results inconsistent with the above. They observed the rate of exhaustion of the oxygen reservoir at the tip of a polarographic probe at the cornea after 90 second periods of wear, without blinking, of a hydrogel lens, a PMMA lens, a silicone rubber lens and of no lens wear. Both PHEMA and PMMA lenses resulted in a greater oxygen deprivation (both had an oxygen uptake rate 2.4 times faster than in the case of no lens wear) than the silicone rubber lens when the oxygen uptake rate was indistinguishable from the normal uptake of the eye. These results suggest that insufficient oxygen permeates through PMMA and PHEMA lenses to cater for the requirements of the cornea whereas a silicone rubber lens interferes little with corneal respiration. These conclusions were supported by observations of the change in oxygen tension within a non-circulating tear pool under the above contact lenses obtained with a micro-polarographic electrode embedded in the appropriate contact lens[77].

From measurements of the epithelial glycogen and lactate levels in the rabbit cornea Burns et al[78] have concluded that PHEMA and PMMA lenses deprive the cornea of oxygen whereas silicon rubber lenses do not. More recently Hamano et al[79] studied the effect of wearing various contact lenses on the oxygen tension in the corneal stroma using an ultra-micro oxygen electrode inserted into the corneas of rabbits. They found that the oxygen tension dropped to zero at a lower rate on wearing a hydrogel lens than a PMMA lens and a silicone rubber lens had no effect on the oxygen tension at all.

As well as studies on the effect of contact lenses on corneal respiration, measurements have been made of the oxygen permeability of a number of contact lenses. Takahashi et al[80] measured the oxygen transmissibilities of PHEMA and PMMA to be about the same and no greater than 4×10^{-10} cc. (S.T.P.) mm. cm.$^{-2}$ sec.$^{-1}$ cm. Hg.$^{-1}$ whereas Fatt and St. Helen[81] have given a higher value for PHEMA of 89×10^{-10} cc. (S.T.P.) mm. cm.$^{-2}$ sec.$^{-1}$ cm. Hg.$^{-1}$. Both values suggest that insufficient oxygen can be transported to the cornea by passage through a PHEMA lens. On the other hand Morrison and Edelhauser[82] have calculated that the oxygen flow rate through a PHEMA lens is greater than the reported corneal utilisation rate. The contrasting values obtained above are probably due to the very different experimental techniques employed and also the experimental conditions used which did not in any way simulate those on the eye.

There are, thus, two differing opinions as to the adequacy of the supply of oxygen through a PHEMA lens. However, the wealth of the evidence indicates that the oxygen permeability of PHEMA is insufficient to maintain normal corneal respiration but that it interferes less than a PMMA lens with corneal respiration whilst a silicone rubber lens has little if any adverse effect.

Despite the fact that both PMMA and PHEMA appear to be insufficiently permeable to oxygen for normal corneal respiration they are used for daily wear contact lenses without any appearance of corneal oedema (a sign of oxygen deprivation) which suggests an additional route for oxygen to reach the cornea. It is well known that the principal source of oxygen for the cornea in the open-eye condition is that dissolved in the tears. In the case of a PMMA lens it is believed that it floats in the tear film such that a tear pool exists between the lens and the cornea and with each blink the lens "rocks" up and down causing fresh tear fluid to be pumped under the lens[70]. It has now been shown experimentally with the aid of a micro-polarographic electrode built into a contact lens that blinking replenishes the tear pool under the lens[83, 84].

With a PHEMA lens a rippling action of the lens on blinking is thought to be responsible for tear flow under the lens[8, 83, 85].

There are thus, two routes by which oxygen can reach the cornea during contact lens wear: by permeation through the lens and via tear flow under the lens. This often leads to difficulties in comparing and interpreting various experimental results on the effect of contact lens wear on corneal respiration. As previously mentioned there has been disagreement between Hill and his associates and the Czech workers over the ability of PHEMA to transmit sufficient oxygen for normal corneal metabolism. Hill and his fellow workers performed their experiments under static conditions, i.e. no blinking, whilst the Czechs carried out theirs under normal blinking conditions. There was agreement on the impermeability of PMMA lenses to oxygen but here the Czechs used a tight fitting lens which even with blinking would not allow replenishment of the tear film under the lens. However, in the case of the PHEMA lens it is probable that blinking caused rippling of the lens which would lead to oxygen rich tears being pumped under the lens. This would account for the Czech conclusion that PHEMA allowed adequate oxygen to permeate through the lens.

1.3.2. Comfort and Visual Acuity

The cornea being much more densely supplied with nerve fibres than the skin is extremely sensitive. A PMMA lens exerts mechanical pressure on the cornea causing a definite foreign body sensation in the eye, so much so, that the initial discomforture can quite often be intolerable to the potential wearer. Although, over a period of a few weeks corneal sensitivity is often reduced and the patient becomes fully adapted to wearing the lens. However, far from being beneficial, this reduction in sensitivity is considered to be clinically undesirable as often the contact lens wearer cannot then detect corneal abrasion so readily.

The hydrogel lens, because of its softness, causes very little initial discomforture and is readily tolerated by the potential wearer. Similarly, the silicone rubber lens whilst not being as comfortable as the hydrogel lens at first, generally requires only a short adaptation period.

Although there have been many improvements in the fitting of hydrogel lenses over the last few years the vision obtained is still not up to the near perfect vision achieved with a PMMA lens. The lack of visual acuity with a PHEMA lens is often attributed to poor fitting, but another reason is its slow rate of recovery after deformation by the eyelid during blinking.

PHEMA lenses because of their softness tend to conform to the toricity of the cornea and are thus, unlike PMMA lenses, unable to correct astigmatism. A silicone rubber lens, however, will correct astigmatism to some degree because it possesses a certain amount of rigidity and elasticity[86, 87].

1.3.3. Microbiological and Pharmacological Aspects of Contact Lens Wear

In order that the contact lens wearer be protected from ocular infection the sterility of the lenses must be maintained. When not in use PMMA and silicone rubber lenses are generally kept in a germicidal storage solution and before being placed in the eye the lenses are treated with a wetting solution to aid the formation of a continuous tear film on the lens and also to provide a mechanical buffer between the lens and cornea for the first few minutes after insertion. The storage solutions and wetting solutions both contain preservatives such as benzalkonium chloride, ethylene diaminetetraacetic acid (EDTA) and chlorobutanol. The majority of solutions used were originally formulated for PMMA lenses and they are not all suitable for silicone rubber lenses. One such instance is with solutions containing chlorobutanol for it is known that silicone rubber "concentrates" the chlorobutanol which may then cause severe ocular discomfort[88].

PHEMA lenses have to be stored in a solution which is isotonic with tears as hypotonicity or hypertonicity of the lens results in a stinging sensation in the eye. The solutions used with PMMA have proved unsuitable for hydrogel lenses as the preservatives used in them can be absorbed by the lens and may be released later in the eye in a more concentrated state which may cause chemical burns[88]. A number of procedures for sterilising hydrogel lenses have been developed[88, 89] including the following:-

(a) Boiling in isotonic salt solution. But as well as being somewhat inconvenient boiling kills only pathogens and not spores.

(b) Treatment with 3% hydrogen peroxide followed by neutralisation with sodium bicarbonate. The danger of neglecting the neutralisation step is, however, obvious.

(c) Experimental isotonic sterilising solutions containing chlorohexidine gluconate or thimerosal are at present being evaluated for clinical use.

Bacteriological studies of contaimination associated with hydrogel contact lenses have been carried out by various workers[90 - 94], whose results, however, were contradictory especially over the possibility of penetration of the lens by bacteria.

It is of interest to note that although tear fluid contains lysozyme which can kill most common bacteria, its effect on bacteria on the surfaces of lenses does not appear to have been investigated.

1.4 TOWARDS AN IDEAL CONTACT LENS

If it were possible to formulate a material having the best properties, relevant to contact lens use, of PMMA, PHEMA and silicone rubber there is no doubt that, based on present clinical information, it would make an excellent contact lens material. But would it be ideal? Kamath[95] has defined an ideal contact lens as one possessing five functional criteria, namely, comfort and safety, visual acuity, ease of wearing, dimensional and optical stability and simple care procedure. Using the cornea as a model he has determined the required physical and chemical properties of his ideal lens (Table 3).

Of course the properties required of a daily wear lens will be less stringent than those required of a continuous wear lens which would remain in the eye for periods of up to two years. For instance, consider the oxygen permeability of the material. Polse and Mandell[15] have established that a minimum oxygen tension of 11 to 19 mm Hg. is required at the corneal surface for normal corneal respiration. To achieve this a much higher oxygen permeability is required for a continuous wear lens than for a daily wear lens, as the oxygen tension under the closed eye-lid is only 55 mm. Hg., one third of that available in the open eye. Also, careful design of a daily wear lens can ensure sufficient tear exchange to occur in the open eye through blinking, which is obviously not applicable during sleep.

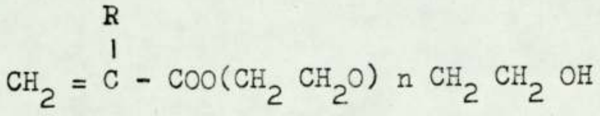
TABLE 3 Kamaths Ideal Contact Lens[95]

PROPERTY	CORNEA	PMMA	PHEMA	SILICONE RUBBER	KAMATH'S IDEAL LENS
Density	1.03	1.18	1.1	1.16	~ 1
Rigidity Modulus x10^{-7}(dynes/cm.^{2})	13	3100	0.2	4	> 150
Tensile Strength x10^{-7}(dynes/cm.^{2})	7	60	0.3	11	> 50
Tear Strength (gms/mm.)	2000	brittle	10	2000	~ 1000
Optical Transmission (%/cm.)	> 98	> 95	> 95	> 95	> 96
Refractive Index	1.37	1.49	1.4	1.43	~ 1.4
Surface Hardness	Shore A.15	Rockwell M.90	Shore A.19	Shore A.96	Rockwell M.90
Surface Finish (Å)	< 50	500	500	--	300
Surface Character	Hydrophilic	Hydrophobic	Hydrophilic	Hydrophobic	Hydrophilic
Oxygen Permeability x10^{10}(cc.mm./cm^{2}sec.cm.Hg.)	520	0.9	3.9	1300	> 80
Water Permeability x10^{15}(cm.^{4}/sec.dyne)	100	0	10	0	Low
Water Content (%)	81	0.4	45	0.12	< 2

1.5. THE STRUCTURE AND PROPERTIES OF HYDROGELS

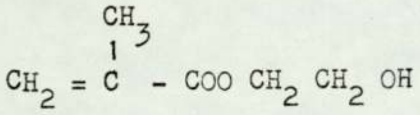
The term hydrogel can be used to describe any water containing hydrophilic polymer network. Although not a strict definition it encompasses such substances as polyelectrolyte complexes, cross-linked acrylamide polymers and cross-linked vinyl lactam polymers. However, the hydrogels which have received the most attention over recent years have been those derived from polymers of hydroxyl containing esters of methacrylic and acrylic acid, in particular poly (2-hydroxyethyl methacrylate) (PHEMA).

2-Hydroxyethyl methacrylate (HEMA) (1, R = CH_3, n = 0; 11) belongs to the family of monomeric esters having the general structure (1). The corresponding diesters, mainly ethylene glycol dimethacrylate (EGDMA) (111, n = 1), are used as cross-linking agents in the preparation of the three-dimensional polymers.



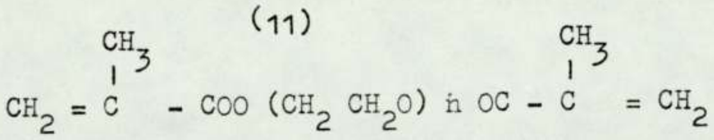
$$CH_2 = \overset{\overset{R}{|}}{C} - COO(CH_2\ CH_2O)\ n\ CH_2\ CH_2\ OH$$

(1)



$$CH_2 = \overset{\overset{CH_3}{|}}{C} - COO\ CH_2\ CH_2\ OH$$

(11)



$$CH_2 = \overset{\overset{CH_3}{|}}{C} - COO\ (CH_2\ CH_2O)\ n\ OC - \overset{\overset{CH_3}{|}}{C} = CH_2$$

(111)

As PHEMA was the first synthetic hydrogel used for biomedical and contact lens applications it has been the most extensively studied. In fact until very recently hydrogels and PHEMA were synonymous for contact lens practitioners. Bearing this in mind a review of the structure and properties of hydrogels must necessarily be mainly concerned with poly (2-hydroxyethyl methacrylate). Particular emphasis is placed on those properties relevant to contact lens applications and to a lesser extent possible permselectivity.

1.5.1. Polymerisation and Copolymerisation

The preparation of cross-linked PHEMA is usually carried out by polymerising HEMA with its diester, ethylene glycol dimethacrylate (EGDMA), using a free radical initiator such as an azo compound, or peroxide or a redox catalyst. For contact lens applications the concentration of EGDMA is generally less than 1% by weight which results in the formation of a soft and elastic hydrogel. The polymerisation of HEMA can be effected in bulk or in a solvent e.g. ethylene glycol or water. Water is, however, a thermodynamically poor solvent for PHEMA and a heterogeneous gel, due to phase separation, is formed if the water content in the polymerisation mixture exceeds 50%. In polymerisations where the water content in the starting mixture is less than 40% or if carried out in a thermodynamically better solvent e.g. ethylene glycol then a homogeneous hydrogel is produced[96].

Purification of HEMA is difficult as it undergoes disproportionation to EGDMA and methacrylic acid even at low temperatures. This means that as the disproportionation reaction competes with the polymerisation, bulk polymerisation always produces cross-linked PHEMA. Soluble PHEMA can be prepared by polymerising to low conversion in a large excess of a thermodynamically good solvent[96].

Very little information is available regarding the copolymerisation of HEMA with other monomers, however its reactivity should be similar to that of methyl methacrylate.

1.5.2. Swelling and the Factors which Govern it.

A cross-linked hydrophilic polymer when placed in water will swell by absorbing water until an equilibrium is reached between the osmotic pressure of the polymer segments which causes the swelling and the opposing and retractive forces arising as the chains between the cross-links elongate. The water uptake at this equilibrium point is known as the equilibrium water content of the hydrogel and is the weight of water in the equilibrated hydrogel expressed as the percentage weight of the hydrogel.

The swelling properties of hydrogels can be compared to those of hydrophobic network polymers in organic solvents[97 - 99], whose swelling depends mainly on (a) the interaction parameter between polymer and solvent, (b) the extent of cross-linking, and (c) the relative swelling at the time of cross-linking i.e. initial dilution of monomers.

PHEMA hydrogels have an equilibrium water content of around 40% which because of the thermodynamically poor solvent power of water for PHEMA is relatively unaffected by the number of cross-links and the initial dilution. For hydrogels to which water has a higher solvent power, such as poly (hydroxypropyl acrylate) and poly (2, 3-dihydroxypropyl methacrylate), the dependence of swelling on the initial dilution and extent of cross-linking is more evident.

1.5.2.1. Effect of Initial Dilution and Solvent Composition

Studies[100, 102] of the swelling properties of PHEMA hydrogels have shown that when HEMA was polymerised in an aqueous medium a transparent homogeneous hydrogel was only obtained if no more than 40% water was used in the polymerisation mixture. The resulting PHEMA hydrogel then had an equilibrium water content of about 40%. However, if water was replaced by a better solvent for PHEMA e.g. ethylene glycol such that a mixture of ethylene glycol and water was used as the diluent in the polymerisation then a homogeneous hydrogel was obtained at a diluent concentration of up to 60%[100, 102]. But the resulting hydrogel, when equilibrated in water still had a water content of 40%. The equilibrium water content of the PHEMA hydrogel was found to be independent of the composition of the diluent.

In marked contrast to PHEMA, Refojo[101] observed that for poly (2, 3-dihydroxypropyl methacrylate) i.e. poly (glycerol methacrylate) (PGMA) hydrogels the water content increased linearly with increasing water content in the monomer mixture. This behaviour was attributed to the solubility of linear PGMA in water.

1.5.2.2. Effect of Cross-Link Density

Using tetraethylene glycol dimethacrylate (TEGDMA) as a cross-linking agent Refojo et al[100] found that the equilibrium water content of PHEMA was independent of the amount of cross-linking agent added over a 3% range in concentration of TEGDMA. Whereas the same variation in the concentration of cross-linking agent in a hydrogel of PHPA reduced the water content from 53% to 49%. A similar dependence of equilibrium water content on the cross-link density was observed by Refojo[101] for PGMA hydrogel. An increase from 1% to 10% of TEGDMA in the monomer mix caused a decrease in the water content of PGMA from 76% to 61%.

1.5.2.3. Effect of Initiator Concentration

Investigations[102] into the effect of initiator concentration on the water content of PHEMA hydrogel showed that an increase in the initiator concentration resulted in an increase in the water content. It was suggested that an increase in the number of growing free radicals was the cause.

1.5.2.4. Effect of the Temperature of Hydration

The equilibrium water content of hydrogels has, not surprisingly, been found to be influenced by the temperature at which equilibration was carried out. A minimum of about 36% in the water content has been observed for PHEMA when equilibrated at about 60°C[100].

PHPA hydrogels showed an inverse temperature dependence, decreasing in water content with increasing temperature up to 50°C, above which the water content approached a constant value of about 33%[100]. On the other hand the water content of a PGMA hydrogel increased when the temperature was raised[101]. It was therefore proposed that the swelling of PHPA hydrogel is an exothermic process and swelling of PGMA an endothermic process. The swelling of PHEMA appeared to be either endothermic or exothermic depending on the temperature of equilibration.

1.5.2.5. Effect of Solutes in the Equilibrating Solution

Hydrogels when used for biomedical applications often come into contact with the physiological solutions of the body and thus the effect of solutes such as sodium chloride and urea on the swelling behaviour of hydrogels is of primary importance.

Sodium chloride was shown by Yasuda et al[102] to have a deswelling effect, producing a marked lowering of the equilibrium water content of PHEMA hydrogel with increasing sodium chloride concentration in the equilibrating solution. In an extensive study on the influence of solutes on the swelling of PHEMA hydrogel, Refojo[103] observed swelling in the presence of urea and its methyl derivatives, and anions such as iodides, acetates, trichloroacetates and thiocyanates, but a deswelling or syneresis in the presence of chlorides, bromides and sulphates.

Studies of the effect of solutes on swelling have also been used to create a better understanding of the mechanism of stabilisation of hydrogels in water. Refojo[103] postulated that PHEMA hydrogel has, in addition to its covalently cross-linked structure, a secondary structure stabilised by hydrophobic interactions between the α-methyl groups. This secondary structure, supposedly, so highly cross-links the hydrogel that the covalent cross-links are overshadowed. Thus, it is the secondary structure that controls the swelling behaviour of the hydrogel. His evidence for this was the increase in swelling of PHEMA hydrogel in dilute urea solutions which he considered to be caused by the breaking of the hydrophobic cross-links by urea in much the same way as urea denatures proteins by destroying hydrophobic bonding[104, 105].

However, investigations by Ratner and Miller[106] have led them to believe that although PHEMA hydrogels do contain sites that can participate in hydrophobic bonding, dilute urea solutions have no effect on such bonds. Furthermore they proposed a secondary structure for PHEMA hydrogels based on hydrogen bonding of the hydroxyl groups which is destroyed by urea solutions.

More recently Dusek et al[107] have examined the effect of urea on the swelling behaviour of PHEMA hydrogels at much higher urea concentrations than used before and found evidence for hydrophobic bonding and its destruction by high concentrations of urea.

1.5.3. Optical Properties

Transparency is obviously the main requisite of a polymer for contact lens use and accordingly transparency of hydrogels under varying conditions has been studied.

As previously mentioned polymerisation of HEMA in the presence of greater than 40% water results in phase separation during the polymerisation producing regions of differing refractive index and thus translucent or opaque hydrogels[100, 102].

An originally homogeneous gel becomes turbid when the solvent power of the swelling agent gets worse; such a change can be induced by a variation in temperature or by the exchange of a good solvent for a poor one. Refojo et al[100] observed that PHPA hydrogel became opaque at temperatures above 30°C if the temperature rise was rapid, and regained its original transparency if allowed to stand for long enough at the higher temperature. Similarly cooling of PHEMA swollen in 1- butanol at a higher temperature induced turbidity[108]. The exchange of a good solvent, ethylene glycol, in PHEMA for water has also been found to cause transient opacity, but transparency was regained when equilibrium was reached[100, 109]. The increase in turbidity observed in the above examples is caused by deswelling which is relatively slow due to the relaxation time of the network being very long. This means that a part of the surplus solvent is separated in the interior of the gel in the form of droplets ("microsyneresis")[108, 110].

The refractive index of a hydrogel is very dependent on its equilibrium water content. In fact, a linear relationship has been found between the refractive index and the water content of a PGMA hydrogel[101]. A value of 1.431 has been obtained for PHEMA hydrogel with an equilibrium water content of 40% and for PHPA hydrogel with a water content of 50% the refractive index was found to be 1.411[100].

1.5.4. Mechanical Properties

In its dehydrated state PHEMA is hard and brittle, resembling poly (methyl methacrylate). But when swollen in water PHEMA hydrogel is soft and exhibits rubberlike behaviour; properties which have made it so appealing for contact lens use. In its swollen state, PHEMA hydrogel has a very low tear and tensile strength and this lack of mechanical strength will affect its life-span as a contact lens. Thus, careful handling of hydrogel lenses is required.

The ultimate tensile characteristics of PHEMA hydrogels have been studied[111] and found to be sensitive to changes of temperature and rate of elongation. Bixler et al[112] have compared the ultimate properties of PHEMA hydrogel, a polyelectrolyte complex and cellophane and their results are shown in Table 4.

TABLE 4

Some Mechanical Properties of Three Water Swollen Polymers [112].

	Water Content %	Tensile Strength (psi)	Modulus (psi)	Elongation (%)
PHEMA	45	60	1000	140
Polyelectrolyte Complex	55	800	8000	18
Cellophane	55	4100	4400	92

Recently Ng[178], using a microindentation apparatus, has examined the deformation behaviour of a number of hydrogels under eye-lid pressure and hence predicted that high water content hydrogel lenses will give poorer visual acuity than low water content hydrogels.

Other mechanical properties such as creep, stress relaxation and equilibrium deformation behaviour of hydrogels, and in particular PHEMA, have been extensively studied and a review of this work has recently been published[113]. However, this work has little relevance to contact lens applications and thus will not be discussed here.

1.5.5. Permeation and Diffusion

The rate of transport of low molecular weight compounds (e.g. water, oxygen, sodium chloride, urea) through hydrogels is an important parameter for many applications.

The necessity of atmospheric oxygen for the maintenance of normal corneal metabolism is well known and so the permeability of hydrogels to oxygen is important for contact lens applications. However, over the years, a number of contradictory values have been obtained for the oxygen permeability of PHEMA hydrogel. Soon after its introduction as a contact lens material Takahashi et al[80] reported its oxygen permeability to be no greater than 4×10^{-10} cc. (STP) mm. cm.$^{-2}$ sec.$^{-1}$ cm. Hg.$^{-1}$. This value has since been used by many workers [74, 76, 95, 114] as evidence than an insufficient amount of oxygen is transported through the hydrogel lens to the cornea for normal respiration. However, the experimental conditions used by Takahashi and his co-workers suggest that their measurements were carried out on a partially dehydrated PHEMA lens which would obviously produce erroneous results. Higher values have been reported by Yasuda[115] who obtained 51×10^{-10} cc. (STP) mm. cm.$^{-2}$ sec.$^{-1}$ cm. Hg^{-1} and more recently by Fatt and St. Helen[81] who obtained 89×10^{-10} cc. (STP) mm. cm.$^{-2}$ sec.$^{-1}$ cm.Hg.$^{-1}$

The diffusion of oxygen through hydrogels from copolymers of HEMA and diethylene glycol methacrylate has been studied[116] and the diffusion coefficient found to be sensitive to changes in the hydrogel structure, particularly the degree of cross-linking. A decrease in the diffusion coefficient was observed with increasing cross-link density which also corresponded with a decrease in water content. Copolymers of HEMA and GMA were used in an investigation of the oxygen permeability of hydrogels by Yasuda et al[102] whose results indicated that for homogeneous hydrogels there was a direct relationship between the oxygen permeability coefficient and the equilibrium water content. But when the hydrogel became translucent or opaque they observed an abrupt increase in the oxygen permeability.

When hydrogels were first suggested as prosthetic materials it was recognised that if the water permeability of the implant was similar to that of the surrounding tissue then interference with the metabolism of the tissue would be greatly reduced. This, along with the possible application of hydrogels for desalination membranes, has led to the study of the water permeability of a number of hydrogels. Extensive investigations have been carried out by Refojo[63, 117, 118] into the water permeability of PHEMA, PHPA, PGMA, cellophane and polyelectrolyte complexes. From his measurements of permeability coefficients he calculated the water diffusion coefficients of the various hydrogels and their "pore radius". Some of his results are shown in Table 5.

The average pore radius provides a rough indication of the size of molecules that will penetrate the hydrogel network. The pore radius given for PHEMA hydrogel is 4Å but this value is probably too small as fluorescein (molecular radius 5.5 Å) is known to be absorbed into PHEMA hydrogel[124]. Fluorescein is used as an aid to the fitting of contact lenses but its uptake by hydrogels prevents its use during the fitting of this type of lens.

TABLE 5

Water Permeability Coefficients, Diffusion Coefficients and Pore Radii of Some Hydrogels[117].

Hydrogel	Equilibrium Water Content (%)	Water Permeability Coefficient $K \times 10^{15}$, cm^2	Water Diffusion Coefficient $D \times 10^5$, cm/sec.	Pore Radius (Å)
PHEMA	38.7	0.075	3.08	4.0
PHPA	41.2	0.087	3.89	4.5
PHPA	62.6	0.28	7.76	6.3
PGMA	80.3	4.65	88.6	21.7
PGMA	83.2	6.08	132.8	26.2
PGMA	88.8	14.79	265	37.0
Cellophane	57.6	1.044	--	--
Polyelectrolyte Complex	66.6	8.18	256	36.4

Refojo's results show, not surprisingly, that for the same family of hydrogels, increasing water content leads to an increase in water permeability. This confirms the earlier findings of White[119] that the water permeability of polyacrylamide hydrogels with low cross-link density is dependent on the amount of polymer in the hydrogel and independent of the amount of cross-linking. However, structure also plays an important part in determining water permeability, for example, the polyelectrolyte complex has a much greater permeability than the acrylic hydrogels with the same water content.

Refojo[117] and White[119] both observed that for hydrogels with less than 60% water content the calculated diffusion coefficients of water were of the same order of magnitude as the self-diffusion coefficient 2.8×10^{-5} cm^2./sec. of water (at 25°C)[120]. But at water contents higher than 60% the diffusion coefficients were very much larger than the self-diffusion coefficient of water. From this they concluded that the transport process was predominantly viscous flow in the high water content hydrogels but in the lower water content hydrogels water permeates by diffusion even under an applied pressure gradient. Their conclusions were confirmed by Yasuda et al[121, 122] who studied the change in the relationship between the diffusive permeability and the hydraulic permeability as a function of the water content of hydrogels. However, Paul[123] has claimed that the equation used by previous workers to calculate diffusion coefficients from hydraulic permeabilities is incorrect. He has developed a modified equation and used it to re-examine White's data for polyacrylamide hydrogels. As a result he concluded that diffusion was the dominant mechanism in homogeneous hydrogels even at high water contents.

As already mentioned hydrogels have been considered as membranes for desalination for reverse osmosis. However, for the process to be economically viable a high water permeability is required and so methods for increasing the permeability to water of hydrogels have been investigated. Refojo[125] has shown that permeation of water through PGMA and PHEMA hydrogels can be increased by the incorporation of silica fillers. Whilst Haldon and Lee[126] have prepared macroporous PHEMA hydrogel membranes with improved water permeability properties by cooling the monomer solution so that the solvent froze and the monomer occupied the interstices between the solvent crystals and then photopolymerising. Hydrogels of varying water permeabilities but much higher than the normal PHEMA hydrogel could be prepared depending upon the experimental conditions used.

Because of the interest shown in hydrogels as semi-permeable membranes especially for desalination by reverse osmosis and haemodialysis, increased attention has been focused on the permeation of solute molecules, such as sodium chloride, through hydrogels. Low salt permeation is a prime requirement for reverse osmosis membranes and high salt permeation a requirement for efficient haemodialysis membranes.

The diffusive permeability of sodium chloride through various hydrogels has been examined as a function of the equilibrium water content by Yasuda et al[127 - 129]. They found a linear dependence of the log of the permeability coefficient on the reciprocal of the volume fraction of water in hydrogels with a water content greater than 25%. Sodium chloride permeability has been shown to be affected[130] by the chemical structure of the hydrogel polymer as well as by its water content. Modification of PHEMA hydrogels by the introduction of ionogenic groups has been brought about by copolymerisation with methacrylic acid and/or 2-(diethylamino) ethyl methacrylate. A lower sodium chloride permeability than with neutral membranes (PHEMA hydrogel) was observed with membranes containing acid groups or basic groups as would be expected according to Donnans excluding effect. Ampholytic membranes (hydrogels containing both basic and acidic units) showed the highest permeability to sodium chloride which was attributed to the electric charge causing an acceleration of the diffusion of both ions. Kopecek et al[131] have also investigated the effect of the hydrophilic character of the polymeric backbone on sodium chloride permeability and found that replacement of HEMA in a HEMA - MMA copolymer by the more hydrophilic 2-(hydroxyethoxy) ethyl methacrylate increased permeability of the hydrogel at the same degree of hydration.

Diffusion studies have also been carried out on other solute molecules such as potassium chloride[132], magnesium sulphate[130] and urea[128]. The transport of urea through PHEMA has been examined[133] and evaluated with respect to the potential use of hydrogels as membranes for haemodialysis.

1.5.6. Applications

Hydrogels were first proposed by Wichterle and Lim[49] for biomedical use where hydrophilicity of the polymer is important with regard to biocompatibility. However, the area of application has now broadened considerably with their possible use as semi-permeable membranes becoming the most important non-biomedical area of interest.

Hydrogels, and in particular PHEMA, in the form of implants have been applied in many branches of surgery[134] including as urether prostheses[135] and vascular implants[136]. For "external use" hydrogels must be kept in contact with body fluids so that they remain in a state of hydration, for example, in the soft lining of dentures[137] and in contact lens applications. In addition to the cosmetic use of hydrogel contact lenses they have been used therapeutically[124, 138, 139] as "bandage lenses" for the treatment of many ocular complaints. Poly (glycerol methacrylate) hydrogels have been suggested for possible use as corneal implants[140, 141].

By utilising the absorption and desorption properties of hydrogels they can be used as vehicles for drugs and medication[134, 143-145].

For instance, a hydrogel device can be used to create a high drug concentration in the region of a tumour growth[142] or in a contact lens form to provide controlled release of therapeutic drugs to the eye[124, 138, 146].

The growing use of semi-permeable membranes in separation processes and the wide range of transport properties available with hydrogels has led to a considerable amount of work being done on the evaluation of various hydrogels for use as membranes in desalination[126, 131, 147 - 151, 155] and haemodialysis[128, 133, 152-155].

Linear PHEMA has been used for surface treating other materials to improve their physiological tolerance, such as in the coating of surgical satures[134, 156] and rubber catheters[134].

CHAPTER 2

EXPERIMENTAL METHODS

EXPERIMENTAL METHODS

2.1. SOURCE AND PURIFICATION OF MONOMERS AND REAGENTS

Monomers

The following monomers were purified by conventional reduced pressure distillation using gas liquid chromatography to monitor purity. The purified monomers were stored in a refrigerator until required for polymer synthesis.

Monomer	Supplier
2-Hydroxyethyl methacrylate	B.D.H.
Hydroxypropyl acrylate	B.P. Chemicals, Wychem Ltd.
N-Vinyl pyrrolidone	Koch Light
Ethylene glycol dimethacrylate	B.D.H.
Methacrylic acid	Koch Light
Methyl methacrylate	B.D.H.
Butyl methacrylate	I.C.I.
N-Hexyl methacrylate	Polysciences
2-Ethylhexyl methacrylate	I.C.I.
2-Phenylethyl methacrylate	Pfaltz and Bauer
2-Ethoxyethyl methacrylate	I.C.I.
2-Phenoxyethyl methacrylate	Pfaltz and Bauer
Lauryl methacrylate	I.C.I.
Ethyl methacrylate	B.D.H.
Styrene	Fisons
α-Methyl styrene	B.D.H.

2-Methyl pent-1-ene and 4-methyl pent-1-ene supplied by Koch Light and B.P. Chemicals, respectively were purified by distillation at atmospheric pressure.

Acrylamide, obtained from B.D.H., was recrystallised from ethyl acetate.

Catalysts Initiators and Solvents

Benzoyl peroxide, supplied by Fisons, was purified by recrystallisation from chloroform.

α-Azo-isobutyronitrile, supplied by B.D.H., was used without further purification.

Anhydrous zinc chloride from Fisons and anhydrous aluminium chloride from B.D.H. were dried in a vacuum oven at 200°C for 2½ hours immediately prior to use.

The following solvents were used as supplied by the manufacturers without further purification.

Toluene	B.D.H.
Tetrachloroethylene	B.D.H.
Benzene	Fisons
T.H.F.	B.D.H.
Methylene dichloride	B.D.H.
Chloroform	B.D.H.

1,4 - Dioxan, supplied by Fisons, was purified according to the standard technique described by Vogel[177].

Reagents used for Surface Treatment

These reagents were used as supplied.

