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SYNTHETIC POLYMERS FOR OPHTHALMIC APPLICATIONS

MARIKO KISHI

**A Thesis Submitted for the Degree of
Doctor of Philosophy**

The University of Aston in Birmingham

October 1987

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SUMMARY

The contact lens represents a well-established important class of biomaterials. This thesis brings together the literature, mostly Japanese and American patents, concerned with an important group of polymers, "rigid gas permeable contact lens materials". A comparison is made, of similarities in the underlying chemical themes, centring on the use of variants of highly branched siloxy compounds with polymerizable methacrylate groups. There is a need for standard techniques to assess laboratory behaviour in relation to *in vitro* performance. A major part of the present work is dedicated to the establishment of such standardised techniques.

It is apparent that property design requirements in this field (i.e. oxygen permeability, surface and mechanical properties) are to some extent conflicting. In principle, the structural approaches used to obtain high oxygen permeability lead to surface properties that are less than ideal in terms of compatibility with tears. PMMA is known to have uniquely good (but not perfect) surface properties in this respect, it has been used as a starting point in attempting to design new materials that possess a more acceptable compromise of transport and surface properties for ocular use.

Initial examination of the oxygen permeabilities of relatively simple alkyl methacrylates, show that butyl methacrylate which has a permeability some fifty times greater than PMMA, represents an interesting and hitherto unexplored group of materials for ophthalmic applications. Consideration was similarly given to surface modification techniques that would produce materials having the ability to sustain coherent tear film in the eye without markedly impairing oxygen transport properties. Particular attention is paid to the use of oxygen plasma techniques in this respect.

In conclusion, similar design considerations were applied to an extended wear hydrogel lens material in an attempt to overcome mechanical stability deficiencies which manifest themselves '*in vivo*' but not '*in vitro*'. A relatively simple structure modification, involving steric shielding of the amide substituent group, proved to be an effective solution to the problem.

Keywords: Contact Lens Materials
Oxygen Permeability
Surface Properties
Plasma Oxidation
Mechanical Properties

This thesis is dedicated to the memory of my beloved father.

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"The ear tends to be lazy, craves the familiar, and is shocked by the unexpected. The eye, on the other hand, tends to be impatient, craves the novel and is bored by repetition".

W.H. Arden, 1962.

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LIST OF ABBREVIATIONS

Material

- PMMA - Polymethyl methacrylate
- pHEMA - Poly(2-hydroxyethyl methacrylate)
- CAB - Cellulose-acetate-butyrate
- TPX - Poly(4-methylpent-1-ene)
- EGD - Ethylene glycol dimethacrylate
- AZBN - α azoisobutyronitrile
- PIBMA - Polyisobutyl methacrylate
- P— - Poly + monomer shown in Table 3.1 indicates polymer version of it.

PARAMETERS

O_2	-	Oxygen
Dk	-	Oxygen permeability (D-diffusion coefficient k or s - solubility coefficient)
ρ	-	Density
SG	-	Specific gravity
P_g	-	Gas/gas oxygen permeability
P_d	-	Dissolved oxygen permeability
θ	-	Contact angle
T_g	-	Glass transition temperature
γ	-	Surface Free Energy
γ^d	-	Dispersive component of surface free energy
γ^p	-	Polar component of surface free energy
γ^T	-	Total surface free energy
E(or Y)	-	Young's modulus
G	-	Rigidity modulus

CHAPTER I
INTRODUCTION

It has been recognised that contact lenses are a far from trivial biomedical use of polymers, requiring fairly sophisticated consideration such as found in many similar applications of polymers. The properties of the lens material that most markedly affect the performance of a contact lens are listed below together with the relevant aspect of eye or lens behaviour that governs its magnitude. Various aspects of the relationship of polymer properties of this type to contact lens performance have been discussed (1-4).

<i>Material Property</i>	<i>Eye-lens Function</i>
Oxygen Permeability	Corneal Respiration
Mechanical Stiffness	Visual Stability & Comfort
Surface Properties	Tear Film Integrity & Deposit Formation

The last two decades have seen an abundance of contact lens materials designed to supercede polymethyl methacrylate (PMMA), the first rigid plastic material to be widely and successfully used in this application. The work presented here describes contact lens materials and their environment from underlying material science principles. The approach is separated into two parts; the first is concerned with background information concerning the contact lens environment and the development that took place in seeking alternatives to PMMA; the second part traces the ways in which these alternatives have progressed by means of an overview of published literature with emphasis on rigid gas permeable materials.

The historical development of materials used in contact lens application is well documented. A brief review of some materials of particular interest are mentioned

in the first section of this chapter. The environment in which these materials are used has been studied in ophthalmic medicine. Relevant information is reviewed to assess the most important requirements for successful performance of these devices in the eye. This is related to the cornea, tear fluid and the eye-lid.

It is apparent from the literature that there is a lack of general appreciation with regard to the relationship of the environmental constraints of the eye itself, and the physical property limitations of the contact lens material. This is particularly true of patent literature published by lens manufacturers. Therefore it was necessary to initiate this study, examining in detail the patent literature with particular emphasis on gas permeable lens materials, to gain an understanding of how these commercial products are developed, and what kind of measures were taken to meet the constraints of the ocular environment. The ultimate aim was to design and develop improved materials, based perhaps upon the concepts from the patent publications, but using the cornea and its environment as a model.

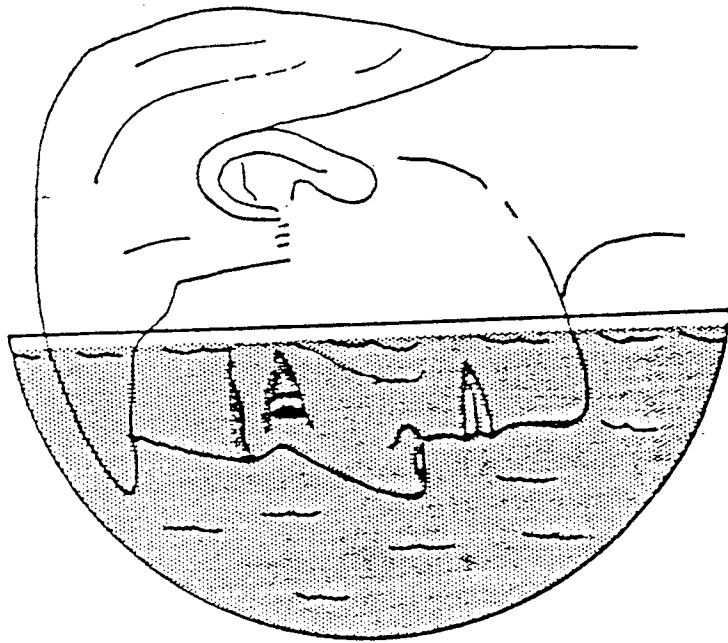
A relatively recent trend in contact lens materials is, what may be termed "Super-Gas-Permeable" materials, where the oxygen permeabilities are claimed to be 10 or more times higher than previously available hard lens materials. The greatest amount of clinical interest in the materials is related to the minimum oxygen requirements of the cornea, which clinical opinion has progressively updated in recent years. With this in mind, many contact lens manufacturers have concentrated upon developing materials with very much higher oxygen permeability than those available previously. This is often fraught with problems as other material properties such as mechanical and surface properties are sacrificed. With hydrogel materials for example, where the degree of gas permeability is closely related to the equilibrium water content, a high water content will result in a fragile material of poor dimensional stability. With hard gas permeable materials the attainment of higher permeability usually entails some compromise in surface properties. It is with this problem that this thesis is concerned, the main thrust of the work being related to rigid gas permeable materials.

1.2. DEVELOPMENT OF CONTACT LENS MATERIALS

The earliest known reference at around 1508 by Leonardo da Vinci consisted of the construction of a large transparent globe intended to model the human eye. This globe being filled with water into which the observer immersed his face, resulted in the 'optical neutralization' of the observer's corneas. The schematic sketch of this idea is shown in Figure 1.1. But it was not until into the 19th Century that contact lenses were prescribed in the form of glass, made using the individual turning technique up until the 1940s. However because of its weight, brittleness and difficulties in processing and design, plastic lenses made of polymethyl methacrylate (PMMA) were used as an alternative. PMMA is a thermoplastic combining excellent optical clarity with acceptable surface properties, toughness, lightweight and physiological inactivity. Its main drawback is its virtual impermeability to oxygen.

1.2.(1). Hydrogels

In 1960 a new class of polymer, hydrogels were introduced by the pioneering work of Wichterle and Lim⁽⁵⁾ in Czechoslovakia, as general purpose surgical materials. The first to be introduced was a covalently crosslinked hydrophilic material, poly (2-hydroxyethyl methacrylate), commonly abbreviated to pHEMA. As a result, alternatives to PMMA as a hard lens material were enthusiastically sought in the 1970s. The presence of water in hydrogels results in a soft three dimensional elastic gel provides biocompatibility, gives comfort and acts as a transport medium for gases in the respiratory process at the corneal surface. Unfortunately, the prolonged wear periods that the hydrogels permitted, highlighted the problems of surface spoilage, manifested as deposition of proteinaceous and other tear fluid debris. Also the water in hydrogels reduces the mechanical stiffness of the material, acting as an internal plasticizer and this leads to a weak and fragile material susceptible to mechanical damage during handling. As a result of these facts, the hydrogels require more complicated cleaning and lens care procedures than do hard lenses.



A hollow glass semispheroid filled with water. One type of contact lens described by da Vinci

Figure 1.1 L da Vinci Globe

1.2.(2). Rigid Thermoplastic Materials

Despite the development of soft hydrogels, research into hard contact lens materials continued, owing to their higher level of visual acuity and mechanical stability on blinking. Amongst many alternative plastic materials that were found in the patent literature were polyethylene, polyvinyl chloride and other halogenated vinyl polymers, polystyrene, cellulose-acetate-butyrate, poly (4-methyl pent-1-ene) and polyamides. Of these various types of hard plastic materials, two were particularly interesting alternatives to PMMA. Cellulose-acetate-butyrate (CAB) offers substantial advantages over PMMA in terms of increased oxygen permeability and over other plastic materials, in providing a range of properties owing to the availability of numerous grades with varying ratios of acetate : butyrate. However, CAB has a rather low elastic modulus causing the material to warp during fabrication and handling stages. It can absorb water which results in poor dimensional stability and discolouration.

Kamather ⁽⁶⁾ introduced poly (4-methylpent-1-ene) (commercially known as TPX) as an alternative contact lens material based on its excellent oxygen permeability (200 times better than PMMA). The major disadvantage of this polymer is its hydrophobic surface which prevents the formation of a continuous layer of tear fluid over the lens. Therefore, contact lenses produced from poly (4-methyl pent-1-ene) require surface treatment to improve its wettability.

1.2.(3). Silicone Elastomer

The silicone elastomer poly (dimethyl siloxane) has extensive medical applications as implant materials and in biomedical machinery. It is highly permeable to oxygen owing to the flexibility of the silicon-oxygen bonds and high solubility of oxygen in the polymer network. A silicone rubber contact lens can maintain the normal respiratory process on the surface of the cornea without the need for tear exchange under the lens. Unfortunately, like many elastomeric materials, silicone rubber is a very hydrophobic material and necessitates surface treatment to render its surface hydrophilic.

However, the effect of surface coating is often temporary and can reduce the oxygen permeability of the bulk. Materials of this type also adsorb lipophilic substances resulting in the accumulation of lipid-like substances on the lens which can have deleterious effects on the physical properties of the lens and the health of the cornea. Additionally, there are problems in the machining of these lenses due to their rubbery nature.

1.2.(4). Polymethacrylates with Organo-silicon Side Groups

A highly successful way of achieving the high oxygen permeability associated with silicone rubber, has been attained by the use of a methacrylate backbone which has organo-silicone side chains. Many such copolymers have been prepared by free radical polymerization; the patent disclosures of Gaylord and Ellis will be dealt with as developments in rigid gas permeable materials in the next chapter.

However, even these materials have limitations as to how much can be copolymerized with other monomers such as methyl methacrylate to give strength and wettability before compatibility problems occur leading to opaque, translucent materials due to phase separation. Additionally the monomers are expensive and difficult to purify by distillation due to their high molecular weight.

1.3. ADVANTAGES AND DISADVANTAGES OF COMMON CONTACT LENS MATERIALS

At this point, it is appropriate to mention why polymethyl methacrylate (PMMA) has long been established as a hard contact lens material. Without doubt, it is related to the unique surface wettability of PMMA in having a similar critical surface tension to the cornea (PMMA, 39 dynes/cm and the cornea, 35 dynes/cm). It is a physiological requirement for the tear fluid to wet the cornea as well as the contact lens above it. PMMA being of low oxygen permeability prevents the diffusion of oxygen through the tear fluid to the cornea. This may be compensated to a limited degree by

rocking of the contact lens (induced by blinking) which pumps fresh tear fluid to the cornea underneath the lens. The contact lens must therefore be rigid to withstand the force of blinking. Unfortunately, such lenses are often uncomfortable and may cause long term erosion of the corneal surface leading to desensitisation. Soft hydrogels have excellent biocompatibility making them comfortable for the wearer. However, in certain corneal disorders such as Keratoconus where the cornea takes the form of a coned pyramid shape rather than a smooth spherical form, a hard rigid material is more suitable.

1.4. THE ENVIRONMENT

In designing of laboratory techniques to evaluate the suitability of a given contact lens material, it is necessary to know the relevant material property requirements. Kamath (7) was the earliest, and almost the only worker to attempt to design materials properties on the basis of the corneal model. A more satisfactory and complete approach involves consideration of the cornea (for oxygen permeability), tears (surface properties) and eyelid (for mechanical stability).

1.4.(1). Cornea and Oxygen Permeability

The cornea is a clear transparent tissue with a smooth and brilliant surface, and is composed of five layers:

- Epithelium
- Bowman's membrane
- Stroma
- Descemet's membrane
- Endothelium.

The sectional view of the cornea is sketched in Figure 1.2. A detailed discussion of the cornea and its structure is beyond the scope of this thesis. The corneal epithelium is exposed to a partial oxygen pressure of 155 mmHg from the atmosphere in an open eye, and 55 mmHg at the palpebral conjunctiva in a closed eye. The quantitative oxygen

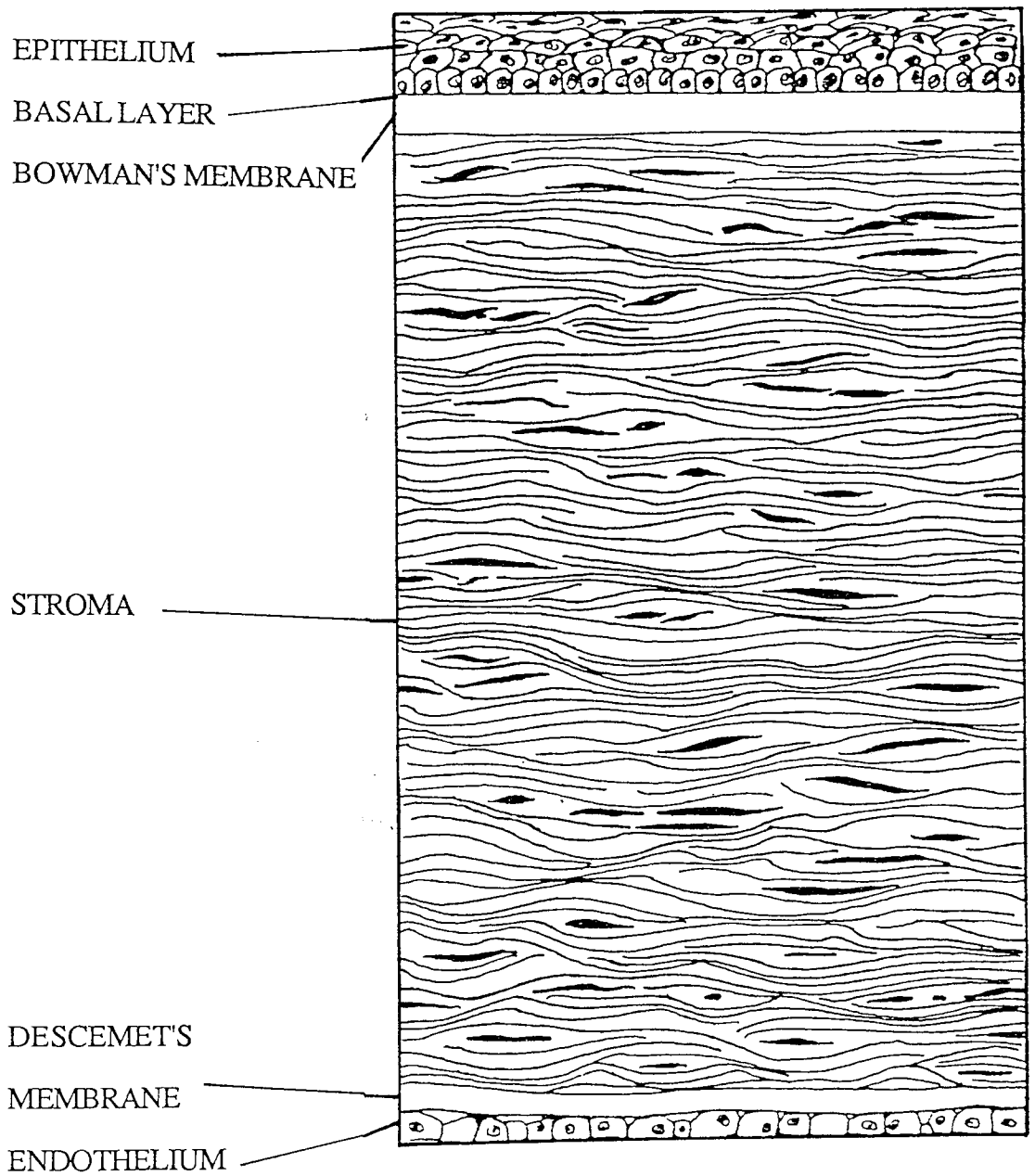


Figure 1.2 Sectional View of the Cornea

requirement for the critical level of atmospheric oxygen to maintain normal corneal thickness is much debated and argued about. Polse and Mandell's experiment in 1970 showed the minimum oxygen tension to be 11 to 19 mmHg⁽⁸⁾. In 1980, Mandell and Farrel revised this to 23 - 37 mmHg⁽⁹⁾. However this was updated in 1984 by two groups of workers. O'Neal, Polse and Sarver estimated the minimum oxygen requirement of 40 mmHg under a contact lens⁽¹⁰⁾. They report these differences to be due to increased metabolic activity accompanying prolonged contact lens wear (the earlier experiments used goggles to induce hypoxia). Australian workers headed by Holden⁽¹¹⁾ indicated that previous experiments had shortcomings in terms of short exposure times to contact lens wear and the range of oxygen concentration studied. Holden suggests that a mean oxygen tension of 74 mmHg is necessary to prevent corneal swelling, but significant differences are observed between individuals.

For daily wear purposes it is accepted that a PMMA lens fitted correctly is just adequate to supply oxygen to the cornea by the pumping action. However with tight eyelids or little tear flow, or for overnight wear when there is no eyelid movement to rock the PMMA lens to pump oxygen, there is a pressing need for alternative materials. With insufficient oxygen supply to the cornea, there is a decrease in epithelial glycogen content and an increase in epithelial thickness leading to symptoms of oedema. The clinical evidence suggests that an oxygen permeability value of 7-10 cc(STP)cm cm⁻² sec⁻¹ mmHg⁻¹ at room temperature is quite adequate for daily wear purposes.

Fatt et al⁽¹²⁾ found that even an impermeable contact lens did not raise the carbon dioxide tension in the cornea above that of a closed eye. They reasoned this owing to the transmissibility for carbon dioxide of the cornea being twenty-fold greater than oxygen, and carbon dioxide transmissibility of most polymers being five-fold greater than oxygen.

1.4.(2) Surface Properties - Tears

The precorneal tear film has been described⁽¹³⁾ as consisting of three layers; a very thin superficial lipid layer, a thicker aqueous layer and a thin mucoid layer

Table 1.1

CORNEAL OXYGEN TENSION REQUIREMENT (Literature Values)

1970	POLSE & MANDELL	11 - 19 mmHg (minimum)
1980	MANDELL & FARREL	23 - 37 mmHg (minimum)
1984	O'NEAL, POLSE & SARVER	40 mmHg (minimum)
1984	HOLDEN ET AL	74 mmHg (mean)

covering the corneal epithelium. A continuous tear film covers the epithelium giving a good optical surface of the cornea. The wetting of the corneal epithelium by the tear fluid in the eye was explained^(14, 15) by the adsorption of mucin contained in the tear film to facilitate spreading of tears by the eyelids over the relatively hydrophobic corneal surface.

The wetting of a contact lens is important, because the adherence of the precorneal 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 eye. This thin layer of tear-fluid on the surface of the contact lenses:

- a) lubricates the inner surface of the eyelid with the lens,
- b) mechanically supports the lens which "floats" on the precorneal fluid, and
- c) prevents the accumulation of oily and sebaceous matter on the lens thus maintaining optical clarity and optimum surface conditions for the fluid flow.

The most convenient way of assessing surface wettability is by contact angle measurement. The contact angle (θ) is the angle between the solid surface and the tangent drawn to the profile of the droplet where it meets the solid surface taken through the liquid. An indication of the ability of a liquid to form a continuous film over a solid surface depends on the surface free energies of the liquid and the solid. In practice, contact lens work has always been limited to studies with aqueous systems rather than the wide range of liquids needed for complete surface energy characteristics; this topic is dealt with in Chapter 4. Clinically, a water contact angle of 60-65° (preferably less) is taken to be the minimum value for a contact lens to hold a coherent film of tear-fluid at the surface (PMMA has a contact angle of 62 - 63° with water).

Unfortunately, most contact lenses suffer from surface spoilage problems after a period of wear and in some cases the lenses become so badly spoiled that the patients can no longer tolerate them. Although the spoilage mechanism and the

detailed study concerning the surface deposition problem on worn contact lenses is outside the scope of this work, it is nevertheless important to realise possible problems that may arise relating to the spoilation affinity of a given contact lens surface.

1.4.(3) Mechanical Stability - Eyelid

Although the varying pressures exerted by the eyelids may cause minute changes in corneal curvature, an acute change in the shape of the cornea does not normally occur to any measurable extent. Similarly, the deformation caused by blinking of rigid contact lens materials in the eye is comparatively small. On the other hand, soft flexible hydrogels may buckle by the action of the eyelid; the fragile nature of hydrogels are usually compensated for by adjusting cross-linking density. The relevance of mechanical stability of these materials lies therefore, more in the fabrication stage and material durability during handling rather than the deformational changes in the eye.

Some aspects of fabrication that must be taken into consideration are machinability, ease of polishing, scratch resistance during handling and toughness to withstand frequent cleaning. In this respect, the assessment of mechanical properties is difficult to define for the contact lens application; there are obviously problems in adapting small contact lens specimens to standard polymer mechanical tests, making direct comparison by measurements difficult between polymer samples in lens form. However, attempts have been made to correlate the response of polymers encountered in a selection of contact lens materials in tensile and compression modes by careful control of the technique and handling of results.

1.5. METHODS OF MANUFACTURE

There are two main methods of manufacture in the production of rigid gas permeable contact lenses.

a) Lathe-Cutting

The polymer is produced by bulk polymerization of a monomer or a

monomer mixture, a crosslinking agent and a free radical initiator, to give rods or buttons. The blanks from the rods or buttons are then lathe-cut, polished and edged. The lathe-cut materials are crosslinked and are therefore mechanically strong. However, the disadvantage is the higher cost of production which is labour intensive. Often, lathe-cut materials have chemical features that prevent them from being moulded (e.g. crosslinking).

b) Compression Moulding

Finished moulded or semi-finished moulded lenses can also be made. The polymer is produced in sheet form, then heated and pressurised to be moulded into desired shapes. The semi-finished lens is then edged to the final product. The advantages offered are the cheaper cost provided the time and temperature of moulding can be kept down. However, the essential factor for the mouldable material is to have a linear uncrosslinked structure. It can subsequently be crosslinked in the mould for the necessary physical stability. A moulded material of sufficient rigidity may easily be made in the lathe-cut form.

c) Other methods

Most of the conventional forming techniques used in the plastics/rubber industries can also be applied to manufacture some types of contact lenses; they include injection moulding and transfer moulding. For the production of covalently crosslinked hydrogels, lathe-cutting from xerogel and spin-casting, in which a liquid monomer mixture in a lens mould is spun to complete polymerisation, have been employed. The finished hydrogel in its dehydrated state (xerogel) is then stored in sterile saline conditions and autoclaved, to produce a soft gel-like material.

Because of high precision techniques involved in the manufacture of such small articles, and the nature of polymerization (ie random copolymerization), reproducibility of contact lenses have often been unsatisfactory resulting in batch to batch variations.

1.6. SCOPE AND OBJECTIVES OF PRESENT WORK

The previous sections have described briefly the background information available to the material scientist whose task is to design and develop novel synthetic materials in ophthalmic application. To 'tailor-make' a polymer which can be used as a contact lens material, bearing in mind the environmental constraints of the cornea and its metabolism, necessitates first the understanding of chemical structures and physical properties of these polymers. It is believed that copolymerization of suitable comonomers would provide a balance of the properties of the corresponding homopolymers.

Rigid gas permeable materials present a wide scope for the design of suitable synthetic products in that the first hard contact lens material PMMA provided well established basic required properties. Hydrogels although more comfortable to the patient have by virtue of their chemical make-up more problems in mechanical stability and surface spoilation. Recent increased competition to provide an 'ideal' contact lens material of 'super oxygen permeability' is centred around rigid gas permeable contact lens materials. Furthermore, much information has been collated from empirical experimental work conducted at these laboratories.

In designing alternative materials to PMMA and hydrogels, it is important to understand and rationalise developments through published literature. To this end, much useful constructive information has been collated by examining the patent literature related to rigid contact lens materials. However, although a broad understanding exists for the environment i.e. cornea, tear and eyelid, there is very little published work which links these requirements with the ultimate material performance of a given contact lens material. This, unfortunately, is particularly apparent in the patent literature. By careful scrutiny of the patent literature, it is possible to rationalise potential alternatives to PMMA.

Synthetic work on copolymerization is designed based on the information from this literature. Polymers with suitable physical properties will be evaluated and correlated with their chemical structure. Only those physical properties deemed to be

relevant in contact lens applications are studied.

However, it is apparent that the testing techniques and methods employed in manufacturer's laboratories are not necessarily of the same standard in terms of testing conditions and procedures. It is therefore necessary to select appropriate testing standards relevant to contact lens applications. This work constitutes a substantial proportion of this thesis. The attempt is made then, to compare the novel synthetic materials with commercial materials under controlled experimental conditions.

CHAPTER II
DEVELOPMENT OF GAS PERMEABLE MATERIALS
AN OVERVIEW OF THE PATENT LITERATURE

2.1. LITERATURE REVIEW

As indicated in Chapter 1, amongst the earliest non-hydrogel polymers that offered any competition to PMMA was silicone rubber. This material, which is substantially poly (dimethylsiloxane) (I) has the highest oxygen permeability of any commercially available polymer (being around 1000 times more permeable to oxygen than PMMA). It is furthermore softer and flexible, and in this respect resembles hydrogels, but unlike hydrogels is exceptionally hydrophobic. Silicone rubber is such an important precursor to many of the current rigid gas permeable materials that the appropriate technology as disclosed in the patent literature must be taken as a basis for later developments.

The earliest silicone rubber patents were concerned with methods of lens manufacture, particularly the use of compression moulding techniques together with questions of mould design, that were able to produce finished lenses with high quality edges⁽¹⁶⁾. Similarly, attention was paid to methods for improvement of the mechanical strengths of poly (dimethylsiloxane) - based compositions. Many of these patents resulted from the work of Polmanteer and Mishler at the Dow Corning Corporation and were based, for example, on the use of endcapped siloxane copolymers containing phenyl groups and blended with a reinforcing silica filler. The use of methyl vinyl siloxane units in the end blocked copolymer provided a degree of functionality that was subsequently utilised in a vulcanization or crosslinking reaction⁽¹⁷⁻¹⁹⁾. This theme was developed by Travnicek (Warner-Lambert Co., and subsequently American Optical Corporation)⁽²⁰⁾, who claimed that a more judicious control of the phenyl to methyl group ratio enabled copolymers to be synthesized whose refractive index was similar to that of the silica filler. As a result, levels of silica loading up to 20% are claimed to produce optically transparent products in contrast to levels of 3~7% in the Dow Corning patents.

The major stumbling-block to the successful use of silicone rubber based lenses has, however, been inadequate wetting properties rather than lack of toughness or durability. This is reflected in a large number of patent specifications that describe the

methods of producing hydrophilic silicone rubber surfaces. The difficulty in obtaining clinically acceptable and permanent hydrophilic surfaces, however, is reflected in the relative lack of success of silicone rubber as a contact lens material. The earliest methods of surface treatment described involved direct chemical attack by alkyl titanate or chlorosulphonic acid followed by hydrolysis (21-23). More sophisticated treatments involving a range of both ionizing and non-ionizing forms of radiation soon followed. A line of development is discernible beginning with the work of Lauzier and Wajs(24). The claims of this invention encompassed the use of ionizing radiation in conjunction with N-vinyl pyrrolidone, allyl alcohol or 2-hydroxyethyl methacrylate (HEMA), in achieving a hydrophilically grafted substrate. A subsequent filing by Merrill used similar hydrophilic monomers with the additional disclosure of the use of glycerol methacrylate(25) in conjunction with much lower levels of radiation. A further modification resulting from work at Essilor International (Compagnie Generale d'Optique) referred to the specific grafting of N-vinyl pyrrolidone onto more complex silicone copolymers(26).

The earliest reference in the patent literature to the use of ultra violet radiation in the production of hydrophilically grafted silicone rubber surfaces seems to be that of the Czechoslovak workers Lim, Kopecek et al, who were active in extending the applications of 2-hydroxyethyl methacrylate and related hydrophilic monomers(27). The technique is also described in a patent assigned to Essilor International, in which Wajs extended his earlier disclosures on N-vinyl pyrrolidone-silicone rubber grafts(24) to similar systems in which non-ionizing U.V. radiation was used to achieve the grafting process (28). A further more complex chemical procedure which claimed to produce a very similar end product was developed at the same time by Toyo Contact Lens Company (Tanaka)(29). This utilized a two stage treatment involving initial immersion of silicone rubber contact lenses in ammonia solution, followed by subsequent immersion in a mixture containing, for example, ethanol, vinyl triethoxysilane and 2-hydroxyethyl methacrylate in the presence of azobisisobutyronitrile (AZBN). Although, the methods differ in detail and complexity they are all essentially free radical

grafting reactions.

One of the most effective methods of generating free radicals is the use of gas plasma or glow discharge techniques. These operate with an electrode system excited by a radio frequency generator (typically 13.5 MHz at a power of 100 watts) around or within a glass chamber containing, for example oxygen at a pressure of 0.1 torr. This type of system has been described in conjunction with unsaturated compounds (e.g. acrylic acid) by Feneberg and Krekeler⁽³⁰⁾, or with water-vapour and saturated acids (e.g. acetic acid and formic acid) by Gesser and Warriner⁽³¹⁾.

It is apparent, therefore, that the extremely high oxygen permeability of silicone rubber is exceptionally difficult to harness in the form of a clinically acceptable contact lens because of the hydrophobic nature of the polymer and the great difficulty experienced in generating a hydrophilic surface on the material with any degree of permanence. A series of patents describe attempts to overcome this latter difficulty with some compromise in oxygen permeability by utilising other flexible polymers that are more readily and permanently surface treated. The first group of these are the carbon-based elastomers such as ethylene-propylene-terpolymer, cis-polyisoprene, styrene-butadiene copolymers, cis-polybutadiene, polyurethane elastomers, and natural rubber. A very broad and early patent filed by the Dow Corning Corporation seeks coverage for the use of these materials in contact lenses⁽³²⁾. A later patent based on work at Aston University in these laboratories describes the way in which solid functional monomers such as acrylamide may be used to produce elastomers with hydrophilic surfaces by incorporation in a preliminary processing operation such as milling⁽³³⁾. In both patents, the technique subsequently used for final lens production is compression moulding.

Some flexible thermoplastic materials have been suggested as being suitable for contact lens manufacture in the patent literature, but none of these have achieved clinical significance. One interesting proposal involves the heating and subsequent quenching of polyethylene to reduce crystallinity and thereby increase optical clarity⁽³⁴⁾. Another describes the use of thermoplastics in general and polyvinyl

chloride in particular to produce lenses of complex laminated design with a flexible central portion (35). A material with much greater apparent potential than other thermoplastics for contact lens use is poly (4-methylpent-1-ene) more commonly known under the tradename TPX. (36, 37). Although less flexible than polyethylene it is appreciably more oxygen permeable (having an oxygen permeability some 200 times greater than PMMA). In addition it is optically clear even at high degrees of crystallinity, and is readily surface treated to an adequate degree of hydrophilicity for contact lens use (37). One major disadvantage of all the conventional olefin-based thermoplastics however, is the fact that they are insufficiently rigid at the temperatures generated in conventional lens lathe-cutting techniques to enable lenses free of distortion to be produced by this, the most widely used of processing methods for non-hydrogel lenses.

A major advance in the development of gas permeable rigid contact lens materials that are susceptible to the conventional lathing and lens polishing processes, is found in the work of Gaylord. There are two distinct aspects of this work. The first encompasses the use of siloxanyl derivatives of methacrylate monomers (e.g. tris-trimethylsiloxy, γ -methacryloxypropylsilane (II))⁽³⁸⁾ and the second the use of fluoroalkyl methacrylates (e.g. 1, 1, 9-trihydroperfluorononyl methacrylate (III))⁽³⁹⁾. Both these lines of work have been subsequently developed and formed the basis of several existing commercial gas permeable contact lens materials.

In the event, the Gaylord patent describing the copolymerization of series of fluoroalkyl acrylates and methacrylates with methyl methacrylate is not unique. It was pre-dated by three quite significant patents describing the use of chemically similar materials in contact lens applications. The first of these was filed in 1967 and assigned to Du Pont by Girard, Sampson and Soper ⁽⁴⁰⁾. In particular, it describes the advantages of contact lenses prepared from polymers derived from perfluoroalkylethyl methacrylates (IV) in terms of its relatively low refractive index (1.39) in comparison to the value of 1.49 for methyl methacrylate. In a subsequent patent, also assigned to Du Pont by A.E. Barkdoll⁽⁴¹⁾, a wider range of polymers based primarily on various perfluoro(methyl vinyl ether)-tetrafluoroethylene copolymers are described together

with means of rendering them hydrophilic. The main thrust of the patent is the production of soft flexible materials processable by compression moulding, but significantly, attention is drawn to the fact that the lenses thus produced are appreciably more oxygen permeable than PMMA. At the same time, a third Du Pont patent filed in the name of C.S. Cleaver⁽⁴²⁾ draws together some of the features of the Barkdoll and the Girard patents. Thus Cleaver describes copolymers of fluoroalkyl methacrylates with methyl methacrylate, the production of lens blanks which were then machined and polished to prescription lenses and the advantageously high oxygen permeability of the resultant lenses. These lenses were not only described in patent literature, but were used with apparently favourable results in a preliminary clinical trial.