Concentrated Sulphuric acid (98%)	Fisons
Potassium dichromate	B.D.H.
Nitric acid (fuming)	Hopkin and Williams
Chlorosulphonic Acid	B.D.H.

2.2. EXPERIMENTAL TECHNIQUES

2.2.1. Analytical Techniques

Infra Red Spectra

These were obtained using a Perkin-Elmer infra red spectrophotometer (model 457). Details of the state of sample etc. are given with the individual spectra.

Gas Liquid Chromatography

Traces were obtained using a Pye series 104 Model 24/34 gas chromatograph. A general purpose silicone gum SE30 column was used with a flame ionisation detector.

Microanalysis

Elemental analysis for the quantitative determination of carbon, hydrogen and nitrogen was carried out on an F & M 185 CHN analyser.

2.2.2. Polymer Synthesis

2.2.2.1. Solution Polymerisation

a) Free radical polymerisations were carried out on a 0.5 litre scale using conventional techniques and precautions.

In a typical experiment a polymerisation mixture consisting of 15.6g. (0.12M) 2-hydroxyethyl methacrylate, 6.32g. (0.04M) 2-ethoxyethyl methacrylate, 4.16g. (0.04M) styrene and 0.063g. (0.25% by wt.) AZBN was dissolved in 250ml. 1,4-dioxan contained in a 3-necked, 500ml. flask which was equipped with a stirrer, condensor, thermometer and a nitrogen bleed. Polymerisation was carried out under nitrogen in a water bath at 65°C for 8 hours. The contents of the flask were then allowed to cool and added drop-wise into 2.5 litres of vigorously stirred ether. A fine white precipitate was obtained. This was filtered, washed with ether then redissolved in 1,4-dioxan and reprecipitated as above. The white precipitate was dried in a vacuum oven at 60°C. The yield was 30%

b) Ultra-violet light initiated polymerisations were carried out in the presence of a Friedel-Crafts catalyst (eg. zinc chloride).

In a typical experiment a 3-necked, 250ml. flask fitted with a stirrer, condensor, thermometer and a nitrogen bleed, was charged with 100ml. T.H.F., 13.8g. (0.1M) zinc chloride, 13g. (0.1M) 2-hydroxyethyl methacrylate, 8.4g. (0.1M) 4-methyl pent-1-ene and 0.1g. α-azo-isobutyronitrile. Polymerisation was carried out at 22°C and effected by uv light of 3650 Å wavelength from a Gallenkamp Ultraviolet Mercury Discharge Lamp (L.H. - 530). The uv source was removed after 2 hours and the contents of the flask carefully poured into 2½ litres of vigorously stirred ether. A white precipitate was obtained which was filtered, washed with ether and dried under vacuum at 60°C. The yield was 32%.

2.2.2.2. Bulk Polymerisation

Both rods and membranes were produced by bulk polymerisation. Membranes were required for physical measurements (e.g. oxygen permeability) and the rods, if promising, could be lathe cut into contact lenses for clinical trials.

a) In Rod Form

Rods were prepared by polymerising a mixture of monomers in the presence of a free radical initiator and, if required, a cross-linking agent in a sealed length of polyethylene tube. Polyethylene tubes were generally used because it was found that they facilitated the removal of the polymerised rods whereas difficulty was often encountered in removing rods from glass test tubes.

By way of an example a monomer mixture of 2-hydroxyethyl methacrylate, 2-ethylhexyl methacrylate and styrene in a molar ratio of 70:20:10 and AZBN (0.1% by wt.) were weighed into a polyethylene tube (150mm. x 12.5mm.) sealed at one end. The mixture was flushed with nitrogen and the tube was sealed with an appropriate rubber bung covered with a thin polyethylene film and secured with adhesive tape. Polymerisation was carried out in a water bath at 65°C for 20 hours and finally in an oven at 90°C for 3 hours to ensure complete conversion. The rod was reasily removed by cutting open the polyethylene tube.

b) In Membrane Form

Hydrogel membranes or sheets were prepared by bulk polymerisation in a suitable glass mould. Two glass plates (12.5cm x 10cm.) each with one side covered with a thin transparent sheet of poly(ethylene terephthalate) as an aid to mould release, were placed together with the coated surfaces facing one another and separated by a 0.2mm. thick polyethylene gasket. The mould was held together by spring clips.

In a typical preparation a monomer mixture of 2-hydroxyethyl methacrylate, 2-ethoxyethyl methacrylate and styrene in a molar ratio of 70:20:10 and AZBN (0.1% by wt.) was purged with nitrogen and introduced into a glass mould by way of a syringe. The mould was then placed in an oven at 65°C for 72 hours followed by 2 hours post-curing at 90°C. When the polymerisation was completed the spring clips were removed from the mould and the mould halves separated leaving the polymer sheet adhering to only one of the halves. This was then placed in distilled water and the polymer sheet allowed to hydrate. The hydrogel in its hydrated state could then be easily removed from the poly (ethylene terephthalate) covered glass plate.

Originally glass plates without a covering of poly (ethylene terephthalate) were used to form the mould. However, it was found that following polymerisation the mould could not be opened until after a lengthy period hydration of the polymer sheet achieved by removing the gasket and soaking the complete mould in distilled water.

The more conventional release agents had no effect and although poly(ethylene terephthalate) was not the complete answer it nevertheless provided a substantial improvement in mould release.

2.2.3. Polymer Properties

2.2.3.1. Contact Angles

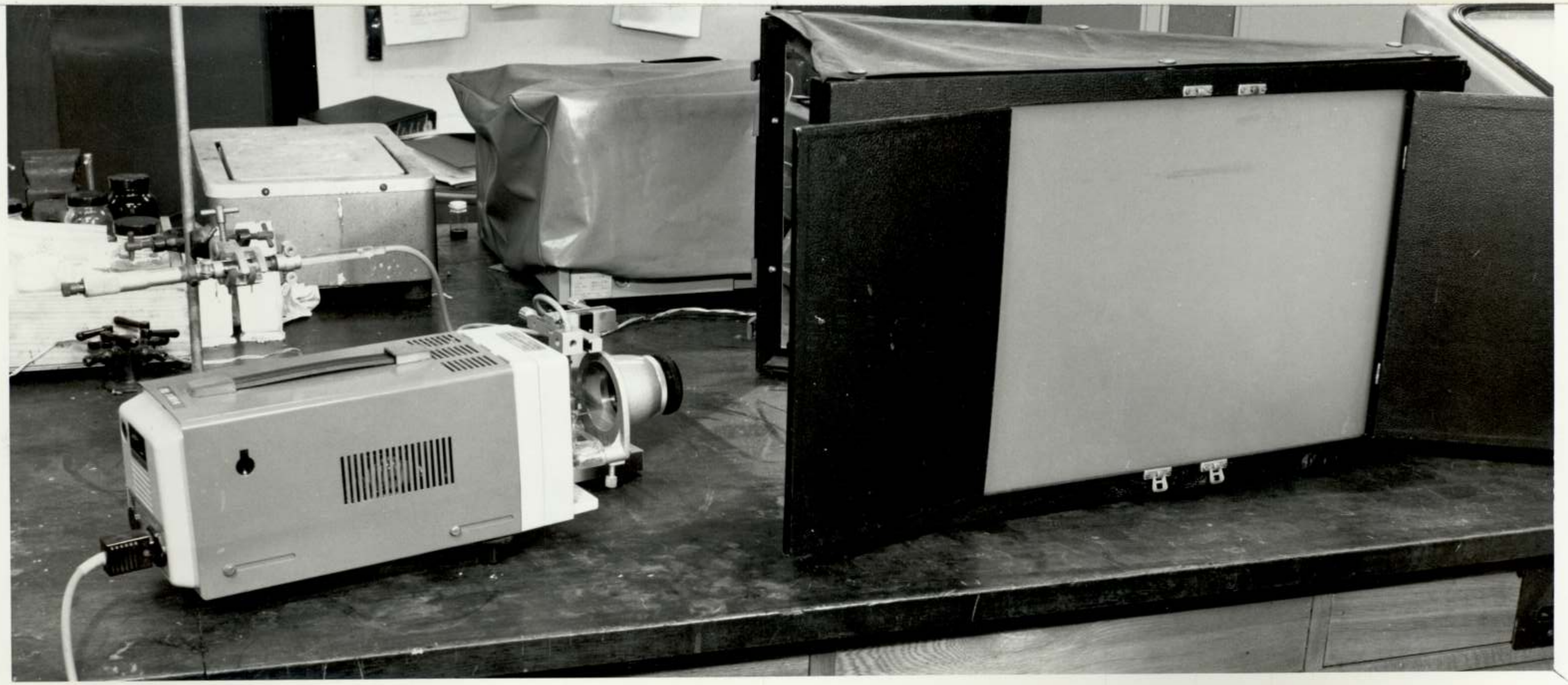
Contact angles were measured by the sessile drop method using a technique developed from the widely used methods of this type.

Prior to contact angle measurements the polymer surfaces were cleaned by washing with a detergent solution followed by a thorough rinsing with distilled water and finally drying in a vacuum desiccator. It has previously been shown that a detergent will not remain on the polymer surface after thorough rinsing with water[179].

The sessile drop of distilled water was formed on the surface of the polymer (usually a compression moulded disc) through a G.25 hypodermic needle, the position of which could be accurately controlled with the aid of a Prior micromanipulator. By supporting the polymer sample in a glass cell with optically perfect sides the sessile drop could be exposed to an atmosphere saturated with water vapour thus eliminating evaporation. The volume of the drop was controlled by an Agla micrometer syringe and was built up slowly enabling several measurements of the equilibrium advancing contact angle to be made.

With the aid of a Rank Aldis Tutor 2 projector fitted with a short, 5cm., focal length lens an enlarged image of the sessile drop was projected on to a back projection screen (Plates 1 and 2). A photograph of the image could be taken for later examination (Plate 3) or a direct measurement made on the screen by drawing a tangent to the drop surface at the three phase interface and measuring the contact angle with a protractor. At least six measurements were made on each polymer sample and each measurement was the average of the contact angles on either side

PLATE 1   Layout of Contact Angle Apparatus



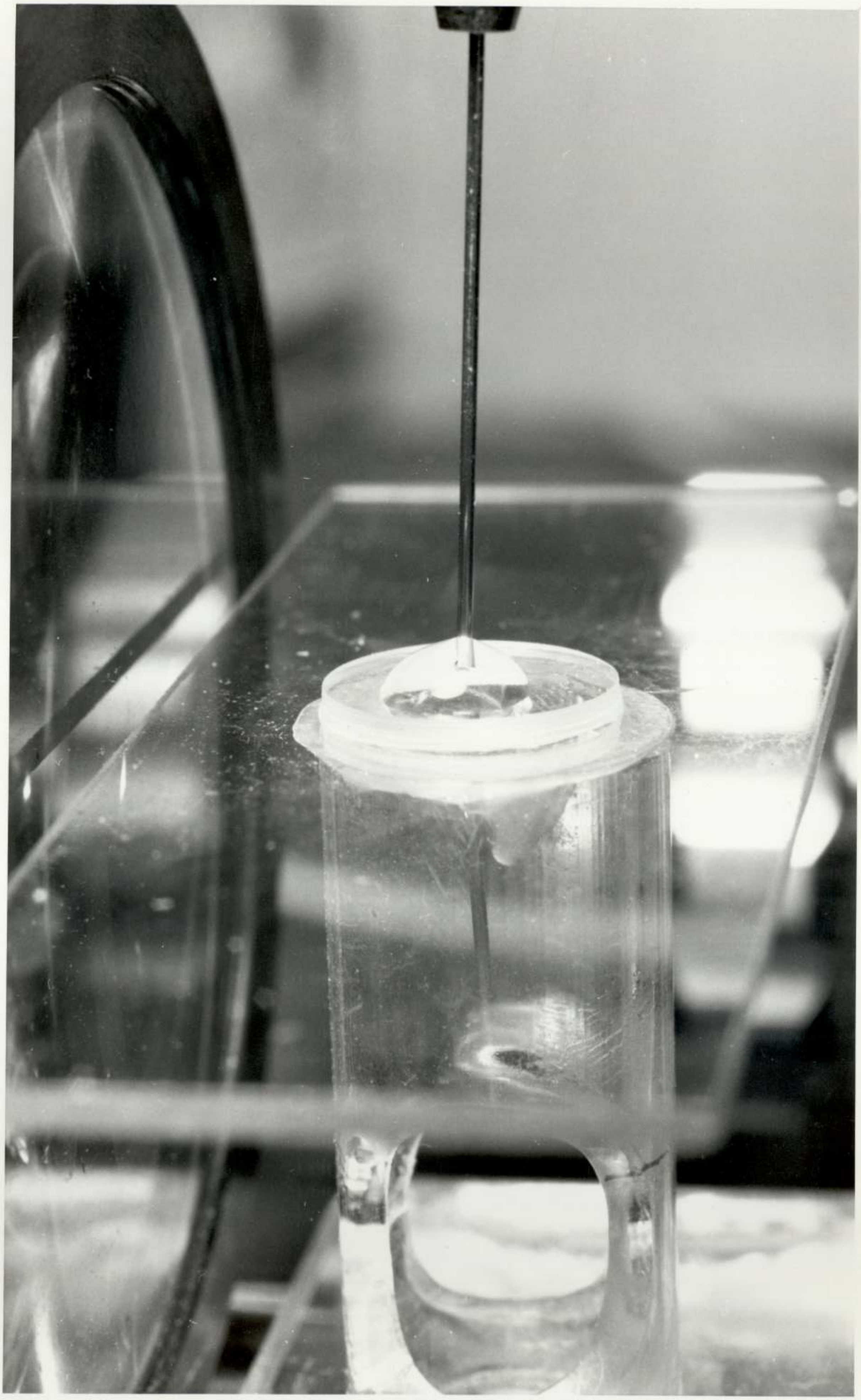


PLATE 2   Formation of Water Droplet

PLATE 3 Projected Image of Water Droplet on Polymer Disc

of the sessile drop.

2.2.3.2. Equilibrium Water Content

The hydrogels were most conveniently characterised by their water contents when swollen to equilibrium in distilled water at room temperature.

The equilibrium water content (E.W.C.) of a hydrogel membrane, for example, was measured after allowing the membrane to hydrate in distilled water for at least three weeks, more than sufficient for the attainment of equilibrium. Not less than three samples were then cut with a cork-borer (1cm. in diameter) from the hydrated sheet. The surface water of each sample was carefully removed with a tissue and the sample quickly transferred to and weighed in a closed weighing bottle of known weight. The lid of the weighing bottle was partially opened and the sample allowed to dehydrate to constant weight in a vacuum oven at 60°C. When a constant weight was reached the weight was noted and the E.W.C. was calculated according to Equation 1.

$$\text{E.W.C.} = \frac{\text{wt. of hydrated sample} - \text{wt. of dehydrated sample}}{\text{wt. of hydrated sample}} \times 100\% \qquad (1)$$

The E.W.C.'s of at least 3 samples were determined in this way and an average E.W.C. was taken.

2.2.3.3. Oxygen Permeability

The transport of gases through polymers has been the subject of a great deal of research motivated by the considerable industrial interest in related applications, in particular, the design of better gas and vapour barriers for packaging. Accordingly almost all the recorded measurements of the gaseous permeability constants of polymers have been obtained using the high vacuum time-lag technique developed by Barrer.[180]

In the case of the contact lens in position on the eye there is a film of tear fluid on both the posterior and anterior surfaces of the lens. This means that the contact lens acts as a barrier to the oxygen dissolved in the tears. Thus, in order to simulate the conditions under which the contact lens will be used and to give more meaningful results, measurements of oxygen permeability should be made in a system whereby water contacts both sides of the polymer. This is also of practical value when hydrogels are being tested as it prevents the hydrogel from partially dehydrating which would certainly occur in the high-vacuum technique and lead to erroneous and misleading results.

Although a number of methods are available for the analysis of dissolved oxygen only the membrane electrode method allows continuous measurements of dissolved oxygen concentration to be made. For this reason and its accuracy of measurement the membrane electrode was used in this work to study the oxygen permeability of contact lens materials.

2.2.3.3.1. Principle of the Membrane Electrode

A membrane electrode (essentially an electrolysis cell) operates on the principle of polarographic analysis. The oxygen electrode which can measure the concentration of dissolved or gaseous oxygen consists of a gold cathode separated by an epoxy coating from a tubular silver anode. The silver anode is electrochemically connected to the gold cathode by a thin layer of potassium chloride electrolyte, and the entire anode-cathode assembly is separated from the solution to be analysed by an oxygen permeable PTFE membrane that fits firmly against the gold and silver surfaces. When oxygen diffuses through the membrane it is electrochemically reduced at the cathode by an applied voltage of 0.8 volts. This reaction causes a flow of current between the anode and the cathode proportional to the oxygen concentration.

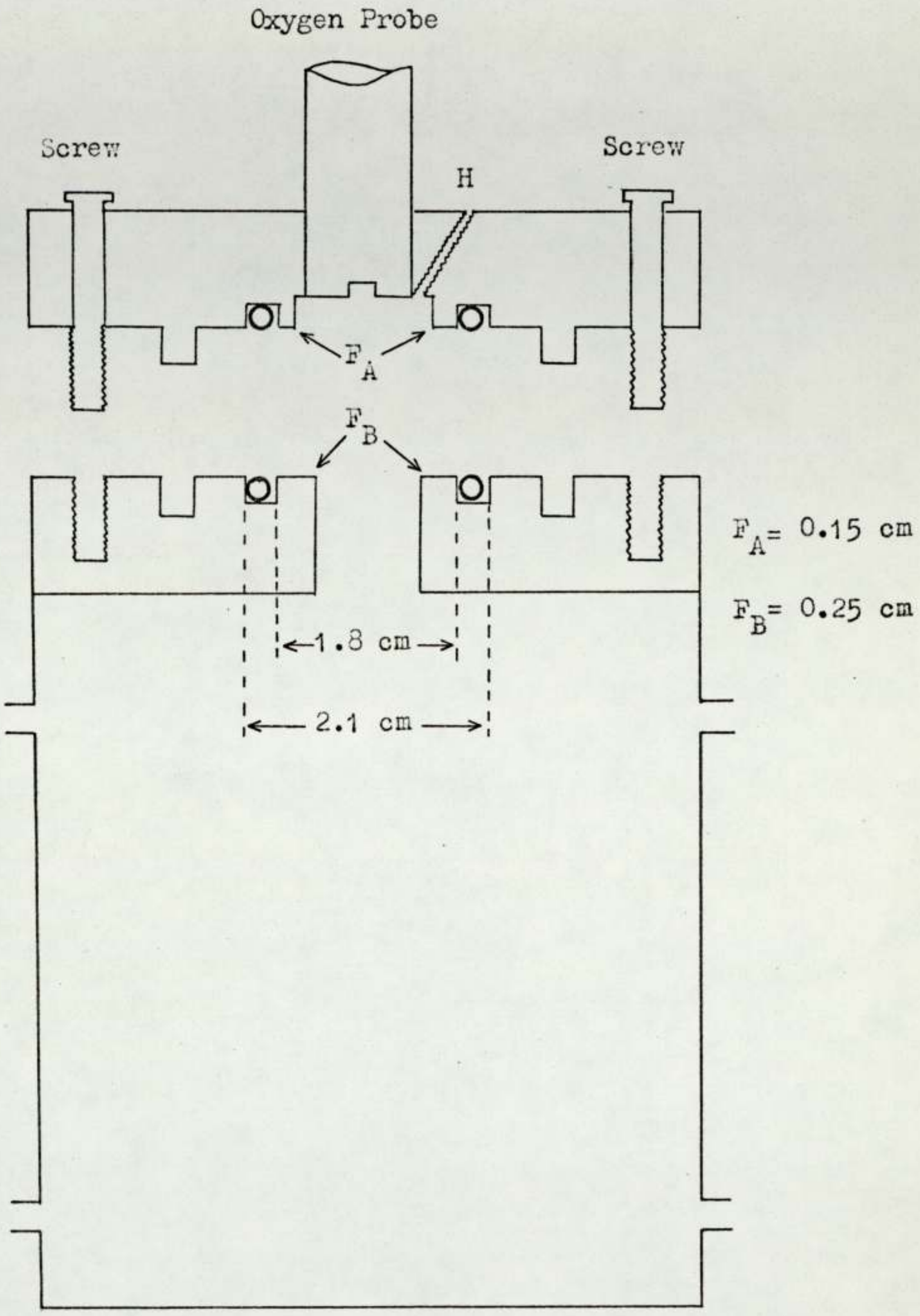


FIGURE 3 The Oxygen Permeation Cell

The chemical reactions occurring at the electrodes of a polarographic oxygen probe are:-

$$O_2 + 2H_2O + 4e^- \qquad 4OH^- \text{ (cathode)} \qquad (2)$$

$$4Ag + 4Cl^- \qquad 4AgCl + 4e^- \text{ (anode)} \qquad (3)$$

2.2.3.3.2. Description of the Permeation Cell and Layout of the Measuring Apparatus

The permeation cell was constructed from perspex in a cylindrical form (height 8.8cm and diameter 5.1cm.) as shown in Fig. 3. The cell consisted of two parts designed so that when clamped together by the six holding screws the top chamber was separated from the bottom chamber by the test sample supported between the two rubber "O" rings.

The top part of the cell contained the I.M.I. 3601A oxygen sensor (Fig. 4) which was firmly secured in a perspex tube attached to the cell such that the tip of the oxygen sensor was flush with the top of the upper chamber. A hole (H)(which could be sealed with a nylon screw) was bored through the top part of the cell so that nitrogen-saturated water could be introduced into the upper chamber.

The bottom part of the cell was equipped with water inlet and outlet positions as well as a magnetic follower.

The layout of the oxygen permeability apparatus is shown in Fig. 5 and Plate 4. The oxygen sensor was connected to an I.M.I. oxygen monitor, the output of which was linked to a recorder (Model EPR-2TB, TOA Electronic Ltd.). The permeation cell was placed on a magnetic stirrer and the water inlet and outlet positions were connected to a water bath thermostatted by an immersion thermostat unit.

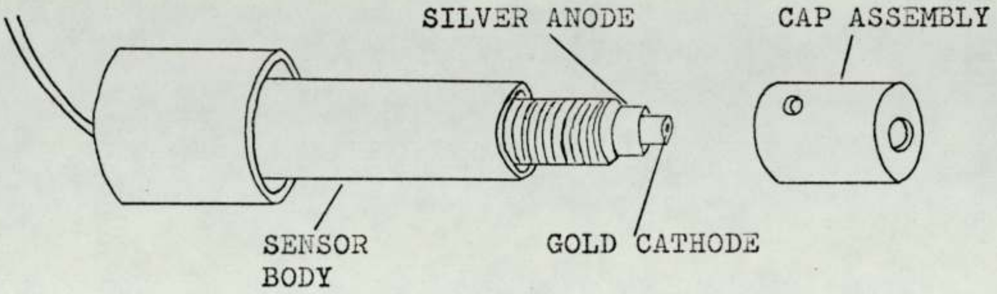


FIGURE 4 Exploded View of Oxygen Sensor

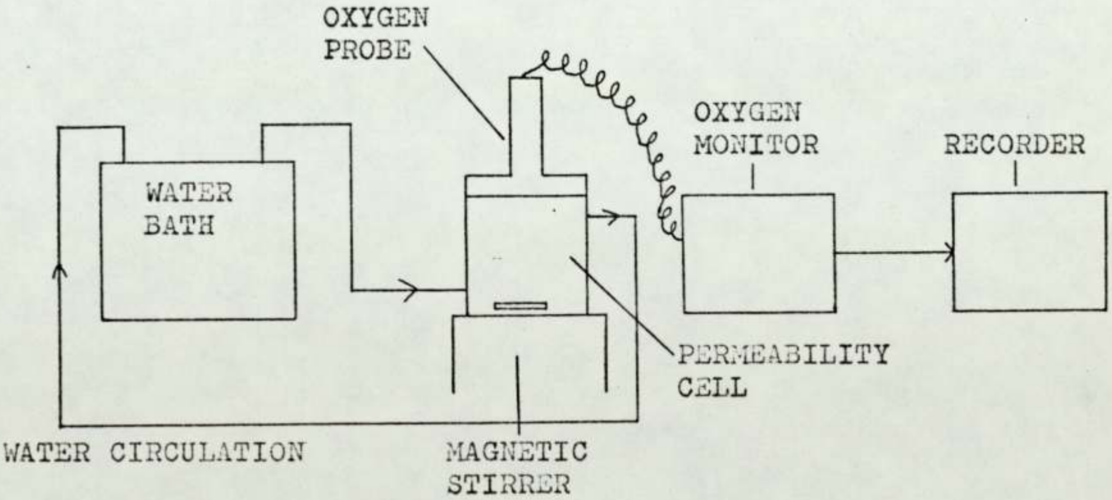
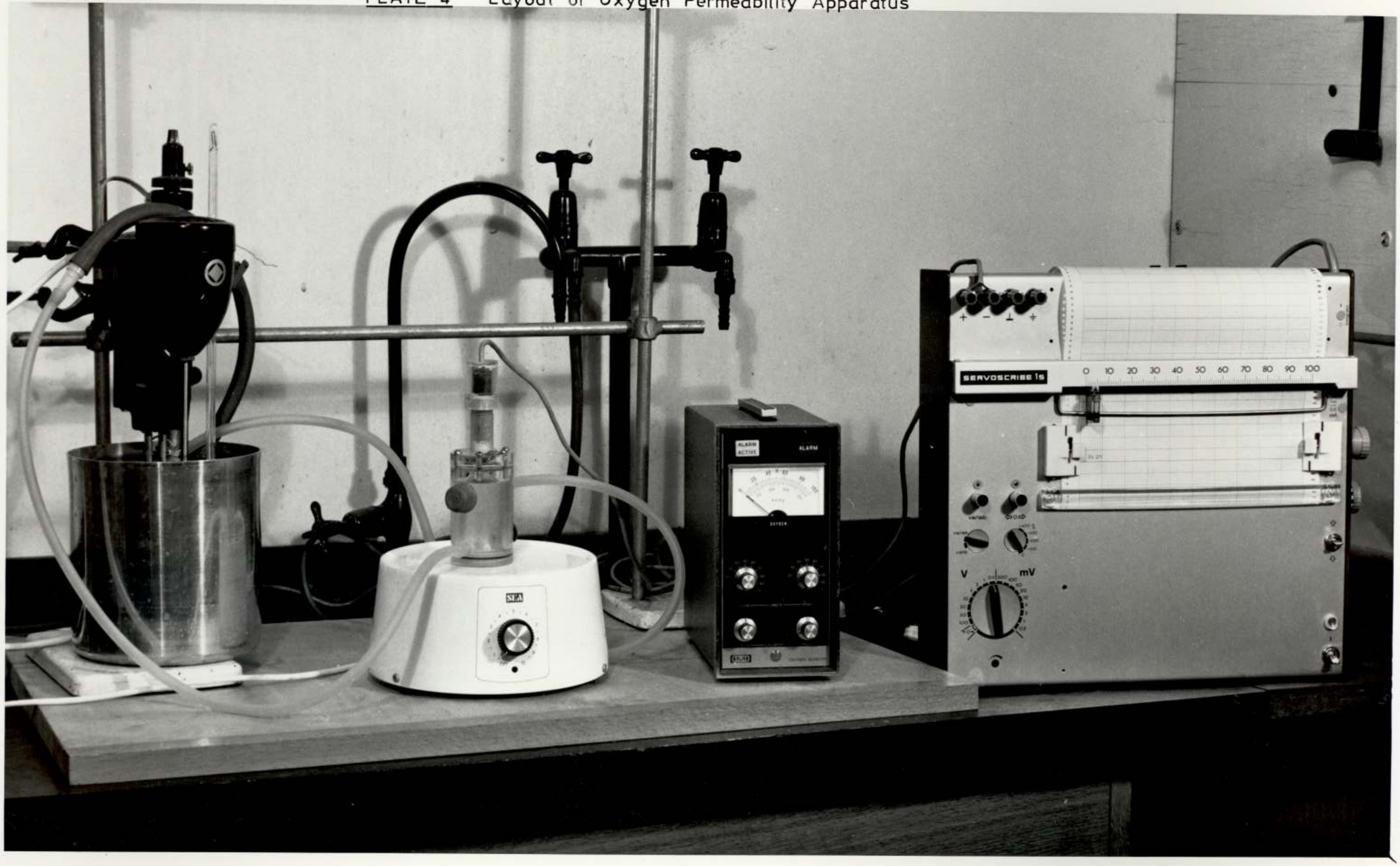


FIGURE 5 Layout of Apparatus for Measuring 'Dissolved' Oxygen Permeability Coefficients

PLATE 4 Layout of Oxygen Permeability Apparatus



2.2.3.3.3. Testing Procedure

The oxygen sensor was first calibrated by exposing it to a nitrogen atmosphere and adjusting the "LOW" knob on the oxygen monitor until a zero reading was obtained. Oxygen was then substituted for the nitrogen and the "HIGH" knob adjusted to obtain a full scale deflection on the monitor. The oxygen sensor was then allowed to equilibrate in air and the oxygen monitor then read 159mm. Hg.. The calibration was checked prior to each oxygen permeability measurement.

For hydrogels a test sample of diameter 1.8cm. was cut from a hydrated (at 25°C) polymer sheet with a cork-borer (Griffin and George; Size 12). Its thickness was then measured with a thickness guage and an average taken of about half a dozen readings. To counteract any dehydration which may have occurred during the thickness measurement the sample was allowed to re-equilibrate in distilled for one hour.

In the case of the more robust hydrophobic materials, such as poly(4-methyl pent-l-ene), a slightly larger disc (diameter 2.1cm.) was cut and its thickness measured with a micrometer. The difference in sample size was due to the slightly different sample mounting techniques. Poly (4-methyl pent-l-ene) and the like were clamped in the permeation cell between the two rubber "O" rings. This, however, was found to lead to rupture of the more delicate hydrogels and the following procedure was thus adopted for use with hydrogels.

Because of the fragile nature of some of the test samples, especially the high water content hydrogels, great care had to be exercised during the sample mounting. In order to prevent leaks and rupturing of the sample a layer of plasticine was applied to the top and bottom flanges (F_A and F_B) of the permeation cell. During the clamping operation uniform pressure was applied by careful adjustment of the six holding screws and this prevented twisting or rupturing of the sample. The bottom part of the cell was then filled with nitrogen saturated water (obtained by boiling distilled water and then bubbling through, overnight, with nitrogen) at 25°C and the top part of the cell was flushed with nitrogen by way of hypodermic needle introduced through the aperture (H). Any leak in the system due to improper clamping or the presence of holes in the sample could be detected at this stage. When a zero reading was obtained on the oxygen monitor the top chamber was filled with nitrogen-saturated water at 25°C injected through the aperture with a Hamilton syringe while the entrance to H was blanketed with nitrogen to prevent contamination with air. This intricate operation required a great deal of care and dexterity to avoid damaging the sample with the hypodermic needle and to prevent the formation of gas bubbles in the small trough at the end of the oxygen probe as these were found to give erroneous readings on the oxygen monitor. The volume of nitrogen saturated water added was noted and the aperture was sealed, whilst still under a nitrogen blanket, with a nylon screw. The nitrogen-saturated water in the bottom part of the cell was drained away and replaced with air-saturated water at 25°C recirculated from a thermostatted water bath. The water in the bottom chamber was rapidly stirred with a magnetic stirrer and the increase in oxygen concentration in the top chamber due to the diffusion of oxygen through the sample was followed on the recorder.

When equilibrium was reached the experiment was terminated and the oxygen probe was allowed to equilibrate in air before the next measurement. At least three measurements were made for each material.

2.2.3.3.4. Theory of Dissolved Oxygen Permeability

The oxygen permeabilities of the membranes studied were measured under unsteady-state conditions. One side of the membrane was in contact with a large reservoir of dissolved oxygen solution whilst on the other side of the membrane the build up of oxygen partial pressure was recorded as a function of time.

Conventionally the oxygen flux, F, from the lower part of the cell (high oxygen concentration side) through the membrane is given by

$$F = \frac{P\,(p_1 - p_2)}{L} \qquad (4)$$

where F is the oxygen flux (cc. cm^{-2}. sec^{-1})

P is the dissolved oxygen permeability coefficient

(cc.(S.T.P.) mm. cm^{-2}. sec.^{-1} $(\text{cm. Hg.})^{-1}$)

p_1 is the partial pressure of oxygen in water on the high oxygen concentration side (cm. Hg.)

p_2 is the partial pressure of oxygen in water on the low oxygen concentration side (cm. Hg.)

L is the thickness of the membrane (mm.)

The oxygen flux, F, into the top part of the cell (low oxygen concentration side) can also be given by

$$F = \frac{V}{A}\, S_w\, \frac{d_{P2}}{dt} \qquad (5)$$

where A is the cross-sectional area of the membrane (cm^2.)

V is the volume of water in the top part of the cell (cc.)