Although Cleaver's concept of the fluorine-containing contact lens was first filed in mid-1971 (a full year before the date of filing of Gaylord patent) over a decade elapsed before significant commercial use was made of fluorocarbon based contact lenses. The reason appears to be fairly straightforward and to reflect the immediate advantage in oxygen permeability of the siloxanyl methacrylates over the relatively simple fluorinated methacrylate esters described by Gaylord or the Du Pont workers. This is illustrated in their permeabilities, quoted by Gaylord in his two patents. Whereas the oxygen permeabilities claimed for materials described in the fluoroalkyl methacrylate patent are some three to four times greater than that of PMMA, typical examples described in the siloxy methacrylate patent are claimed to have permeabilities 15 to 20 times greater than PMMA. There is internal evidence in these Gaylord's patents that the base line value of PMMA taken may be some three times too high. If this is the case, as seems likely, some revision of the permeabilities claimed is necessary. Thus, the fluorinated materials would become some ten times more permeable than PMMA, whereas the siloxanyl copolymers would be around 50 or so times more permeable than PMMA.

On the other hand, it has to be said that the permeabilities quoted by Du Pont workers, reflected in values claimed by Cleaver are probably unduly optimistic. In this patent, compositions broadly similar to those described by Gaylord is claimed to

produce materials some 200 times more oxygen permeable than PMMA! The long delay in commercial use of fluorine-based gas permeable materials is a consequence of the fact that more complicated structures than those described in any of these early patents are required to achieve oxygen permeabilities as commercially attractive as this. On the other hand, the relative simplicity and effectiveness of the siloxanyl methacrylate concept resulted in direct commercial utilization of this group of materials.

It was, however, some three or four years after the publication of Gaylord's first patents before the so-called siloxy-methacrylate gas permeable contact lens materials began to achieve significant market penetration in the contact lens world. This time period corresponds, coincidentally, to the appearance of the third Gaylord patent⁽⁴³⁾ in late 1978, which is a continuation-in-part, following a series of interim abandonments of various of the original siloxanyl-methacrylate patent. Its claims are somewhat more restricted than those of the original; its scope is limited to a method for correcting visual defects. In addition, the maximum percentage of siloxy-methacrylate in the compositions described has been reduced from 70% to 60%. A new assignee also appears on this patent, this being Syntex (U.S.A.) Inc. who in the next few years gained control of the major proportion of key patents in this area.

Within a twelve month period in 1978 and early 1979, at about the time of appearance of Gaylord's third patent, three workers began to file their separate series of patents related to siloxymethacrylate-based contact lens materials. These were, in advancing order of the priority date for the first written filing, Kyoichi Tanaka (Toyo Contact Lens Co. Ltd.), Edward Ellis (Polymer Technology Corporation), and Nick Novicky whose later patents (and presumably rights to the earlier) were assigned to Syntex (U.S.A.) Inc. The Ellis and Novicky patents form a clear line of continuation from early Gaylord's work, and because of this, are best considered together. Tanaka's work, for which parallel filings exist in Japan and the United States, has some slight and significant differences and are conveniently considered separately.

Early in 1978, two patents were filed in the names of Edward Ellis and

Joseph Salamone that used Gaylord's basic concept with slight but significant modification. The first of these (filed 8th January) ⁽⁴⁴⁾ described the electrostatic binding of a polyelectrolyte complex coating to the surface of an otherwise hydrophobic contact lens in order to render the material hydrophilic. This highlights a very real problem associated with the incorporation of substantial proportions of hydrophobic organosilicone monomers into materials for contact lens use. Indeed, the examples in the patent, are significantly based on the siloxymethacrylate copolymers and exemplify the incorporation of a small amount of methacrylic acid or dimethylaminoethyl methacrylate to induce a surface negative charge. The second patent ⁽⁴⁵⁾ again uses Gaylord's basic composition based on (II) modified with methacrylic acid (a hydrophilic monomer referred to but not exemplified by Gaylord), and by the incorporation of an itaconate ester (e.g. dimethyl itaconate (V)). A subsequent Ellis patent ⁽⁴⁶⁾, describes the advantages of radiation cure of these materials.

Novicky's first patent ⁽⁴⁷⁾ describes the shortcomings of the prior art contact lenses based on siloxy monomers in terms of their inadequate mechanical properties, inadequate resistance to ocular spoilation, and modest oxygen permeability. The advantages that he claims for his disclosure fall into two areas. The first is an improved synthesis of the siloxane intermediates and the second the use to which such an intermediate may be put in the preparation of more highly branched siloxanyl-methacrylates than are described in Gaylord's original patent. Examples of these structures illustrated below are (mono (tris-trimethylsiloxy-siloxanyl) bis-(pentamethyl disiloxanyl) methacryloxypropylsilane (VI) and bis (tris-trimethylsiloxy-siloxanyl) pentamethyl disiloxanyl methacryloxypropylsilane (VII)). A further feature of the patent is the importance attributed to the use of methacrylic acid and N-vinyl pyrrolidone (rather than 2-hydroxyethyl methacrylate) and cyclohexyl methacrylate as comonomers. Although, the use of the former compounds which are incorporated to improve hydrophilicity, is described (but not exemplified) by Gaylord, he makes no specific mention of cyclohexyl methacrylate amongst the many other alternatives to methyl methacrylate that he lists. Furthermore, Gaylord specifically refers to the

advantages associated with the use of a lower rather than higher degree of branching in the siloxanyl substituents. Novicky's second patent (48) which was filed in August 1979, some months after the appearance of the early Ellis patents continues his earlier theme in which emphasis is placed upon highly branched siloxanymethacrylates such as (VI) and (VII), together with low temperature methods for their manufacture with improved yield. In addition, however, the scope of the invention is extended to include itaconate esters in broadly similar quantities to those described by Ellis.

Two further Novicky patents were filed in rapid succession in September 1979. In chemical terms, these represent a very limited addition to previously described concepts. The first(49) of them describes a group of unsymmetrically substituted silicone monomers typified by tris(nonamethyltetrasiloxanyl) methacryloxy-propyldimethylsilane (VIII) together with a siloxanyldimethacrylate crosslinking agent decamethyl pentasiloxanyl di(methacryloxypropylmethylsilane) (IX). The combinations of monomers exemplified in the patent give oxygen permeabilities claimed to be significantly but by no means dramatically higher than those previously described. The second of these patents(50) is restricted to combinations of three more examples of branched siloxanyl methacrylate monomers (similar to (VI) and (VII)) together with a few additional and more exotic methacrylate esters such as 3-hydroxy-2-naphthyl methacrylate. Both of these patents make specific claims for the use of itaconate esters in combination with all the other components (i.e. siloxanyl methacrylate, alkyl methacrylate, crosslinking agent and hydrophilic monomer) described.

Ellis returns to the patent literature, with a lengthy patent (51) filed at the end of 1981, in which a complex array of unsaturated multifunctional and mono-functional organosilanes is described (e.g Tetra (γ -methacryloxypropyl dimethylsiloxy) silane (X)) which are suggested for use in various combinations together with an extensive range of hydrophilic and hydrophobic monomers (including cationically and anionically charged methacrylates). Many of the siloxanyl compounds described in this and other patents would present severe problems in isolation, purification and

characterisation, suggesting that the chemistry involved is speculative rather than established. Some aspects of the Ellis invention are however contained and extended in a U.K. patent application, filed some 12 months later (52). In the same period Ellis disclosed the synthesis and use of methacrylate monomers (53) containing branched siloxy substituents but differing from previous compounds, in that the siloxy chains are terminated by acetoxy groups. The silicon content of the monomers is relatively low and obviously involve some sacrifice in oxygen permeability at the expense of improved wettability.

The patents of Tanaka et al (Toyo Contact Lens Co. Ltd.), have certain similarities to the work of Gaylord and its subsequent amplification by Novicky and Ellis. Tanaka's patents were filed initially in Japan in late 1977 and then as a group on the same day (March 1978) in the United States. The central and main distinguishing feature of these patents is the use of a monomer that contains a hydroxyl group as well as the branched siloxy and methacrylate units. The synthesis of the monomer, methylbis(trimethylsiloxy)silylpropylglyceryl methacrylate (XI) and other species of similar structure is described (54), together with their copolymerization with a range of monomers of the type described by Gaylord (55, 56, 57). To the attempts to harness the high permeability of siloxy polymers during this period must be added two similar pieces of work from Dow Corning, and Bausch & Lomb. The Dow Corning patent (58) describes techniques for preparation of cured phenyl substituted polysiloxanes which have oxygen permeabilities similar to those of silicone rubber whilst being hard enough to be fabricated by conventional hard contact lens techniques. No measurement of surface properties and their effective modification is described which appears to place the materials at a disadvantage in comparison to siloxy polymers based on vinyl polymerization. A subsequent Dow Corning Patent (59) describes a technique based on treatment with alkali and trimethoxychlorosilane for surface modification of more conventional siloxymethacrylate based contact lens materials. The Bausch & Lomb patents (60, 61, 62) (Deichert et al) combines, to a degree, vinyl polymerization with the use of the polydimethylsiloxane backbone. The central feature of the patents is the use

of polysiloxanes endcapped with acrylate end groups. This is brought about typically by reaction of 1, 3-di(4-hydroxybutyl)tetramethyldisiloxane with methacryloyl chloride to form 1, 3-di(4-methacryloylbutyl)tetramethyldisiloxane (XII) followed by insertion of dimethylsiloxane groups using octamethylcyclo tetrasiloxane. One significant feature (63) which is taken up in later work, is the inclusion of polycyclic acrylates such as isobornyl acrylate. Monomers of this type had appeared several years earlier in contact lens literature, particularly associated with the work of Mortarano. Such monomers would be expected to influence both mechanical properties and permeabilities of copolymers in which they are incorporated.

Two further significant ideas emerged at the end of the 1970s both naming Mitchel Shen as a co-inventor. The first of these, assigned to Wesley-Jessen Inc., encompassed the use of alkyl substituted polystyrenes (64, 65, 66), and the second (Biocontacts Inc., (67)) described the way in which the ester interchange reactions could be employed to convert a hard lens (manufactured therefore by conventional lens techniques) to a lens with a lower glass transition temperature. In the Wesley-Jessen patents the introduction of progressively more bulky alkyl groups as in the series vinyl toluene, isopropyl styrene, and t-butyl styrene is shown to produce a progressive improvement in oxygen permeability. The patents describe several ways of improving surface wettability of the polymers including treatment with U.V. light in the presence of oxygen, treatment with chromic acid, and use of a glow discharge (oxygen plasma) technique. Although the second of the patent areas (67) envisaged the physiological compatibility associated with lower glass transition temperature as the main advantage of the materials produced, subsequent work (68) indicates that the oxygen permeabilities compare well with those of other commercial gas-permeable contact lenses. The essence of the invention involves copolymerization of butyl methacrylate and acrylic acid (or anhydride) followed by the use of direct and/or indirect esterification reactions with butanol, pentanol or propanol to form a substantially complete esterification.

In the post 1980 period, several significant features characterise the patent scene. A very marked expansion in Japanese patents coverage emerges, principally as a

result of work assigned to Hoya Lens K.K. and Toyo Contact Lens Co. Ltd., with the significant additional incursion of Syntex and Paragon Optical into the Japanese patents literature. Many of this substantial group of patents deal with concepts that have been described above in connection with the development of ideas in the U.S. patents literature. A significant number of original ideas have emerged during this period, however, which may form the basis for new and interesting contact lens materials. These include silyl acetylene polymers, pentafluorostyrenes, urethane siloxanol acrylates, and polyperfluoro-alkylene oxide copolymers. The Syntex patent filed in June 1981 ⁽⁶⁹⁾ in the name of Novicky describes contact lens materials made from a mixture of monomers typified by the structures (VI), (VII) and (VIII), and previously disclosed in three U.S. patents ⁽⁴⁷⁻⁵⁰⁾. The disclosure describes the materials as copolymers made up of at least one silicone monomer of the type (10 - 60 weight %), together with 40 - 90% by weight of an ester of either acrylic, methacrylic or itaconic acid.

The Paragon patent ⁽⁷⁰⁾, on the other hand naming Ratkowski and Pin Chan Loo as inventors describes less complex siloxy monomers that are closely related to the widely used precursor material trimethoxymethacryloxy propylsilane (XIII) (alternatively named γ -methacryloxypropyltrimethoxysilane). Typical examples of the structures described are illustrated below. These are identical with the structures described within the first claim of the Gaylord's first patents ⁽³⁸⁾. These simple derivatives have not been widely exploited since the permeabilities have been generally held to be inferior to those obtained with monomers that are more branched and contain a higher proportion of siloxy units. In view of this, it is surprising that the oxygen permeabilities of the materials described in this Japanese patent are higher than those of the Boston lens based on the Ellis patents ⁽⁴⁴⁻⁴⁶⁾ for example. One particular feature of this Paragon patent and its American counterparts ⁽⁷¹⁾ is the inclusion of some 10% of trimethylethoxysilane into the copolymer described. This has the potential to behave as a reactive plasticizer facilitating the injection moulding properties of the derived copolymers.

A small group of patents were filed between 1981 to 1984 by Toyo Contact Lens Co. Ltd.; several concepts were contained within these patents, the underlining theme being the use of silicon in polymers for contact lens use. The first of the group filed in 1981 (72) describes the production of polymers from a well-established polysiloxanyl methacrylate together with itaconic acid and its derivatives and fluoroalkyl substituted methacrylates. Although none of these components is in itself new, the patent describes a novel technique for producing hydrophilic surfaces. The procedure is based on the use of sugar esters or ethers, which may be subsequently ring opened with acids to increase the hydrophilicity of the pendant group. The technique of incorporating carbohydrate derivatives of this type is well known in polymer science and had, indeed been adapted for use in contact lenses by Masatake Murakami and his coworkers at Nagoya University who developed the so-called Bio-contact lens (73) which was based on dextran-methyl methacrylate copolymers.

Other aspects of silicone chemistry developed by Toyo in this period include siloxanyl substituted styrenes (74) (for example, para(trimethyl silyl) styrene (XIV)). Materials based on this monomer crosslinked with ethylglycol dimethacrylate were claimed to have excellent oxygen permeability, good hardness and light transmission properties, but no specific methods of controlling surface hydrophilicity are claimed. The use of fluoroalkyl groups briefly referred in an earlier patent (72), is described in great detail in a subsequent UK patent application (75). The patent describes a vast array of combinations, but most significantly the use of the novel glycerol based monomer (XI) described in an earlier Toyo patent in conjunction with conventional 'Gaylord' monomers, and methacrylates containing long ($C_3 - C_{16}$) fluoroalkyl groups.

One further and interesting idea disclosed by Toyo in this period is the use of acetylenic rather than vinyl monomers (76). Thus, a contact lens material made from a copolymer of t-butyl acetylene (XV) and 1-trimethylsilyl acetylene (XVI) is claimed to have an oxygen permeability of some 100 times greater than that of PMMA.

Although this is only of the same order as materials based on branched siloxy methacrylates, it is achieved by susceptibility to glow discharge treatment using either oxygen or inert gases or alternatively hydrophilic monomers which are grafted onto the polymer surface. One interesting feature of the Japanese patent literature is the way in which identical or very similar ideas are patented by different companies within a short period of time. Thus, the use of 1-trimethylsilyl acetylene (XVI) described by Toyo is also claimed for contact lens use in a patent filed some three months earlier by Toray industries (77). The earlier patent is in some senses more broadly based since it describes the introduction of ethyl and propyl groups onto the silicone, and the use of a range of cationic initiators. Although the initial polymerization is carried out in toluene, conventional lens fabrication procedures are described together with advantageous properties, including oxygen permeability for the lens.

Although Hoya Lens K.K. have no published patent material before 1980, the group of patents that have appeared since that time shows a systematic and well organised approach to the subject in conjunction with well formulated applications accompanied by comprehensive and well presented data. The two earliest Hoya patents appearing between mid 1980 and 1982 deal with direct alternatives to PMMA as a hard contact lens material. The first of these (78), describes the advantage of mixtures of alkyl and cycloalkyl methacrylates used in conjunction with small amounts of hydrophilic monomer and a crosslinking agent. All the methacrylates described have been mentioned in the extensive lists contained in previous patents, but this Hoya work provides a uniquely detailed account of relative advantages of specific members of this group of compounds. The effect of branching on oxygen permeability of methacrylates is highlighted and illustrated by the fact that the oxygen permeability increases along a series of methyl methacrylate, sec-butyl methacrylate, t-butyl methacrylate, in the ratio 1:30:50. The second patent (79) utilizes the high permeability of t-butyl methacrylate in conjunction with the beneficial effects accorded by the use of vinyl esters of fatty acids such as lauric and stearic. These long chain esters are claimed to increase the toughness of the polymer, and to exert a beneficial effect on oxygen permeability. There is

obviously an upper limit to the amount of, for example, lauryl ester that can be incorporated and although the patent claims incorporation of up to 70%, such levels produce a dramatic lowering of the glass transition temperature and resultant impairment of machinability. Incorporation of 30% of the lauryl ester is shown to double the oxygen permeability of poly t-butyl methacrylate, but more modest increases of around 20% are associated with the more realistic levels of incorporation. Glycerol methacrylate and 2-hydroxyethyl methacrylate, are used in a conventional manner at levels of around 1%, to improve wettability. A closely related idea involving typically copolymers of lauryl methacrylate, diethylene glycol monomethyl ether methacrylate and a crosslinking agent was subsequently patented by Toyo (80).

Sandwiched between the filing dates for the two Toyo patents (72, 75) dealing with fluoroalkyl methacrylates in conjunction with siloxy methacrylates, Hoya filed an application (81) dealing with the same topic. However, all three of these patents were predated by a Hoya application (82) dealing specifically with the properties of fluoroalkyl methacrylate themselves. Here again, the nature of the work is not novel since fluoroalkyl methacrylates are referred to in the early groups of Gaylord and related patents (39-42). As with the branched alkyl methacrylates the properties, specifically permeability of the individual homopolymers are carefully described in preparation for their use in the later mixed-monomer patents (81). It is interesting to compare the increase in relative permeability along the series of homopolymers, methyl methacrylate, trifluoroethyl methacrylate, hexafluoroisopropyl methacrylate (1:60:100); the ground is clearly seen in this patent for the development of fluorinated gas permeable materials which penetrated the market towards the mid-1980s.