S_w is the solubility of oxygen in water

(cc. (S.T.P.) $(\text{cc. } H_2O)^{-1}$ $(\text{cm. Hg.})^{-1}$)

From Equations (4) and (5)

$$dp_2 \cdot \frac{1}{p_1 - p_2} = \frac{PA}{LVS_w} dt \qquad (6)$$

Integration of this equation with the boundary condition of $p_2 = 0$ at $t = 0$ gives

$$\ln \frac{(p_1 - p_2)}{p_1} = - \frac{PA}{LVS_w} t \qquad (7)$$

A plot of $\ln \frac{(p_1 - p_2)}{p_1}$ against t yields a negative slope k where

$$k = \frac{PA}{LVS_w} \qquad (8)$$

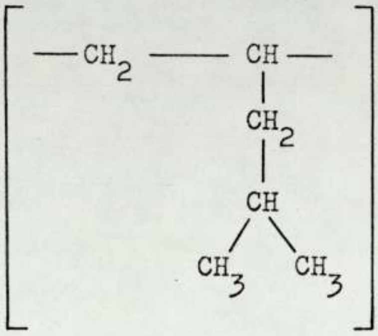
thus $$P = \frac{kLVS_w}{A} \qquad (9)$$

CHAPTER 3

COMMERCIALLY AVAILABLE POLYMERS AS POTENTIAL CONTACT LENS MATERIALS

temperature (Tg) of P4MP1 has been quoted as 29°C which would mean that when placed on the eye (temperature 34°C) it would be above its Tg, thus possibly lending itself to greater comfort. Of course, there is the inevitable drawback, in that the hydrophobic nature of P4MP1 indicates that it would not be wet by the tears and therefore a simple but nevertheless effective method[183, 184] is required to render the polymer more wettable.

P4MP1 (IV) because of its secondary and tertiary C - H bonds is susceptible to oxidative attack. Thus treatment with chromic acid was selected as a surface oxidation process to increase the wettability of P4MP1 and also as one that could be comfortably used by a contact lens manufacturer with little chemical expertise.


(IV)

3.1. MATERIALS AND METHODS

Poly (4-methyl pent-1-ene), supplied by I.C.I. in the form of granules, was compression moulded into discs (diam. 8.5mm.) and contact lenses (diam. 10mm.) by Kelvin Lenses Ltd. The lenses were normally moulded from the discs (blanks) and both were used in the surface treatment investigations.

The lenses and discs were cleaned with a soap solution, thoroughly rinsed with distilled water and dried prior to immersion under varying conditions of time and temperature in a bath of chromic acid (prepared from potassium dichromate, concentrated sulphuric acid and water in the ratio 1:12:1.7 by weight). Other reagents also used for surface treatement were fuming nitric acid, concentrated sulphuric acid and chlorosulphonic acid.

In recent years research into new materials for contact lenses has been concentrated on hydrogels. However, because of the inherent problem of the failure of hydrogel lenses to correct corneal astigmatism and not altogether satisfactory optical performance of commercially available hydrogel lenses, the so-called "hard lens" will undoubtedly maintain its important position in the contact lens market for a number of years to come.

Since its introduction[33] for contact lens use in 1947, poly (methyl methacrylate) (PMMA) has, because of its optical properties, stability and commercial availability been the most popular contact lens material. Improvements over the years in design and fitting of the PMMA lens have helped to maintain its popularity, but despite this it does have a number of deficiencies, in particular, its rigidity (a prime factor in governing comfort) and virtual impermeability to oxygen.

It would obviously be advantageous to develop a material showing improvements in these respects whilst retaining the toughness and ease of sterilisation which have such a marked effect on convenience in day to day handling. Although a tailor made polymer would provide these properties and more there are a number of commercially available polymers which as a short term approach warrant investigation as potential contact lens material. One of the more promising is isotactic poly (4-methyl pent-1-ene) (P4MP1) sold by I.C.I. under the tradename TPX. P4MP1 has a number of desirable propeties which recommend it for contact lens use; optical properties comparable to PMMA, physiological inactivity, more flexible than PMMA, a relative density of 0.83 making it the lightest known thermoplastic, and an oxygen permeability at 25°C reported[182] to be 275×10^{-10} cc. (STP) mm. cm.$^{-2}$ sec.$^{-1}$ (cm. Hg.)$^{-1}$, many times greater than that of PMMA. In addition the glass transition temperature (Tg) of P4MP1 has been quoted as 29°C which would mean that when placed on the eye (temperature 34°C) it would be above its Tg, thus possibly lending itself to greater comfort. Of course, there is the inevitable drawback, in that the hydrophobic nature of P4MP1 indicates that it would not be wet by the tears and therefore a simple but nevertheless effective method[183, 184] is required to render the polymer more wettable.

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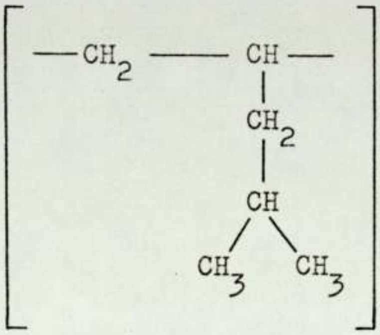

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Observations were made of the effect of surface treatment on other potential contact lens materials.

Polymer	Supplier
Polypropylene (70% isotactic/30% atactic)	Hercules Chemical Co.
Polypropylene (40% isotactic/60% atactic)	Hercules Chemical Co.
Poly (dimethylsiloxane) D414-S5505	Dow Dorning
Ethylene propylene terpolymer (Enjay 3509)	Esso

After immersion the discs and lenses were throughly rinsed (sufficient to remove any traces of the surface treatment reagent) and dried in a vacuum desiccator. The effect of surface treatment on clarity and surface polish was assessed visually. The advancing contact angles with water were measured according to the procedure described in Section 2.2.3.1. The reproducibility of readings was ± 2°. The surface of P4MP1 was also examined by attenuated total reflectance infra red spectroscopy.

3.2. RESULTS

3.2.1. Preliminary Study

It was necessary from the outset of this study to determine whether contact angles measured on flat discs were equivalent to those measured on contact lenses as equivalence would ensure that results obtained from preliminary investigations on discs would be applicable to contact lenses. For a variety of polymers no difference was found in measurements made on a polymer in both lens and disc form. However, contact angle measurements on lenses were found to be more difficult and subject to slightly larger errors because of the necessity of having to draw two tangents instead of one.

The contact angles of water on a number of potential contact lens materials were determined and compared with PMMA (Table 6). The contact angle data shows that these polymers are much less

TABLE 6

Wettability of Polymers with Potential as Contact Lenses

Polymer	Contact angle of water on disc (degrees)
Poly (methyl methacrylate)	64
Poly (4-methyl pent-1-ene)	93
Poly (dimethylsiloxane)	96
Polypropylene (70% isotactic/30% atactic)	91
Polypropylene (40% isotactic/60% atactic)	91
Ethylene propylene terpolymer	94

wettable than PMMA and are thus unlikely to be tolerated on the eye unless provided with a more hydrophilic surface.

3.2.2. Surface Treatment of Poly (4-Methyl Pent-1-ene)

The effect of immersion of P4MP1 in chromic acid at 20°C and at 60°C on the contact angle of water is shown in Figures 6 and 7, respectively. At both temperatures there is a rapid initial decrease in the contact angle but little subsequent drop with increasing time of immersion.

There was no visual effect with surface treatment until after twenty to thirty minutes exposure to chromic acid at 60°C when there was a noticeable worsening of clarity and loss of surface polish. When examined under a microscope and compared to untreated P4MP1 it was evident that there was a marked increase in surface roughness. No loss of clarity or surface polish was observed when P4MP1 was surface treated at 20°C for up to at least 45 minutes.

The surfaces of the treated samples were examined by attenuated total reflectance (ATR) infra red spectroscopy for the presence of oxidation products. However, despite the sensitivity of the ATR technique to detect small changes in surface chemistry there

FIGURE 6 Change in the Equilibrium Advancing Contact Angle of Water on Poly(4-methyl pent-1-ene) with Time of Immersion in Chromic Acid at 20°C

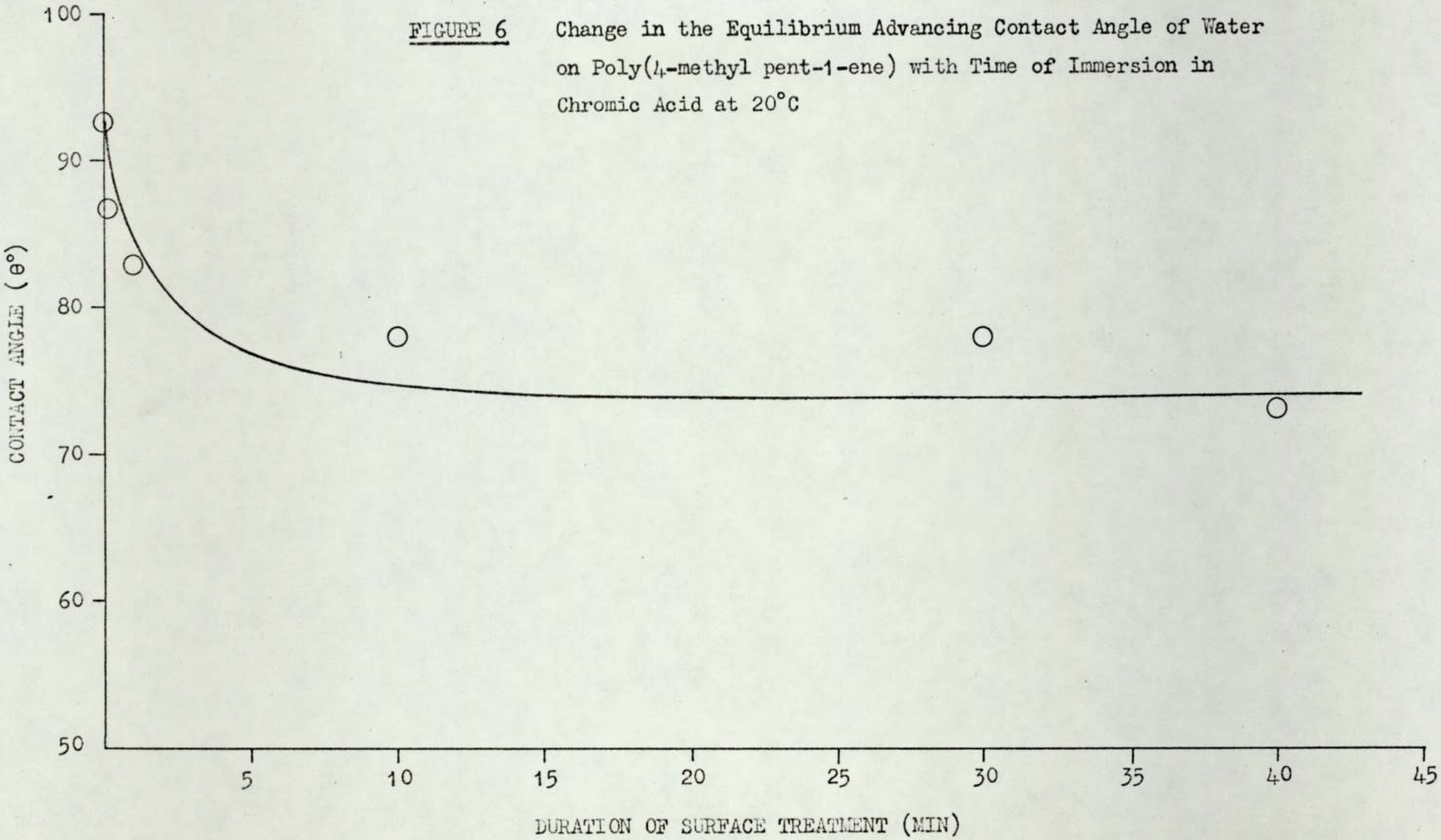
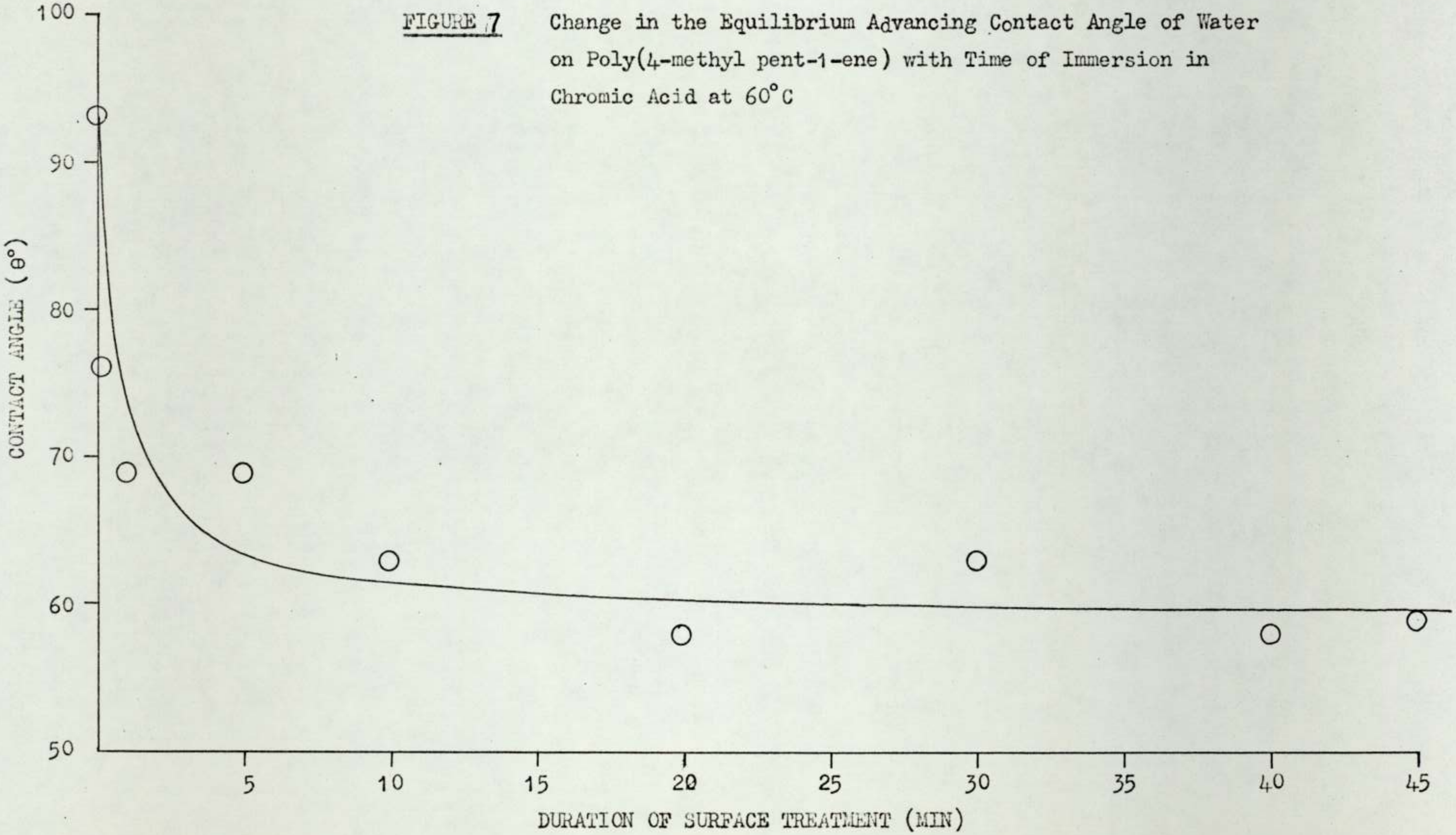


FIGURE 7 Change in the Equilibrium Advancing Contact Angle of Water on Poly(4-methyl pent-1-ene) with Time of Immersion in Chromic Acid at 60°C



was no difference in the spectra of untreated P4MP1 and the most strongly treated (60 minutes at 60°C) sample.

As the optical finish of lenses surface treated at 60°C was not quite as good as untreated lenses, it was of practical interest to determine whether or not the optical finish could be restored without destroying the improved hydrophilicity. The results are shown in Table 7 from which it can be seen that a secondary process of moulding or polishing substantially increases the contact angle i.e. reduces wettability. Improved optical quality, however, was observed in the moulding of lenses from surface treated discs but the moulding of 16mm. discs from 8.5mm. discs resulted in fogging of the disc surface corresponding to the original area of the surface treated disc.

TABLE 7

The Effect of Moulding and Polishing on the Wettability Towards Water of Chromic Acid Treated Poly (4-Methyl Pent-1-ene)

P4MP1 Sample	Surface Treatment	Contact Angle	Secondary Process	Contact Angle
8.5mm. Disc		93°		
8.5mm. Disc	1 hr. 60°C	59°	Compression moulded into 10mm. Lens	87°
8.5mm. Disc	10 mins. 60°C	63°	Compression moulded into 10mm. Lens	87°
8.5mm. Disc	10 mins. 60°C	63°	Compression moulded into 16mm. disc.	92°
10mm. Lens	10 mins. 60°C	63°	Polished with silicate optical polish	84°

Observations made on the surface treatment of P4MP1 with reagents other than chromic acid are summarised in Table 8. Treatment with fuming nitric acid resulted in improved wettability but had an undesirable effect on the optical quality of the P4MP1 surface. However, there was little change in wettability after treatment with concentrated sulphuric acid and even more surprising was the increased contact angle produced on immersion in chlorosulphonic acid.

TABLE 8

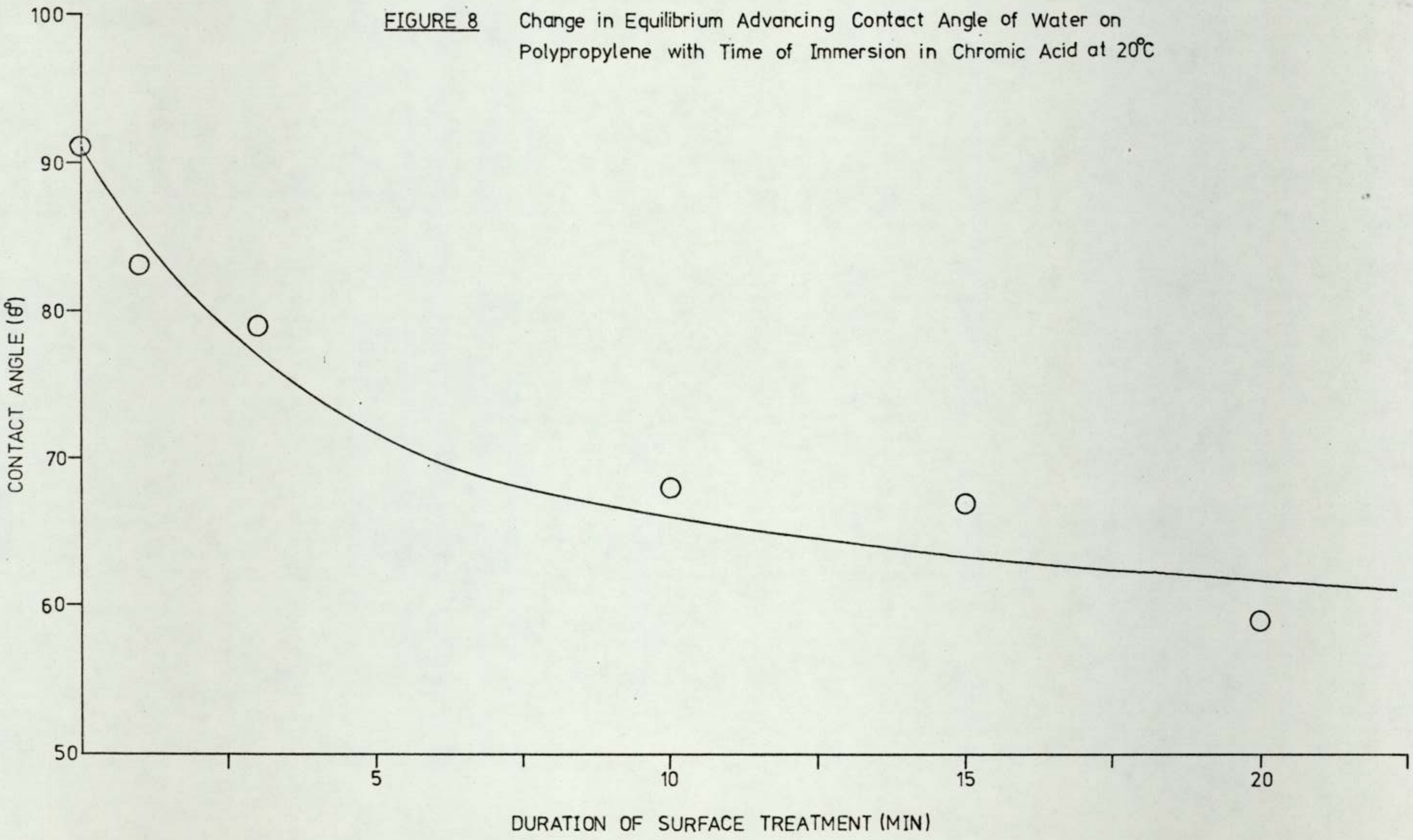
The Effects of Fuming Nitric Acid, Concentrated Sulphuric Acid and Chlorosulphonic Acid on the Surface of Poly (4-Methyl Pent-1-ene)

Reagen	Conditions	Contact Angle (Degrees)	Effect on Optical Properties
Fuming nitric acid	30 mins. 20°C	75	Brown tinge
Fuming nitric acid	30 mins. 60°C	59	Brown tinge and white spots
Concentrated Sulphuric Acid	60 mins. 60°C	92	No effect
Chlorosulphonic Acid	30 mins. 20°C	98	Slight loss of clarity
Chlorosulphonic Acid	5 hrs. 20°C	103	Loss in clarity

3.2.3. Observations of the Surface Treatment of Other Polymers With Contact Lens Potential

Poly (dimethylsiloxane) was found to have little resistance to the attack of chromic acid at 60°C. Immersion of lenses for 1 minute resulted in opacity and after 5 minutes the surface layer flaked off when the lenses were gently rubbed between the fingers. The final

FIGURE 8 Change in Equilibrium Advancing Contact Angle of Water on Polypropylene with Time of Immersion in Chromic Acid at 20°C



destruction was signalled after ten minutes when the lenses began to break up.

Polypropylene (70% isotactic/30% atactic) was treated with chromic acid at 20°C (Figure 8) with increasing loss in clarity with time of immersion. With the higher atactic content (40% isotactic/60%atactic) polypropylene the loss in clarity was much worse under the same conditions of treatment.

Ethylene propylene terpolymer (EPT) lenses when treated with chromic acid at 20°C and 60°C also lost their optical clarity. However, it was observed that if 100 parts (by weight) was masticated on a water cooled two roll mill with 4 parts dicumyl peroxide and then compression moulded to give optically clear sheet a contact angle with water of 60° was obtained. By comparison the untreated polymer had a contact angle of 94°.

3.2.4. Results of Clinical Trials[185]

Before a complete clinical trial could be undertaken on P4MP1 lenses it was necessary to correlate surface treatment and thus the resulting contact angle with the clinical phenomenon of a continuous tear film over both surfaces of the lens. The assessment of a continuous film over both surfaces was made with the aid of 2% fluorescein instilled into the eye. An examination using a biomicroscope enabled the homogeneity of the tear film to be determined. From the results shown in Table 9 it is apparent that for satisfactory wetting on the eye P4MP1 lenses need to be surface treated sufficiently to produce a contact angle of about 60°.

A fitting set was thus manufactured and subject to a suitable chromic acid surface treatment (10 mins. at 60°C). A group of twenty-one patients was assembled and clinical evaluations of the treated lenses obtained.

TABLE 9

The Effect of the Wettability of Poly (4-Methyl Pent-1-ene) on the Homogeneity of the Tear Film

Advancing Contact Angle (Degrees)	60 - 65	65 - 70	70 - 75	> 75
% Number of cases in which a Complete Anterior Tear Film was Observed	100	50	30	0

Comfort was assessed on a 0 to 4 scale according to which:-

0 - Presence of lenses not felt.

1 - Lenses felt but not irritating.

2 - Lenses irritating but not painful.

3 - Lenses moderately painful.

4 - Lenses painful.

The level of comfort achieved by the patients was a mean of 1.2 (standard deviation 0.45).

Visual acuity, quality of vision and induced astigmatism were found to be similar to that encountered with PMMA lenses. The disturbance to the epithelium was assessed using a conventional staining technique. Over a period of 21 one hour wearing periods, seven instances of stipple stain were observed, two instances of punctate stain, and one instance each of arcuate and line stain. No area of stain exceeded 10% of the corneal surface. No incidence of central epithelial oedemawas encountered.

Some clinical work was also carried out on ethylene propylene terpolymer (subject to mastication with dicumyl peroxide on a two roll mill) lenses having contact angles with water of 60°. These lenses were, however, found to cause pain in the eyelid of the wearer subjectively similar to that due to an abrasive action.

3.3 DISCUSSION

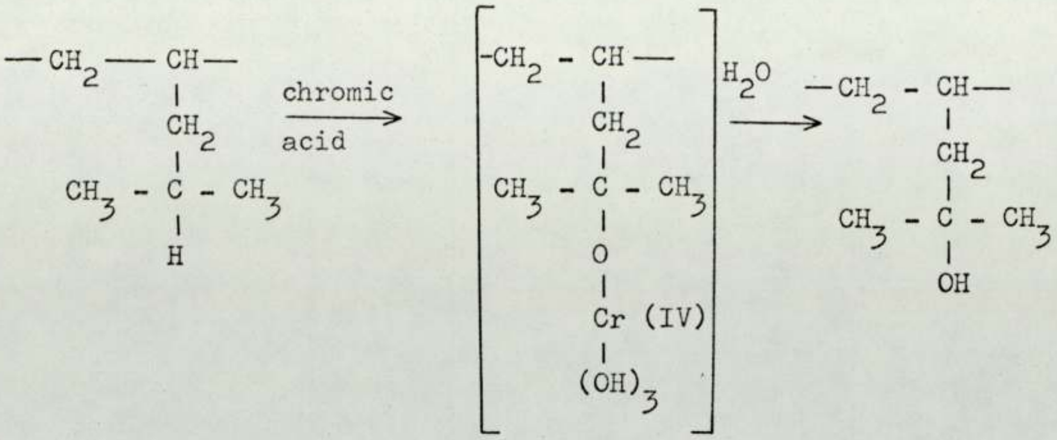
The lack of an apparent difference between contact angles measured on discs and those measured on lenses is not altogether surprising, as the curves of the lenses used were not very steep and only small drops of water were formed on the very top of the lenses. There is also an acceptable method[186, 187] for measuring contact angles, in which a liquid drop is placed on the surface of a polymer in the form of a flat sheet and the sheet is then tilted until the drop can be seen to be advancing slowly. It is then rotated gently in the reverse direction until the drop is just static and the advancing contact angle is thus measured. In the case of the measurements on contact lenses the advancing contact angle was obtained by building the drop up from a syringe whilst ensuring that the drop did not move down the side of the lens. Thus, in both cases a static rather than dynamic advancing contact is measured.

Comparison of contact angle results with data from the literature is often difficult because of the sensitivity of contact angles to the method of sample preparation and also because of the hysteresis of contact angles which has in the past made reliable results difficult to obtain. Contact angle hysteresis describes the difference between the advancing contact angle, θ_A, observed when a liquid boundary advances over a clean, dry, solid surface and the receding contact angle, θ_R, observed when a liquid boundary recedes from a previously wetted surface. It has been attributed to surface roughness[188 - 191] and porosity[188] of the solid surface such that entrapment of liquid in the valleys, crevices or pores of the solid occurs when the liquid advances over it. When the liquid recedes the uncovered surface can contain trapped liquid, in which case θ_R will be smaller than θ_A.

Unfortunately many authors do not fully describe their methods of contact angle measurement which makes it difficult for the reader to ascertain whether or not the more useful advancing contact angle has made measured. In this work the equilibrium advancing contact angles, as described by Zisman[166], have been determined (Section 2.2.3.1.).

Of the polymers investigated in this study only poly (methyl methacrylate) and polypropylene have previously had their contact angles with water reported. Values from the literature of 65° and 67° for PMMA[192, 193] and 93° for polypropylene[194] compare favourably with the contact angles reported here (Table 6) of 64° and 91°, respectively. The remaining polymers in Table 6, with their abundance of methyl groups would be expected to exhibit similar contact angles to that of polypropylene and this is indeed the case.

The wettability of a surface is determined mainly by the nature of the outermost atoms or exposed groups of atoms. It is apparent, therefore, that the decrease in the contact angle observed (Figures 6 and 7) during immersion of P4MP1 in chromic acid is brought about by the introduction of hydrophilic groups on to the surface, produced by the oxidative attack on the C-H bonds in the polymer. It has previously been shown[195] that for low molecular weight alkanes the relative rates of reaction of $-\overset{|}{\underset{|}{C}}-H$, $-CH_2-$, and $-CH_3$ groups towards chromic acid oxidation are of the order 7-18,000:114:1. Thus the structure of P4MP1 with its two tertiary C-H bonds per repeat unit suggests that it is very susceptible to oxidative attack. The attack of chromic acid, or more correctly chromium VI in an acidic medium, has been reported[196] to proceed through a chromium IV ester intermediate to give an alcohol. For P4MP1 one possible reaction scheme is shown in Equation 10. The tertiary alcohol can then rapidly form an olefin[197] and undergo scission to yield aldehydes and ketones which may be further oxidised to carboxylic acids. It is apparent, therefore, that the possible groups on the surface of P4MP1 responsible for the reduced contact angle (increased wettability) are $>C=O$, $-COOH$ and $-OH$. However their concentration appears to be too low for detection



(10)

by ATR infra red spectroscopy.

Immersion of P4MP1 in chromic acid at 60°C results in a rapid decrease in the contact angle with water and then little subsequent change which suggests that attack is continuing into the polymer and thus contributing little to the wetting properties of the surface. However, there is a noticeable loss in clarity due to the increase in surface roughness of the P4MP1, a result of the etching of the polymer surface by chromic acid. Etching of the surface probably occurs through loss of soluble oxidised polymer fragments and through the mechanical loss of larger fragments caused by deep penetration into the amorphous regions of the polymer. It is known that roughening of the surface affects the measurement of contact angles. Wenzel[198] showed that the roughness factor, r, (the ratio of the true area of the solid to the apparent area) is related to the apparent or measured contact angle θ' and also the true contact angle, θ, (measured on a smooth surface). Thus,

$$r = \frac{\cos\theta'}{\cos\theta} \qquad (11)$$

One consequence of Wenzel's equation which deserves consideration is that when $\theta < 90^\circ$ then $\theta' < \theta$. Thus if a liquid exhibits an acute contact angle on a solid surface, roughening of that surface will make the apparent contact angle, θ' , less than the true angle. In other words the liquid will appear to wet the surface more when the surface is roughened. It can be postulated, therefore, that when P4MP1 is attacked by chromic acid rapid surface oxidation occurs, reducing the contact angle to below 90°, followed by roughening (etching) of the surface and further oxidation; a combination which causes still further reduction in the contact angle.

The observations regarding the secondary processing of chromic acid treated P4MP1 are obviously of interest in any discussion concerning the relative contributions of surface oxidation and etching in increasing wettability. These results (Table 7) show that after surface treatment a process which restores the smoothness of the surface also causes a substantial increase in the contact angle. This would suggest that surface roughness is an important factor in the increase in wettability of P4MP1 after chromic acid treatment. However, it is possible that the secondary process is just destroying the oxidised surface layer. For example, the polishing could mechanically remove the oxidised surface layer leaving a less oxidised sub-layer as the new surface. Moulding could also lead to the replacement of the surface, although it is generally considered that during moulding from a disc polymer flows from the centre of the disc to fill the mould. But in the moulding of lenses there will undoubtedly be shear forces involved in producing the curvature required which could aid the formation of a new surface.

The moulding of the 16mm disc from a 8.5mm disc proved to be interesting when it was noticed that on the surface of the moulded disc there was an area of haziness equal in size to the original disc. This did not appear due to any roughness of the surface so it was more than likely due to the presence of oxidation products on the surface. Surprisingly, there was little difference between the contact angle on the hazy part and that on any other part of the surface which indicates that whatever the oxidation products are they do not possess a high concentration of hydrophilic groups.

It is therefore reasonable to assume that in just the same way that wettability of P4MP1 appears to be increased by a combination of surface oxidation and roughening, the treated polymer has its wettability reduced by a combination of destruction of the oxidised surface and a decrease in roughness. However, it does seem to be difficult to assess the relative contributions, made by the oxidised surface and the roughness, to the improved wettability of P4MP1.

Polypropylene (70% isotactic/30% atactic), found to be less resistant to oxidative attack by chromic acid (Figure 8) than P4MP1, has only one tertiary C-H site per repeat unit compared to P4MP1's two. However, the higher crystallinity of P4MP1 makes it less susceptible to attack. This is emphasised by the greater roughening and thus oxidative attack on the polypropylene samples with the greater atactic content (60%) and thus higher amorphous nature. Similar arguments apply to the extensive attack on ethylene propylene terpolymer samples except that in this case the presence of the ethylene units reduces the concentration of tertiary C-H bonds.

Polydimethylsiloxane contains only primary C-H bonds which indicates reasonable stability to oxidative attack. However, in practice it was found to have little resistance to chromic acid which is undoubtedly due to the combined effects of hydrolytic and oxidative action.

Immersion of P4MP1 in fuming nitric acid, a powerful oxidising agent, resulted in increased wettability but was accompanied by a marked yellowing of the surface. The yellowness can be attributed to either extensively oxidised polymer or to nitration products. Concentrated sulphuric acid had little effect on the wettability of P4MP1, whereas surprisingly, treatment with the more powerful sulphonating agent, chlorosulphonic acid, actually resulted in an increase in the contact angle and a decrease in clarity. A reasonable explanation for this phenomenon lies yet again with Wenzel's Equation. For if on immersion in chlorosulphonic acid soluble sulphonation products were formed, the surface of P4MP1 would become rougher but no hydrophilic groups would be present on the surface. Thus, from Equation 11 when $\theta > 90^\circ$ roughening of the surface leads to an apparent contact angle, θ', greater than θ.