The Hoya (83) work in parallel with work on alkyl and fluoroalkyl methacrylates, also investigated prior to exploitation, the effect of aromaticity in polymers. The first of two patents on this topic extended the ideas originally described in the earlier U.S. patents assigned to Wesley-Jessen (64-66). The work describes the fairly conventional use of alkyl and branched alkyl substituents in the aromatic ring in conjunction with a methyl group on the polymer backbone (for example,

α -methyl styrene). In addition, however, polar hydroxyl, nitro and amino groups are described, and more significantly, a crosslinking process based on bis-phenol-A-dimethacrylate (XVII). The specific advantage of this crosslinking agent is illustrated by the fact that when incorporated at 15 weight % level, the permeability is some six times higher than the equivalent polymer containing divinyl benzene as a crosslinker. The final Hoya patent ⁽⁸⁴⁾ illustrates the logical extension of the ideas previously disclosed, and is based upon polymers and copolymers of pentafluorostyrene. Pentafluorostyrene is shown to have an oxygen permeability of some three times greater than that of styrene itself, whilst the various combinations of pentafluorostyrene and acrylates (both fluorocarbon and hydrocarbon based) are appreciably greater than this, being some 200 times more permeable than PMMA.

Several United States patents appeared in the 1980s, many of them concerned with relatively minor variations and loopholes in the network siloxymethacrylate patents based on Gaylord's original work. Two of these are attributable to Russell A. Neefe, in whose name patent applications associated with hydrogels have also been filed. In the first ⁽⁸⁵⁾ of the two patents claiming improvement in gas permeable contact lens materials, he claims an improved method of synthesis of Gaylord's most widely used monomer (1,1,1-tris(trimethyl siloxy) methacryloxypropylsilane) (II). This is subsequently used in conjunction with other monomers including the crosslinking agent 1, 3-bis(γ -methacryloxypropyl) 1,1,3,3-tetra (trimethyl siloxy) disiloxane (XVIII) first described by Ellis ⁽⁵¹⁾ and related to Novicky's previously disclosed compound, (IX) ⁽⁴⁹⁾. A further feature of this patent is the use of N-1, 1(dimethyl-3-oxobutyl) acrylamide more commonly known as diacetone acrylamide to improve hydrophilicity of the material. In the second patent ⁽⁸⁶⁾, Neefe makes the broad claim to improved oxygen permeability by the use of specific combinations of complex siloxanyl methacrylates, itaconic esters, and 2-hydroxyethyl methacrylate as a wetting agent. All of the compounds exemplified have appeared in the patent literature, but since no physical property data are included it is impossible to know

whether these specific combinations have the advantages claimed for them.

The same general comment must be made of the work of Foley and McCarry⁽⁸⁷⁾ in which they claim that the relatively simple expedient of incorporating terminal Si-H in place of Si-CH₃ groups has a beneficial effect. In the absence of recorded data, it is impossible to know if the claim is valid. The claims of Ivani^(88, 89) on the other hand are relatively simple and specific, and well documented. The patents deal with copolymers of siloxymethacrylates and vinyl acetate, and in particular the relatively simple siloxy monomers first described by Gaylord. The presence of vinyl acetate is claimed to improve the permeability and wettability properties of the material, and the figures are quoted in support of the claim. In contrast, the relatively recent patent of Wittmann and Evans assigned to Cooper Vision and published in 1985⁽⁹⁰⁾, is relatively long and complex. Despite this, it contains no specifically new material; the claims rest upon the beneficial effect that accrue, when between five and seven monomers previously known individually are used together. The particular elements of combination are typically a siloxanyl methacrylate and a mixture of bulky methacrylate esters (such as isobutyl methacrylate, isobornyl methacrylate), together with a mixture of hydrophilic monomers (such as vinyl pyrrolidone, dimethyl aminoethyl methacrylate and methacrylic acid), and a crosslinking agent (tetraethyl glycol dimethacrylate). The permeabilities quoted are of the same order as those described in previous patents in this field. It seems probable that the majority of the group of patents discussed above, depending as they do upon the elements of previous disclosures, are designed to seek to achieve commercial freedom within the field rather than to make innovated claims.

Two relatively recent patents ^(91, 92) from the 3M Co. take a series of ideas that have been previously disclosed in patent literature, and assemble them to produce materials that are in some way novel. Both patents utilise the concept of a long flexible oxygen-permeable chain with polymerizable acrylate or methacrylate groups at each end. Two candidates were chosen for this flexible, permeable chain. One of these is the siloxane backbone that has formed the basis of so many patents in this review.

This principle of endcapped polysiloxane chains was utilised, notably by Dow Corning (17-19) and Bausch and Lomb (60-62). Shorter and frequently more branched siloxy units have also been described in otherwise similar dimethacrylates (49, 51), of the type illustrated in structures (VIII, VIX and X). The main distinguishing feature of the compounds disclosed in the 3M patents is the inclusion of a urethane group between the terminal acrylates and central siloxyblock exemplified in (XIX). As with the great majority of the siloxymethacrylate patents reviewed here, the siloxymonomer (i.e. XIX) is copolymerized with methyl methacrylate and 2-hydroxyethyl methacrylate to produce clear buttons which are then subjected to conventional lens machining techniques.

As an alternative to the central polysiloxane block, a perfluoropolyether segment may be used. An example of the resultant dimethacrylate is shown in structure (XX), although it is not a requirement of the claim, in this case, that the urethane group be included. The values of n in (XX) (and in (XIX)) can vary quite widely and independently but might, for example, be in the region of 20. The thinking behind compounds of this type clearly goes back to much earlier 3M's patent (93) and is connected not with contact lens materials but is concerned with perfluoroalkylene oxide elastomers and urethane derivatives of these. Similarly, work on fluorine-containing contact lens materials can be traced back to the work of Barkdoll, Girard, Cleaver and Gaylord (39-42), and indeed the much later Hoya and Toyo patents (72, 75, 81, 82). One of these materials gave very satisfactory results in early clinical trials (94), but the manufacturer, Du Pont, decided not to pursue the project. Unlike the earlier material, lenses based on the 3M patent are not susceptible to lathe-cutting, being too soft and flexible. They are typically based on combinations of the fluoromonomer (e.g. XX), methyl methacrylate and a hydrophilic monomer such as N-vinyl pyrrolidone. On the other hand, this disadvantage is offset by the extremely high permeability (600 times greater than PMMA) claimed for the material.

The readily discernible trend in methacrylate-based contact lens materials described in the patent literatures and discussed here is one of increasing oxygen permeability. Although a range of variants have been disclosed, the essential structural

developments have centred around the incorporation of higher proportions of more highly branched siloxanyl derivatives, and the use of fluorocarbon in the place of hydrocarbon substituents. Much attention has been paid to the comprehensive coverage of all possible structural variants of the Gaylord's original disclosures. Despite this, logical extensions of the concept still remain to be exploited and are available to future workers who possess the appropriate imagination and synthetic skills. On the other hand, problems associated with the wettability of alkyl siloxanes, and discussed in some detail in an earlier section of this review, have not been convincingly solved. Many of the ranges of techniques discussed in references (21-31) in connection with silicone rubber have been adapted to improve the wettability of a wider range of alkyl substituted siloxy polymers.

The most widely used technique to improve wettability of siloxy methacrylate based materials is the copolymerization of hydrophilic monomers such as methacrylic acid, 2-hydroxyethyl methacrylate, and N-vinyl pyrrolidone. Surprisingly, in some cases up to 30% of N-vinyl pyrrolidone or 2-hydroxyethyl methacrylate have been specifically claimed with no indication that water uptake reaches levels that impair dimensional stability of lenses (95, 96). This contrasts with the more reasonable observation that the incorporation of 1% of the novel wetting agent propylene glycol monomethacrylate leads to 0.5% water absorption coupled with an improvement in surface hydrophilicity (97). Direct gas plasma treatment of lenses (98) together with plasma polymerization of N-vinyl pyrrolidone (99), and conventional free radical grafting of N-vinyl pyrrolidone (100) onto the materials surface are also used. Variants on the theme of chemical modification of these materials include the use of diethylene glycol allyl methyl ether (101, 102) in conjunction with chloroplatinic acid, and a more complex procedure involving initial surface grafting of methyl methacrylate and subsequent transesterification with ethylene glycol (103).

PROPERTIES OF COMMERCIAL RIGID GAS PERMEABLE MATERIALS

The influence of the disclosures, previously outlined and contained in the patent literature, is reflected in the nature and the properties of commercially available contact lens materials. Table 2.1 gives an overview of commercially available rigid gas permeable materials together with information on chemical type, oxygen permeability, wettability, mechanical properties and refractive index. This information has been compiled from various sources including manufacturer's literatures, reviews and results compiled by other workers (104-108), and measurements made in these laboratories. In addition, values for PMMA, cellulose-acetate-butyrate, silicone rubber and poly(4-methylpent-1-ene) are included for comparisons.

One of the problems in making comparisons between materials and particularly in comparing manufacturer's claims is that there is no rigid standardisation of experimental techniques to provide a basis for such comparisons. The first point to consider is the range and reliability of oxygen permeability measurements. Complications in making true permeability measurements on materials arise from the curvature and varying thickness of individual contact lens samples, the thickness dependence (or the barrier effect) (109), and the lack of widely available standards for instrument calibration especially in the high Dk region in which many of the recently developed materials are claimed to lie.

The problems associated with the use of increasing quantities of siloxymethacrylates to achieve high oxygen permeabilities are two-fold. Firstly, incompatibility, phase separation, and deterioration in mechanical properties limit the amount of such monomers that can be incorporated. Secondly, their use requires the incorporation of hydrophilic monomers containing hydroxyl, carboxyl, amide or imide groups to improve wettability. As a result, measurement of wettability by contact angle techniques becomes a much more difficult procedure to carry out in the standard reproducible fashion. In this case, contact angle hysteresis (110, 111), the effect of soaking (106) on water uptake by and thus wettability of materials, coupled with the

popularities among manufacturers of the inverted or captive air bubble technique, and even surfactant solutions rather than water in measurement, produce wide variations in the reported values. These various factors coupled with the relevance of in vitro measurement to clinical performance of materials of this type will be discussed in the subsequent chapter.

TABLE 2.1 TABLE OF PROPERTIES

NAME OF LENS AND MANUFACTURER	MATERIAL TYPE	DK (X Unit)	CONTACT ANGLES		HARDNESS	REFRACTIVE INDEX (N)
			DRY	SOAKED		
BOSTON I (Polym.Tech.)	Siloxymeth. Copolym.	10.1(a) 7.9(b) 12(c)	65°(d) 80.8°(e)	42°(f) 33.3°(g)	85SD(1) 83.5SD(k)	1.46
BOSTON IV "	Siloxymeth. Copolym.	14(a) 26.3(c)	79°(d)	119R (m)		1.468
AIRLENS (Wesley Jessen)	Butyl Styrene	21(c, 35°C)			86SD	1.53
ALBERTA N (Calgary Concal Cont)	Perfluoroalkyl Itaconate-siloxane	42(c, 35°C)			120R (m)	1.445
CALGARY XL 30 (Concal Contact)	Siloxymeth. Copolym.	12.8(a) 8.73(c)	65°(d)	28°(f)		1.48
EQUALENS (Polym.Tech.)	Fluorosiloxane	72(c, 35°C)	55.3°(d) 30°(c)			1.439
FLUOROFICON A (3M)	Perfluoropolymer	70+ (c,20°C) 90(c,35°C)		44°(f)		
HYPERM (Hydron Europe)	Siloxymeth. Copolym.	12.2(a) 14(c)	71°(d)	84SD(k)		
MENICON O ₂ (Toyo)	Siloxymeth. Copolym.	5 8(c)	16°(f)		81.5SD(k)	1.481
MENICON SUPER O ₂ (Toyo)		52(c)				
OPTACRYL 60)	Siloxymeth. Copolym.	9.1(a) 7.4(a) 12(c)	65°(d) 75.9°(e)	25°(g)	88SD(1)	1.467
OPTACRYL K) (Optacryl)		23(c,25°C) 32(c,35°C)		25°-30°(j)	86SD(1)	1.467
OPTACRYL Z)		82(c) 84(c,35°C)		25°-30°(j)	80SD(1)	1.46
POLYCON I) (Syntex)	Siloxymeth. Copolym.	6.5(a) 3.1(b) 5(c)	67°(d) 76.6°(e)	25°(f) 30.4°(g)	83SD(k)	1.49
POLYCON II)		6.5(b) 12(c)	82.7°(e)		84.5SD(1)	1.473
POLYCON HDK		50(c,35°C)		25°(h)	85SD(m)	1.465

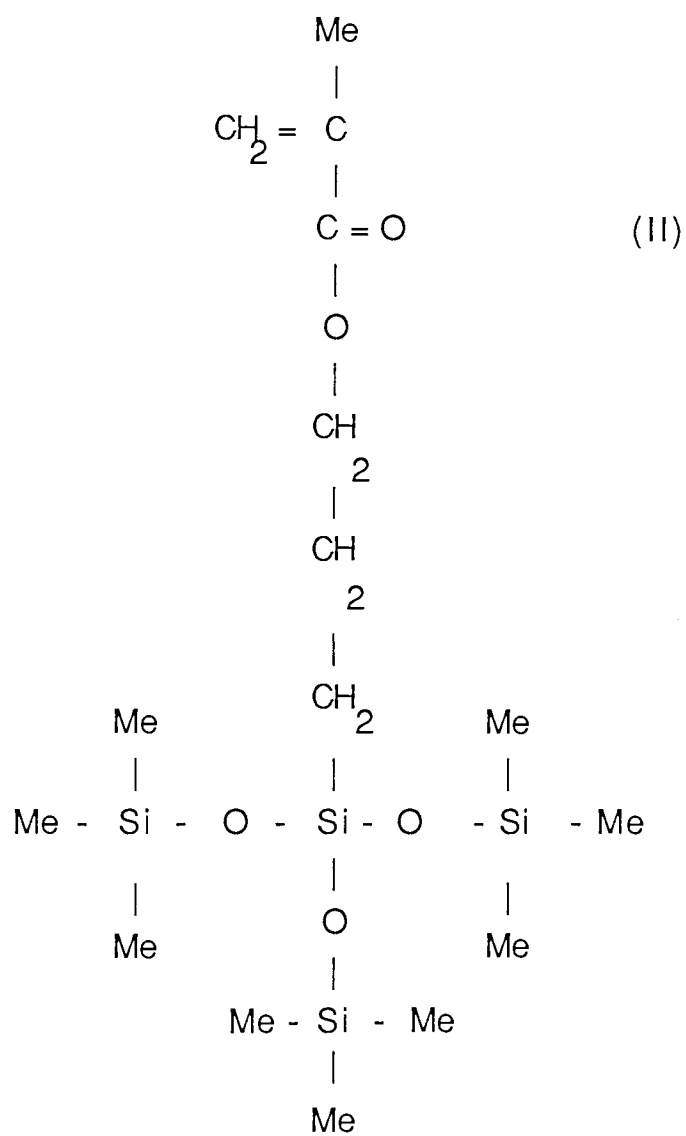
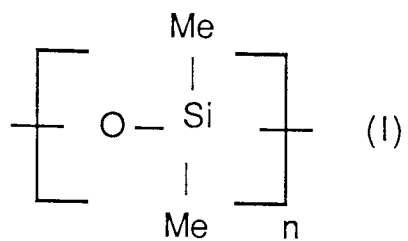
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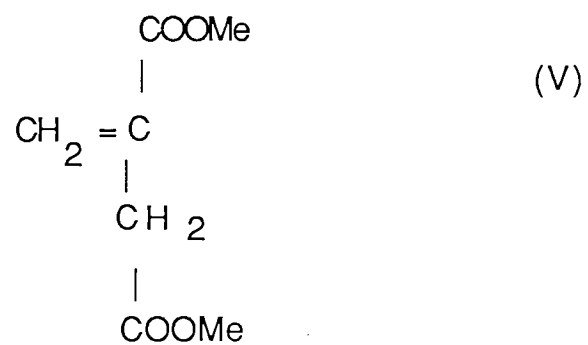
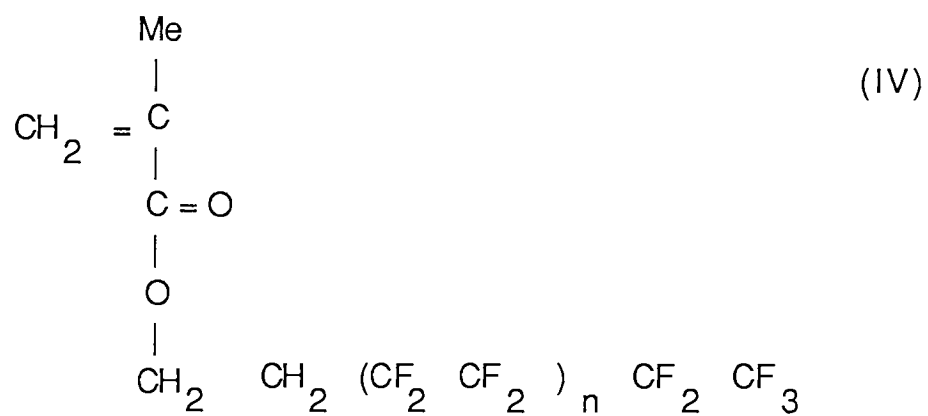
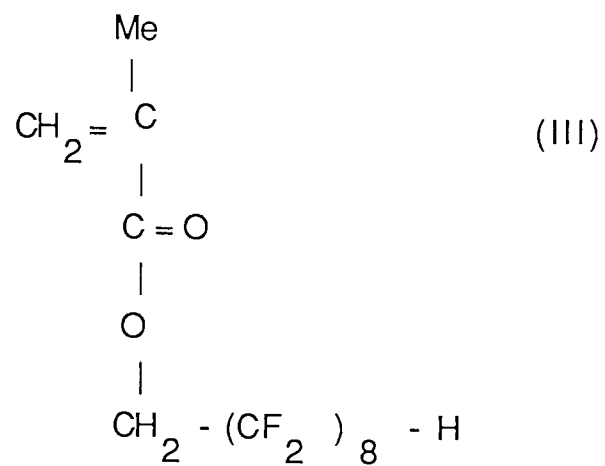
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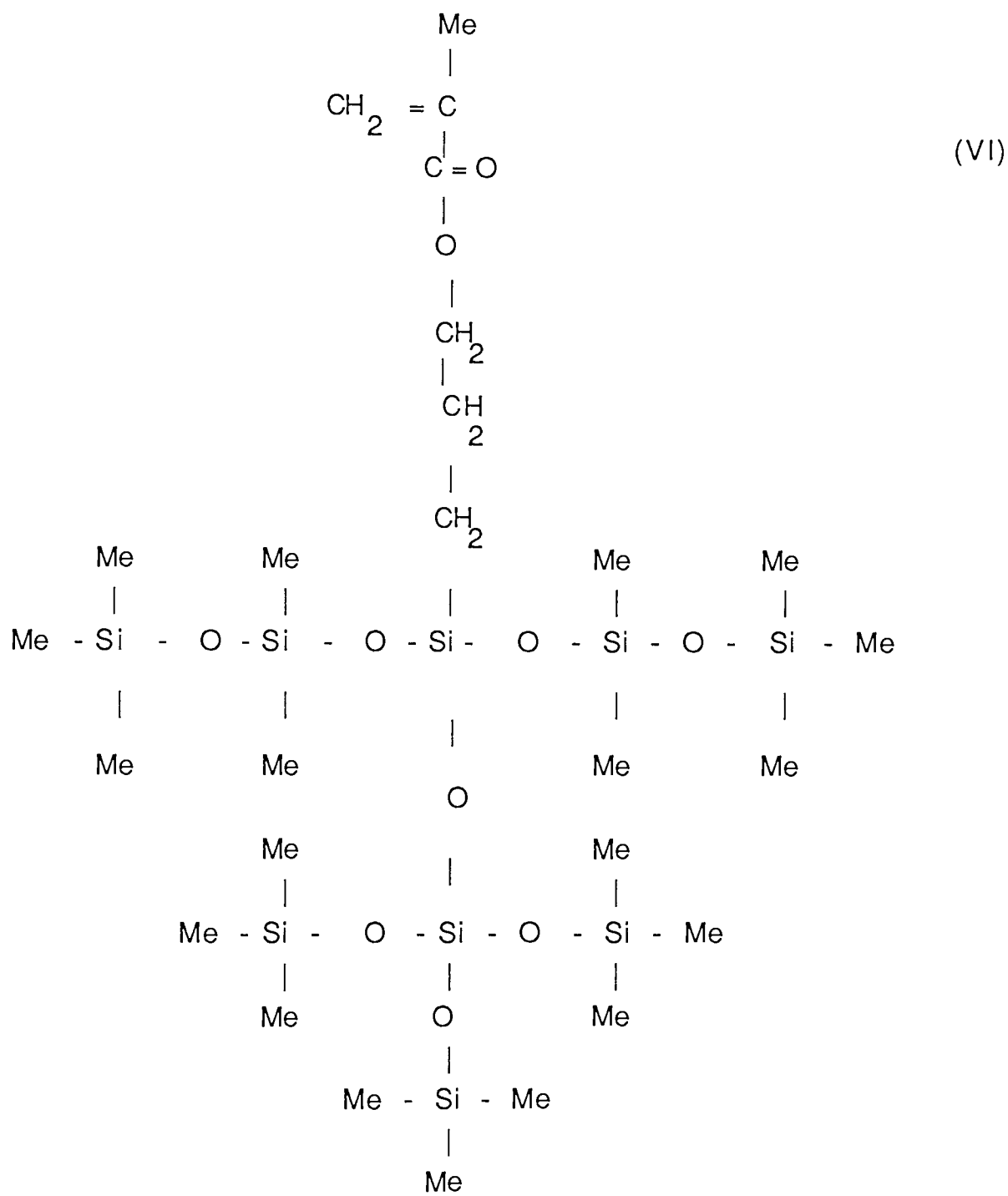
NAME OF LENS AND MANUFACTURER	MATERIAL TYPE	DK (X Unit)	CONTACT ANGLES		HARDNESS	REFRACTIVE INDEX (N)
			DRY	SOAKED		
PARAPERM O ₂)		7.9(b) 12.2(c)	80°(e)	46°(f) 23.1°(g)	85SD(1)	1.48
PARAPERM EW) Paragon		56(c, 35°C)	68.3°(d) 92°(g)		10.6V(m)	1.475
PARAPERM Plus)		39(c, 35°C)	91°(g)		11.3V(m)	
REVLENS (Bioflex)		117(c)				
SILPERM		12(a)	90°(d)	50-55°(f) 15°(h)		
SILCON (Dow Corning)	Silicone Mat.	10.1(b)	92.8°(unt)		82SD(1)	1.52
TPX		20(a)	31.4° (treat)			
PMMA	Methyl Metha. Polym.	0.1(a)	63°(d)		88.51SD(k)	
PARACAB	CAB	12(a) 5(g)			77.5SD(k)	