The increase in wettability of ethylene propylene terpolymer following mastication on a two roll mill with dicumyl peroxide is most probably the result of a surface oxidation process, the mechanism of which is probably similar to that of thermal oxidation. The surface oxidation which occurs during mastication could begin with hydrogen abstraction to yield hydrocarbon radicals followed by a rapid reaction of these radicals with oxygen to give peroxy radicals. They can then abstract further hydrogen atoms from the polymer to yield hydroperoxides on the surface which would account for the observed decrease in the contact angle with water.

Clinical Trials

It has long been recognised that wetting of contact lenses is a primary requirement for the physiological compatability of the lens and the patient[157, 158]. However, despite calls for the improved wettability of lenses there has previously been no attempt to correlate the wettability of lenses to water with the formation of a continuous tear film over the surface.

Comparison of the contact angles with water on P4MP1 lenses with the homogeneity of the tear film (Table 9) show that for satisfactory wetting a contact angle of $60^\circ - 65^\circ$ is required. This compares favourably with the fact that PMMA lenses, with a contact angle of 64°, will, a short time after insertion (without the aid of a wetting solution) be wet by the tears[199]. The spreading of the tear film over a lens which exhibits a contact angle of about 60° with water is easily explained by the lower surface tension of tears 46 dynes/cm.) compared to water (72.8 dynes/cm.).

Although the observed relationship between the contact angle with water and the homogeneity of the tear film cannot be rigidly applied to every polymer it does, however, provide a useful method of screening potential contact lens materials.

The clinical results on the treated P4MP1 lenses resembled those that would have been anticipated had the patients been wearing conventional PMMA lenses. This suggests that the greater flexibility of P4MP1 was not sufficient to significantly affect the initial patient comfort response and that the much superior oxygen permeability had little extra beneficial effect under the conditions used i.e. daily wear. This lack of an observed beneficial effect of P4MP1's reportedly high oxygen permeability is probably because "rigid" lenses "pump" oxygen enriched tears under the lens to the cornea and this acts as the main oxygen supply route.

The lack of patient comfort observed during the wearing of ethylene propylene terpolymer lenses is possibly due to the high coefficient of friction generally possessed by elastomers. It also appears that although a continuous tear film is formed on the lens this does not provide sufficient lubrication between the lens and the eye lid.

CHAPTER 4

THE COPOLYMERISATION OF 4-METHYL PENT-1-ENE WITH SOME HYDROPHILIC MONOMERS

Polymers for biomedical applications are often required to possess a spectrum of properties which are not generally found in any one polymer. The contact lens is no exception with as yet no one polymer meeting the stringent requirements of the ideal lens (see Section 1.4). Poly (2-hydroxyethyl methacrylate) has many desirable properties for contact lens use but appears to lack a sufficiently high oxygen permeability. On the other hand poly (4-methyl pent-1-ene) is reported to have a high oxygen permeability but is non-wettable by tear fluid. It is, however, well known that copolymerisation is often effective in matching the potentialities inherent in polymer structure with applications. Therefore, if copolymerisation could effectively combine the desirable properties of poly (2-hydroxyethyl methacrylate) and poly (4-methyl pent-1-ene) the result would be an excellent contact lens material.

Also included in this 'hydrophilic-hydrophobic' copolymerisation study is N-vinyl pyrrolidone which because of its greater hydrophilicity should enable higher water content copolymers to be prepared. Poly (N-vinyl pyrrolidone) has been used as a blood-plasma extender and has been studied extensively for signs of toxicity and shown to be physiologically inactive[202, 203].

The copolymerisation of 4-methyl pent-1-ene with either of the hydrophilic monomers immediately poses a problem as 2-hydroxyethyl methacrylate and N-vinyl pyrrolidone are generally polymerised by free radical techniques whereas the structure of 4-methyl pent-1-ene indicates that it is unlikely to be susceptible to free radical polymerisation. In fact, Poly (4-methyl pent-1-ene) is obtained by a Ziegler-Natta catalysed polymerisation. Unfortunately it is well known that, in general, polar monomers deactivate Ziegler-Natta type catalysts[204 - 206].

However, a technique for copolymerising polar and non-polar monomers has been patented by Serniuk et al[200, 201]. In their method a monomer that contains strongly negative groups and that responds to free radical initiation but not cationic polymerisation, e.g. methyl methacrylate, is complexed with a Friedel-Crafts halide or Lewis acid and the complexed monomer is copolymerised in the presence of a free radical initiator with a second monomer that responds to cationic polymerisation but not free radical polymerisation e.g. 2-methyl pent-1-ene.

It was evident, therefore, that the most likely chance of achieving a successful copolymerisation of 2-hydroxyethyl methacrylate or N-vinyl pyrrolidone with 4-methyl pent-1-ene would be in adapting Serniuk's method to include the above monomers.

Although this investigation has been concerned mainly with obtaining an end-product i.e. a copolymer of 4-methyl pent-1-ene with a hydrophilic monomer, where possible tentative suggestions have been made in relation to a mechanism which is capable of explaining the observed results.

4.1. EXPERIMENTAL

Copolymerisations were carried out using the technique described in Section 2.2.2.1.(b). The conditions used and any variations in the copolymerisation process are tabulated in the following section. The products of the copolymerisations were isolated using techniques normally employed in polymer synthesis (e.g. precipitation into a non-solvent) and the extent of copolymerisation was assessed qualitatively by i.r.spectroscopy and quantitatively by C H N analysis.

In order that any copolymers produced may be considered as useful contact lens materials it must be possible to compression mould them into lenses. Only non-crosslinked polymers were considred to be mouldable; linearity being assessed by solubility. Limited processing trials were carried out by Kelvin Lenses Ltd.

4.2. RESULTS

Copolymerisation of 4-methyl pent-1-ene (4MP1) with 2-hydroxyethyl methacrylate (HEMA) and with N-vinyl pyrrolidone (NVP) was attempted under a variety of conditions using different catalyst systems, solvents and temperatures as shown in Tables 10 and 11. Some of these results were obtained with the collaboration of David Cobbett[223] and Barry Beerman[224]. Although 4MP1 was found not to have copolymerised with either of the hydrophilic monomers a number of interesting results were obtained which should help to explain this unexpected behaviour.

In the absence of free radical initiators both HEMA and NVP were found to rapidly homopolymerise at room temperature under the influence of zinc chloride. The homopolymerisations occurred both in the dark and in the light. The polymerisation of NVP was found to occur with a perceptible evolution of heat and was also more rapid than the polymerisation of HEMA. In the absence of both free radical catalysts and zinc chloride there was no evidence of polymerisation of HEMA and NVP after 24 hrs. at room temperature. 2, 2-Diphenyl - 1 - picrylhydrazyl was found to be discoloured during the zinc chloride catalysed polymerisations of HEMA and NVP both in the presence and absence of light. This would appear to indicate the presence of free-radicals in the polymerisations.

Not surprisingly free radical catalysts did not produce copolymers of 4MP1 with either HEMA or NVP. When free radical catalysts were used in conjunction with a Friedel-Crafts halide, zinc chloride, there was still no evidence of copolymerisation, in fact, homopolymers of HEMA and NVP were obtained in every case. This lack of copolymerisation was observed despite variations in temperature, time of reaction and polarity of the solvent.

TABLE 10. Attempted Copolymerisation of 2-Hydroxyethyl Methacrylate With 4-Methyl Pent-1-ene

Molar Ratio of HEMA:4MP1	Solvent	Catalyst System	Temp./Time	% Yield Based on Total Monomers	Solubility in Methanol	Melt Processability	Infra-Red Analysis	Comments
HEMA		Molar ratio of $ZnCl_2$: HEMA 0.5:1	22°C/3 hrs.		Insoluble but swells	No	Poly HEMA	Cross-linked poly HEMA produced
HEMA		Molar ratio of $ZnCl_2$:HEMA 0.5:1 In the dark	22°C/3 hrs.		Insoluble but swells	No	Poly HEMA	Cross-linked poly HEMA produced
1:4	Benzene	0.1% by wt. α-azo- isobutyronitrile (AZBN)	52°C/24 hrs.	16%	Soluble	Possible if mould adhesion problems can be overcome	Poly HEMA	Linear poly HEMA
1:1	Benzene	Molar ratio of $ZnCl_2$:HEMA 1:1 0.1% by wt. AZBN Using ultra-violet light	22°C/3 hrs.	33%	Soluble	" " "	Poly HEMA	" " "
1:1	Tetrachloroethylene	" " "	0°C/3 hrs.	20%	Soluble	" " "	Poly HEMA	" " "
1:1	Tetrahydrofuran	" " "	22°C/3 hrs.	32%	Soluble	" " "	Poly HEMA	" " "

TABLE 10 Continued

Molar Ratio of HEMA:4MP1	Solvent	Catalyst System	Temp./Time	% Yield Based on Total Monomers	Solubility on Methanol	Melt Processability	Infra-Red Analysis	Comments
1:1	Tetrahydrofuran	As above but 1% by wt. AZBN	20°C/18 hrs.	39%	Insoluble but swells	No	Poly HEMA	Cross-linked poly HEMA
1:4	Tetrahydrofuran	Molar ratio of $ZnCl_2$:HEMA 0.5:1 0.35% by wt. AZBN Using ultraviolet light	0°C/3 hrs.	22%	Soluble	Possible if mould adhesion problems can be overcome	Poly HEMA	Linear poly HEMA
1:6	Tetrahydrofuran	" " "	0°C/3 hrs.	13.6%	Soluble	" " "	Poly HEMA	Linear poly HEMA
1:4	50/50 mixture by volume of Methanol and Tetrahydrofuran	Molar ratio of $ZnCl_2$:HEMA 1:1 0.35% by wt. AZBN Using ultraviolet light	0°C/3 hrs.	18.8%	Soluble	" " "	Poly HEMA	Linear poly HEMA

TABLE 11. Attempted Copolymerisation of N-Vinyl Pyrrolidone With 4-Methyl Pent-1-ene

Molar Ratio of NVP:4MP1	Solvent	Catalyst System	Temp./Time	% Yield Based on Total Monomers	Solubility in Water	Melt Processability	Infra-Red and C H N Analysis	Comments
NVP		Molar ratio of $ZnCl_2$:NVP 0.5:1	22°C/1 hr.		Soluble	Possible but mould release problems result in broken mouldings	Poly NVP	On addition of NVP to $ZnCl_2$ exothermic reaction occurred
NVP		Molar ratio of $ZnCl_2$:NVP 0.5:1 In the dark	22°C/1 hr.		Soluble	" " "	Poly NVP	" " "
1:1	Benzene	0.1% by wt. AZBN	52°C/16 hrs	43%	Soluble	" " "	Poly NVP	
1:4	Benzene	0.1% by wt. AZBN	52°C/21 hrs	10%	Soluble	" " "	Poly NVP	
1:1	Tetrahydrofuran	Molar ratio of $ZnCl_2$:NVP 0.5:1 0.3% by wt. AZBN	52°C/8hrs.	32%	Soluble	" " "	Poly NVP	
1:1	Benzene	Molar ratio of $ZnCl_2$:NVP 1:1 0.1% by wt. AZBN Using ultra-violet light	22°C/3 hrs.	39%	Soluble	" " "	Poly NVP	

TABLE 11 Continued

Molar Ratio of NVP:4MP1	Solvent	Catalyst System	Temp./Time	% Yield Based on Total Monomers	Solubility in Water	Melt Processability	Infra-Red and C H N Analysis	Comments
1:2	Tetrahydrofuran	Molar ratio of $ZnCl_2$:NVP 1:3 0.5% by wt. AZBN Using ultraviolet light	$0^{\circ}C$/2 hrs.	21%	Yes	Possible but broken mouldings due to mould release problems	Poly NVP	
1:4	Tetrahydrofuran	Molar ratio of $ZnCl_2$:NVP 1:2 0.4% by wt. AZBN Using ultraviolet light	$0^{\circ}C$/3 hrs.	10%	Yes	" " "	Poly NVP	
1:2	50/50 mixture by volume of methanol and tetrahydrofuran	Molar ratio of $ZnCl_2$:NVP 1:1 1% by wt. AZBN Using ultraviolet light	$22^{\circ}C$/8 hrs.	34%	Yes	" " "	Poly NVP	

TABLE 12. Attempted Copolymerisation of N-Vinyl Pyrrolidone and 2-Hydroxyethyl Methacrylate with 2-Methyl Pent-1-ene

Molar Ratio of Monomers	Solvent	Catalyst System	Temp./Time	% Yield Based on Total Monomers	Solubility	Melt Processability	Infra-Red and C H N Analysis	Comments
HEMA:2MP1 1:1	Tetrahydrofuran	Molar ratio of $ZnCl_2$:HEMA 1:1 0.1% by wt. AZBN Using ultra-violet light	20°C/3 hrs.	34%	Soluble in Methanol	Possible if mould release problems can be overcome	Poly HEMA	Linear Poly HEMA
NVP:2MP1 3:1		Molar ratio of $ZnCl_2$:NVP 1:3 0.1% by wt.AZBN using ultra-violet light	22°C/20 hrs.	48%	Soluble in Water	" " "	Poly NVP	Exothermic reaction observed
NVP:2MP1 1:1	Benzene	Molar ratio of $ZnCl_2$:NVP 1:1 0.1% by wt.AZBN Using ultra-violet light	22°C/3 hrs.	36%	Soluble in Water	" " "	Poly NVP	

Replacement of 4MP1 with 2-methyl pent-1-ene(2MP1) in a number of experiments (Table 12) did not result in successful copolymerisation. Identical results were obtained from experiments with both 4MP1 and 2MP1.

In the attempted copolymerisations with NVP linear, water soluble poly (vinyl pyrrolidone) was obtained, however the linearity of poly HEMA produced in similar copolymerisation attempts was found to be dependent on the polymerisation conditions. Cross-linked polymers were produced when the concentration of HEMA in the monomer-solvent mixture was high. The cross-linking of poly HEMA is due to the presence, as an impurity in the monomer, of the diester, ethylene glycol dimethacrylate. Although every effort was made to completely purify the HEMA the diester can never be completely removed because at elevated temperatures HEMA undergoes disproportionation[110] to the diester so that the amount of impurity can actually increase with repeated distillation. Disproportionation can also occur (slowly) at low temperatures such that with storage the diester content increases. Linear poly HEMA was however obtained in many cases due to the fact that cross-linking efficiency decreases with dilution of the initial polymerisation mixture.

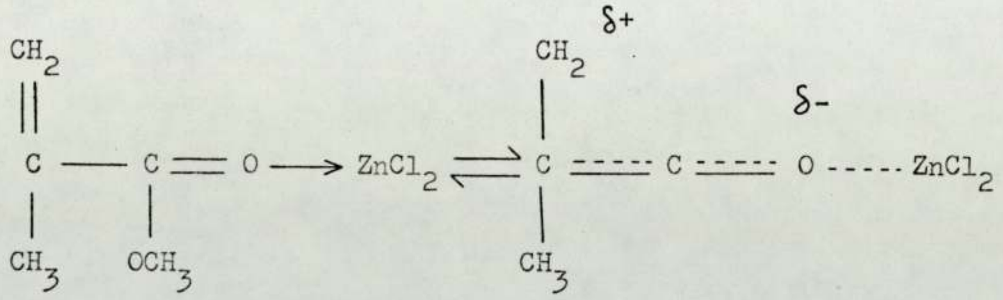
As only homopolymers were obtained in this work the processing trials were necessarily confined to poly HEMA and poly NVP. A great deal of difficulty was experienced with mould release which resulted in the majority of the mouldings being broken. The mould release problems are of course directly related to the hydrophilic nature of poly HEMA and poly NVP. Investigation into the moulding behaviour of hydrogel polymers is still being carried out with the aim of obtaining the optimum conditions for successful compression moulding which would make it a viable technique for the production of hydrophilic contact lenses.

4.3. DISCUSSION

The failure to achieve copolymerisation of 4MP1 with HEMA or NVP using conventional free radical catalysts is of course due to the lack of a radical stabilising factor in the 4MP1 monomer unit. This lack of reactivity in the presence of free radical catalysts is consistent with the behaviour of other more widely studied α-olefins e.g. propylene.

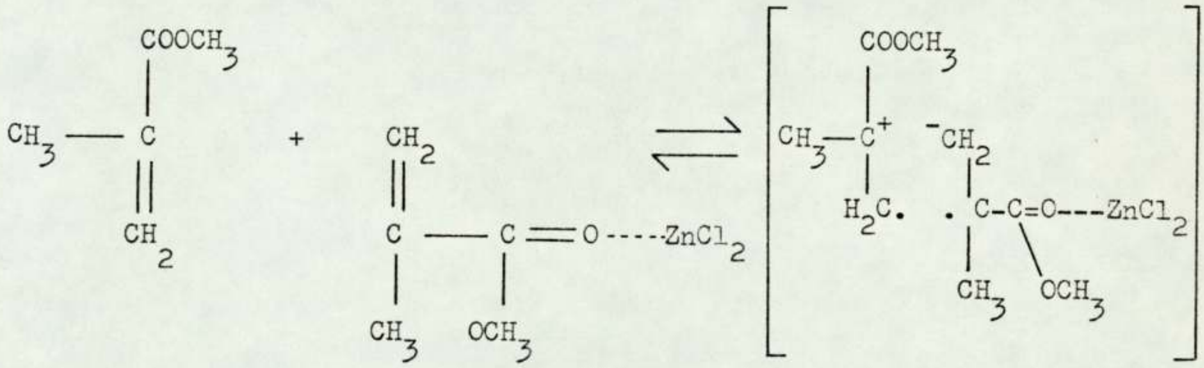
When a free radical catalyst was used in conjunction with a Friedel-Crafts halide there was still no evidence of copolymerisation. This is somewhat surprising considering that Sernuik et al[200, 201] using a similar catalyst system successfully copolymerised monomers comparable to HEMA and 4MP1 e.g. methyl methacrylate and 2-methyl pent-1-ene. An explanation of the lack of copolymerisation obtained in the present work is most likely to be found by consideration of the homopolymerisation behaviour of HEMA and NVP and the mechanisms proposed for the copolymerisation of polar with non-polar monomers in the presence of a Friedel-Crafts halide and a free radical initiator.

Both HEMA and NVP can be homopolymerised using classical free-radical techniques. However, in the presence of zinc chloride but in the absence of a free radical catalyst rapid homopolymerisation of both monomers occurred. It is well known that for free radical initiated polymerisation of polar monomers containing pendant nitrile or carbonyl groups e.g. acrylonitrile and methyl methacrylate in the presence of metal halides such as zinc chloride and aluminium chloride, increased rates of polymerisation are observed[207 - 214]. This effect has been attributed to the formation of a complex between the polar group of the monomer and the metal halide, resulting in an increase in the reactivity of the complexed monomer[210]. It has been proposed by Imoto[209, 211] that the increased reactivity is due to the delocalisation of the electrons in the double bond of the polar electron acceptor monomer (Equation 11).



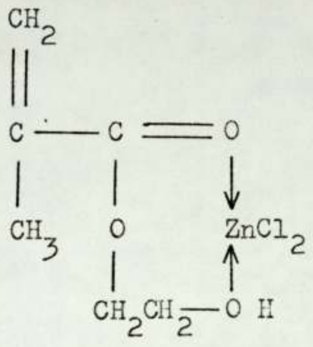
(11)

Gaylord[215, 216] has gone one step further and suggested that the increased reactivity of the complexed monomers in homopolymerisation is the result of the formation of a donor-acceptor charge transfer complex between the uncomplexed monomer (donor) and the metal halide complexed monomer (acceptor) (Equation 12). The charge transfer complex can then readily undergo spontaneous or radical initiated homopolymerisation.



(12)

Equimolar complexes of methyl methacrylate-zinc chloride and acrylonitrile-zinc chloride have been readily isolated[210,211,213, 217,218] and characterised. However, even in the dark it was not possible to isolate complexes of zinc chloride with either HEMA or NVP owing to their spontaneous polymerisation, which occurred even at room temperature. HEMA and NVP differ from previously studied polar monomers in one major respect which is that they both have more than one functional group capable of complexation with a metal halide. This of course raises the possibility that complexes formed between HEMA or NVP and a metal halide may not be as straightforward as those previously encountered e.g. methyl methacrylate-zinc chloride and acrylonitrile-zinc chloride especially if the metal halide is zinc chloride which has the ability to form more than one co-ordination bond. Although it is not possible to be definite about the structure of complexes of zinc chloride with HEMA or NVP there are a number of realistic possibilities. Assuming that all the polar sites on the two monomers are available for complexing the most probable complex structures are shown below.



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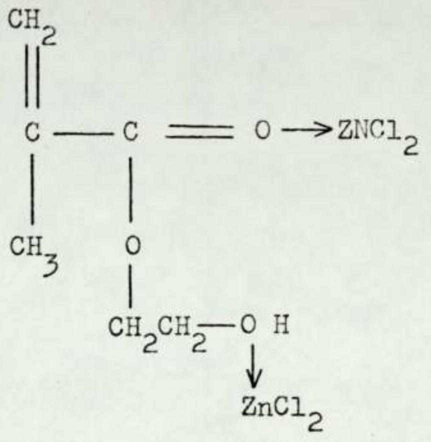
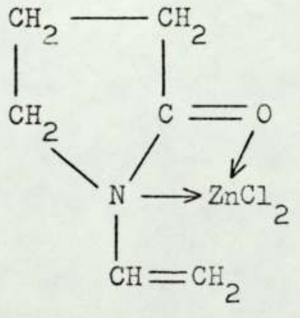
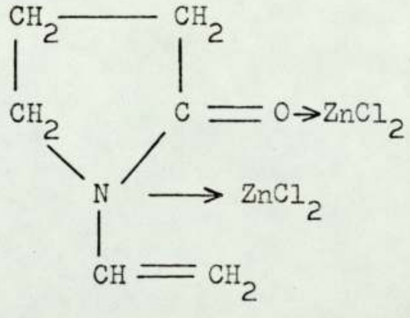


(VI)

COMPLEXING OF ZINC CHLORIDE WITH HEMA



(VII)



(VIII)

COMPLEXING OF ZINC CHLORIDE WITH NVP

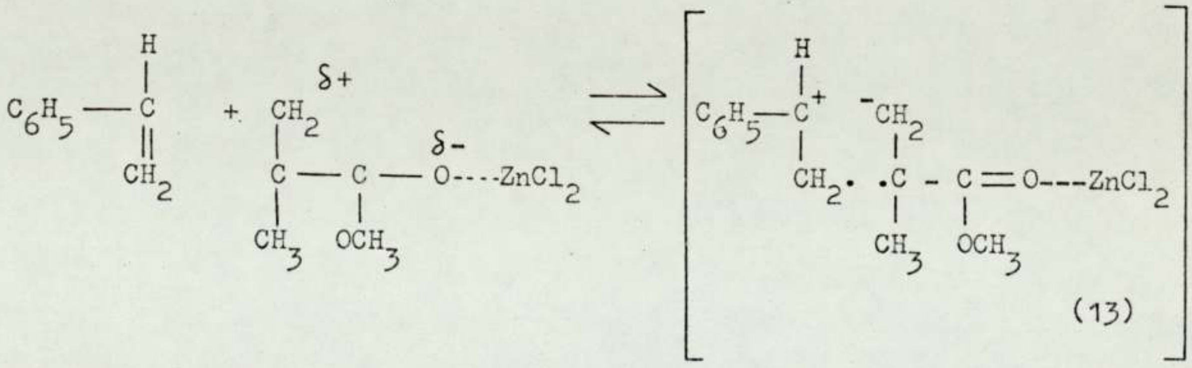
In general complexes of zinc chloride with polar monomers have not been found to spontaneously polymerise but do so thermally, under the influence of free radicals or with ultra-violet light. The spontaneous polymerisation of HEMA and NVP in the presence of zinc chloride can be explained by referring to the above complex structures

(V, VI, VII, VIII) which almost certainly would have greater electron-accepting properties and thus increased reactivity than if only one site on each monomer were available for complex formation.

It is as yet uncertain how the actual polymerisation occurs. On the one hand some Russian workers[214, 219] regard the polymerisation of polar monomers in the presence of zinc chloride as proceeding in a classical free radical manner whereas Gaylord[215, 216] has proposed the formation of a charge transfer complex between the uncomplexed monomer and the complexed monomer (see Equation 12). The charge transfer complex can then undergo homopolymerisation.

It has been suggested[202] that NVP is susceptible to cationic polymerisation as evidenced[220] by its polymerisation in the presence of boron trifluoride etherate at room temperature. It is, however, more probable that polymerisation occurred as a result of complex formation as boron trifluoride is quite capable of complexing with NVP.

The enhanced reactivity of polar monomers in the presence of metal halides can be extended to copolymerisation with electron-donor monomers such as styrene, resulting in the formation of alternating copolymers. This behaviour has been attributed to the interaction between the electron-donor monomer e.g. styrene and the metal halide-complexed electron-acceptor monomer e.g. methyl methacrylate resulting in the formation of a charge transfer complex (Equation 13) which can undergo spontaneous or radical initiated homopolymerisation to yield alternating copolymer, irrespective of the initial monomer composition.

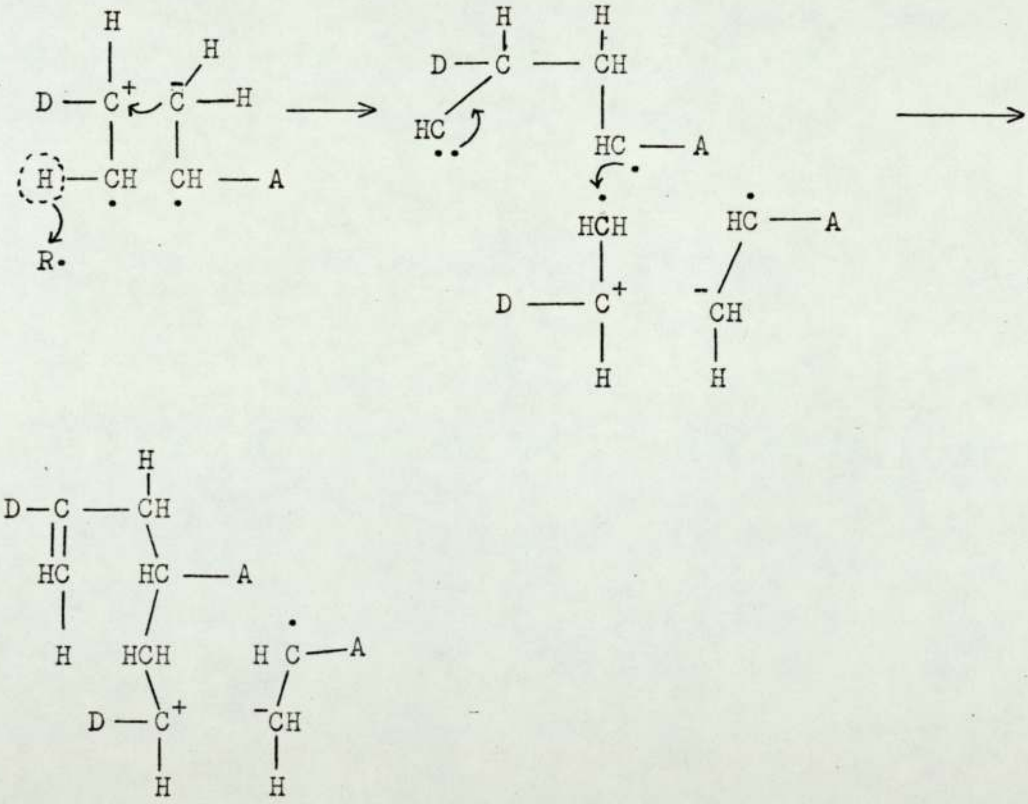


(13)

This is an analogous situation to that of homopolymerisation discussed earlier so that there is, of course, a corresponding free-radical mechanism in which polymerisation proceeds in a classical manner by the alternating addition of donor and acceptor monomers.

The exact mecahnism by which a charge transfer complex may undergo homopolymerisation has not been elucidated although Gaylord[221] has proposed a scheme which he suggests is consistent with the known characteristics of copolymerisation or homopolymerisation in the presence of metal halides.

Briefly, polymerisation of charge transfer complexes is initiated as a result of hydrogen abstraction. A radical catalyst may only promote excitation of ground state charge transfer complexes, or alternatively may abstract a hydrogen from a complex (Equation 14).

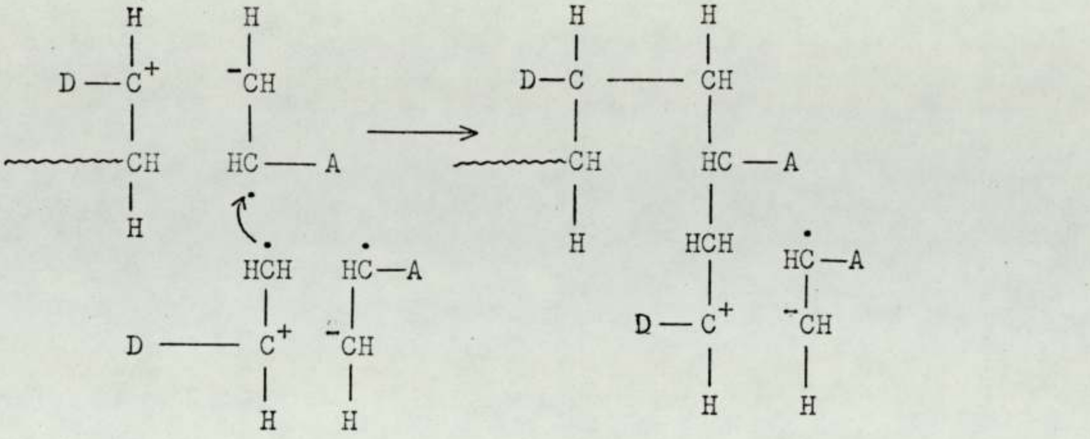


(14)

D denotes an electron-donating substituent and A is an electron-withdrawing substituent complexed with a metal halide.

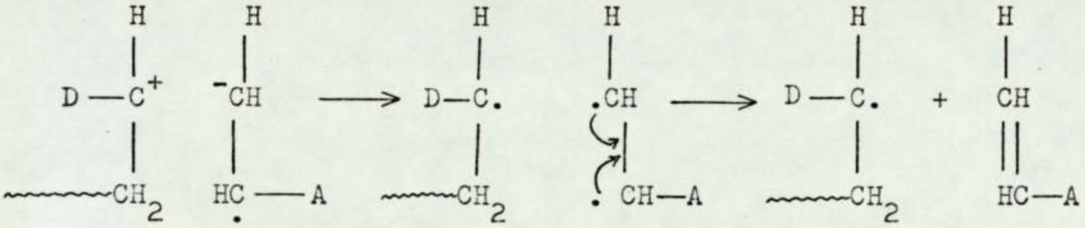
Thermal and/or uncatalysed reactions may be initiated by hydrogen abstraction by an excited complex from solvent or monomer, by inter-complex hydrogen transfer or by coupling of complexes.

Irrespective of the mode of initiation, the propagation step involves the addition of a comonomer complex to the ion pair chain end (Equation 15).

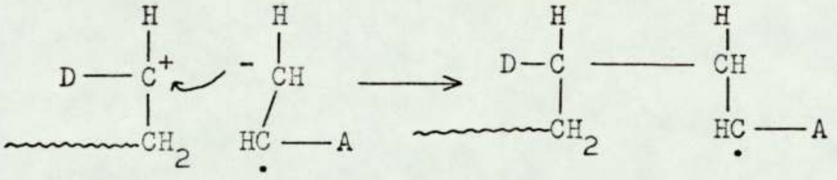


(15)

Termination occurs through reverse electron transfer or intramolecular coupling (Equations 16 and 17).



(16)



(17)

The radical species generated in Equations (16) and (17) may then undergo disproportionation or coupling.

The discolouration of 2,2-diphenyl-1-picrylhydrazyl (DPPH) during the spontaneous polymerisations of HEMA and NVP in the presence of zinc chloride could be evidence for a free radical mechanism. It must be recognised however, that DPPH is well known for hydrogen abstraction[222] which has been proposed by Gaylord[221] as the initiation step in the polymerisation of charge transfer complexes (e.g. Equation 14).

The lack of copolymerisation in the presence of zinc chloride of either HEMA or NVP is apparently due to complex formation which enhances homopolymerisation. In other words the complexed monomers preferentially reacted with their respective uncomplexed monomer rather than with the electron-donor monomer, 4MPl.

Substitution of 4MPl by 2MPl did not result in copolymerisation even though 2MPl is a stronger electron-donor than 4MPl.

Although no successful copolymerisations were achieved in this work it does suggest that given the right conditions it may be possible to prepare alternating hydrophilic-hydrophobic polymers which could possess very interesting properties. Towards this end investigations are required into the use of very strong electron-donor monomers such as styrene or butadiene which may prove to be more reactive towards complexed HEMA and NVP than the respective uncomplexed monomers and result in copolymerisation.

Almost certainly the best chance of achieving copolymerisation of HEMA or NVP with 4MPl will be to first prepare an electron-acceptor complex of HEMA or NVP which does not undergo spontaneous polymerisation. This may be possible with a Friedel-Crafts catalyst or Lewis Acid which has less co-ordination strength than zinc chloride.

CHAPTER 5

HYDROGEL POLYMERS: THE RELATIONSHIP BETWEEN POLYMER COMPOSITION AND EQUILIBRIUM WATER CONTENT

In Chapter 4 it was suggested that the most profitable approach to meeting the requirements of the ideal contact lens (Section 1.4) lies in copolymerisation. A suitable copolymerisation system would involve both hydrophilic and hydrophobic monomers such that the best properties, relevant to contact lens wear, of each homopolymer would be incorporated into the resulting copolymer. Attempted copolymerisation between 2-hydroxyethyl methacrylate (HEMA) and 4-methyl pent-1-ene (4MP1) was described in Chapter 4. For the work discussed in this chapter HEMA was again included as a hydrophilic monomer together with its structural isomer 2-hydroxypropyl acrylate (HPA). Cross-linked polymers formed from hydroxyalkyl acrylates and methacrylates and other hydrophlic monomers are, because of their ability to imbibe substantial quantities of water without dissolution, termed hydrogels (Section 1.5.).

A number of hydrophobic vinyl monomers are available which readily undergo free radical polymerisation and which may provide the necessary structural features for an improved contact lens material. Styrene is one such hydrophobic monomer, which has been included because bulky side groups attached to a polymer main chain disrupt chain symmetry and regularity of the polymer giving a more open structure. It is reasonable to suppose that such a structure may possibly have increased oxygen permeability. Styrene also has a similar reactivity ratio[225] (0.38) to HEMA (o.34) which indicates that polymerisation should produce a random copolymer. Ng[178] has recently shown that the incorporation of small amounts of styrene into hydrogels through copolymerisation produces dramatic changes in their properties. The resulting hydrogels had increased strength, they were, however, deleteriously affected in having reduced flexibility.

It was considered that the presence of an internal plasticiser could lead to increased flexibility and thus a more comfortable contact lens with possibly higher oxygen permeability. The introduction of a third monomer which can act as an internal plasticiser has thus been considered[226]. Long chain methacrylate esters were considered to be the ideal choice as the plasticising monomer because they enable a wide range of structural variability to be achieved whilst remaining within a fairly narrow range of reactivity ratios.

Since water is a crucial constituent of a hydrogel it is important to know the amount of water imbibed by a hydrogel when swollen to equilibrium. In fact as the equilibrium water content (E.W.C.) reflects the bulk hydrophilicity of a hydrogel it is a useful method for hydrogel characterisation. Thus, in this chapter the effect of varying the structure of hydrogels (through hydrophilic-hydrophobic copolymerisation) on the E.W.C. is considered.

In the latter part of this chapter the effect of incorporating monomers more hydrophilic than HEMA or HPA is considered. The monomers used were those whose uncross-linked homopolymers are water soluble eg. N-vinyl pyrrolidone (NVP), acrylamide (ACM) and methacrylic acid (MAA).

5.1. EXPERIMENTAL PROCEDURE

Polymerisations were carried out in bulk using the techniques described in Sections 2.2.2.2.(a) and 2.2.2.2.(b). The majority of polymers were prepared in the form of membranes as membranes were required for physical measurements such as oxygen permeability (see Chapter 6). A number of variations in the general polymerisation technique had to be employed when acrylamide was one of the comonomers. The limited solubility of acrylamide in HEMA and

HPA resulted in the necessity of heating the monomer mix to 60°C in order to bring about solution. The monomer solution was then filtered before polymerisation. The exothermic nature of polymerisations involving acrylamide meant that, in order to produce bubble free polymers, polymerisations in rod form had to be mainly carried out at 40°C, whilst membrane polymerisations because of easier heat dissipation could be effected at 60°C.

The hydrogels were allowed to hydrate in distilled water for at least 3 weeks prior to the measurement of the equilibrium water content (Section 2.2.3.2.).

It should be noted that the E.W.C. as defined in this work is not the only term used to describe the water uptake of a hydrogel. Confusion can arise when the term "percentage water absorbtion" is used as a measure of the water content. In this case

$$\text{Water absorption} = \frac{\text{weight of water in hydrogel}}{\text{weight of dehydrated hydrogel}} \times 100$$

For the sake of convenience the following abbreviations are used in this chapter and hereafter.

EA	ethyl acrylate
MMA	methyl methacrylate
BMA	n-butyl methacrylate
HMA	n-hexyl methacrylate
EHMA	2-ethylhexyl methacrylate
LMA	lauryl methacrylate
EEMA	2-ethoxyethyl methacrylate
POEMA	2-phenoxyethyl methacrylate
St	styrene
MAA	methacrylic acid
ACM	acrylamide
DAACM	diacetone acrylamide
NVP	N-vinyl pyrrolidone

5.2. RESULTS AND DISCUSSION

5.2.2. Effect of Monomer Structure on the Physical Characteristics and Optical Properties of Hydrogels: General Observations

Membranes and some rods were prepared and examined in the dehydrated and hydrated state. The results are shown in Tables 13-18. Although the assessment of flexibility and clarity was only subjective a number of significant trends were observed.

In the dehydrated state terpolymers containing HEMA were found to be more rigid than those containing HPA. This can be attributed to restriction of main chain rotation in the HEMA terpolymer due to the presence of the methyl group on the main chain. It was expected that the introduction of alkyl methacrylates into HEMA-St copolymers would lead to an increase in flexibility and this was indeed the case with lauryl methacrylate and 2-ethoxyethyl methacrylate. Their flexibilising effect appears to be due to the long methacrylate side chains acting to prevent optimal approach of chains thus decreasing the interchain attraction due to dipole/dipole interactions, van der Waals forces and hydrogen bonding. No increase in flexibility was observed, however, on the introduction of 2-phenoxyethyl methacrylate because it appears that although the bulky phenyl group is joined to the main chain by a flexible link it still provides a high energy barrier to rotation. Similarly, the incorporation of 2-ethylhexyl methacrylate, the homopolymer of which has a glass transition temperature (Tg) intermediate between poly POEMA and poly EEMA, has little observed effect on the flexibility of HEMA-St copolymers. This is simply due to the fact that the Tg of the terpolymer in the composition range studied, although lower than the copolymer, is still above room temperature.

The terpolymers were found to be more flexible in the dehydrated state and the magnitude of the increase in flexibility appeared dependent on the amount of water absorbed and its interaction with polar sites within the polymer. It is apparent that the absorption of water causes a separation of the polymer chains thus reducing interchain attraction and so leading to an increase in general mobility.

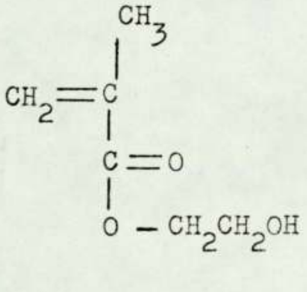
The majority of the terpolymers studied were transparent in the dehydrated state which suggests that they were, at least visually, homogeneous. However, translucence was observed in HEMA-LM-St terpolymers whilst the corresponding terpolymers containing HPA in place of HEMA were transparent. It is therefore probable that the observed translucence is due to an abnormal distribution of the flexible hydrophobic lauryl group in the relatively molecularly immobile HEMA matrix.

Hydration to equilibrium of the transparent terpolymers resulted mainly in optically clear hydrogels although in a few cases translucent hydrogels were obtained. The translucence is possibly due to the formation of clusters of water molecules in the polymer network giving rise to a microphase separation of regions having different refractive indices. The formation of water clusters would be affected by the configuration adopted by the terpolymer. For instance, terpolymers containing 2-phenoxyethyl methacrylate could have hydrophobic phenyl groups stacked together resulting in hydrophobic areas with an absence of water and hydrophilic areas with clusters of water molecules.

5.2.3. Effect of Monomer Structure on the Equilibrium Water Content of Hydrogels

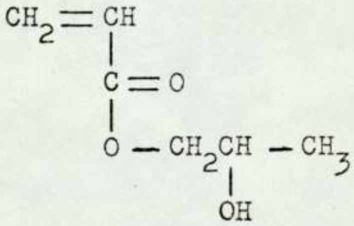
The effect of the partial replacement of HEMA and HPA by various alkyl and alkoxy methacrylates on the water contents of HEMA-St (90:10) and HPA-St (90:10) copolymers has been studied and the results are shown in Tables 13 - 18 and which for convenience and ease of comparison are also portrayed in Figures 9 - 13. The equilibrium water contents of HEMA-St and HPA-St copolymer series as found by Ng[178] are shown for comparison.

It is known that 2-hydroxyethyl acrylate is more hydrophilic (as shown by a higher E.W.C.) than 2-hydroxypropyl acrylate and that similarly 2-hydroxyethyl methacrylate is more hydrophilic than 2-hydroxypropyl methacrylate. Obviously the presence of the extra methyl group in the side chain is effective in reducing the E.W.C. The effect of backbone substitution is also important and is reflected in the effect of hydrophobic substituents. For example, although HEMA (IX) and HPA (X) are isomers poly HPA has a higher equilibrium water content (51%) than poly HEMA (41%). This is a general effect and shows that the methyl group on the HEMA backbone has more steric effect in restricting the water absorption than the extra methyl group in the side chain of HPA.



$CH_2{=}C(CH_3){-}C({=}O){-}O{-}CH_2CH_2OH$

(IX)



$CH_2{=}CH{-}C({=}O){-}O{-}CH_2CH(OH){-}CH_3$

(X)

Undoubtedly a balance of effects--steric and polar--exists. Styrene has a bulky hydrophobic phenyl group directly substituted on the backbone and when copolymerised with HEMA and HPA there is a sharp drop in the E.W.C. (Figures 9 and 10). A much less dramatic change in the E.W.C. occurs when HEMA is copolymerised with methyl methacrylate (Figure 9). This is attributed to the lower steric hindrance of the methacrylate side chain compared to the phenyl group of styrene and also the less hydrophobic nature of MMA due

TABLE 13. Effect of EHMA Content on Some Properties of HEMA Based Hydrogels.

Hydrogel	Molar Composition	Clarity		Physical Character		Water Content (%)
		Dehydrated	Hydrated	Dehydrated	Hydrated	
HEMA-EHMA-St	80:10:10	Transparent	Transparent	Rigid	Flexible	17.8
HEMA-EHMA-St	70:20:10	Transparent	Transparent	Rigid	Flexible	13.5
HEMA-EHMA-St	60:30:10	Transparent	Transparent	Rigid	Semi-rigid	9.5
HEMA-EHMA-St	50:40:10	Transparent	Transparent	Rigid	Semi-rigid	7.2
HEMA-St	50:50	Transparent	Transparent	Rigid	Rigid	5.0
HEMA-EHMA	50:50	Transparent	Transparent	Rigid	Semi-rigid	7.1
HEMA-EHMA-St	70:15:15	Transparent	Transparent	Rigid	Flexible	13.0
HEMA-EHMA-St	60:20:20	Transparent	Transparent	Rigid	Semi-rigid	9.0

FIGURE 9 Effect of EHMA and Styrene on the Equilibrium Water Content (20°C) of HEMA based Hydrogels. HEMA–MMA Copolymers are shown for comparison

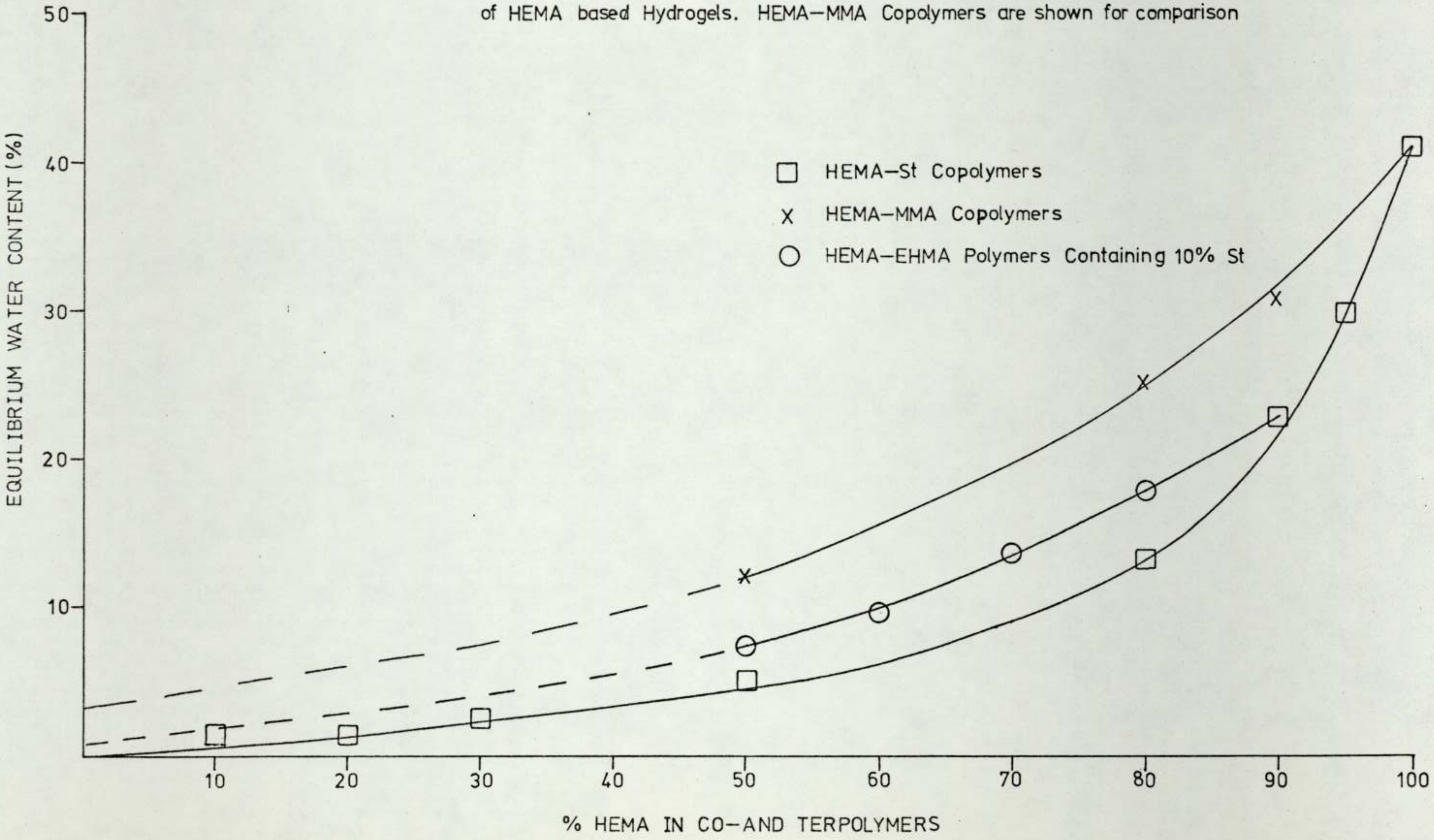


TABLE 14. Effect of EHMA Content on Some Properties of HPA Based Hydrogels.

Hydrogel	Molar Composition	Clarity		Physical Character		Water Content (%)
		Dehydrated	Hydrated	Dehydrated	Hydrated	
HPA-EHMA-St	80:10:10	Transparent	Transparent	Flexible	Flexible	30.4
HPA-EHMA-St	70:20:10	Transparent	Transparent	Flexible	Flexible	20.5
HPA-EHMA-St	60:30:10	Transparent	Transparent	Flexible	Flexible	12.3
HPA-EHMA-St	50:40:10	Transparent	Transparent	Flexible	Flexible	9.2
HPA-St	50:50	Transparent	Transparent	Semi-rigid	Semi-rigid	5.9
HPA-EHMA	50:50	Transparent	Transparent	Flexible	Flexible	10.4
HPA-EHMA-St	60:20:20	Transparent	Translucent	Semi-rigid	Flexible	11.4

FIGURE 10 Effect of EHMA and Styrene on the Equilibrium Water Content (20°C) of HPA based Hydrogels

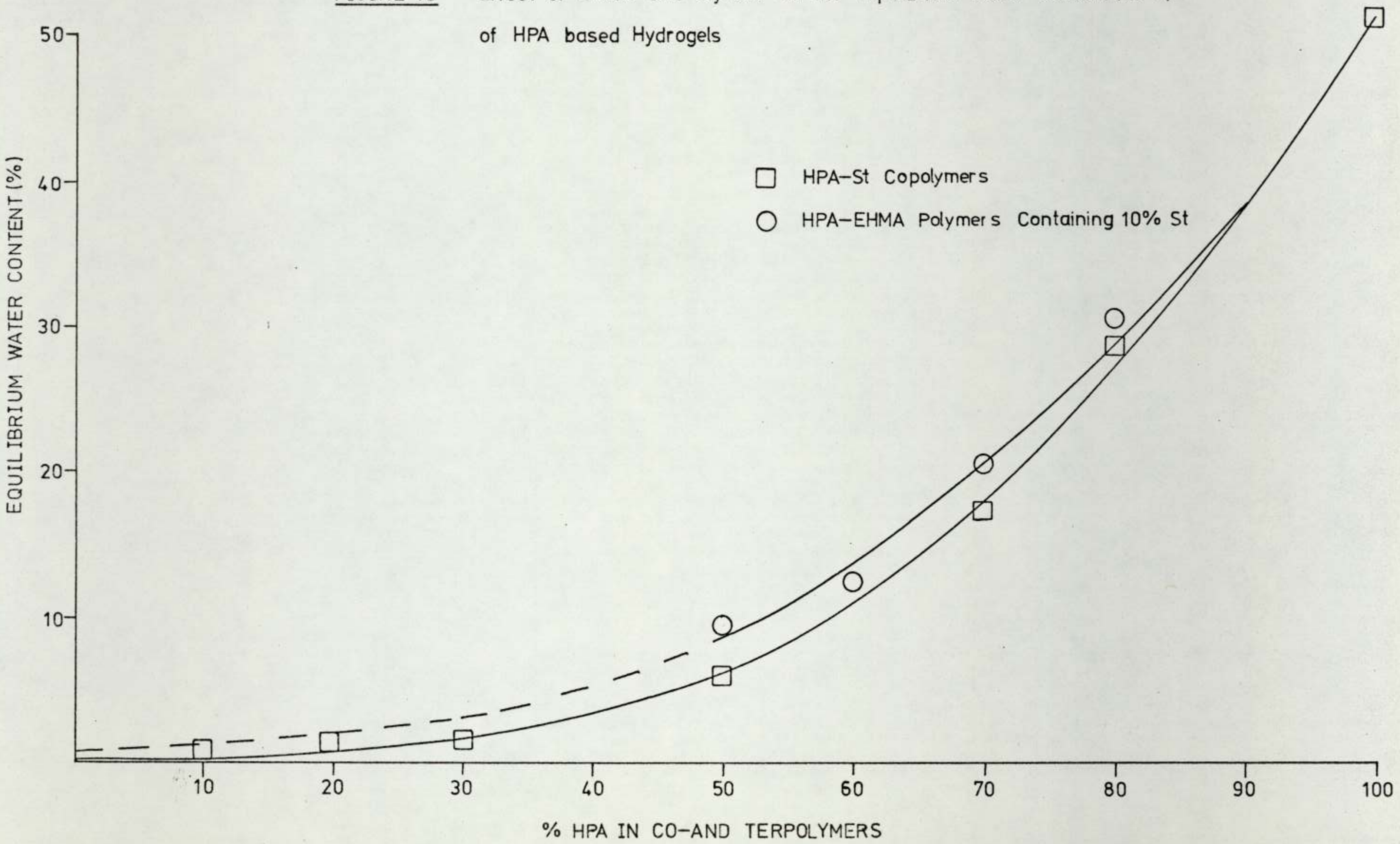


TABLE 15. Effect of EEMA Content on Some Properties of HEMA Based Hydrogels.

Hydrogel	Molar Composition	Clarity		Physical Character		Water Content (%)
		Dehydrated	Hydrated	Dehydrated	Hydrated	
HEMA-EEMA-St	80:10:10	Transparent	Transparent	Rigid	Flexible	20.7
HEMA-EEMA-St	70:20:10	Transparent	Transparent	Rigid	Flexible	16.5
HEMA-EEMA-St	60:30:10	Transparent	Transparent	Rigid	Flexible	13.9
HEMA-EEMA-St	50:40:10	Transparent	Transparent	Semi-rigid	Semi-rigid	9.9
HEMA-St	50:50	Transparent	Transparent	Rigid	Rigid	5.0
HEMA-EEMA	50:50	Transparent	Transparent	Semi-rigid	Flexible	14.6
HEMA-EEMA-St	70:15:15	Transparent	Transparent	Rigid	Flexible	14.3
HEMA-EEMA-St	60:20:20	Transparent	Transparent	Rigid	Semi-rigid	11.0

FIGURE 11 Effect of EEMA and Styrene on the Equilibrium Water Content (20°C) of HEMA based Hydrogels

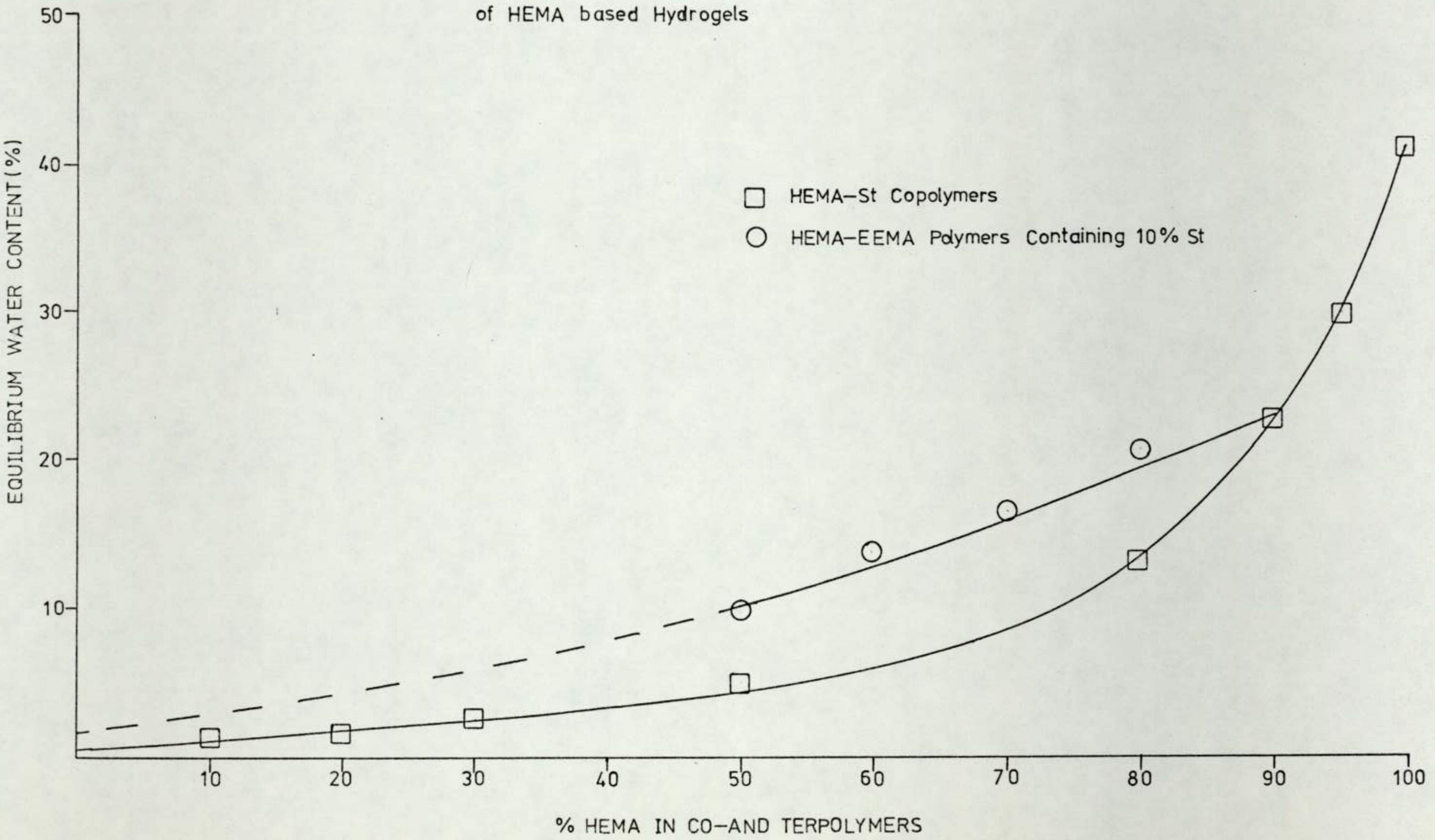


TABLE 16. Effect of EEMA Content on Some Properties of HPA Based Hydrogels.

Hydrogel	Molar Composition	Clarity		Physical Character		Water Content (%)
		Dehydrated	Hydrated	Dehydrated	Hydrated	
HPA-EEMA-St	80:10:10	Transparent	Slight Translucence	Flexible	Flexible	33.1
HPA-EEMA-St	70:20:10	Transparent	Slight Translucence	Flexible	Flexible	25.1
HPA-EEMA-St	60:30:10	Transparent	Slight Translucence	Flexible	Flexible	18.8
HPA-EEMA-St	50:40:10	Transparent	Slight Translucence	Flexible	Flexible	12.8
HPA-St	50:50	Transparent	Transparent	Semi-rigid	Semi-rigid	5.9
HPA-EEMA	50:50	Transparent	Slight Translucence	Flexible	Flexible	15.0
HPA-EEMA-St	60:20:20	Transparent	Slight Translucence	Flexible	Flexible	15.2

FIGURE 12 Effect of EEMA and Styrene on the Equilibrium Water Content (20°C) of HPA based Hydrogels

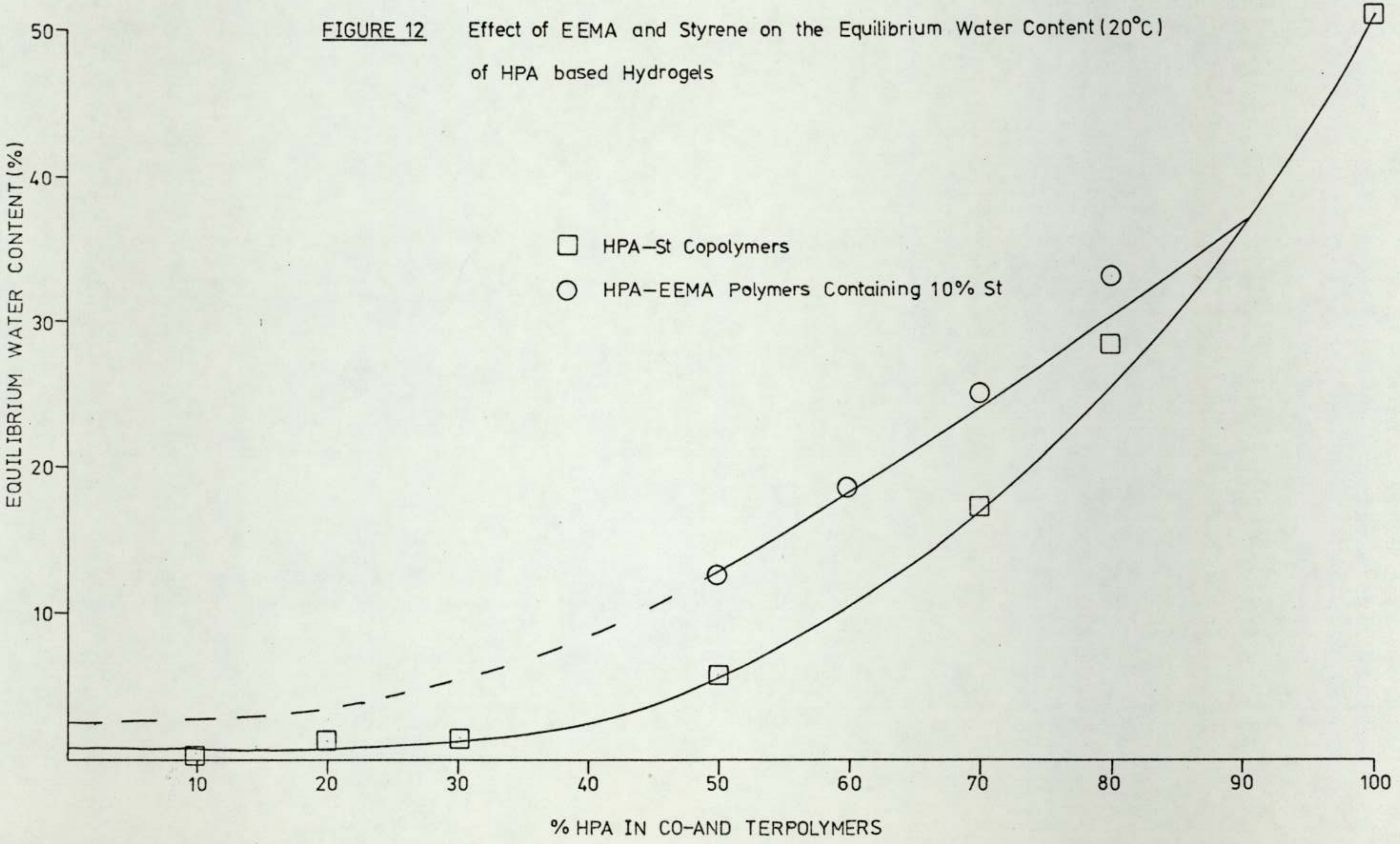


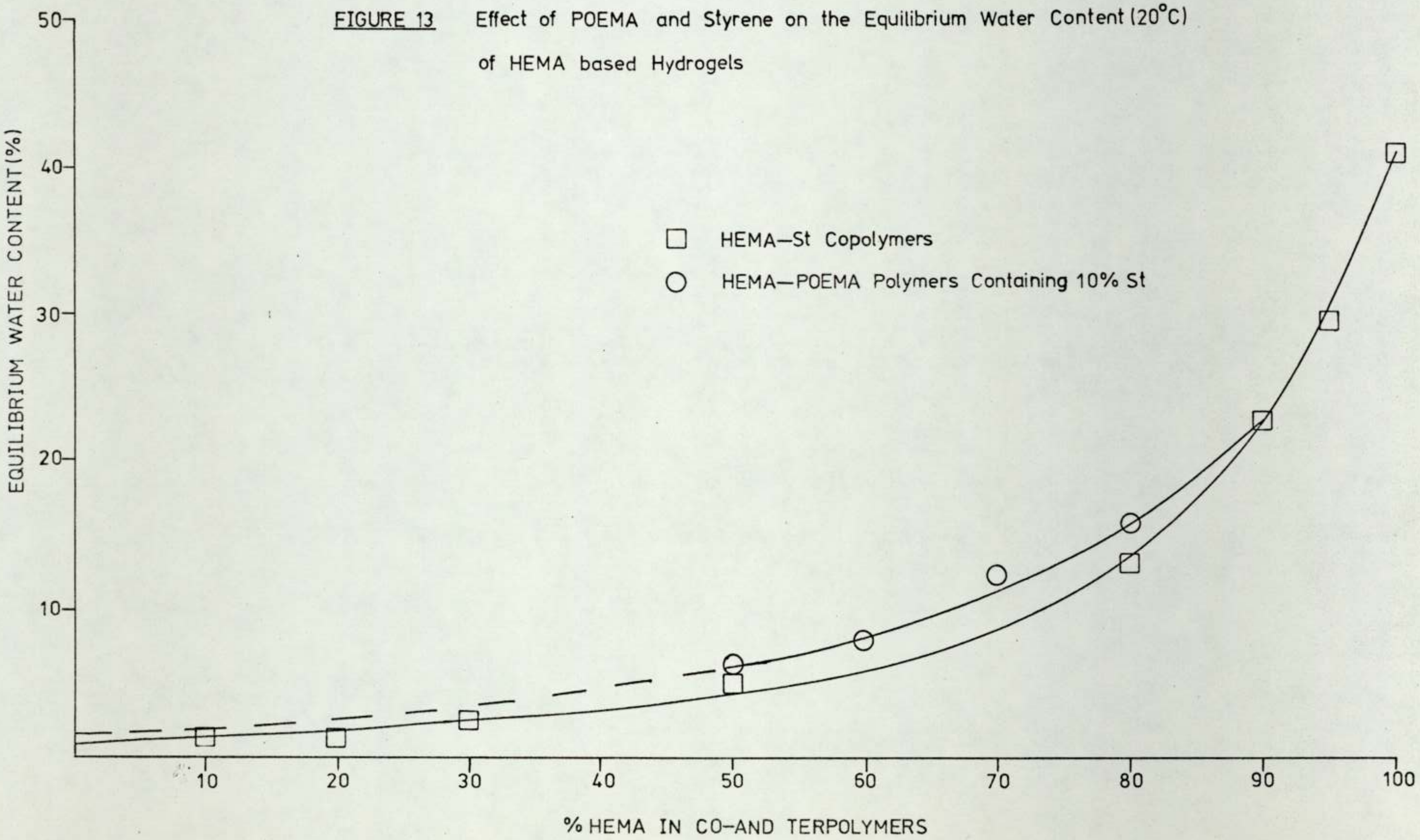
TABLE 17. Effect of POEMA Content on Some Properties of HEMA Based Hydrogels.

Hydrogels	Molar Composition	Clarity		Physical Character		Water Content (%)
		Dehydrated	Hydrated	Dehydrated	Hydrated	
HEMA-POEMA-St	80:10:10	Transparent	Transparent	Rigid	Flexible	15.9
HEMA-POEMA-St	70:20:10	Transparent	Transparent	Rigid	Semi-rigid	12.2
HEMA-POEMA-St	60:30:10	Transparent	Slight Translucence	Rigid	Semi-rigid	8.0
HEMA-POEMA-St	50:40:10	Transparent	Slight Translucence	Rigid	Rigid	6.1

TABLE 18. Effect of LMA Content on Some Properties of HEMA and HPA Based Hydrogels.