Footnotes

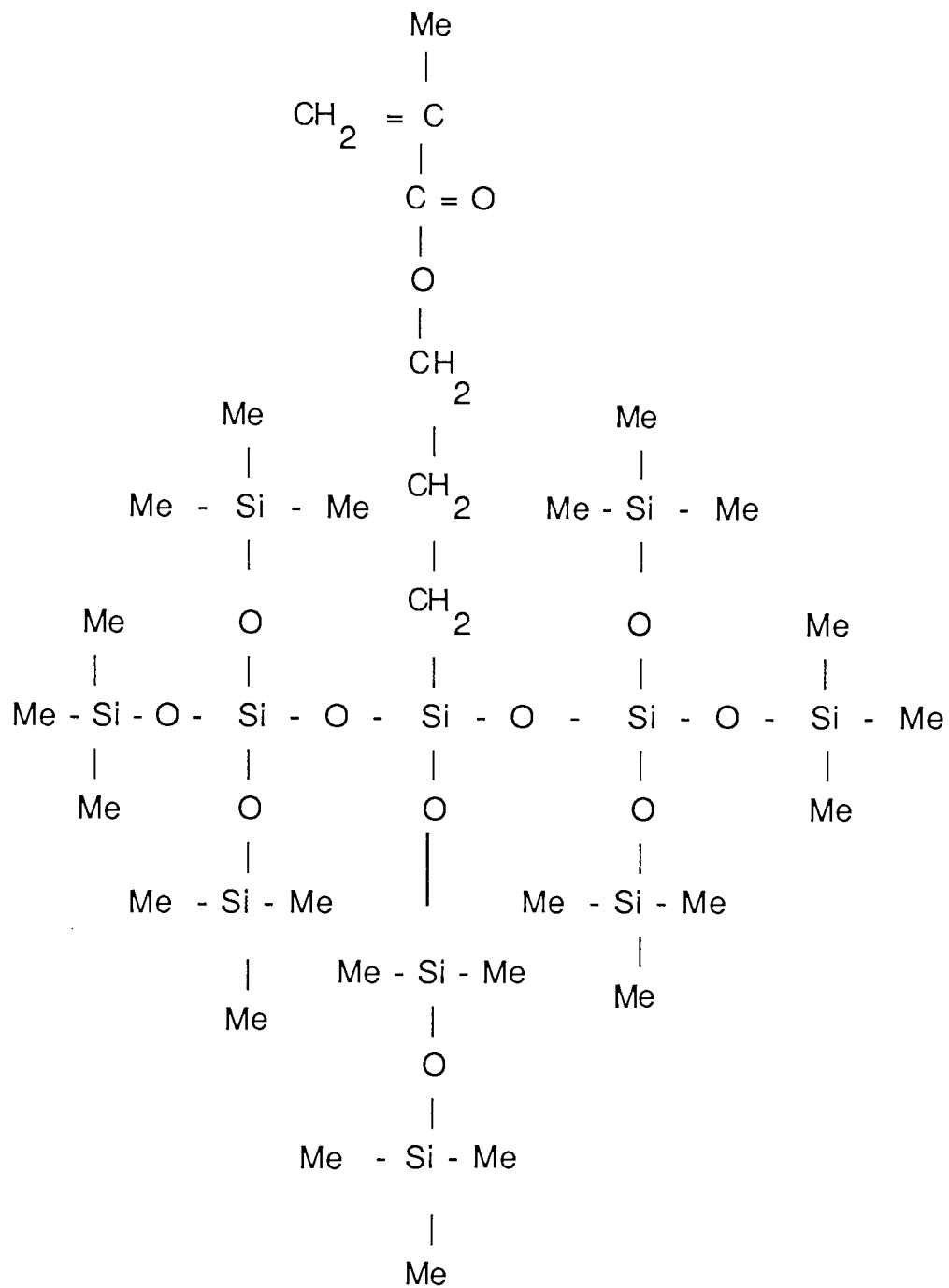
DK	a)	Aston 20°C	Contact Angles (Soaked)	f)	Japanese review
	b)	Fitzgerald 20°C		g)	P. Honan
	c)	Manufacture ?°C		h)	Other
Contact Angles (Dry)	d)	Aston 20°C	Hardness	k)	P. Walker
	e)	J. Fitzgerald		l)	J. Fitzgerald
	j)	Other		m)	Others

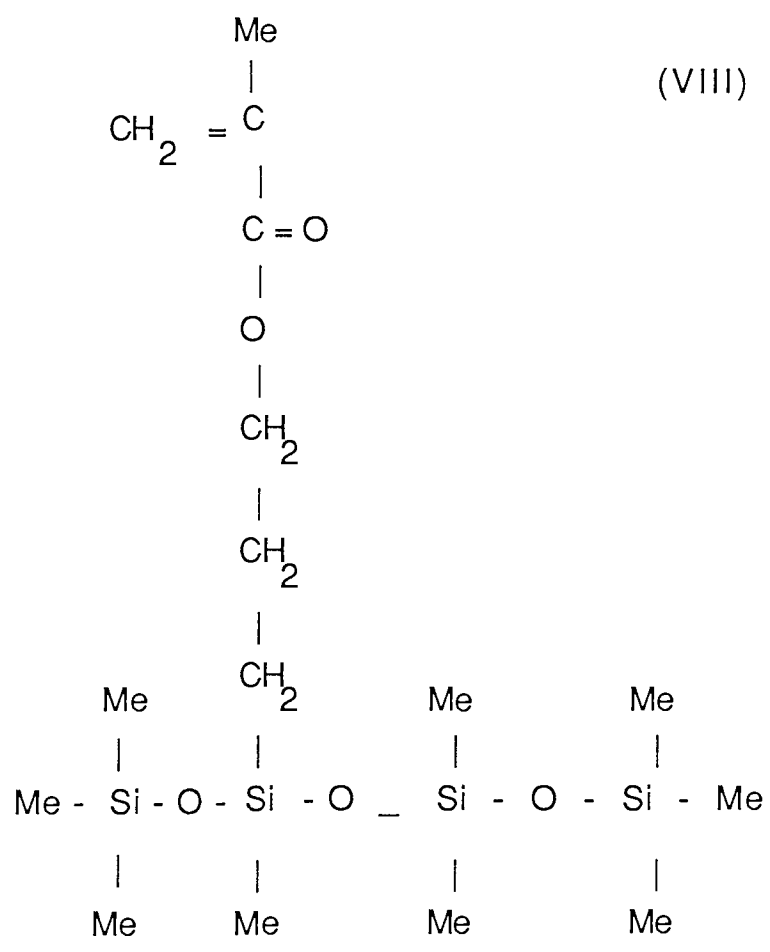




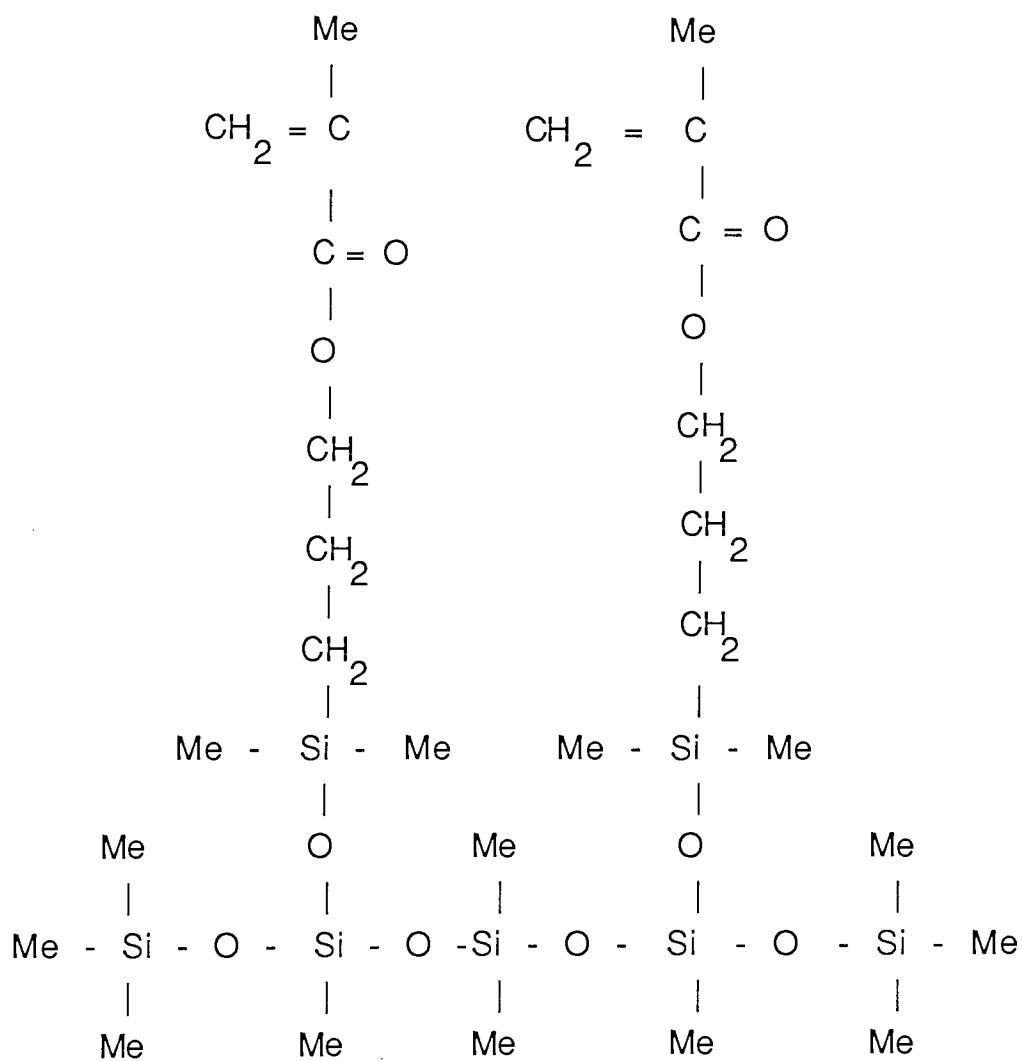


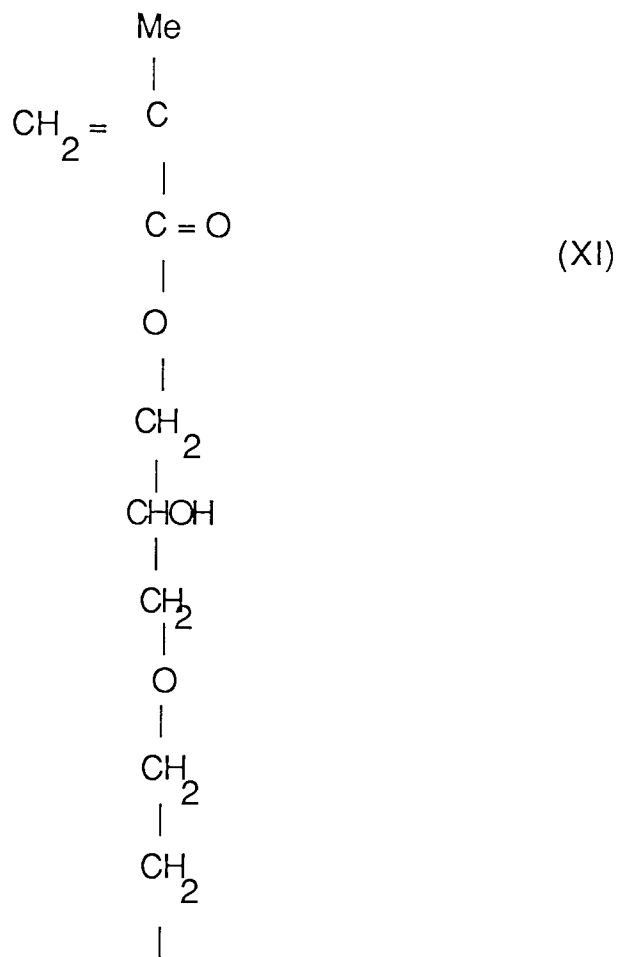
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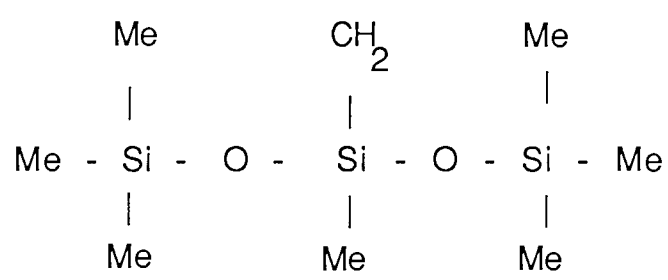