Hydrogels	Molar Composition	Clarity		Physical Form		Water Content (%)
		Dehydrated	Hydrated	Dehydrated	Hydrated	
HEMA-LMA-St	70:15:15	Translucent	Translucent	Rigid	Flexible	14.9
HEMA-LMA-St	60:20:20	Translucent	Opaque	Semi-rigid	Flexible	10.1
HPA-LMA-St	60:20:20	Transparent	Translucent	Flexible	Flexible	11.4

FIGURE 13 Effect of POEMA and Styrene on the Equilibrium Water Content (20°C) of HEMA based Hydrogels



to the presence of the carboxylate ester group. Even the phenyl group in 2-phenoxyethyl methacrylate does not quite have the same effect on water content as styrene. This is no doubt due to the presence of the carboxylate ester group and the polar ethereal oxygen in POEMA and also the distance of the phenyl group from the main chain.

As an extension to this work the E.W.C.'s of 50:50 (molar) copolymers of HEMA with methacrylates and acrylates have been studied[227] (Table 19). Figure 14 shows that as the length of the methacrylate side chain increases the E.W.C. decreases rapidly until a fairly constant value is reached. It appears that when the length of the alkyl substituent in the methacrylate side chain reaches C_4 (i.e. butyl) the effect on the E.W.C. of increasing the number of methylene groups is balanced by the increased flexibility. This is further emphasised by the similar water contents of HEMA-EHMA-St (60:20:20) (9.0%) and HEMA-LMA-St (60:20:20) (10.1%). In this case the length of the lauryl methacrylate side chain is about twice that of EHMA. Although the fact that EHMA is branched could be a complicating factor it does appear that branching when it is remote from the backbone does not have a significant effect on the water content.

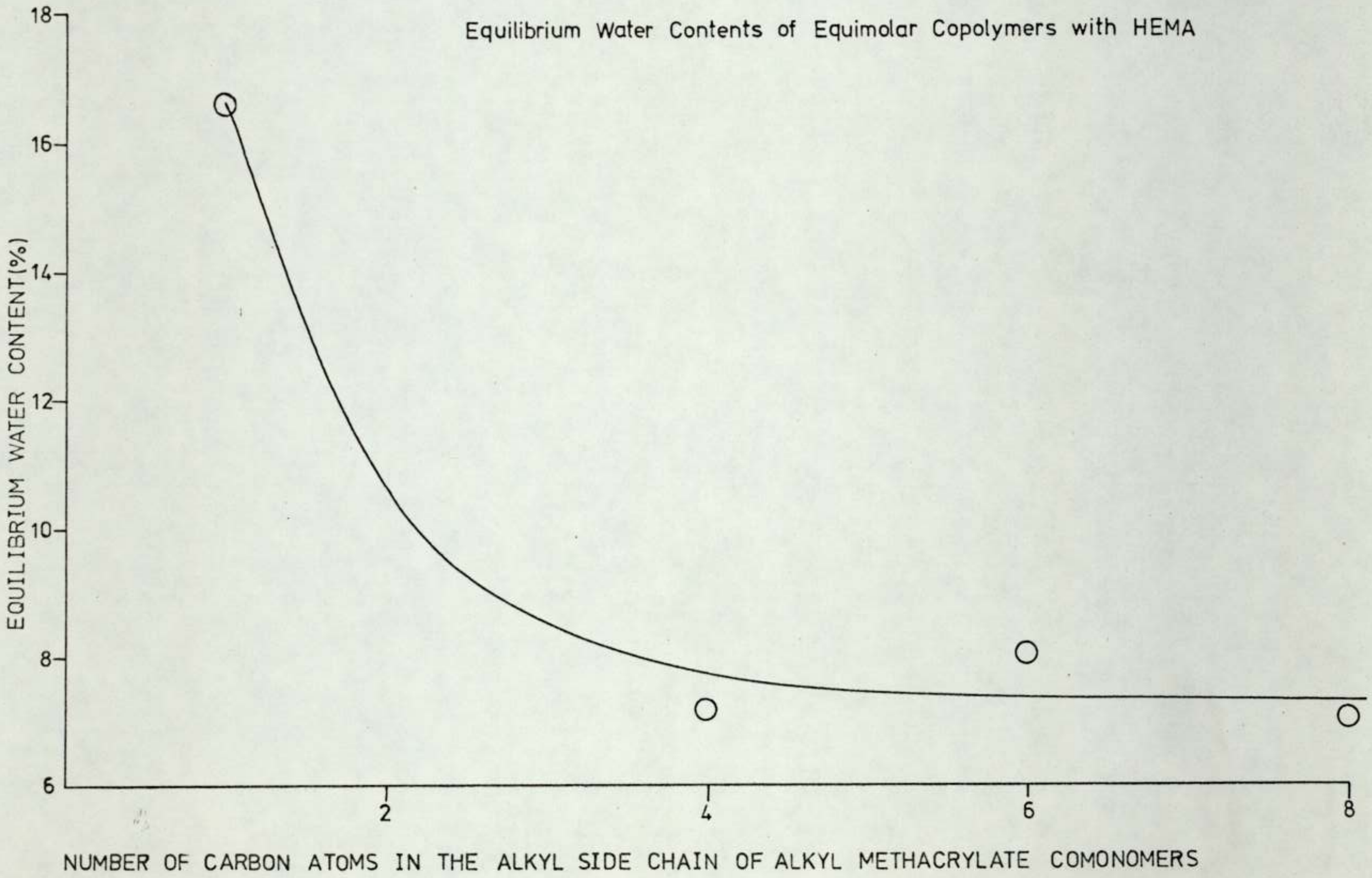
Replacement of methyl methacrylate by its structural isomer ethyl acrylate in a 50:50 copolymer with HEMA resulted in an increase in E.W.C. from about 16% to 19% showing once again that the presence of the sterically hindering methyl group on the main chain is more effective in reducing E.W.C. than an increase in side chain length.

A comparison of the E.W.C.'s of HEMA-BMA (50:50) and HEMA-EEMA (50:50) shows that replacement of a butyl group ($CH_2CH_2CH_2CH_3$) with a 2-ethoxyethyl group ($CH_2CH_2OCH_2CH_3$) results in an increase in water content from 7.2% to 14.6%. Similarly

TABLE 19. Effect of Comonomer Structure on the Equilibrium Water Content of HEMA Based Hydrogels.

HYDROGEL	MOLAR COMPOSITION	EQUILIBRIUM WATER CONTENT (%)
HEMA - EA	50:50	18.9
HEMA - MMA	50:50	16.6
HEMA - BMA	50:50	7.2
HEMA - EEMA	50:50	14.6
HEMA - HMA	50:50	8.1
HEMA - EHMA	50:50	7.1
HEMA - St	50:50	5.0

FIGURE 14 Effect of the length of Side Chain of Alkyl Methacrylates on the Equilibrium Water Contents of Equimolar Copolymers with HEMA



terpolymers containing EEMA (Figures 11 and 12) have higher water contents than terpolymers containing EHMA (Figures 9 and 10). The presence of the polar ethereal oxygen is apparently responsible for the higher E.W.C.'s observed.

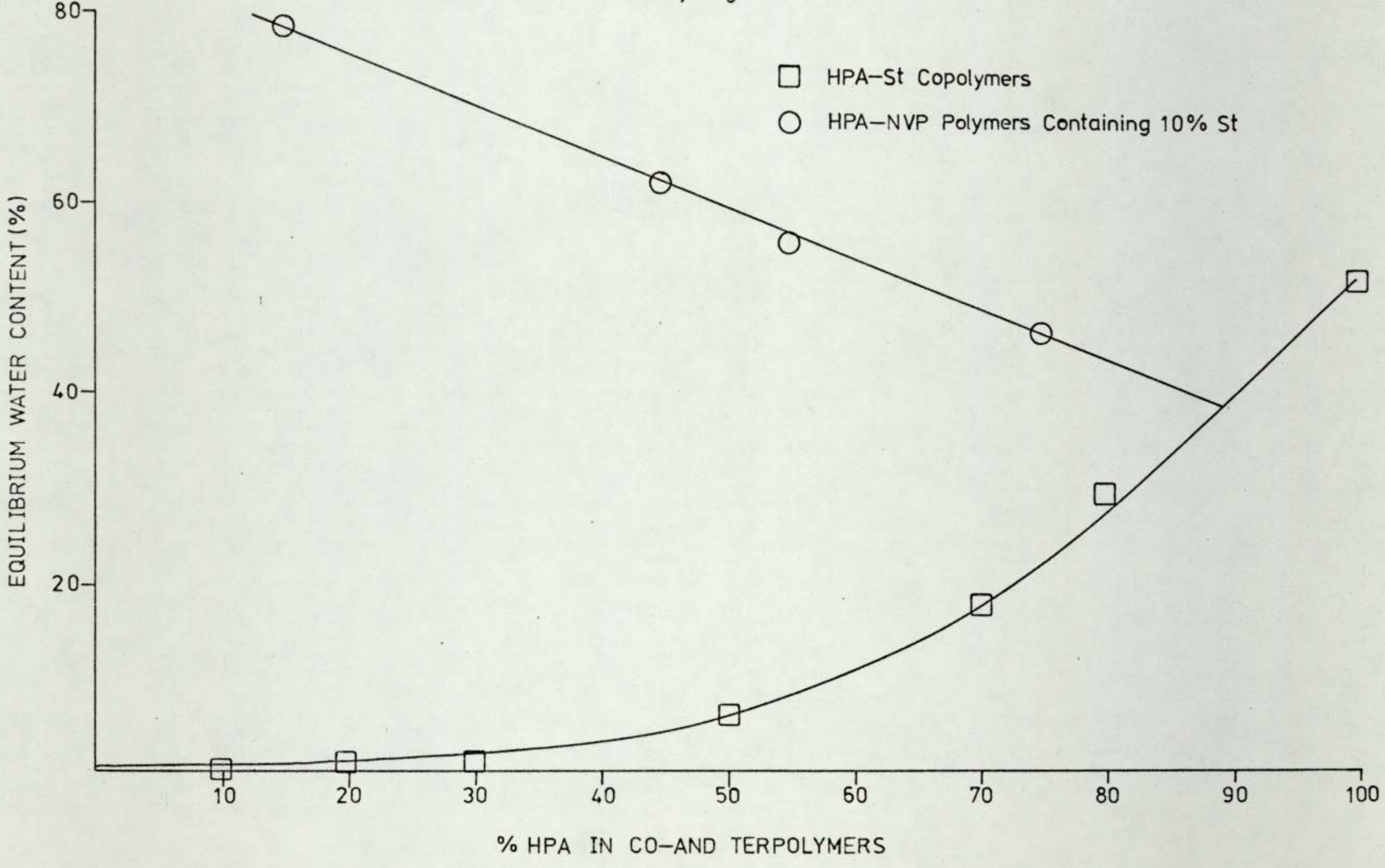
The precise nature of monomers affects not only the water uptake but also such important features of hydrogels as mechanical properties and the nature of the water binding processes. Studies currently in progress show that mechanical properties are related in a fairly complex way to the interaction of the constituent monomers with each other and with the water in the hydrogel. The nature of the water binding processes and the effect on such properties as permselectivity is referred to in more detail in Chapter 8.

The effect of the non-hydrophilic component in a hydrogel on E.W.C. is shown by previous results to be a function of the hydrophobic content and its mode of incorporation. The effect of the incorporation of monomers more hydrophilic than HEMA or HPA has been illustrated by Ng[178] who showed that partial replacement of, for example, HEMA by NVP led to a greater E.W.C.

The effect of the nature of monomers more hydrophilic than HEMA or HPA on the E.W.C. is now considered. Figure 15 shows that the gradual replacement of HPA by NVP in a (90:10 molar) HPA-St copolymer results in a linear increase in water content. This suggests that there is little hydrogen bonding or dipole interaction between the constituent monomers. In other words there is stronger interaction between water and the hydrophilic monomer units than between the monomer units themselves which results in the almost complete utilisation of the available hydrogen bonding sites for water absorption.

Rather more complex effects were expected when hydrophilic monomers capable of strong hydrogen bonding were used in co-and terpolymers.

FIGURE 15 Effect of NVP and Styrene on the Equilibrium Water Content (20°C) of HPA based Hydrogels



The results obtained during this work together with those obtained recently by Anderton[227] and Skelly[228] are shown in Table 20.

Amides are capable of strong hydrogen bonding, indeed acrylamide is known to form plurimolecular aggregates with itself and with many solvents[229]. However, the results in Table 20 and Figure 16 illustrate that the relationship between E.W.C. and composition in copolymers of HEMA or HPA with acrylamide varies in a normal and uncomplicated manner and is indeed similar to that previously discussed. (This contrasts with the abnormal variation in E.W.C. observed with copolymers containing methacrylic acid which will be discussed later). Little or no interaction occurs between acrylamide units or between acrylamide units or between acrylamide and HEMA or HPA units in the co-and ter-polymers studied. This is possibly because the probable random nature of the co-and ter-polymers together with the shielding and steric effects reduce the amount of hydrogen bonding possible between chains whilst maximising the amount of polymer-water interaction. The introduction into HEMA-ACM copolymers of MMA and EEMA as termonomers predictably causes a decrease in E.W.C. owing to their hydrophobic nature. HPA-EA-ACM (50:25:25) has a considerably higher E.W.C. than HEMA-MMA-ACM (50:25:25) which again emphasises the steric effect of the methyl group on the backbone of methacrylates in restricting their water absorption.

The replacement of MMA by the hydrophilic MAA in the terpolymer system HEMA-MMA-ACM (25:50:25) does not result in a large increase in E.W.C. as might reasonably be expected. On the contrary there is a slight reduction. This would suggest that MAA was of a similar hydrophobic nature to MMA, however, uncross-linked poly MAA is water soluble which indicates quite the opposite. It appears that the explanation for this behaviour lies in the strong

<u>FIGURE 16</u> Equilibrium Water Contents (20°C) of Some HEMA–ACM Copolymers

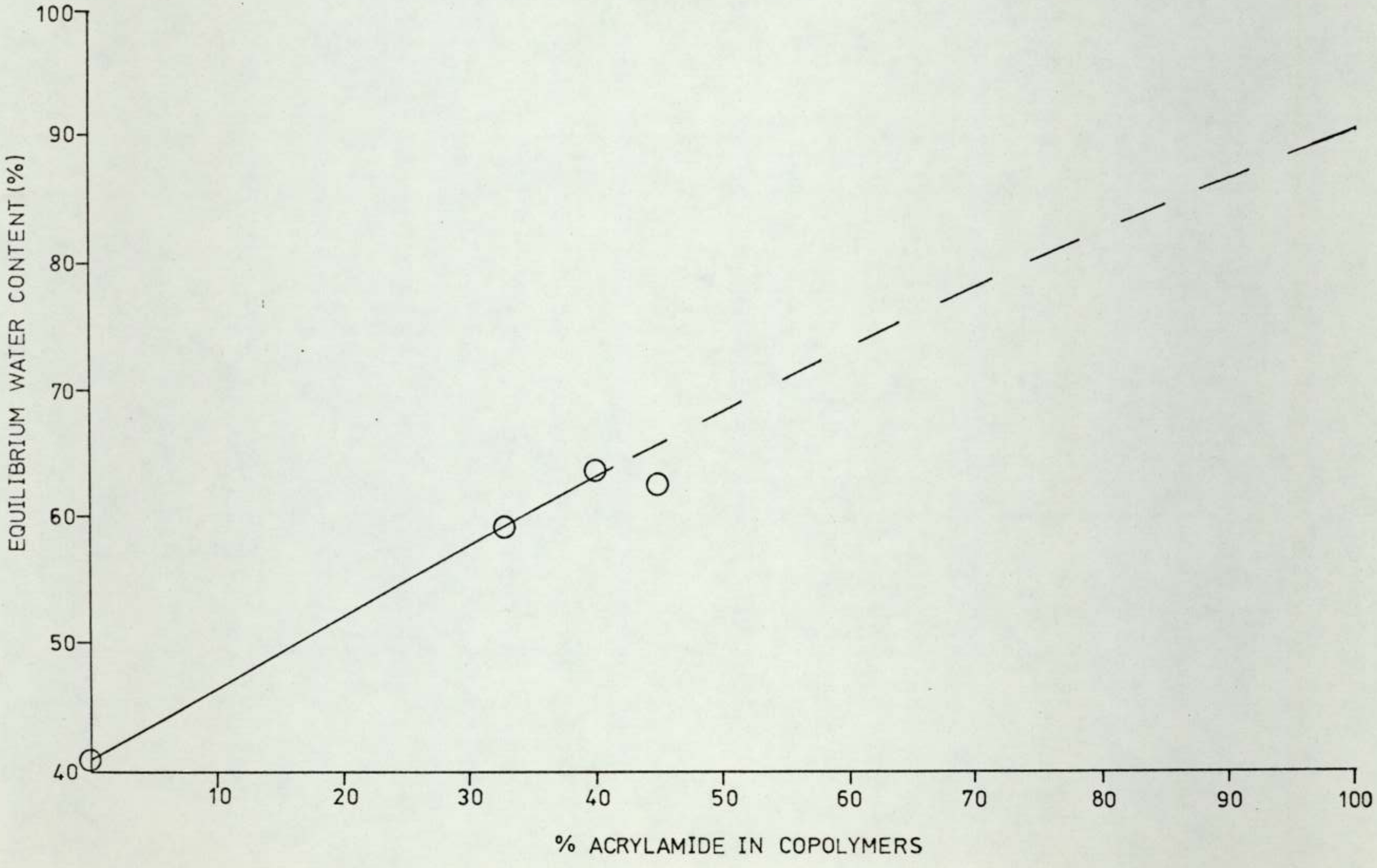


TABLE 20. Effect of the Hydrophilic Monomer Structure on the Equilibrium Water Content of Hydrogels.

MONOMERS IN HYDROGEL	MOLAR COMPOSITION	EQUILIBRIUM WATER CONTENT (%)
HEMA - ACM	66:33	59.3
HEMA - ACM	60:40	63.7
HEMA - ACM	55:45	62.5
HPA - ACM	66:33	71.6
HEMA - MMA - ACM	50:25:25	36.5
HEMA - MMA - ACM	25:50:25	28.7
HEMA - EEMA - ACM	25:50:25	29.9
HPA - EA - ACM	50:25:25	59.5
HEMA - MMA - ACM	25:50:25	28.7
HEMA - MAA - ACM	25:50:25	27.3
HEMA - MMA - ACM	50:25:25	36.5
HEMA - MAA - ACM	50:25:25	38.5
HEMA - MAA - NVP	50:25:25	54.5
HEMA - MAA	50:50	27.7
MAA - ACM	50:50	40
MAA - NVP	50:50	40
NVP - ACM*	50:50	89.5
NVP - DAACM*	50:50	66.2

All the hydrogels were cross-linked with 1% by wt. ethylene glycol dimethacrylate except * which had 1 mole% added cross-linking agent.

hydrogen bonding ability of MAA. Hydrogen bonding can occur in the terpolymer between different MAA units and between MAA units and ACM or HEMA units. As a result of this hydrogen bonding there would be a reduction in the number of sites available for interaction with water and also a secondary cross-linking effect which together would account for the observed low E.W.C. of HEMA-MAA-ACM (25:50:25).

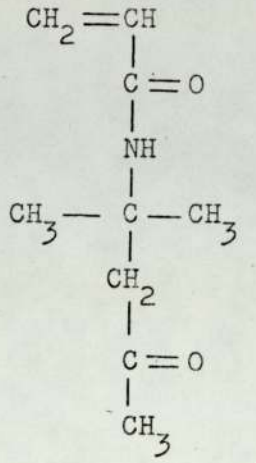
An increase in E.W.C. is observed when there is a decrease in MAA content with a corresponding increase in HEMA content, HEMA-MAA-ACM (50:25:25). This can be explained by a reduction in the number of hydrogen bonding sites (from MAA) for monomer unit--monomer unit interaction which reduces secondary cross-linking and leaves an increased concentration of HEMA and ACM units available for interaction with water.

MAA-ACM (50:50) has a higher E.W.C. than MAA-HEMA (50:50) which is not altogether surprising as the ACM units in the copolymer not participating in inter-unit hydrogen bonding will because of their greater hydrophilicity have a higher water uptake than the corresponding HEMA units.

Interaction between MAA and NVP is indicated by the low water content of MAA-NVP (50:50). Additional evidence for interaction is supplied by previous workers[230, 231] who have shown that poly MAA complexes with poly NVP in aqueous solution. In view of the known complexing behaviour of poly MAA and poly NVP it is surprising that HEMA-MAA-NVP (50:25:25) should have a substantially higher E.W.C. than the corresponding acrylamide terpolymer. However, it is possible that NVP may be present in blocks in the terpolymer and thus with the added presence of HEMA interaction between MAA and NVP would be greatly reduced leaving many NVP units available for interaction with water.

Little interaction is evident between NVP and ACM as NVP-ACM

(50:50) has an extremely high water content. The replacement of ACM by diacetone acrylamide (DAACM) results in a straightforward decrease in E.W.C. due to the substitution of an amide hydrogen by a hydrophobic group (XI).



(XI)

From the above results it is apparent that significant interactions which affect the E.W.C. only occur in the presence of methacrylic acid. It thus seems plausible to assume that the unusually low water contents observed are related to the formation of strong hydrogen bonds between methacrylic acid units and other units in the hydrogels. Further experimental work, however, is required for a fuller interpretation of the observed phenomenon.

5.2.4. Terpolymers Obtained by Solution Polymerisation

In order to compression mould hydrogel contact lenses it is necessary to produce non-crosslinked polymers which are subsequently cross-linked during moulding. These can most conveniently be obtained by solution polymerisation as described in Section 2.2.1. (a).

A number of terpolymers having similar monomer feed ratios to those obtained by bulk polymerisation were synthesised. For example, a monomer mix of HEMA-EEMA-St in a mole feed ratio of 60:20:20 was polymerised and a fine white powder soluble in 1, 4-dioxan and dimethylformamide obtained. A moulding apparatus (from Kelvin Lenses Ltd.) consisting of a mould and heating block was used to mould a disc at 135°C from the terpolymer powder. Severe mould release problems were encountered and only broken bits of the disc could be removed from the die. On hydration the moulded hydrogel became opaque which may possibly be due to incomplete fusion of the particles during moulding or the presence of hydrophobic blocks in the terpolymer.

Due to the polar nature of the hydrogels the severe mould release problems experienced in this example occurred also when other terpolymers were moulded. Investigations into the problems of moulding conditions and mould release are at present being undertaken and are beyond the scope of this thesis.

It is relevant to note, however, that the problem illustrated above can be overcome if the polymer is pressed into sheet using a temperature of 130°C and a pressure of 10 tons per square inch and "melinex" as a mould release film. Discs punched from such sheet can then be conveniently compression moulded into contact lenses at lower temperatures (~100°C) with little difficulty.

CHAPTER 6

'DISSOLVED' OXYGEN PERMEABILITIES OF HYDROGELS

An adequate supply of oxygen to the cornea is recognised as a primary requirement for the maintenance of the normal aerobic metabolism of the cornea and thus the prevention of corneal oedema (Section 1.1.3.). The most important pathway for the transport of oxygen to the cornea is from the air by dissolution in the tear film which oxygenates the cornea. The presence of a contact lens in position on the eye can therefore act as a barrier to the oxygen dissolved in the tears.

PMMA lenses are virtually impermeable to oxygen; they are, however, fitted in such a way that with each blink the lens "rocks" causing fresh tear fluid to be pumped under the lens[70, 83, 84]. In the case of hydrogel lenses it is thought that rippling of the lens on blinking causes fresh tear flow under the lens. Since, however, much still needs to be learnt about the fitting of hydrogel lenses the transport of oxygen through hydrogel materials cannot be neglected as an important pathway for the supply of oxygen to the cornea.

Of still greater importance is the oxygen transport through contact lenses when they are considered for continuous (as distinct from daily) wear. For in this case the lenses are worn during sleep when blinking is at a minimum and it is thought that the only significant route by which oxygen can reach the cornea is through the lens. It is apparent, therefore, that oxygen permeability is a vitally important property to consider in the design of hydrogel polymers for use in both continuous and daily wear lenses.

Permeabilities of polymer membranes to oxygen have been extensively studied; most measurements, however, have been made using the high vacuum time-lag technique developed by Barrer[180]. This method, however, is not applicable to the contact lens situation. When the contact lens is on the eye there is a film of tear fluid on both the posterior and anterior surface of the lens. Thus, the contact lens acts as a barrier to the oxygen dissolved in the tears. It is, therefore, more realistic to consider the 'dissolved' oxygen permeability rather than the 'gaseous' oxygen permeability of potential contact lens materials.

In Chapter 5 the relationship between polymer composition and equilibrium water content of a range of hydrogels derived from various combinations of hydrophilic and hydrophobic vinyl monomers was discussed. In this Chapter the 'dissolved' oxygen permeability coefficients of a number of these hydrogels have been determined and the relationship between oxygen permeability, water content and hydrogel structure examined.

The surface treatment of poly (4-methyl-pent-1-ene) (P4MP1) and its potential as a contact lens material was discussed in Chapter 3. It is therefore relevant to consider the effect of surface treatment on the 'dissolved' oxygen permeability of P4MP1.

'Dissolved' oxygen permeability coefficients were determined using the apparatus and experimental techniques described in Section 2.2.3.3.

6.1. RESULTS AND DISCUSSION

6.1.1. Effect of Surface Treatment on the 'Dissolved' Oxygen Permeability of Poly (4-Methyl Pent-1-ene)

It has been observed by Ng[178] that the 'dissolved' oxygen permeability coefficient (Pd) of P4MP1 is lower than its 'gaseous' oxygen permeability coefficient (Pg) at the same temperature and that Pd of the material increased with sample thickness becoming equal to Pg when the sample was infinitely thick. Similar behaviour has been observed by Hwang et al[232] for silicone rubber.

The above observations have been attributed to the additional resistance to oxygen permeation at the boundary layer between water and the polymer film.

The contribution of the boundary layer resistance is small if the oxygen transfer rate in the polymer membrane is low. Therefore, the 'dissolved' oxygen permeability coefficients of a polymer of low oxygen permeability is nearly equal to its 'gaseous' oxygen permeability coefficient. However, the boundary layer resistance becomes more and more significant as the overall transport resistance of a membrane becomes smaller. The Pd of silicone rubber which has the highest oxygen permeability of existing polymers has been found to be considerably smaller than the corresponding Pg[232].

The effect of surface treatment on the 'dissolved' oxygen permeability coefficient of P4MP1 has been studied and the results are shown in Table 21. Surface treatment with chromic acid was carried out as described in Chapter 3 and surface hydrophilicity was assessed by advancing contact angle measurements with water (Section 2.2.3.1.). The 'dissolved' oxygen permeability coefficients were determined by Ng[178] at 34°C. (Temperature of the eye).

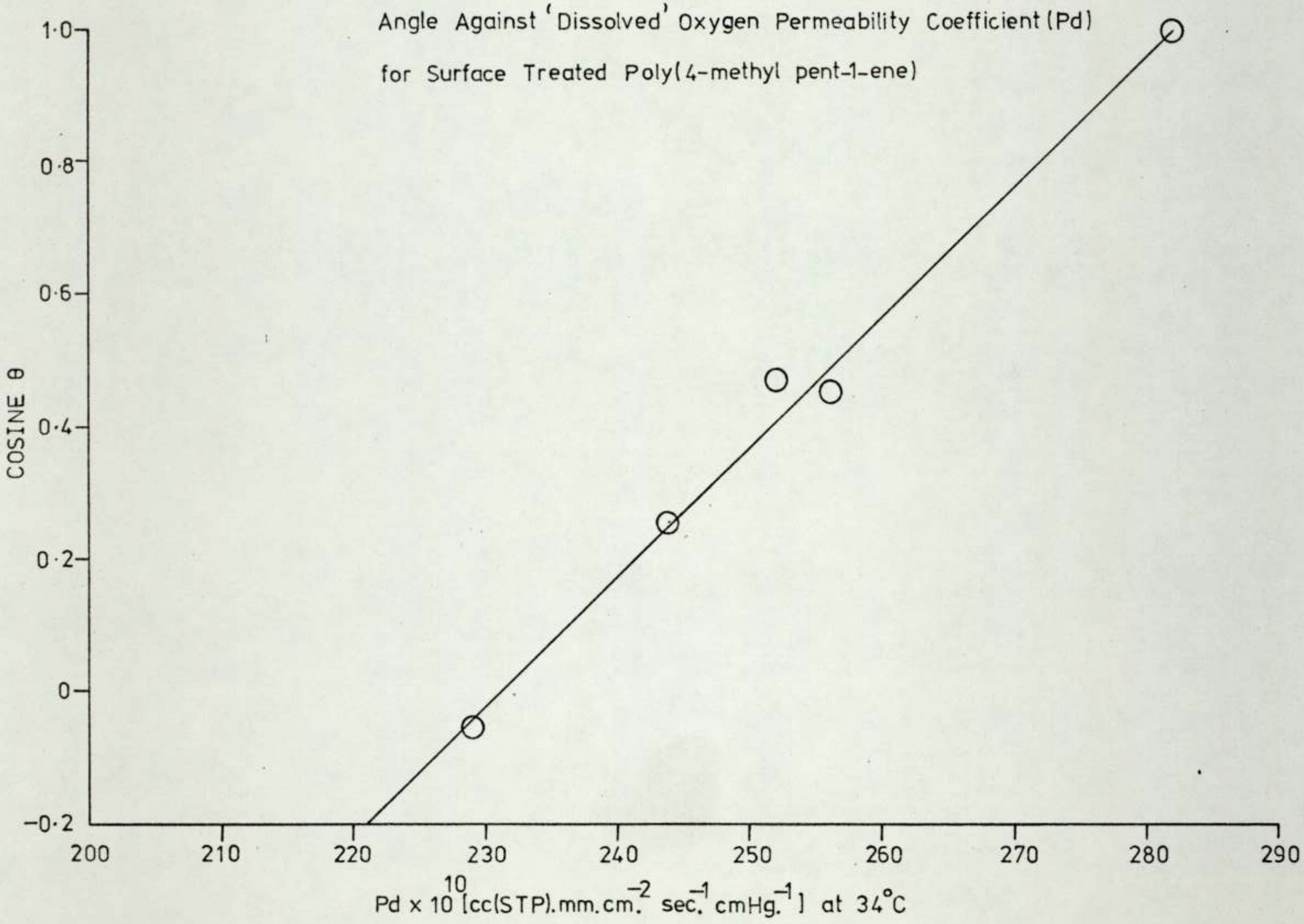
The results show that Pd increased with increasing hydrophilicity. In other words the boundary layer effect appeared to be reduced as the wettability of the P4MP1 surface increased.

The oxygen transport resistance due to the boundary layer may be a function of many factors such as the shape of the interface, wettability of the surface and the velocity of the liquid at the interface. The actual nature of the boundary layer and the relative importance of the above factors on its effect is beyond the scope of this work. It is, however, interesting to note that a good linear relationship is obtained if the results of Table 21 are plotted in the form Pd vs. Cos θ (Figure 16A). This form of plot is analagous to the Fox and Zisman[165, 166] treatment of surface tension data referred to in Section 1.2.2. and emphasises the surface dependence of the boundary layer effect.

TABLE 21. Effect of Surface Treatment on the 'Dissolved' Oxygen Permeability Coefficient (Pd) of Poly (4-methyl pent-1-ene) at 34°C. Film Thickness (L) = 0.23 mm.

Sample Treatment	Contact Angle (θ°)	Pd x 10^{10} (cc.(STP).mm.cm.$^{-2}$sec.$^{-1}$cmHg^{-1})
Untreated	93 ± 2	229
Chromic Acid 15 mins at 20°C	75 ± 2	244
Chromic Acid 15 mins at 60°C	63 ± 2	256
Chromic Acid 30 mins at 60°C	62 ± 2	252
Ideal Value (no boundary effect)	0	282

FIGURE 16A Plot of the Cosine of the Equilibrium Advancing Water Contact Angle Against 'Dissolved' Oxygen Permeability Coefficient (Pd) for Surface Treated Poly(4-methyl pent-1-ene)



6.1.2. The Effect of Structure and Water Content on the 'Dissolved' Oxygen Permeability Coefficients of Hydrogels.

In contrast to the behaviour exhibited by P4MP1, the 'dissolved' oxygen permeability coefficients of the hydrogels studied in this work showed no dependence on sample thickness (~0.1mm to 0.3mm.) . This would appear to indicate a negligible boundary layer effect for the transport of oxygen through hydrogels.