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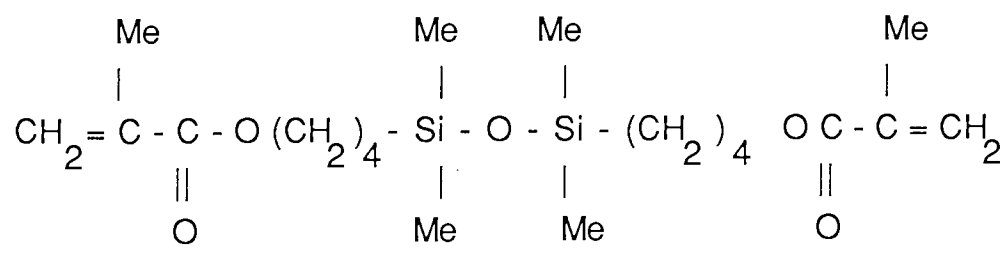


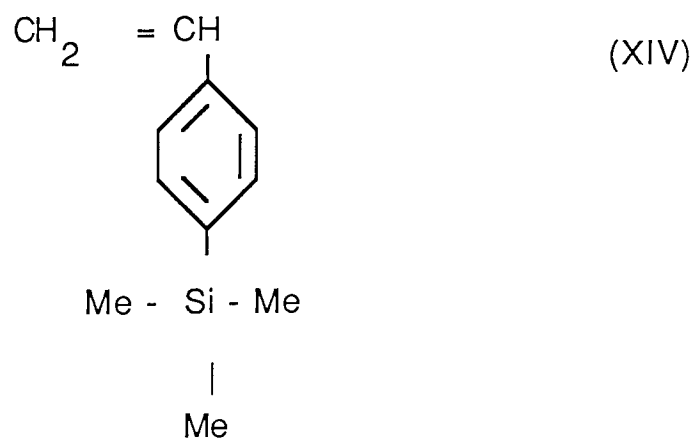
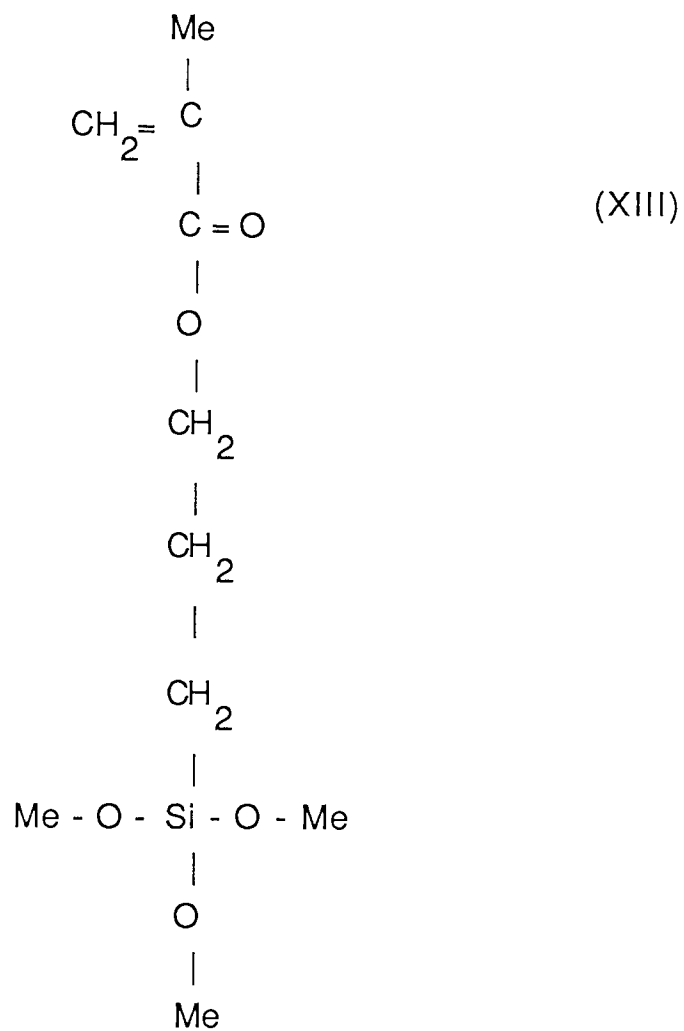


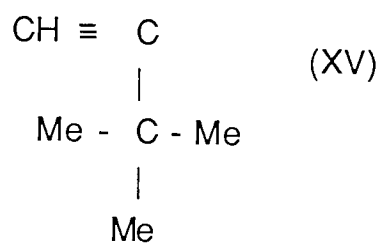
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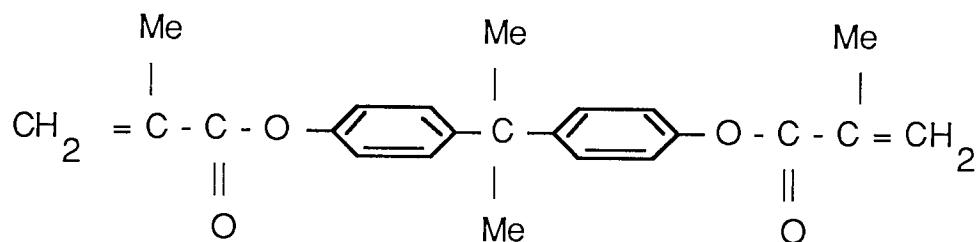
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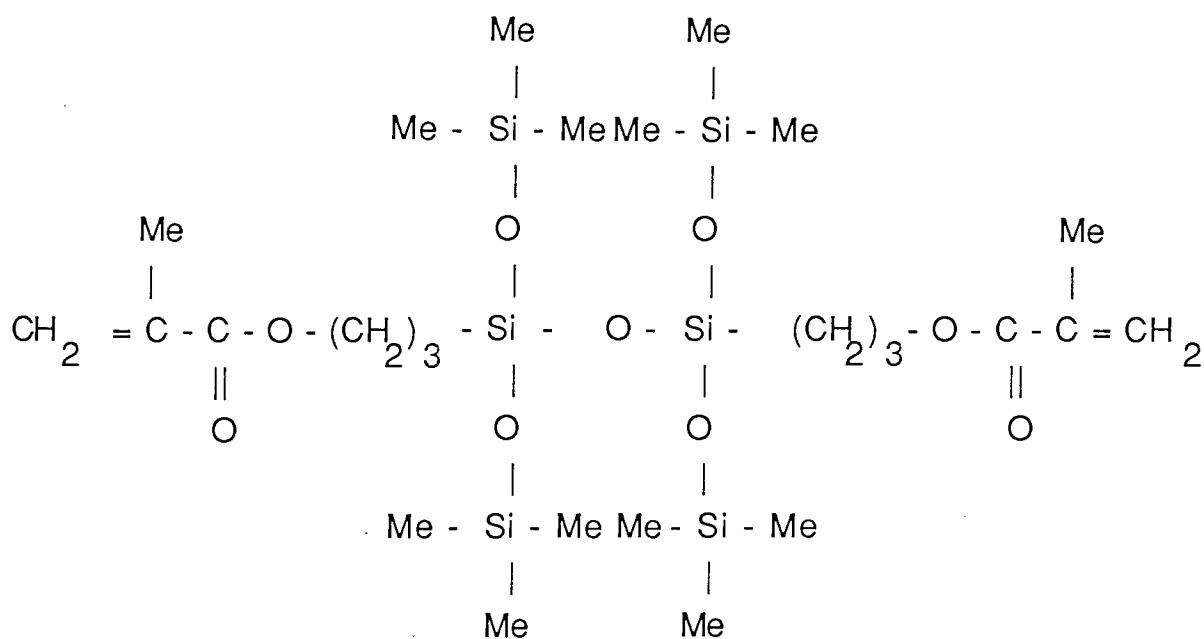




(XVII)



(XVIII)



CHAPTER III
EXPERIMENTAL TECHNIQUES

3.1 INTRODUCTION

This chapter describes the preparation and synthesis of polymers used in this thesis, together with their characterisation and evaluation techniques related to the requirement for contact lens materials applications.

Two types of potential contact lens materials were produced in this project, and a general outline to the synthesis of these polymers is described. The list of reagents used and their molecular weights (where known) are shown in Table 3.1 together with the suppliers. The schematic structures of the reagents are shown in Figure 3.1a and 3.1b. The monomers used can be divided into the types of materials used for hard gas permeable materials and those for hydrogels. In this chapter, experimental procedures and techniques common to these both types of materials are mentioned. Any experimental preparation or techniques that are relevant to the hydrogel type of materials are detailed in Chapter 7.

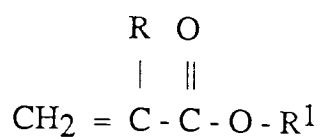
3.2 REAGENTS AND PURIFICATION

The reagents used in this work were purified before polymerization by reduced pressure distillation. Any inhibitors in the crude monomer were removed first by successive washings in dilute hydroxide solution, then the water layers were removed in a separating funnel until no colour was apparent. The washed solution was dried overnight with anhydrous magnesium sulphate before being distilled by vacuum. High boiling point monomers or those which polymerize at or below normal boiling points at atmospheric pressure were distilled at lower temperatures using a vacuum pump. For lower boiling point monomers, methyl methacrylate, iso-butyl and iso-propyl

TABLE 3.1 REAGENTS USED

<u>Monomer</u>	<u>Molecular Weight</u>	<u>Supplier</u>
Methyl methacrylate (MMA)	100.00	B.D.H.
Ethyl methacrylate (EMA)		
Butyl methacrylate (BMA)		
Isobutyl methacrylate (IBMA)	142.2	Fluka
Isopropyl methacrylate (IPMA)	128.2	Pfaltz and Bauer
t-Butyl acrylate (tBA)	128.2	Pfaltz and Bauer
t-Butyl methacrylate (tBMA)	142.0	Pfaltz and Bauer
Hexyl methacrylate (HMA)	170.2	Pfaltz and Bauer
Octyl methacrylate (OMA)	226.0	Pfaltz and Bauer
Lauryl methacrylate (LMA)	254.0	I.C.I.
Cyclohexyl methacrylate (CHMA)	170.2	
Glycidyl methacrylate (GMA)	102.7	
2-Hydroxyethyl methacrylate (HEMA)	103.1	optical grade monomer (Kelvin lenses)
Maleic anhydride (Ma)	98.11	
Styrene (styrene)	104.1	B.D.H.
N-vinyl pyrrolidone (NVP)	111.1	Koch Light
Diacetone acrylamide (DAAc)	169.2	Fluka
N-tertbutyl acrylamide (NtBAcr)	127.2	Polyscience
N-isobutyl methacrylamide (NiBMAcr)	157.2	Polyscience
N-isopropyl acrylamide (NipAcr)	113.16	Pfaltz and Bauer
<u>Initiator</u>		
α - Azoisobutyronitrile (AZBN)		
Cyclohexyl t-butyl perdicarbonate		
<u>Crosslinking agent</u>		
Ethylene glycol dimethacrylate (EGD)	198.2	





Nomenclature of Monomer	R ¹	R
MMA	CH ₃	CH ₃
BMA	(CH ₂) ₃ CH ₃	
IBMA	CH ₂ CH(CH ₃) ₂	CH ₃
IPMA	CH(CH ₃) ₂	CH ₃
tBA	C(CH ₃) ₃	H
tBMA	C(CH ₃) ₃	CH ₃
EMA	CH ₂ CH ₃	CH ₃
HMA	C ₆ H ₁₃	CH ₃
OMA	C ₈ H ₁₇	CH ₃
LMA	C ₁₂ H ₂₅	CH ₃
CHMA	C ₆ H ₁₂	CH ₃
GMA	$\begin{array}{c} \text{O} \\ / \quad \backslash \\ \text{CH}_2\text{CH}-\text{CH}_3 \end{array}$	CH ₃
HEMA	CH ₂ CH ₂ OH	CH ₃
EGD	$\begin{array}{c} \text{O} \quad \text{CH}_3 \\ \parallel \quad \\ (\text{CH}_2)_2\text{OC}-\text{C}=\text{CH}_2 \end{array}$	CH ₃

Figure 3.1a Structures of Reagents

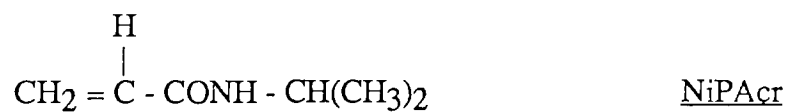
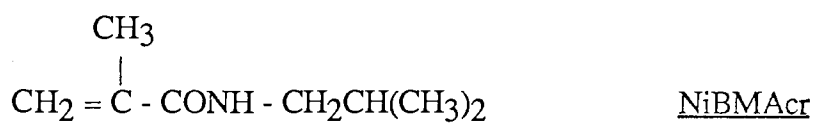
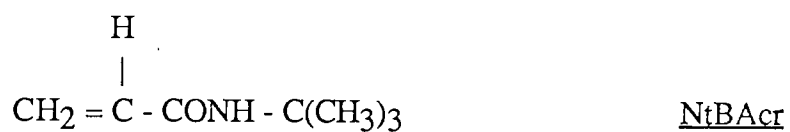
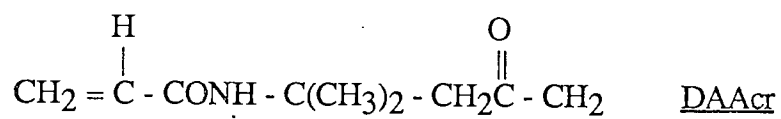
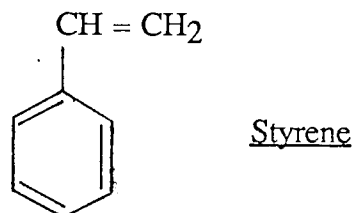
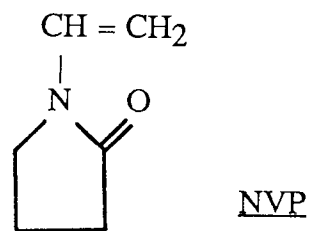
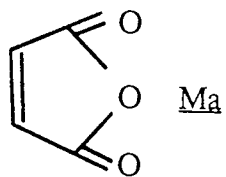


Figure 3.1b Structures of Reagents

methacrylates, a water pump was used which reduces boiling points sufficiently to permit distillation at a temperature of approximately 40° - 80°C but not too low as to lead to excessive loss into the cold trap. The distillation of monomers was carried out under a stream of nitrogen to de-gas the system and to prevent bumping. The experimental set up is shown in Figure 3.2. For higher molecular weight monomers, such as lauryl methacrylate and octyl methacrylate, an oil pump was used to reach lower pressures so that monomers could be distilled at temperatures below 80°C. For tert-butyl methacrylate and tert-butyl acrylate, as their prices are so high for the small quantity supplied (£570/100g and £435/100g respectively), they were not distilled to avoid loss. The purification of 2-hydroxyethyl methacrylate is more complex, since the monomer readily dissociates to methacrylic acid and ethylene glycol dimethacrylate under normal distillation. The monomer used in this work was pre-purified 'optical' grade supplied with an analysis certificate. In all cases except octyl and lauryl methacrylate, the purities of the monomers were found to be 99% or better, by GLC analysis. Although those two exceptions could not be purified as readily as the lower boiling point methacrylates, the purification process did serve to remove polymerization inhibitors.

3.3 POLYMERIZATION METHODS

In the synthesis of copolymers (or terpolymers), three methods of bulk polymerization were used depending upon the physical state and shape the copolymer was required i.e. sheet, rod or buttons.

3.3.(1) Prepolymerization Technique

Each comonomer formulation for the hard gas permeable materials was pre-polymerized before being synthesized by free radical polymerization. The reasons

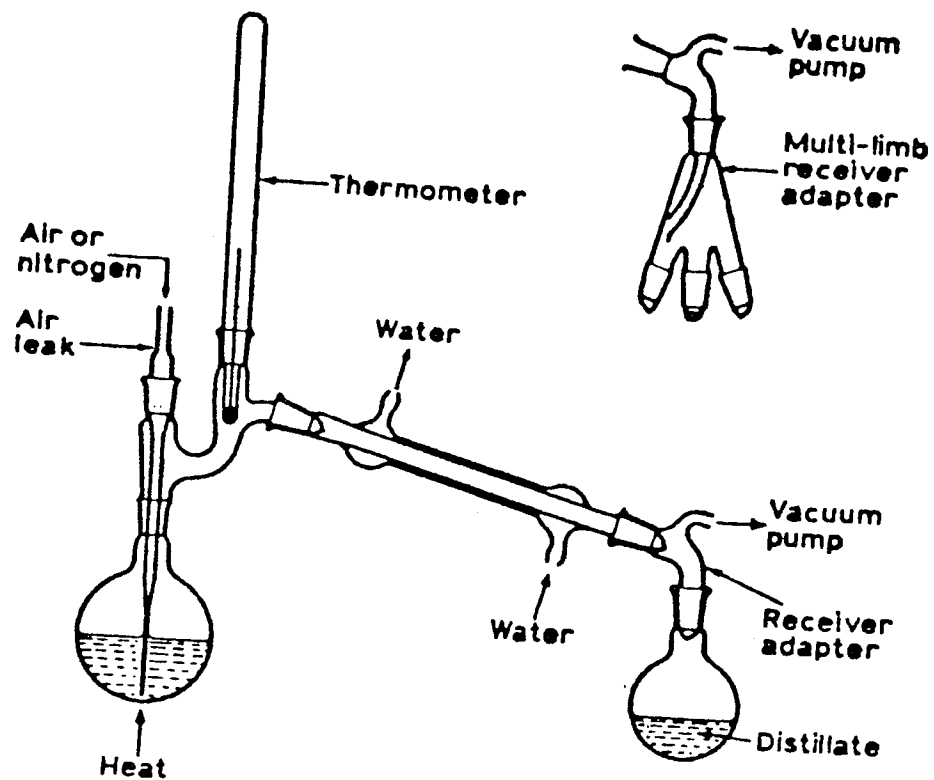


Figure 3.2 Vacuum distillation apparatus

being:

- a) The monomers used in the work are so volatile such that excessive loss can occur if polymerization is attempted from the monomer mix without any pre-polymerization.
- b) Thinning of the polymerized sheet will occur due to shrinkage in the mould because of the large difference in the polymer and monomer densities which occur particularly with methacrylates.

By using cyclohexyl t-butyl perdicarbonate as the initiator, it was possible to bulk polymerize the mixture at a low temperature of 40°C. This particular initiator was used because of its high reactivity allowing the polymerization to be carried out at low temperatures (40°C- 50°C) which minimises the potential for loss by more volatile monomers during the polymerization with consequent irregularity in the polymer mixture. Nitrogen was bubbled through the filtered comonomer mixture and the flask was heated to 40°C in a water bath. After a period of 30 minutes to 7 hours depending on the formulation, a fairly viscous solution was obtained.

Typically, a formulation would consist of 90% molar ratio of isobutyl methacrylate (9.0g) with 10% molar ratio of glycidyl methacrylate (0.722g) and with 0.5% weight ratio of the initiator. The experimental set-up is shown in Figure 3.3.

3.3.(2) Thin Film Polymerization

Thin sheets of polymer were prepared after they have been prepolymerized as described in the earlier section. Uniform thin (0.2mm) films are required for physical property evaluations. Polymer sheets processed in plastic moulding are normally of thickness about 1mm.

After pre-polymerization, a fairly viscous comonomer solution is

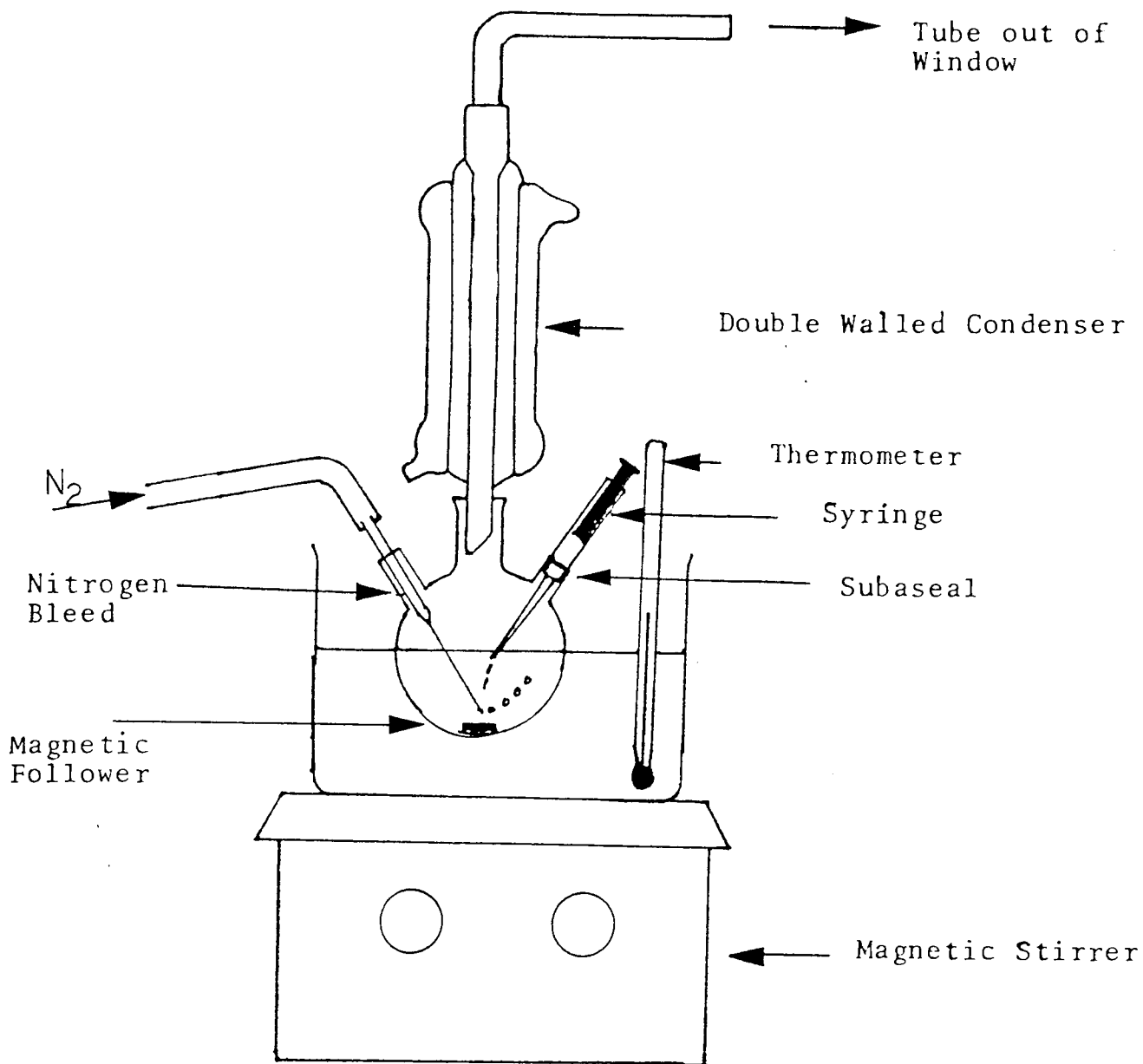


Figure 3.3 Experimental set up for pre-polymerization

obtained, which can subsequently be injected into the mould cavity. The apparatus (sketched in Figure 3.4) consists of two glass plates covered with Melinex sheets (polyethylene terephthalate) separated by a gasket made of polyethylene of thickness 0.2mm ($\pm 10\%$). The Melinex helps to release the polymer sheets from the glass plates and the gasket, also giving a smooth finish. The glass plates and the gasket were clamped tight on three sides using spring clips to hold the polymer solution and to prevent air bubbles entering the system. Approximately 2 - 3 mls of the pre-polymerized comonomer mixture was injected from the unclamped side of the glass plate into the mould cavity. This side was clamped after the introduction of the monomer to form a tight seal. The glass plates with the monomer were placed in an oven at 50°C to 60°C for three days, then post-cured for two hours at 90°C to complete the polymerization; the shrinkage of polymer in the mould is reduced and thus uniform sheet of polymer should be produced. Also the glass plates were placed at an angle from the horizontal in the oven to displace any air bubbles from the centre to the sides.

After the post-curing, polymer sheets were removed from the glass plates and polyethylene gasket. In cases where the separation of the plates caused damage to the sheets, the sheets with the Melinex were put back in an oven at 50°C for 15- 30 mins, which heated the polymer to above its glass transition temperature (T_g) thus making it flexible and easy to remove. Discs of polymer were cut using a cork borer for oxygen permeability measurements; discs were stored in labelled glass jars to keep them dry and clean.

3.3 (3) Manufacture of Rods

Attempts were made to produce lathe-cut materials with improved oxygen permeability and surface properties by making rods. The comonomer solution containing

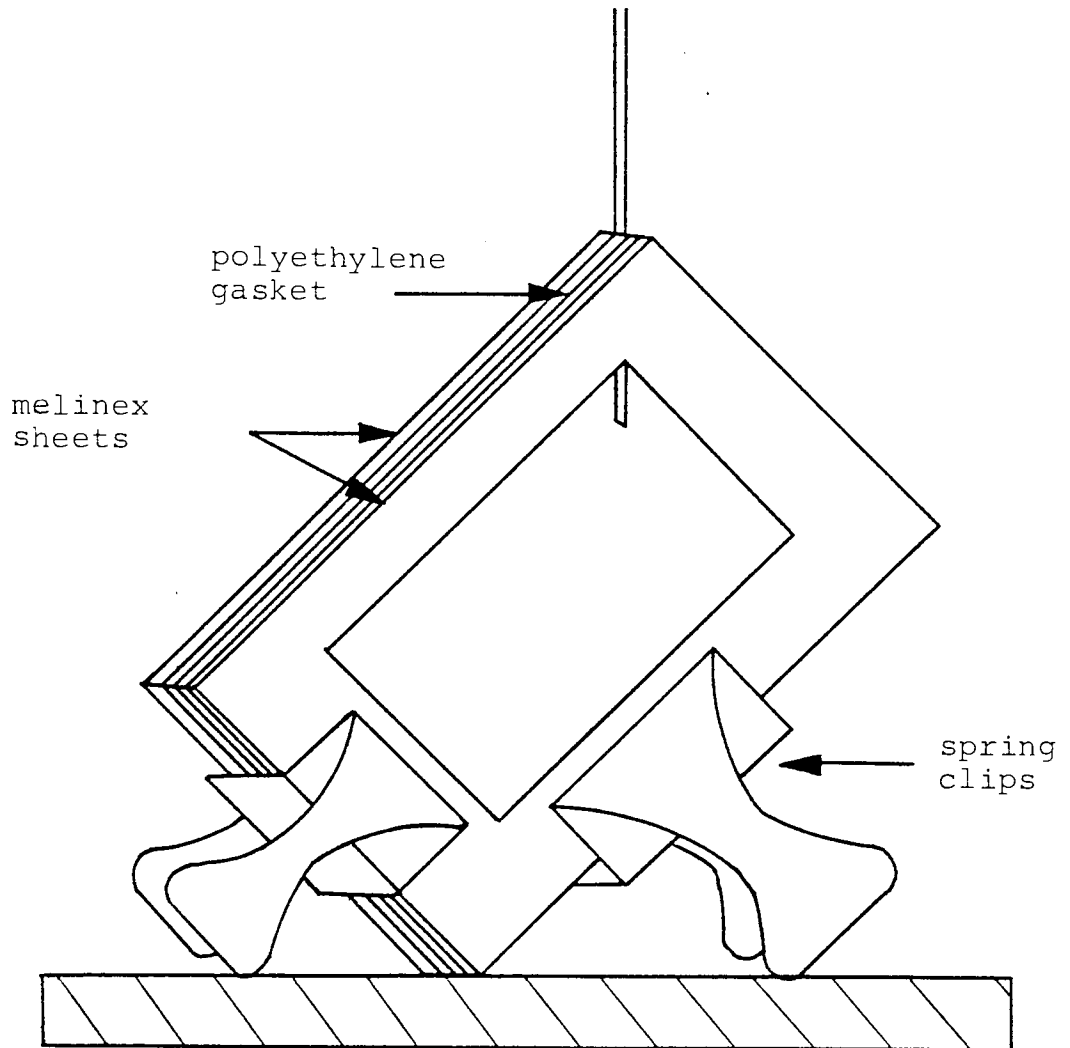


Figure 3.4 Thin-film apparatus

a free radical initiator, α -azoisobutyronitrile (AZBN) and a cross-linking agent ethylene glycol dimethacrylate was put into a dry clean polyethylene tube of diameter 12mm and nitrogen was passed through for 15 minutes to degas the mixture. The polyethylene tube is about 15cm in length and sealed at one end by heating it gently and squeezing the warmed ends. The open end of this tube with the solution is then sealed with a cork and poly(tetra fluoroethylene) tape. The sealed tubes were then placed in a water bath at 50^o - 60^oC for three days followed by post-cure at 90^oC for 3 hours. The complete polymer rod was then sent to Kelvin Lenses Research Laboratories to be made into contact lenses suitable for further testing, whilst noting the machinability and processability of the formed rods.

3.3 (4) Manufacture of Buttons

In some cases, especially hydrogel rods, where there were problems with severe exotherm with compositions of high N-vinyl pyrrolidone content, attempts were made to reduce the exotherm effect by producing buttons where the heat would dissipate more effectively. A mould for buttons was produced by the workshop in the Department of Chemistry, using aluminium blocks. The mould has two parts; a bottom part with several small bores to hold the polyethylene hollow buttons, the top part as a top-plate. Clean polyethylene sheet was placed between the two sections to separate them and to ensure a good seal. After purging nitrogen through the comonomer mixture, each button was filled to the rim and placed in the mould. After ensuring that the polyethylene sheet was in position, the top-plate was screwed on tightly. The whole casing was then placed in an oven at 60^oC for 4 days and each button removed and post-cured at 90^oC for several hours.

3.4 MATERIALS TESTING

3.4 (1) Density Measurements

The densities of the synthesized materials were determined using a density gradient column. The positioning of partially mixed liquids in a vertical tube will give rise to a stable column having a density gradient. A density column was initially set up using solutions of carbon tetrachloride (specific gravity SG 1.59) and xylene (SG 0.86) at different proportions. The column was calibrated using coloured marker floats of known density and the positions of the floats at equilibrium were measured with a cathetometer. The polymer samples were cut into small different shapes for identification, and the positions of these samples were noted and their densities determined from the calibration graph. It was discovered after several trials that the alkyl methacrylate group of copolymers were found to be soluble in the original column mixture. After consulting the Polymer Handbook⁽¹¹²⁾, a second column of ethylene glycol (SG 1.1088) and methanol (SG 0.79) was tried (see Table 3.2). These two solutions were chosen because they are non-solvents for higher alkyl methacrylates. This second density column was found to be stable and thus the densities of the synthesized materials were determined as described earlier. This density calibration graph is sketched in Figure 3.5.

3.4 (2) Oxygen Permeability Measurements

Two types of permeability apparatus were used to give gas (particularly oxygen) permeabilities of polymer material relevant to contact lens applications. A description of the apparatus, experimental set-up and procedure for the Davenport Gas Permeability Apparatus and Schema Versatae Flux Meter are given in this section.

TABLE 3.2 DENSITY GRADIENT COLUMN SYSTEM II

<u>SOLUTION NUMBER</u>	<u>ml ETHYLENE GLYCOL</u> <u>(SG = 1.1088)</u>	<u>ml METHANOL</u> <u>(SG = 0.79)</u>
1	25	0
2	22	3
3	20	5
4	17	8
5	14	11
6	11	14
7	8	17
8	5	20
9	3	22
10	0	25

Table 3.2 shows the densities of marker floats for the calibration line (Figure 3.5).

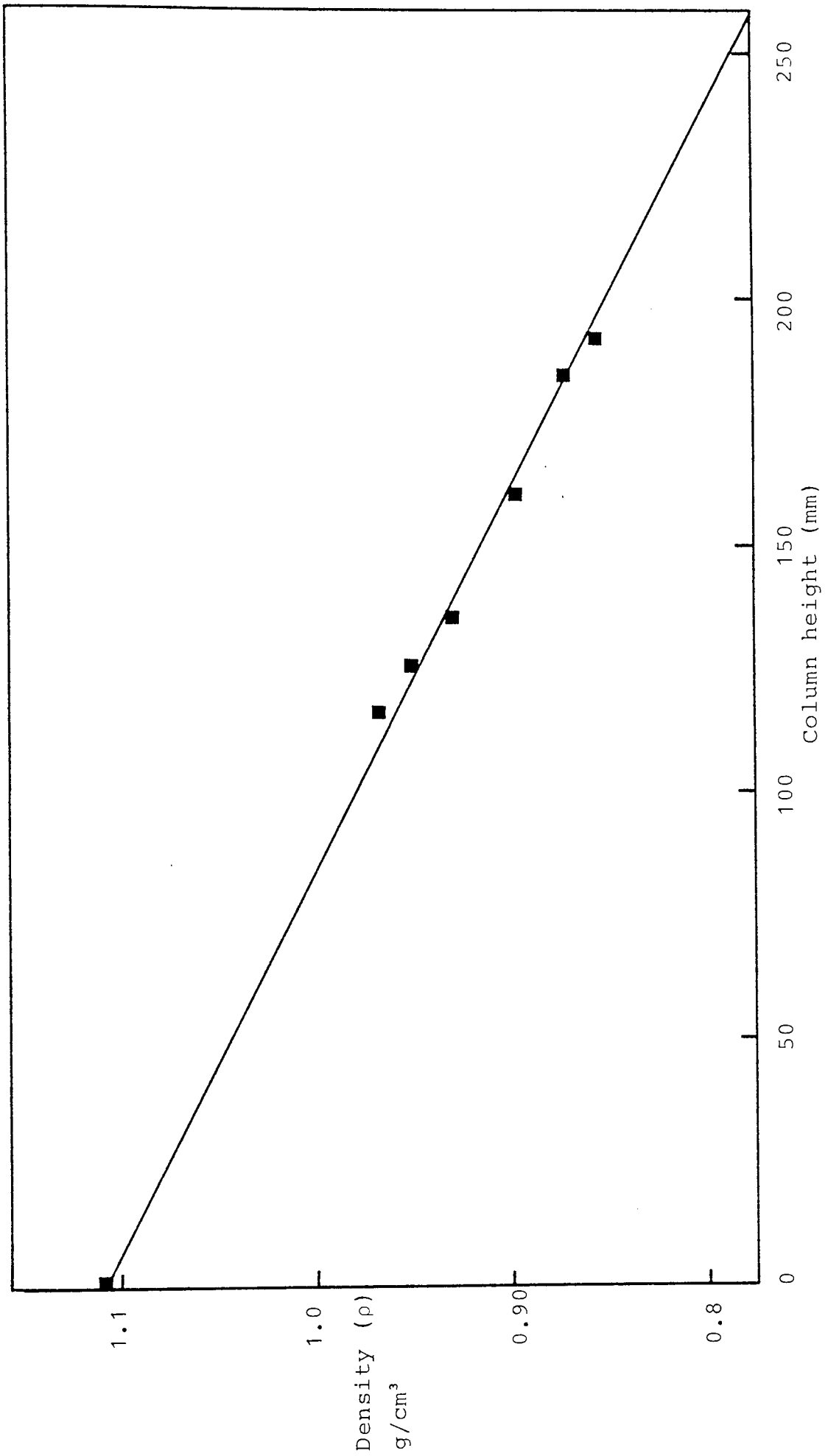


Figure 3.5 Density calibration gradient (ethylene glycol and methanol)

3.4 (2a) Gas Permeability Measurements by Davenport Apparatus

i) Description of Apparatus

The measurement of the gas permeability coefficients of the polymer membranes was carried out using the "Davenport Gas Permeability Apparatus".