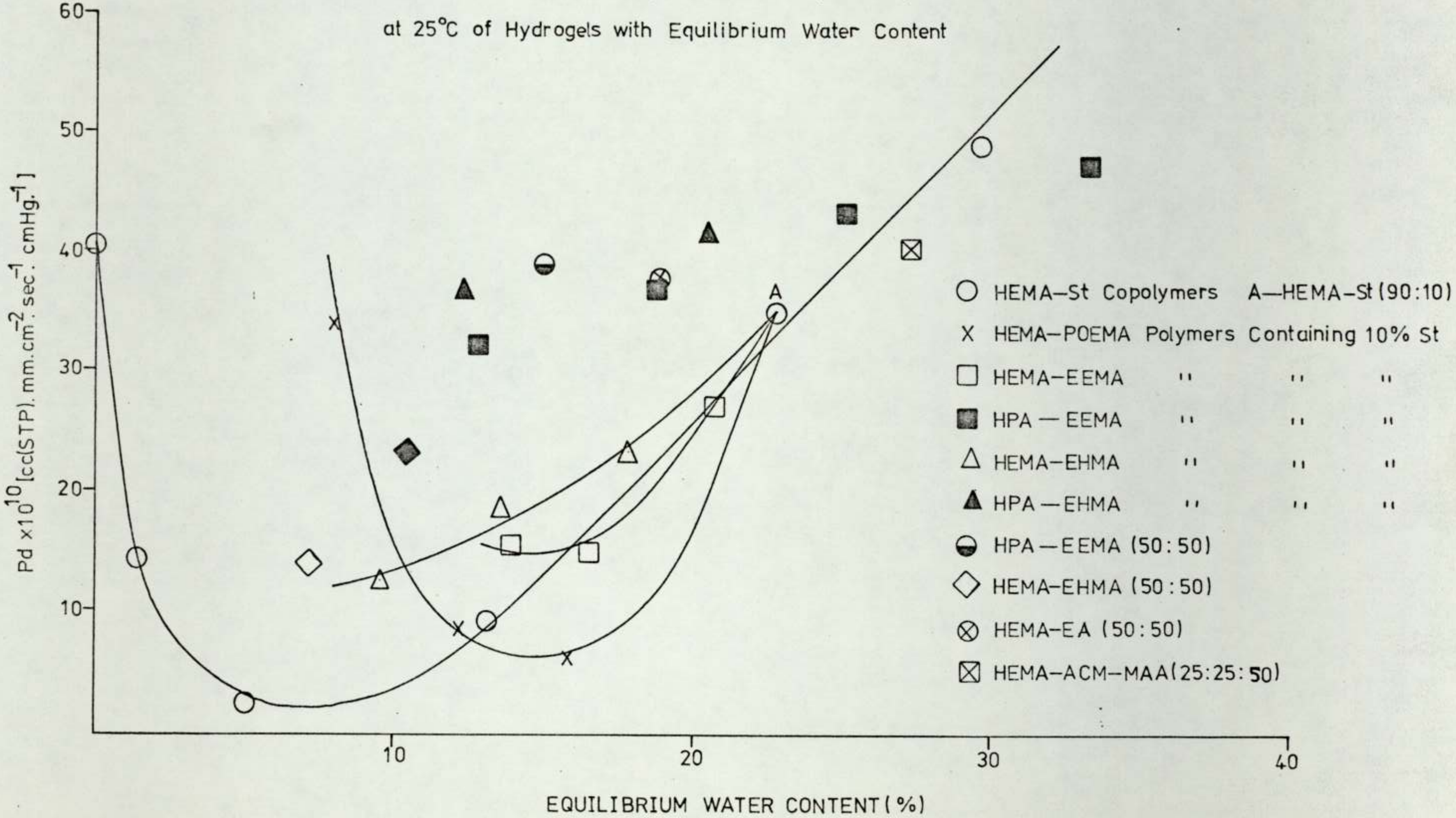
The 'dissolved' oxygen permeability coefficients of hydrogels having a variety of chemical structures and equilibrium water contents were measured at 25°C and the results are shown in Table 22. For convenience the Pd values shown in Table 22 were plotted as a function of water content (Figure 17). In addition the Pd values obtained by Ng[178] for a series of HEMA-St copolymers have been included for the purpose of comparison.

From the scatter of results in Figure 17 it is apparent that there is little correlation between the equilibrium water content and Pd of low water content hydrogels. This of course does not mean that Pd is independent of water content but that there are a number of competing factors involved in controlling the 'dissolved' oxygen permeability. This is clearly illustrated by a closer examination of the results.

Consider first the HEMA-St copolymer series in which an increase in HEMA content (and thus an increase in water content) resulted in a decrease in Pd until a minimum was reached, whereupon a further increase in HEMA content produced a rise in Pd. This behaviour can be attributed to the relative effects of the chemical structure of the copolymers and their water contents on the permeability to oxygen.

According to the hole theory of diffusion the rate of diffusion is dependent on a) the number and size distribution of pre-existing holes, and b) the ease of the hole formation. The

FIGURE 17 Variation in 'Dissolved' Oxygen Permeability Coefficients (Pd) at 25°C of Hydrogels with Equilibrium Water Content



former depends on the ease and degree of packing of the polymer chains and is related to the free volume of the chains whilst the ease of hole formation will depend on the segmental chain mobility, i.e. chain stiffness, and on the cohesive energy of the polymer.

The observed permeability behaviour of the HEMA-St copolymers and other terpolymers in Figure 17 can conveniently be explained with reference to the above theory of diffusion.

An increase in the HEMA content of the HEMA-St copolymers from none to about 50% causes an increase in the cohesive energy of the polymer due to the presence of the polar side chain. This, of course, results in a decrease in the rate of oxygen diffusion. It is apparent that the accompanying increase in water content (to about 10%) has no appreciable effect on the Pd. However, above a HEMA content of about 70% further increases in the amount of HEMA results in a marked increase in water content and correspondingly an increase in Pd. At these higher water contents the water increases chain separation which causes a reduction in the cohesive forces and an increase in free volume resulting in an increased rate of diffusion. Thus, as the water content increases it begins to overwhelm the structural factors in controlling the oxygen permeability. It is probable that at lower water contents the water is strongly bound to the polar sites in the copolymer and is unavailable for gas diffusion and may even help to reduce oxygen permeability by increasing the tortuosity of the diffusion path.

Similar behaviour to that of HEMA-St copolymers is observed for the HEMA-POEMA-St terpolymer system but with the minimum occurring at a higher water content. It is, therefore, apparent that POEMA is more effective in increasing the oxygen permeability of low water content hydrogels than styrene. This can

TABLE 22. 'Dissolved' Oxygen Permeability Coefficients (Pd) and Equilibrium Water Contents of Various Hydrogels at 25°C.

Molar Composition	Sample Thickness (mm.)	Water Content (%)	Pd x 10^{10} (cc(STP).mm.cm.$^{-2}$sec^{-1} cm Hg^{-1})
HEMA-POEMA-St (80:10:10)	0.24	15.9	6.0
HEMA-POEMA-St (70:20:10)	0.23	12.2	8.4
HEMA-POEMA-St (60:30:10)	0.26	8.0	34.0
HEMA-EEMA-St (80:10:10)	0.13	20.7	27.2
HEMA-EEMA-St (70:20:10)	0.18	16.5	15
HEMA-EEMA-St (60:30:10)	0.18	13.9	15.5
HPA-EEMA-St (80:10:10)	0.12	33.1	47.3
HPA-EEMA-St (70:20:10)	0.11	25.1	43.3
HPA-EEMA-St (60:30:10)	0.16	18.8	37.0
HPA-EEMA-St (50:40:10)	0.15	12.8	32.2
HPA-EEMA (50:50)	0.11	15.0	38.9
HEMA-EHMA-St (80:10:10)	0.21	17.8	23.2
HEMA-EHMA-St (70:20:10)	0.23	13.5	18.6
HEMA-EHMA-St (60:30:10)	0.21	9.5	12.6
HEMA-EHMA (50:50)	0.22	7.1	14.0
HPA-EHMA (50:50)	0.06	10.4	23.4
HPA-EHMA-St (70:20:10)	0.10	20.5	42.7

TABLE 22 Continued

Molar Composition	Sample Thickness (mm.)	Water Content (%)	Pd x 10^{10} (cc(STP). mm. cm.$^{-2}$sec^{-1} cm Hg^{-1})
HPA-EHMA-St (60:30:10)	0.10	12.3	36.8
HEMA-EA (50:50)	0.19	18.9	37.9
ACM-HPA-EA (25:50:25)	0.26	59.5	243
ACM-HEMA-MAA (25:25:50)	0.24	27.3	40.5
Poly (HEMA)	0.21	40.5	77.0
HEMA-St (95:5)	0.16	29.7	49.0
HEMA-St (90:10)	0.20	22.8	35.0
HEMA-St (80:20)	0.11	13.1	9.2
HEMA-St (50:50)	0.10	5.0	2.5
HEMA-St (10:90)	0.14	1.4	14.4
Polystyrene	0.16	0	40.6

be accounted for by consideration of the position of the phenyl group in the two monomers. In styrene the phenyl group is attached directly to the backbone whilst the phenyl group in POEMA is at the end of a flexible side chain. This would be responsible for different packing arrangements resulting in a larger free volume for POEMA containing polymers which would explain the greater effect of POEMA than styrene on Pd.

EHMA and EEMA do not have the same dramatic effect on Pd that is observed with styrene and POEMA. They do, however, show a flattening of the curve if not a minimum with decreasing water content. This suggests that although EHMA and EEMA prevent optimal approach of the main chains in the terpolymers thus decreasing inter-chain attraction and, therefore, at low water contents should lead to an increase in Pd, their effect is not great and is balanced by the factors which cause a decrease in oxygen permeability e.g. decreasing water content.

It is very noticeable that the HPA containing hydrogels studied in this work have, in general, a higher Pd than HEMA containing hydrogels at similar water contents. This can be attributed to restriction of main chain rotation in the HEMA hydrogels by the presence of the methyl group on the main chain. This is further supported by comparing the effect of ethyl acrylate with that of methyl methacrylate on Pd. HEMA-EA (50 - 50) has a Pd of 37.9×10^{-10} cc (STP). mm. cm^{-2}. sec^{-1}. cmHg.^{-1} compared to a value[178] of only 12.7×10^{-10} cc (STP). mm. cm.^{-2} sec.^{-1} cmHg.^{-1} for HEMA - MMA (50:50). Undoubtedly the effect of the methyl group in restricting oxygen permeability will be overwhelmed at higher water contents by the plasticisation action of the water.

The low Pd value of HPA-EHMA (50:50) when compared to the Pd values obtained for HPA-EHMA-St terpolymers is rather surprising.

It is possible, however, that with the exceptionally thin membranes of HPA-EHMA (50:50) used for the Pd measurements there was a boundary layer effect which would account for the anomalous Pd value.

Permeability in this work has been discussed in terms of the effect of polymer structure on the rate of diffusion. It should, however, be noted that the permeability coefficient is a function of both the diffusion constant and the solubility of the gas in the polymer. It is difficult though to isolate the effects on permeability that are due to changes in diffusion rate or due to changes in solubility.

Although the work in this chapter has been mainly concerned with 'dissolved' oxygen permeability coefficients of low water content hydrogels, it is interesting to note the high Pd value obtained for ACM-HPA-EA (25:50:25) with an equilibrium water content of 59.5%. This is, however, in keeping with the observations made by Ng[178] who found that for hydrogels with water contents greater than about 25% Pd increased exponentially with increasing water content. This was clearly shown by a plot of log Pd against equilibrium water content which gave a straight line passing through the 'dissolved' oxygen permeability coefficient of water at 25°C (930×10^{-10} cc (STP). mm. $cm.^{-2}$ $sec.^{-1}$ $cmHg^{-1}$). These results tend to suggest that for high water content hydrogels water forms a solvent phase and permeation of oxygen occurs mainly through this liquid phase; the chemical structure of the polymer having little effect. This contrasts markedly with the permeability characteristics of low water content hydrogels. In this region the chemical structure of the polymer and the extent and nature of the binding processes between water and the polymer play a major part in controlling the oxygen permeability.

6.1.3. Prediction of the Permeability Requirements for Contact Lenses

In order that the cornea should show no sign of swelling it has been found[15] that a minimum oxygen tension of 11 to 19 mm Hg. is required at the anterior surface of the corneal epithelium. If the average value is taken, then 15 mm Hg should also be the critical oxygen tension under a contact lens during wear in either an open-eye or closed-eye condition.

It has been reported[81, 114] that in the case of tight fitting contact lens, the oxygen flux (F) across the epithelial surface is given by

$$F = \alpha p_2^{\beta} \tag{18}$$

α and β are two empirical constants

$\alpha = 0.24 \times 10^{-6}$ cc (STP). cm.^{-2} sec.^{-1} $(\text{mm Hg})^{-0.5}$

$\beta = 0.5$

p_2 is the oxygen tension at the epithelial surface.

Using the value of 15 mm Hg for p_2 the critical oxygen flux through a contact lens should be 0.93×10^{-6} cc(STP) cm^{-2} sec.^{-1} i.e. about 3.5 μl. cm.^{-2} hr.^{-1}. This is less than the range 3.7 to 7.8 μl. cm.^{-2} hr.^{-1} reported by Hill and Fatt[11] for the oxygen flux into the cornea of an open eye but higher than the value, 2.8 μl. cm^{-2} hr.^{-1}, recently measured[233] for the oxygen consumption rate of the corneal epithelium. It appears that an oxygen flux of about 3.5 μl. cm.^{-2} hr.^{-1} can be taken as a minimum but sufficient flux to maintain corneal transparency.

It is generally accepted that the oxygen tension at the epithelial surface of the open-eye is 155 mm Hg. but this value does not take into account the effect of the tear film on the surface of the epithelium. Oxygen dissolved in the tear film is supplied to the cornea which suggests that the oxygen tension in the tear film is the boundary condition required. Even with a contact lens on the eye a tear film necessarily covers the lens and thus supplies the oxygen for transport through the lens.

With the aid of the oxygen electrode used in the oxygen permeability studies, the oxygen tension in distilled water was measured at 34°C. When stirred an oxygen tension of 122 mm Hg. was obtained for water but when unstirred the oxygen tension was only 61 mm Hg. As tear fluid can be considered to be a stirred liquid due to the action of the eyelids it is reasonable to assume an oxygen tension in the tear film of 122 mm Hg. It is possible, however, that the oxygen tension in tear fluid may be lower than in distilled water due to the presence of solutes.

In order to obtain the oxygen tension in the tear film under the closed-lid Fatt and Bieber[14] measured the oxygen tension of the palpebral conjunctiva which they assumed to be in equilibrium with the tear film under closed-eye conditions. The value they obtained was 55 mm Hg. It is worth noting that their experimental procedure involved calibrating their oxygen electrode in aerated water which they assumed to have an oxygen tension of 155 mm Hg. It is difficult, even with rapid bubbling of air through water, to envisage a figure as high as 155 mm Hg. being obtained. It is probable, therefore, that value for the oxygen tension in the tear film of 55 mm Hg. is also too high. A recalculation shows that it may be as low as 43 mm Hg. if an oxygen tension of 122 mm Hg is used as the calibration figure.

With the aid of Equation 19 the previously discussed information can be used to determine the critical 'dissolved' oxygen permeability coefficient (Pd) at 34°C of a hydrogel for a given contact lens thickness (L) for both the open-eye and closed-eye situation.

$$F = \frac{Pd}{L} \times (\Delta p) \qquad (19)$$

Δp is the difference in oxygen tension across the lens.

The correlation between Pd and L for a contact lens in the open-eye and closed-eye condition is shown in Figure 18.

The values of Δp used are those obtained from the literature

open-eye $\Delta p = 155 - 15 = 140$ mm Hg.

closed-eye $\Delta p = 55 - 15 = 40$ mm Hg.

and those obtained in this work

open-eye $\Delta p = 122 - 15 = 107$ mm Hg.

closed-eye $\Delta p = 43 - 15 = 28$ mm Hg.

It should be mentioned that the correlation in Figure 18 is not applicable to polymers which exhibit boundary layer effects causing a dependence of Pd on thickness.

Poly HEMA has a water content of 40% and a Pd[178] at 34°C of 145×10^{-10} cc (STP) mm. cm.^{-2} sec.^{-1} cmHg.^{-1}. Commercial Poly HEMA lenses are normally 0.3mm or 0.4mm thick and therefore, according to Figure 18, not suitable for continuous wear (closed-eye condition) or for daily wear (open-eye condition) under tight conditions i.e. when the only pathway for oxygen is through the lens. Poly HEMA lenses (for daily wear) are of course worn successfully by many patients because oxygen flux through the lens is supplemented by oxygen dissolved in the tear fluid which because of a rippling action during blinking is transported under the edge of the lens.

Using the 'dissolved' oxygen permeability measurements of Ng[178] at 34°C (Figure 19) and the correlation between Pd and L (Figure 18) it is possible to predict the water content at 34°C required of a hydrogel to be suitable for daily or continuous wear.

In order to make these predictions the line in Figure 18 obtained when $\Delta p = 107$ has been used for the open-eye situation and it has been assumed that for the closed-eye condition the optimum pressure difference is somewhere between 40 and 28 mm Hg.

On this basis, for a contact lens of thickness 0.1mm to be suitable for daily wear, the lens material should have a Pd at 34°C

FIGURE 18 Theoretical Correlation of 'Dissolved' Oxygen Permeability Coefficient (Pd) Required to Produce an Oxygen Flux of $0{\cdot}93 \times 10^{-6}$ cc(STP).cm^{-2}.sec^{-1} with Increasing Contact Lens Thickness at 34°C

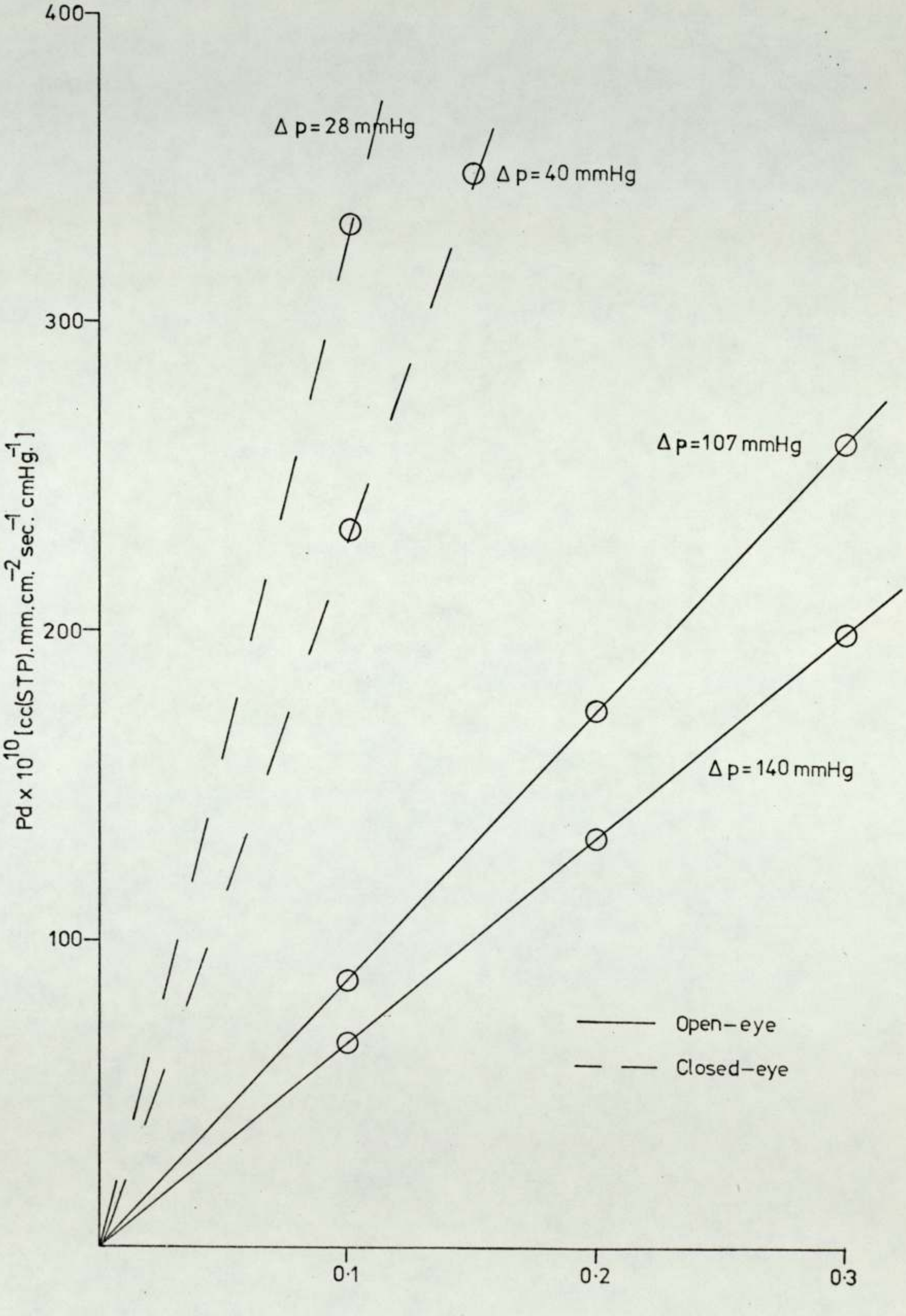
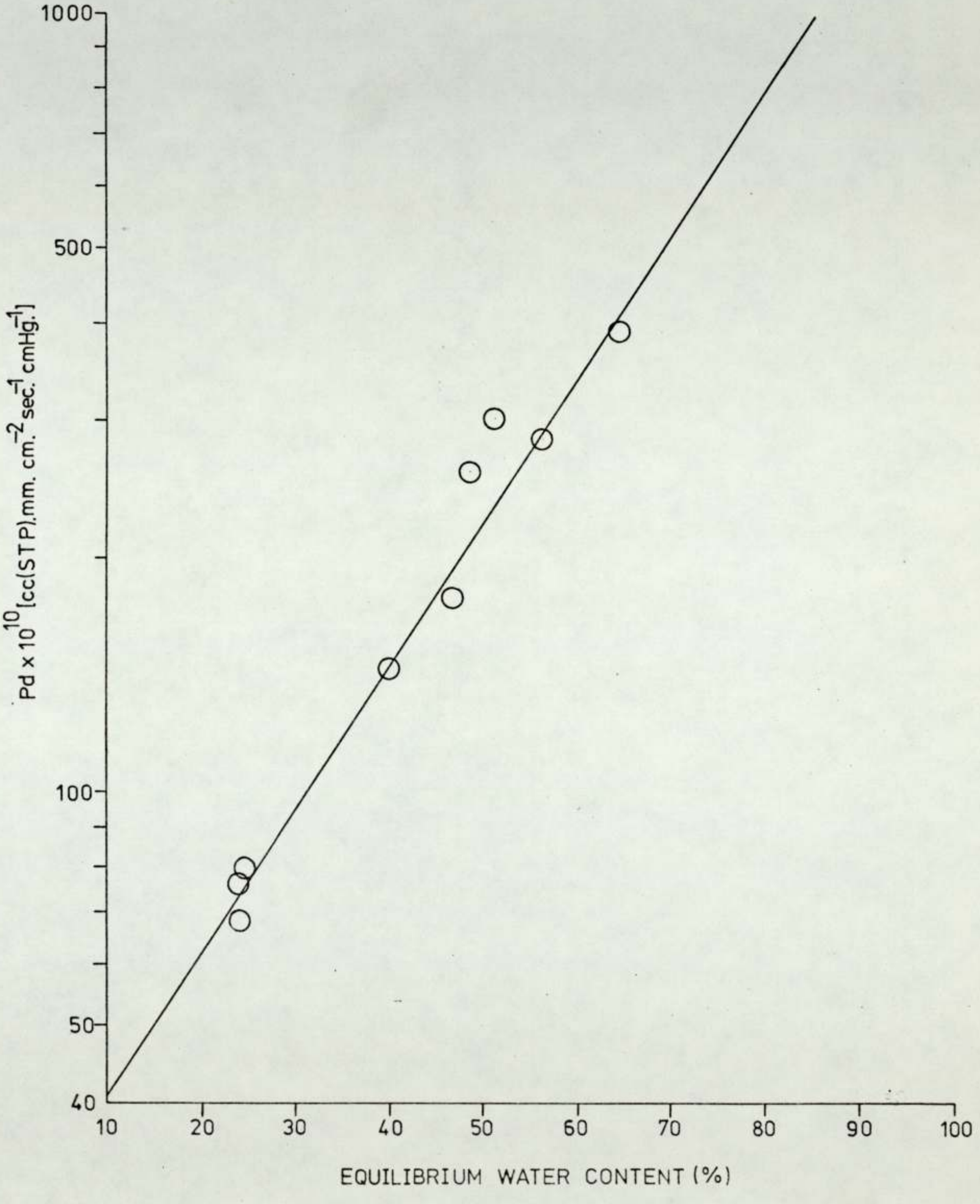


FIGURE 19 Variation in Log Pd of Hydrogels at 34°C with Equilibrium Water Content



of at least 85 x 10^{-10} cc (STP). mm. $cm.^{-2}$ $sec.^{-1}$ cm $Hg.^{-1}$ which from Figure 19 indicates a required water content of 27% or more.

In order that a hydrogel lens may be considered for continuous wear it must have a sufficient oxygen permeability such that under closed-eye condition the normal aerobic metabolism of the cornea is maintained. Thus, for a contact lens of thickness 0.1mm the lens material should have a Pd at 34°C of between 230 x 10^{-10} and 330 x 10^{-10} cc (STP). mm. $cm.^{-2}$ $sec.^{-1}$ cm $Hg.^{-1}$ This means that a hydrogel of water content between 50% and 60% at 34°C would be required. Such a thin lens, however, would present difficulties in manufacture as lathe-cutting or compression moulding such a lens in its dehydrated form (and therefore even thinner) would require highly sophisticated techniques.

For a continuous wear 0.2mm lens the required oxygen permeability would be double that for a 0.1mm lens and the water content would thus have to be between 67% and 76% at 34°C.

A 0.2mm lens for daily wear requires a Pd of 175 x 10^{-10} cc (STP). mm. $cm.^{-2}$ $sec.^{-1}$ cm $Hg.^{-1}$ corresponding to a water content of 45%. This, of course, represents the Pd required assuming only oxygen transport through the lens but as previously mentioned this can be supplemented by tear flow under the lens. This tear flow is, however, dependent upon lens design and the fitting of the lens and is therefore not always adequate. It is obviously advisable to adhere to the additional safety margin offered by a contact lens with a Pd greater than 175 x 10^{-10} cc (STP). mm. $cm.^{-2}$ $sec.^{-1}$ cm $Hg.^{-1}$ In the case of the continuous wear lens fitting techniques will have little effect under closed-eye conditions. It should be mentioned, though, that the correlation between Pd and contact lens thickness (Figure 18) was obtained assuming that in the closed-eye situation the only available oxygen supply is from the capillaries of the palpebral conjuctiva. During sleep, however, the eye-lids are not firmly closed so there may be some extra oxygen available from the atmosphere. It is also known that during sleep rapid eye-ball movement occurs which may contribute to tear replenishment under the lens.

Other complicating factors to the above theoretical approach include the following:-

a) The equilibrium water content of a hydrogel is lower in a 0.9% saline solution (isotonic with tear fluid) than in distilled water.

b) The solubility of oxygen in tear fluid may be lower than in distilled water due to the presence of solutes.

c) The structure of water in hydrogels may be affected by the presence of solutes in the tear fluid and this may affect the oxygen permeability.

d) The oxygen consumption rate of the cornea varies from one person to another and is not constant for a given individual.

This latter factor, especially, stresses the need for a clinical correlation between oxygen permeability and the maintenance of normal corneal metabolism under continuous wear conditions. A minimum figure for the 'dissolved' oxygen permeability coefficient required for a hydrogel lens for continuous wear and suitable for the majority of patients would then be available.

6.1.4. Some Comments on the Method Used for 'Dissolved' Oxygen Permeability Measurements

The study of the permeability of polymer membranes to dissolved oxygen has not until recently been pursued. There are thus no standard methods or apparatus available for the measurement of the 'dissolved' oxygen permeability coefficient.

Although the apparatus (see Chapter 2) used in this work was found to give reproducible results several difficulties were found to be associated with the technique.

The filling of the top chamber with nitrogen-saturated water, injected through the aperture with a syringe, whilst under a blanket of nitrogen, required a certain amount of dexterity in order to avoid damaging the sample with the hypodermic needle and to prevent the formation of gas bubbles in the small trough at the end of the oxygen electrode. The amount of water required to fill the top chamber was about 0.25 to 0.5 ml, thus uncertainty in its measurement could lead to large errors in the permeability coefficient. This was, however, somewhat alleviated by using a 0.5 ml. Hamilton syringe which read to 0.01 ml.

It is probable that the measurements would be made easier and more accurate if a permeation cell with a larger top chamber was constructed. This would, however, necessitate stirring up the top chamber as well as the bottom which may present its own difficulties.

The plot of log $(p_1 - p_2)/p_1$ vs. t was found in many cases (especially for low permeable polymers) to curve upwards. This can possibly be attributed to two main causes:

a) Insufficient mixing of oxygen and water in the top chamber. This is, however, unlikely as the permeability of water to oxygen is many times greater than that of the low permeable polymers.

b) High oxygen consumption by the electrode. This is the most likely cause but there seems little that can be done about it.

CHAPTER 7

SURFACE PROPERTIES OF HYDROGEL POLYMERS

The wettability of contact lens materials is important because the adherence of the pre-corneal tear film, in the form of a thin capillary layer, is recognised as being a primary requirement for the physiological compatibility of the lens and the patient (Section 1.2.2.). Thus, the surface properties of hydrophobic contact lens materials e.g. PMMA and silicone rubber and methods of rendering them more hydrophilic have received a lot of attention.[38-41, 171-176]

The ability of hydrogel-forming polymers to imbibe water and the obvious ease of wetting of hydrogels has resulted in their surface properties being neglected as far as contact lenses are concerned. This is simply because hydrogels have a critical surface tension above the minimum value for tear film spreading discussed in Chapter 1. Consideration has, however, been given to the surface properties of hydrogels in relation to their blood compatibility.[234]

Recently it has become apparent that mucous adhesion to the surface of a hydrogel contact lens occurs especially in lenses with a high water content.[199, 259, 260] In Chapter 6 it was suggested that high water content hydrogels would be needed for continuous wear contact lenses in order to satisfy the oxygen requirements of the cornea. This indicates that mucous build-up could be a significant problem with continuous wear lenses. The build-up of mucous debris on a lens causes a decrease in vision and makes a lens uncomfortable especially when particles become dislodged under the lens. Mucous can also provide nutrition for pathogens, and infections such as conjunctivitis may result.[235] This would obviously necessitate the frequent removal of the lens for cleaning and sterilisation. Since the wettability of, and adhesion to, a substrate are known to be interrelated[258] it is probable that the hydrophilicity of the surface of a hydrogel is responsible for the build-up of mucous debris, it is important thus, to determine the surface characteristics of a hydrogel for contact lens use.

The widespread use of water contact angles as criteria for assessing the wettability characteristics of hydrophobic lens materials as discussed in Chapters 1 and 3, makes a contact angle study the most obvious starting point for determining the surface hydrophilicity of a hydrogel. In order that contact angle measurements should be relevant to the situation of the contact lens on the eye they must be made on hydrogels in the hydrated state. It should be mentioned, however, that surface studies on dehydrated hydrogels are of considerable importance in relation to mould adhesion problems encountered in the moulding of hydrogel polymers. The relationship between surface properties of dehydrated hydrogels and mould adhesion is at present under investigation and beyond the scope of this thesis.

Poly HEMA, because of its widespread use, is the most obvious hydrogel on which to start an investigation of surface properties. The effect of hydrophobic substituents on surface hydrophilicity has been examined in this work using copolymers of HEMA with styrene.

7.1 EXPERIMENTAL PROCEDURE

15mm hydrogel discs were cut from a membrane with a cork-borer and prior to contact angle measurements water was gently removed from the surface of the hydrogel samples using Kleenex Medical Wipes. The advancing contact angles of water on the hydrogels were measured using the sessile drop technique (Section 2.2.3.1.).

A further technique for characterising the hydrophilic nature of solid surfaces has recently been developed by Hamilton.[236] This technique involves the measurement of octane contact angles on solid surfaces whilst under water (Figure 20). It is, therefore, apparent that this method would be most suitable for the surface characterisation of hydrogels. The hydrogels would easily remain in their hydrated state and the problems of the removal of surface water from hydrogels would be eliminated.

Octane and water have surface free energies of 21.8 and 72.0 dynes/cm, respectively, at 20°C. Fowkes[237] has demonstated that the surface free energy value for octane is due to dispersion forces only, but that the surface free energy value of water consists of two components, dispersion forces (21.8 dynes/cm) and polar forces (50.2 dynes/cm). As the dispersion force contributions to the surface free energy values of octane and water are identical, octane underwater contact angles would be expected to have an identical value on those solid surfaces which can interact only through dispersion forces, but have different and higher values on those surfaces that have the ability to interact through polar forces. Hamilton has calculated that in cases where only dispersion forces are present the contact angle for the octane/water/solid system should be 50°. The stronger the polar forces, i.e. the more hydrophilic the surface, the larger the octane/water contact angle is. Octane/water contact angles ranging from 50° to nearly 180° are, therefore, possible depending on the magnitude of the surfaces' polar forces.

Hamilton's technique was adapted for use with hydrogels and the following procedure was used.

Hydrogel samples were cut from a hydrated membrane and stuck to microscope coverslips using a spray-adhesive. The hydrogel surfaces were then cleaned using a detergent solution followed by a thorough rinsing with distilled water. The samples were then allowed to re-equilibrate in distilled water for several hours.

The coverslips, onto which the hydrogel samples were attached, were supported in a glass cell containing octane-saturated

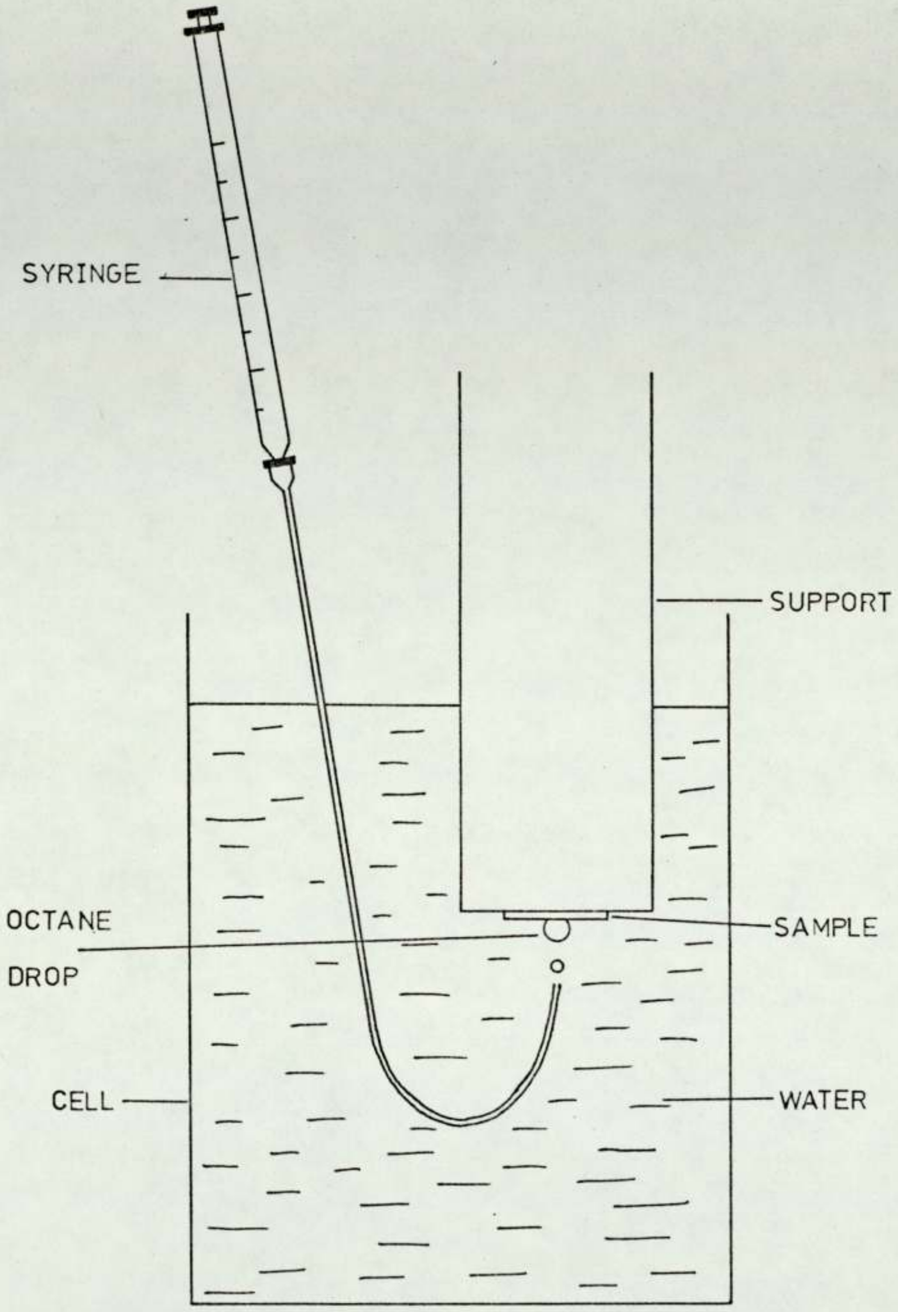


FIGURE 20 Cell for Measuring Octane/Water/Solid Contact Angles

water. Sessile drops of octane were formed on the hydrogel surface by releasing octane drops from a syringe (Figure 20). As octane has a lower density than water the octane droplet floats upwards, touches the sample surface and forms the interface. Enlarged images of the sessile drops were projected onto a back projection screen and the contact angles were measured as described in Section 2.2.3.1. At least 3 samples of each hydrogel were used and at least 3 measurements made on each sample.

7.2. RESULTS AND DISCUSSION

Difficulties were encountered in the measurement of the advancing contact angle with water on hydrated poly HEMA using the conventional technique and reproducible results were not obtained. It was apparent that the extent to which the hydrogel surface was dried affected the measured contact angle. The contact angles on poly HEMA varied between 0° and about 40°. Attempts to obtain such water contact angles on hydrogels were abandoned because meaningful results were not being obtained.

It is interesting to note, however, that with dehydrated poly HEMA Gott et al[234] obtained an advancing contact angle of 42°. Whilst they found that hydrated samples behaved in a similar way to a duplex film of water and exhibited zero contact angle. Upon visual inspection of the water swollen poly HEMA no layer of water was obvious.

More recently Holly and Refojo[238] have investigated the contact angle of water on poly HEMA hydrogels having water contents ranging from 32 to 43%. The results they obtained were independent of water content and varied over a range 58° to 85°. The difference in the results obtained in this work and theirs is difficult to explain especially as their technique of measurement was in many ways similar to that used here. Although no comments on the reproducibility of the results appears in their paper the large and inconsistent variation in contact angles over a small water content range suggests poor reproducibility.

They do, however, attempt to explain why such large contact angles were obtained by suggesting, that when a hydrogel is swollen to equilibrium, it is energetically more favourable for the polymer chain segments to orientate in such a way as to expose the hydrophobic parts of the polymer towards the surface and to bury the polar sites in the aqueous phase within the gel.

The difficulties encountered in this work in obtaining meaningful contact angle measurements of water on hydrogels has led to the use of an apparently more reliable technique for hydrophilic surface characterisation. The method devised by Hamilton[236] appeared to be most suitable and easily adapted for use with hydrogels. Its most important advantage is the fact that measurements are made under water and thus removes the need to dry the surface of a hydrogel.

Octane/water contact angles measured on some hydrophobic polymers and on a series of hydrogels (copolymers of HEMA and styrene) are shown in Table 23.

The contact angles obtained on polyethylene and P4MP1 are the same as the value of 50° calculated by Hamilton for cases where dispersion forces only are present. Hamilton reported the octane/water contact angle on polytetrafluoroethylene to be also 50°. This shows that the octane/water contact angles are insensitive to differences in dispersion force interactions of surfaces.

Octane/water contact angles do, however, reflect changes in surface hydrophilicity as shown by the higher value for PMMA than for either polyethylene or P4MP1. This is further emphasised by the increase in contact angle observed with increasing HEMA content

TABLE 23. Octane/Water Contact Angles on Hydrogels and on Hydrophobic Polymers.

Polymer	Equilibrium Water Content (%)	Octane/Water Contact Angle (deg)
Polyethylene	0	50 ± 2
P4MP1	0	50 ± 2
PMMA	~ 0	78 ± 2
Poly HEMA	40.5	148 ± 2
HEMA-St (90:10)	22.8	136 ± 2
HEMA-St (80:20)	13.1	126 ± 2
HEMA-St (50:50)	5.0	108 ± 2
HEMA-St (10:90)	1.3	93 ± 2
Polystyrene	0	55 ± 2

in the HEMA-styrene copolymer series. Obviously an increase in the concentration of hydroxyl groups at the surface of the HEMA-styrene copolymers is responsible for the increased octane/water contact angle.

For convenience the octane/water contact angles on the hydrogel series have been plotted against HEMA content (Figure 21). A small increase (10 mole%) in HEMA content produces an initial sharp increase in the octane/water contact angle. This is followed by a more gradual increase in contact angle with increasing HEMA content. The initial sharp increase in contact angle can be attributed to the sensitivity of the contact angle to the hydrophilicity of the surface. The gradual increase in the octane/water contact angle which follows the sharp increase represents the increasing dominance of the polar component at the surface.

Equilibrium water content reflects the bulk hydrophilicity of a hydrogel and the octane/water contact angle provides a measure of surface hydrophilicity. It is thus interesting to compare Figure 21 with a plot of equilibrium water content vs. HEMA content for the same HEMA-styrene copolymer series (Figure 22). The copolymerisation of a small amount of styrene with HEMA results in a sharp drop in the equilibrium water content whereas only a gradual drop in the octane/water contact angle is observed. This indicates that the steric hindrance of the phenyl group in styrene which plays such an important part in restricting the water uptake of HEMA-styrene copolymers does not have such a dominant effect on the surface hydrophilicity.

The fact that styrene has a much greater effect on the equilibrium water content than on the hydrophilicity of the surface of a hydrogel is clearly illustrated by a plot of octane/water contact angle vs. equilibrium water content (Figure 23). Thus, in

FIGURE 21 The Dependence of the Octane/Water Contact Angle on the Composition of Some HEMA–Styrene Copolymers

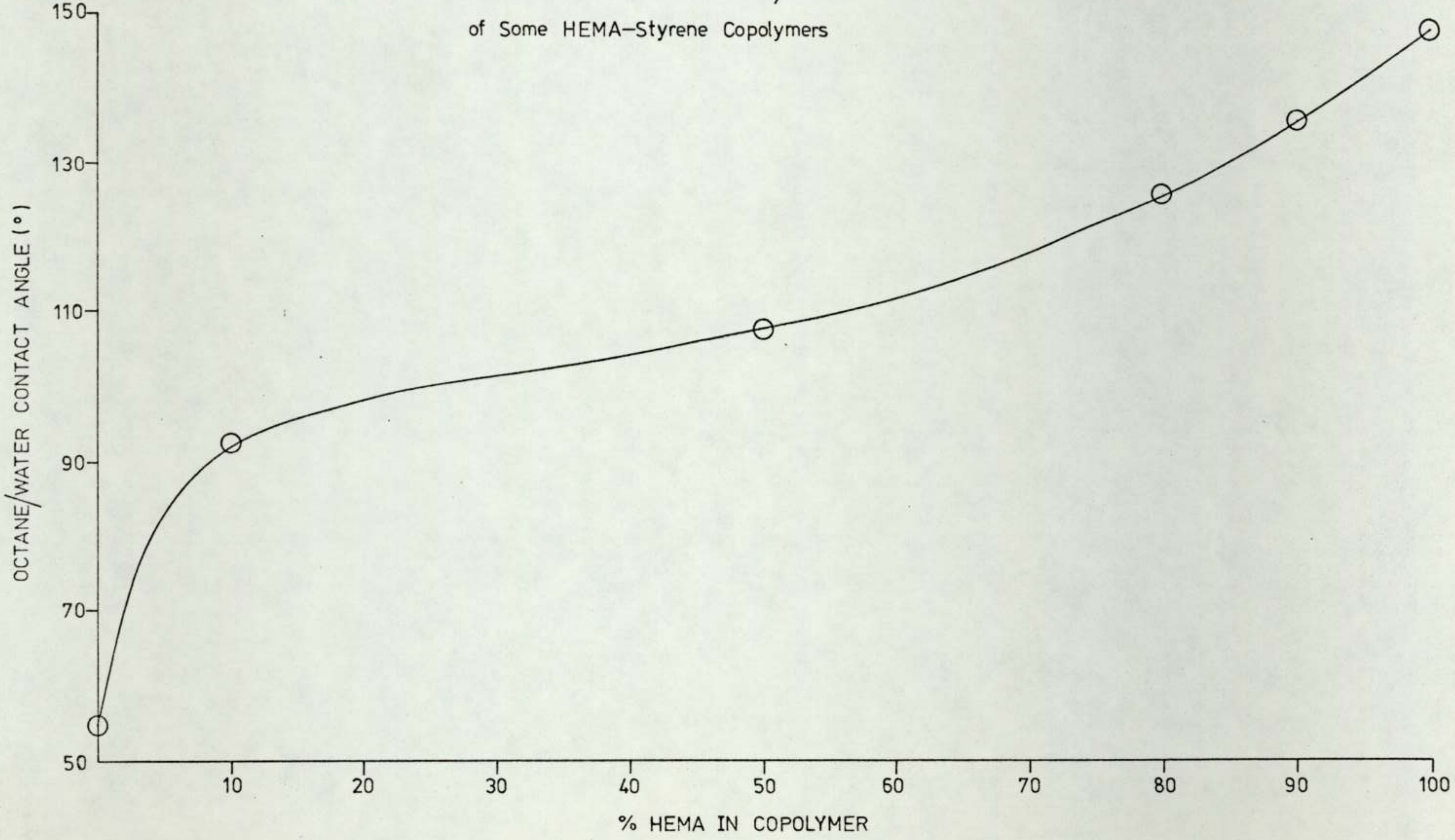


FIGURE 22 Equilibrium Water Contents (20°C) of Some HEMA–Styrene Copolymers

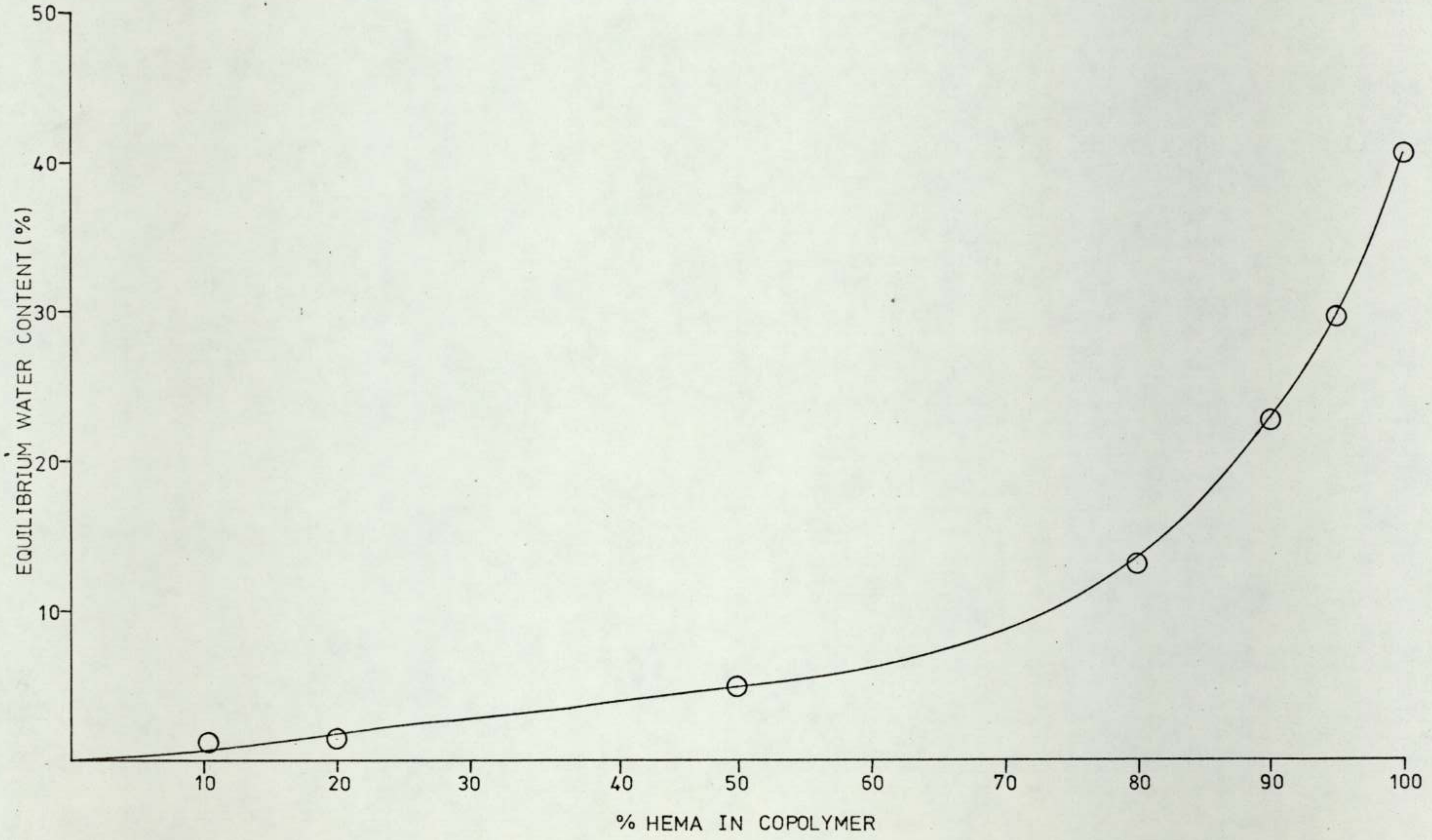
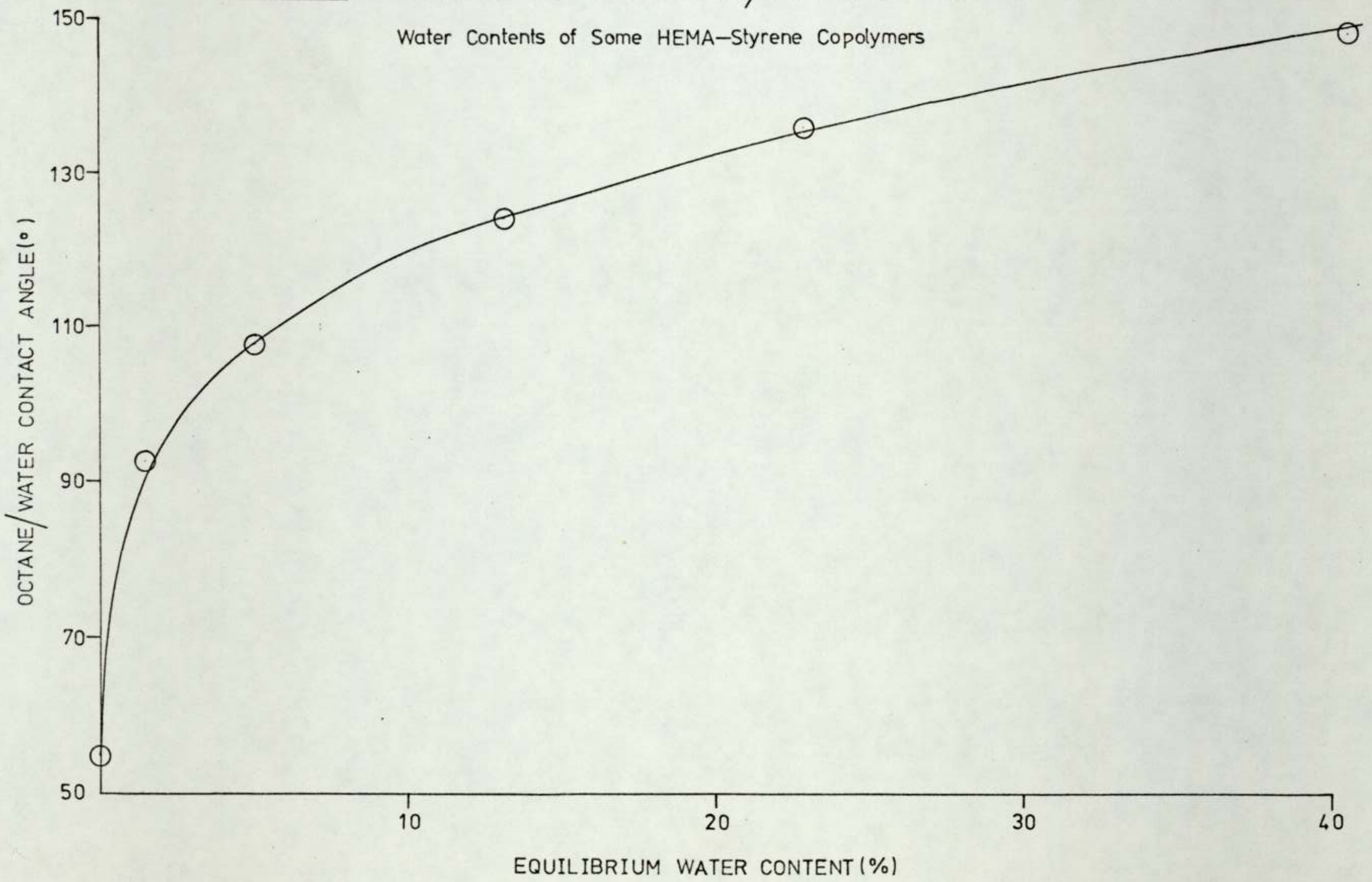


FIGURE 23 The Relationship Between Octane/Water Contact Angles and Equilibrium Water Contents of Some HEMA–Styrene Copolymers



order to reduce the surface hydrophilicity of a high water content hydrogel the introduction of styrene by way of copolymerisation would not be acceptable, as a large decrease in water content would result before any noticeable decrease in surface hydrophilicity.

Obviously what is required is a monomer which will reduce dramatically the surface hydrophilicity without affecting the water content by much. It has been suggested that the incorporation of small amounts of fluorinated alkyl acrylates and methacrylates[239] e.g. trifluoroethyl methacrylate may substantially affect the surface hydrophilicity whilst only having a slight effect on the water content. The limited amount of work done in this direction suggests that fluorinated alkyl acrylates and methacrylates do have a desired effect on surface hydrophilicity.[240]

Whilst the work described here does provide a useful method for determining the hydrophilicity of a surface it is not certain whether mucous build-up on the surface of a hydrogel contact lens is wholly dependent on the hydrophilicity of the surface, although it does appear that mucous build-up is more of a problem with high water content hydrogels. It is obvious that there is a need to correlate surface hydrophilicty as measured in this work with clinical information on the mucous deposition on contact lense. This, however, may prove difficult for as yet there is no straightforward way of quantitatively assessing the mucous build-up on a lens.

CHAPTER 8

GENERAL DISCUSSION, CONCLUSIONS AND SUGGESTIONS FOR FURTHER WORK

8.1. GENERAL DISCUSSION

The most important features of hydrogels taking properties as a whole are the equilibrium water content and the nature of the water within the gel. Earlier studies on hydrogels, however, have tended to overlook the fact that water may be able to exist in different "states" in a hydrogel. A most important analogy can be drawn with biological systems as in such systems the concept of different "states" of water has been used for several years in relation to transport phenomena and permselectivity of biological membranes.[243, 244]

It is apparent that many of the concepts associated with transport phenomena in biological systems can be applied to the study of commercially important separation processes such as reverse osmosis. On the other hand much can be learnt from a study of purely synthetic systems in which the isolation of structural factors and their effect in terms of water binding can be readily achieved.

The properties of hydrogels most relevant to contact lens wear which have been considered in this work are permeability to oxygen and surface properties. The mechanical properties especially deformation under eye-lid load have been investigated elsewhere[178] and are beyond the scope of this work. It is worth noting, however, that the mechanical properties retain some dependence on the molecular structure of the polymer even in high water content hydrogels.

In the design of polymers for contact lens applications two approaches have been examined in this work:-

a) The surface modification of existing polymers having otherwise attractive properties.

b) The use of copolymerisation to combine some of the desirable properties of the respective homopolymers.

The first approach, although successful when using poly (4-methyl pent-l-ene), in imparting a surface of sufficient hydrophilicity for contact lens wear did not on a clinical basis provide advantages over PMMA.

The second approach, however, provides for structural variation and allows the possible use of the cornea as a model for the design of contact lenses. Although the idea of using the cornea as a model is attractive the synthesis of a polymer to mimic the complex structure of the cornea presents formidable difficulties. The surface properties and bulk properties of the cornea are separately governed by the epithelium and the stroma, respectively, and their natures are quite different. Thus, the cornea has a water content of 81% yet has a hydrophobic surface (only just wettable by the tear fluid). The reason why nature has given the cornea a hydrophobic surface may be more apparent when the problem of mucous build up (see Chapter 7) encountered by wearers of high water content lenses with their very hydrophilic surfaces is considered.

Of the three types of property (mechanical, surface and permeability) that govern the suitability of a synthetic hydrogel for continuous wear (as distinct from daily wear) contact lens use the most critical is oxygen permeability. This is because mechanical properties govern comfort, surface properties the long term resistance to mucous deposition, and oxygen permeability the respiration of the cornea. If the supply of oxygen to the cornea is insufficient to maintain the normal metabolism of the eye then corneal oedema with consequent lack of corneal transparency and the onset of considerable pain are encountered following the first period of sleep. In Chapter 6 it was concluded that hydrogels with high equilibrium water contents (c.f. the cornea) would be required to fulfil the oxygen requirements for continuous wear. Promising high water content hydrogels have been prepared (Chapter 5) using acrylamide[245] as one of the hydrophilic monomers. In fact a contact lens from

HPA-ACM (66:33) with a thickness of 0.15mm and water content 71.6% has recently been worn continuously (day and night) for a period of two weeks without any sign of corneal oedema.

The "dissolved" oxygen permeability coefficient of HPA-ACM (66:33) can be estimated from Figure 19 to be about 400 to 500 x 10^{-10} cc (STP).mm.cm.$^{-2}$ sec.$^{-1}$ cmHg^{-1} (assuming there is no dramatic change in water content at 34°C). This is interesting because according to the work in Chapter 6 and in particular Figure 18, for a contact lens of 0.15mm thickness a "dissolved" oxygen permeability of between 350 and 460 x 10^{-10} cc (STP). mm. cm.$^{-2}$ sec.$^{-1}$ cmHg^{-1} would be the minimum acceptable for continuous wear. Thus, in this case the theoretical prediction is supported by the available clinical evidence.

Although only covalently cross-linked hydrogels have been considered in this work high water content contact lenses can be obtained using ionically cross-linked polyelectrolyte complexes. It is unlikely, though that they will find wide application in the contact lens field because of their inherent disadvantages, namely the large changes in water content and thus dimensions brought about by minor changes in pH and tonicity such as those experienced on the eye.

The nature of water in both synthetic polymers and biopolymers has been the subject of much speculation in recent years. It is apparent that water can exist in a number of states varying from that which is hydrogen bonded to the appropriate hydrophilic groups within the polymer to that which is only associated with other water molecules in a similar environment. These states are often referred to as "bound" and "free", however, this is certainly an oversimplification as it is probable that these are extreme situations between which there are successive hydration shells each with a decreased interaction with the hydrophilic sites in the polymer as the shell becomes more remote from the "binding site".

A number of terms have been used over the years to describe the various states of water in polymers (particularly synthetic polymers). The more common ones are collected together in Table 24.

A variety of techniques can be used to study the state of water in systems involving water as one of the components. They include infra-red spectroscopy, dilatometry, differential scanning calorimetry (DSC), nuclear magnetic resonance spectroscopy (NMR), specific conductivity and dielectric studies. Of these, the major techniques have been DSC and NMR.

TABLE 24 Terms Used to Describe the States of Water in Water Swollen Polymer Systems.

Description			References
Bound	Free		246 - 249
Non-freezing	Freezing		248, 250, 251
Primary	Secondary		149, 151, 252
Z	Y	X	253, 256
W_3	W_2	W_1	254, 255
Bound	Interfacial	Bulk	253, 256

DSC quite simply allows a quantitative determination to be made of the amount of water in the system that freezes at about the freezing point of water and that fraction which does not freeze even at temperatures as low as -70°C.

Both broad line and pulsed NMR techniques have been used and have helped to clarify the situation somewhat regarding the relative mobility of the different states of water. A rapid exchange is indicated by NMR between "bound" and "free" water. "Bound" water although highly associated with the polymer retains substantial mobility,[249] in fact it is still highly mobile when compared to ice.

The oxygen permeability of hydrogels has been shown to be dependent on water content at high equilibrium water contents but at less than 30% greater dependence on molecular structure and possibly the state of water is observed (Chapter 6). At low water contents most of the water in a hydrogel would be expected to be closely associated with specific groups in the polymer chain but because oxygen is also soluble in the polymer matrix per se, it is difficult to isolate effects on oxygen permeability due to structural features from those due to water binding.

On the other hand where solutes which are only soluble in the water phase are concerned the selectivity characteristics of the membrane will be significantly determined by the nature of the water in the polymer membrane. Thus, for example, if there is only water strongly associated with the hydrophilic sites on the polymer present then water can travel through the membrane by diffusion along the adsorbtion sites whereas permeation of the solute would not occur because of the lower capacity for hydration of solutes by water which is strongly bound to the polymer.[257] An example of this sort of behaviour is the transport of sodium chloride through water swollen membranes. Hydrated sodium ions permeate only very slowly through a membrane if the only water present in the membrane is strongly associated with the polymer. This is presumably due to the slow rate of exchange between water in these two environments. This example of permselectivity is important in desalination by reverse osmosis.

It is relevant to mention that the flow of water through hydrogels indicates the existence of "pores". Yasuda and Lamaze[261] have shown that there is a linear correlation between the swelling ratio ($\frac{1}{1 - H}$), where H is the fractional hydration of the membrane (i.e. H = 0.5 is equivalent to 50% equilibrium water content), and the average pore radius. It is, however, important to remember that the binding of water to the polymer has a marked effect in reducing the effective pore radius of the hydrogel.

A large water soluble permeant such as bromosulphophthalein (molecular weight 486) shows a "cut off" phenomenon. In other words permeation does not occur[228] in this case through homogeneous hydrogels with a water content of less than about 70%. This corresponds to a pore size slightly larger than the bromosulphophthalein molecule. This is consistent with the above ideas.

For hydrogels in biomedical applications the most important properties in addition to transport phenomenon are surface properties. Blood compatibility has in general been assumed to be a simple function of water content. Recently, however, the role of the nature of water in hydrogels and at the hydrogel/blood interface has been given more consideration.[241, 242] It has been suggested that as blood may contain relatively "structured" water, a certain degree of water "structuring" at the interface may be desirable for optimum compatibility.

8.2. CONCLUSIONS

The correlation of the wettability of polymers by water with clinical observations of the homogeneity of the tear film on the surface of a contact lens shows that potential contact lens materials can be screened by determining the contact angle with water of the polymer. In order for tear fluid (surface tension 46 dynes/cm) to completely wet a polymer surface the contact angle with water (72.8 dynes/cm) should be no greater than 60-65°.

Of the non-hydrogel polymers examined poly (4-methyl pent-1-ene) is the most readily modified in such a way that its surface becomes sufficiently wettable to sustain a coherent tear film without unacceptable impairment of its optical properties. The higher oxygen permeability and greater flexibility of poly (4-methyl-pent-1-ene) over that of poly (methyl methacrylate) are not sufficient for significant clinical differences to be detected during daily wear.

Structural variations in hydrogels are conveniently obtained by copolymerisation of a range of hydrophilic and hydrophobic monomers. The equilibrium water contents of the resulting hydrogels is governed by a balance of polar and steric effects. More complex behaviour is observed when methacrylic acid is included as a hydrophilic monomer in hydrophilic--hydrophobic and hydrophilic--hydrophilic copolymerisations. The anomalously low equilibrium water contents which such hydrogels exhibit are probably a result of the strong hydrogen bonding ability of methacrylic acid. As a result of hydrogen bonding between methacrylic acid units in adjacent chains and between methacrylic acid and suitable bonding sites on other hydrophilic units in the polymer there is a secondary cross-linking effect and a reduction in the number of sites available for interaction with water. These effects are consistent with the unexpectedly low water contents obtained.

Over a wide range of water contents the permeation of "dissolved" oxygen through hydrogels is dependent upon the equilibrium water content. At low water contents i.e. less than 30%, however, it also depends on the molecular structure and possibly on the water binding ability of the hydrogel polymer.

Based on the literature values of the critical oxygen tension of 15mm Hg at the corneal surface and the critical oxygen flux of 3.5 μl. cm^{-2} hr.$^{-1}$ into the cornea, a 0.15mm thick hydrogel contact lens for continuous wear requires a minimum "dissolved" oxygen permeability coefficient of between 350 and 460 x 10^{-10} cc (STP). mm. cm.$^{-2}$ sec.$^{-1}$ cm Hg^{-1}. These correspond to in-vivo water contents of between 61% and 68%.

High water content hydrogels, although required in order to satisfy the oxygen requirements of the cornea during sleep, provide problems associated with their hydrophilic surfaces i.e. mucous deposition on the lens surface. The Hamilton contact angle technique provides a useful method for measuring the hydrophilicity of a hydrogel surface. Increasing the hydrophobic content of a hydrogel causes a decrease in the surface hydrophilicity but unfortunately this is accompanied by a large decrease in the equilibrium water content. Obviously a hydrophobic monomer which affects the surface hydrophilicity to a greater extent than the bulk hydrophilicity is required. Such a monomer may well be an acrylate or methacrylate with a fluoroaliphatic side chain.

8.3. SUGGESTIONS FOR FURTHER WORK

Arising from this work several suggestions for further work are made as follows:-

1) Further investigations should be made into the copolymerisation of 4-methyl pent-1-ene with a hydrophilic monomer e.g. 2-hydroxyethyl methacrylate or N-vinyl pyrrolidone. A successful copolymerisation may be achieved if an electron acceptor complex of HEMA or NVP which does not undergo spontaneous polymerisation can first be prepared. This may be possible using an alkylaluminium halide e.g.

ethylaluminium dichloride as the complexing agent.

2) More extensive studies should be made of the observation that the presence of methacrylic acid as a co-or ter-monomer in hydrogels produces unexpectedly low water contents. Comparisons should be made with similar hydrogels containing acrylic acid.

The properties of hydrogels containing methacrylic acid should be studied in relation to their possible use in other fields. For example, properties such as blood compatibility (general biomedical use) and salt retention (membrane separation processes) should be investigated.

3) Techniques such as NMR and DSC should be employed to study the states of water in hydrogels in order that a correlation with and a better understanding of the permeability of hydrogels to solutes such as oxygen and more especially sodium chloride may be obtained.

4) Clinical studies should be carried out to establish the range of "dissolved" oxygen permeabilities necessary to meet the varying requirements of individaul patients during continuous wear.

5) Preliminary clinical studies have indicated that HPA-ACM (66:33) provides a reasonable basis for meeting the problems of visual stability together with the oxygen consumption requirements of the cornea over successive day and night cycles. Further investigations are thus warranted into the suitability of this hydrogel and variations on it for continuous wear lenses.

6) Clinical studies on mucous deposition on hydrogel lenses should be carried out to enable correlations to be made of the degree of mucous build up with the hydrophilicity of the hydrogel surface as determined by the Hamilton contact angle technique. In addition the effectiveness of acrylates and methacrylates with fluoroaliphatic side chains in reducing the surface hydrophilicity of hydrogels should be investigated.

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