The Davenport Gas Permeability Apparatus consists of a stainless steel permeability cell connected through a capillary tube to a manometer and a vacuum system, and is fitted to a vertical mounting. The permeation cell unit has two parts which contain a rubber "O" ring to form a seal when they are clamped together by six vertical studs with nuts. The lower part of the cell is fitted with a changeable insert so that the volume of the free space in this part of the cell is 20, 15, 10 or 5 mls. This variation makes it more convenient to test samples of differing rates of permeability. The manometer unit consists of a manometer connected to the lower part of the cell unit through a capillary tube (1.5 mm bore). On one end of the manometer is a mercury reservoir which can be connected to a vacuum system; behind the capillary was mounted vertically a scale 10 cm. long graduated in divisions of 1 cm. and sub-divisions of 1 mm.

(ii) Procedure

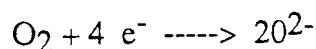
A suitable insert was chosen and placed in the lower half of the Permeation cell. A No.1 Whatman filter paper (5.5 cm diameter) was placed centrally on the top surface of the insert and then a polymer sample (7 cm diameter) put on top of the filter paper. The two parts of the cell were closed and the six studs were tightened with size six nuts. With mercury in the reservoir, the test gas was passed from a cylinder into the top chamber of the cell and then the stop-cock was opened, and the lower cell unit and the manometer were evacuated with a pump attached to a Vacustat Pressure Gauge. When the pressure in the system was steady, and less than 0.01 mm Hg the stop-cock was closed and the

whole apparatus was tilted to get the mercury in the reservoir into the manometer tubes. The mercury level in the capillary tube was read to the second decimal place in cm., with the help of the graduated scale behind it, and a stop-watch was immediately started. The mercury level in the capillary tube fell due to gas transmission through the test polymer, and the readings were taken at time intervals. The height of the mercury was plotted against time, and the measurement was carried on until constant rate of change in the height of mercury was obtained. The gas was then switched off and the mercury was brought back to the reservoir before the next sample was studied.

3.4 (2b) Oxygen Permeability Determination Using Schema Versatae Flux Meter

Oxygen permeabilities of synthesized polymer discs and commercial contact lens materials were measured using a Schema Versatae Oxygen Flux Meter S/V - 920a. Oxygen permeability (P) may be defined as the product of the diffusion coefficient (D) in $\text{cm}^2\text{sec}^{-1}$ and the solubility coefficient (S) in ml O_2 (STP) dissolved per ml of solution. The details of theory on gas permeability are discussed in Chapter 4.

The method used in this technique is to establish a certain concentration on one side of the lens, usually with air or pure oxygen and use a stainless steel polarographic electrode on the other side of the lens to both establish a zero oxygen concentration and to monitor the oxygen flux. The polarographic electrode can do both because at this surface, oxygen is changed to oxygen ions through the following reaction;



The reaction is driven strongly to the right by a bias voltage of 0.75 volts between the negative stainless steel electrode and a positive silver-silver chloride electrode in the same cell. Consequently, the oxygen concentration at the negative electrode is held at zero. Furthermore, since four electrons are assumed to be required to reduce each oxygen

molecule to two ions, the flux of oxygen to the stainless steel cathode is translated to a flow of electrons to the cathode i.e. to an electric current. It is this current that is amplified and displayed as a meter reading or as a pen tracing on a strip chart recorder.

The instrument consists of the control chassis containing power supply, amplifiers and meter; and the cell which holds the synthesized disc or contact lens. A conducting solution was placed in the lower cell to a level where it just covers the stainless steel cathode. The conducting solution is not critical; an isotonic saline buffer with pH of 7 to 9 is adequate.

A piece of wet cigarette paper was placed on the cathode to assist in the reaction of oxygen at the cathode by preventing an air pocket between the cathode and curved lens samples. The upper part of the cell was placed over them and nylon screws tightened until the disc or the lens was pressed firmly against the cathode. The schematic diagram of the apparatus is sketched in Figure 3.6. With the cell assembled and the ZERO control fully anti-clockwise, the RANGE switch was set at 100, and the instrument switched on. As the nitrogen gas is introduced to the cell, the meter reading will finally stabilize; and zero adjustment is made. The gas is then changed to oxygen; a meter reading was made when a new steady state was established. The meter reading is the chosen RANGE (which selected the instrument sensitivity) times the number on the meter scale. The results of (meter reading x thickness) were recorded by converting them to oxygen permeability P using a calibration graph, (Figure 3.7), using poly(4 methyl-pent-1-ene)(TPX) and polystyrene (PS) as extremes of the standard. Unfortunately, no suitable material was available to give values about the mid-point between these two standards. A film of poly (4 methyl-pent-1-ene) was used to check the reproducibility of the instrument during the course of work.

In Schema Versatae, the gas permeability coefficient measured is the

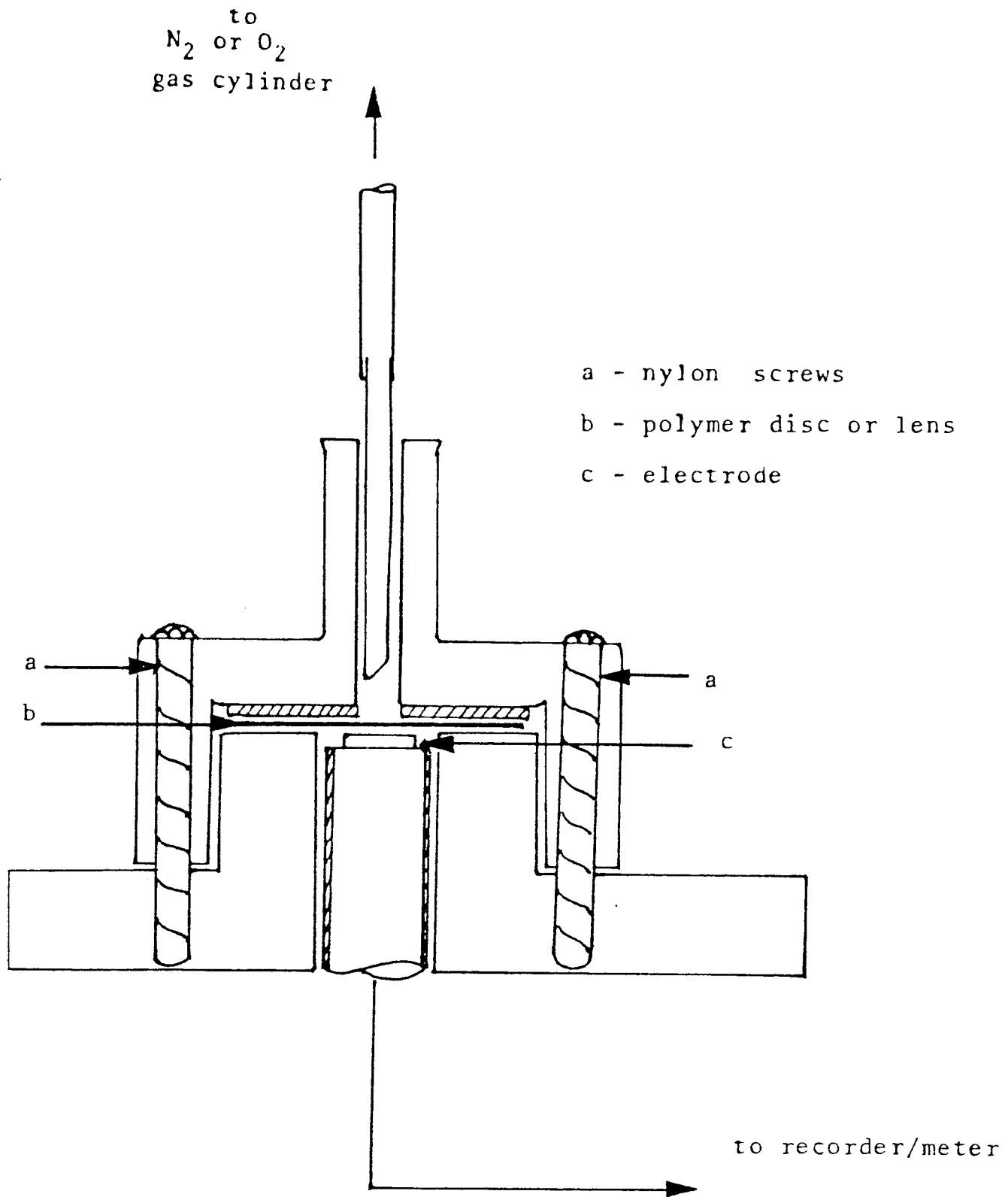


Figure 3.6 Oxygen permeability cell

"dissolved" oxygen permeability (P_d), where the permeability through the membrane from one aqueous phase to another aqueous phase is measured. This is analogous to the situation where a contact lens is covered at its anterior and posterior surface by tear fluid.

3.4 (3) Surface Characterisation

The wetting of a contact lens by tear fluid is of primary importance for the physiological compatibility of the lens and the eye. There are several surface characterisation techniques available to assess their compatibility. In this work, contact angle measurement using a sessile drop technique was chosen due to its ease of handling and reproducibility when enough care is taken. The contact angle (θ) can be obtained in a number of ways, through visual observations of liquid drops or by several indirect methods. A profile of a sessile drop on a lens surface is shown in Figure 3.8. The drop profile, here, is observed through a cathetometer with a goniometer eyepiece and contact angles are thus obtained directly. An alternative procedure involves projection of an enlarged image of the drop on a screen and measuring the contact angle with a protractor (113, 114). This sessile drop method only requires very small quantities of the liquid on small samples, and is fairly easy to manipulate with reasonable reproducibility, provided care is taken to achieve the same drop size and the same experimental conditions. Prior to the measurement, the polymer surfaces were cleaned with a surfactant such as a sterile commercial contact lens cleaner, followed by a thorough rinsing with distilled water until any residuals and dirt had been washed off. Then the samples were dried by gently blotting with clean filter paper and mounted on a clean microscope slide. A small drop of a liquid was carefully placed on the surface using a clean hypodermic syringe and the contact angle was measured directly through

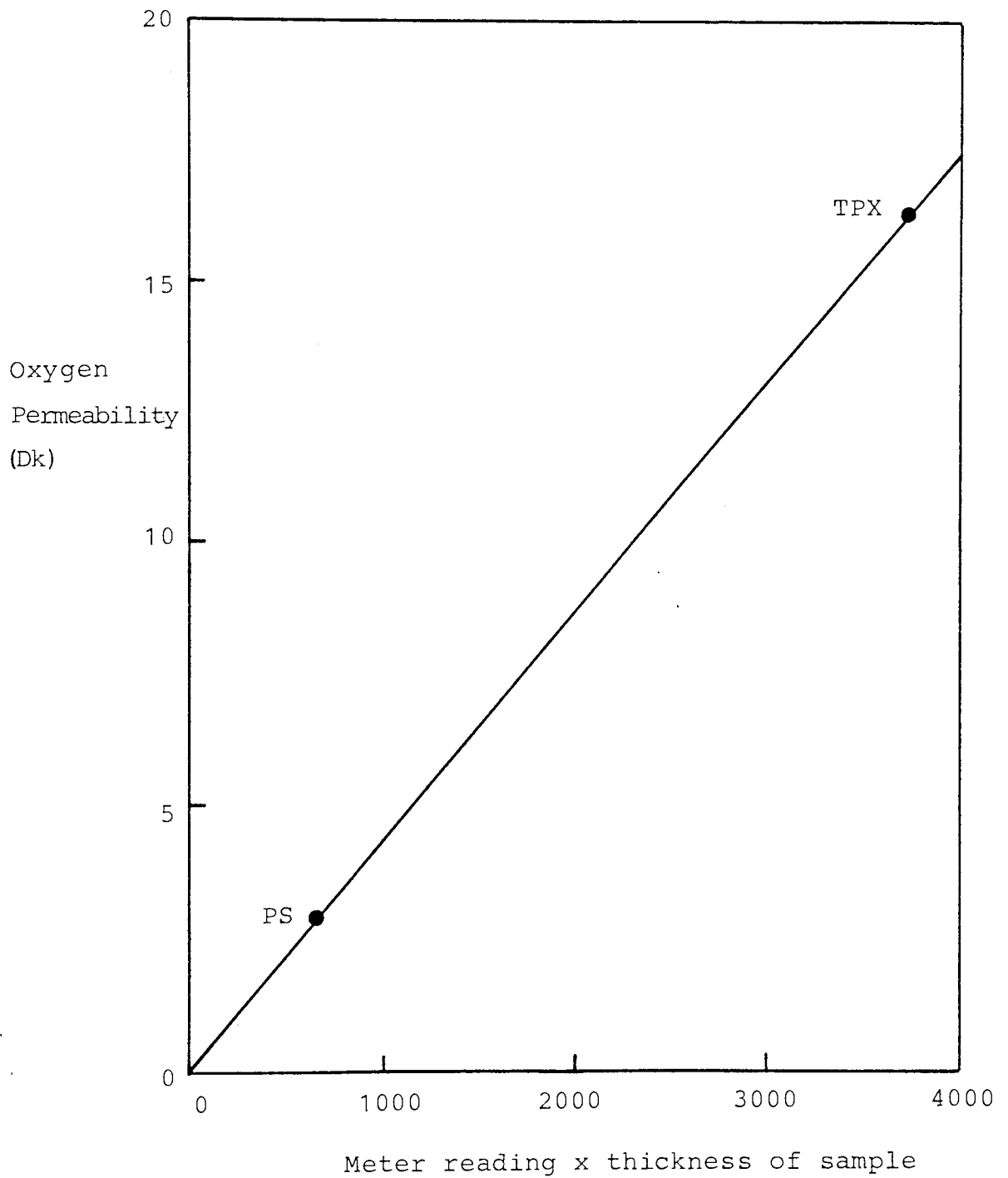


Figure 3.7

Calibration graph of oxygen permeability ($\times 10^{-11}$, ccO_2 (STP) $\text{cm}/\text{cm}^2 \text{sec. mmHg}$) for polymers using Schema Versatae flux meter.

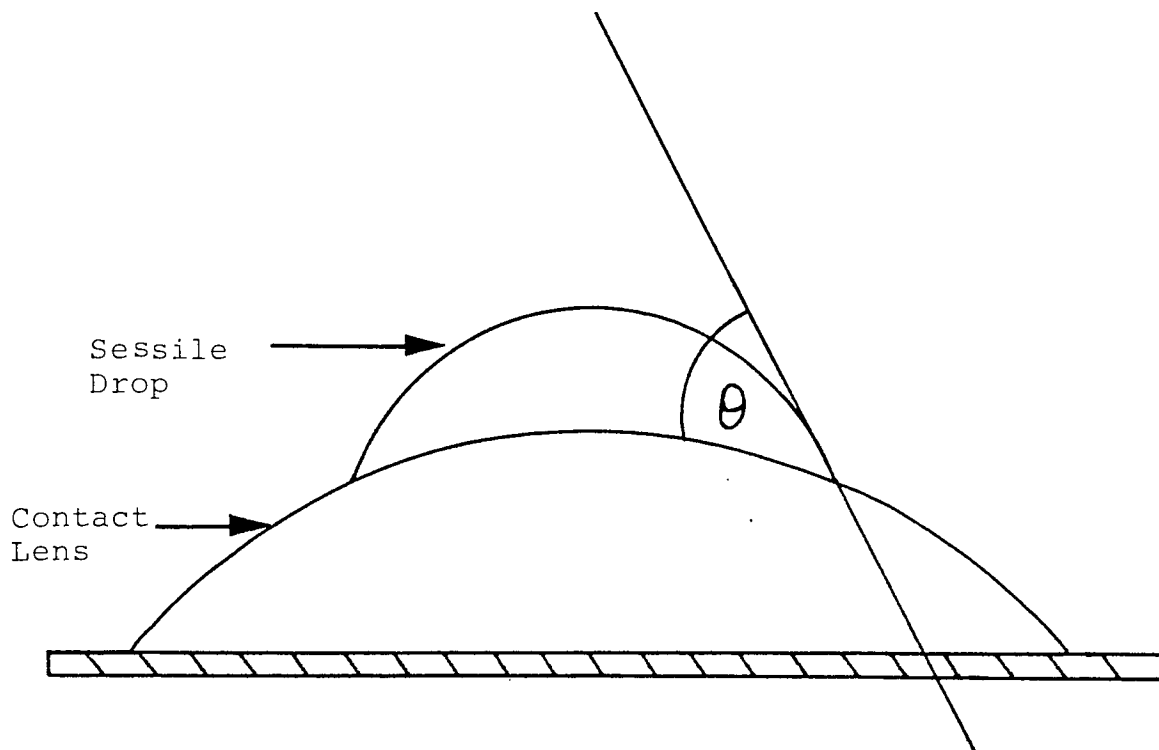


Figure 3.8 Profile of a sessile drop on a contact lens surface showing the contact angle (θ)

the liquid at the point of contact with the solid. At least six measurements were taken on each surface, each reading being the average of the contact angle on either side of the sessile drop. The contact angles of distilled water and methylene iodide (or diiodomethane CH_2I_2) were measured for each material surface to determine the surface free energy of the sample. The measurements were taken initially of dry clean material surfaces, then the effect of soaking on these surfaces was determined by observing the contact angles of the sample after soaking in commercial solutions. In the 'wet' contact angle measurements, after the soaking, the lens surfaces were blotted by filter paper to remove excess fluid, then the same procedure was taken to find the contact angle. The principles behind the surface wettability of polymer materials are discussed in more detail in Chapter 4.

3.4 (4) Mechanical Testing

The requirement of the mechanical properties appropriate to both hard polymers and soft hydrogels are difficult to define, however the most relevant areas of mechanical performance of these materials lie in the fabrication stage and during handling. The study of mechanical behaviour in these respects can conveniently be obtained from carefully controlled tensile and compression testing.

3.4 (4.1) Tensile Testing

In the tensile test, a polymer sample is stretched by applied tensile stress. The resultant stress-strain relationship provides some information in terms of tensile strength, elastic modulus and % elongation at break of the sample. In this work, an Instron tensometer was used operating at room temperature ($20^\circ - 25^\circ\text{C}$). There are two

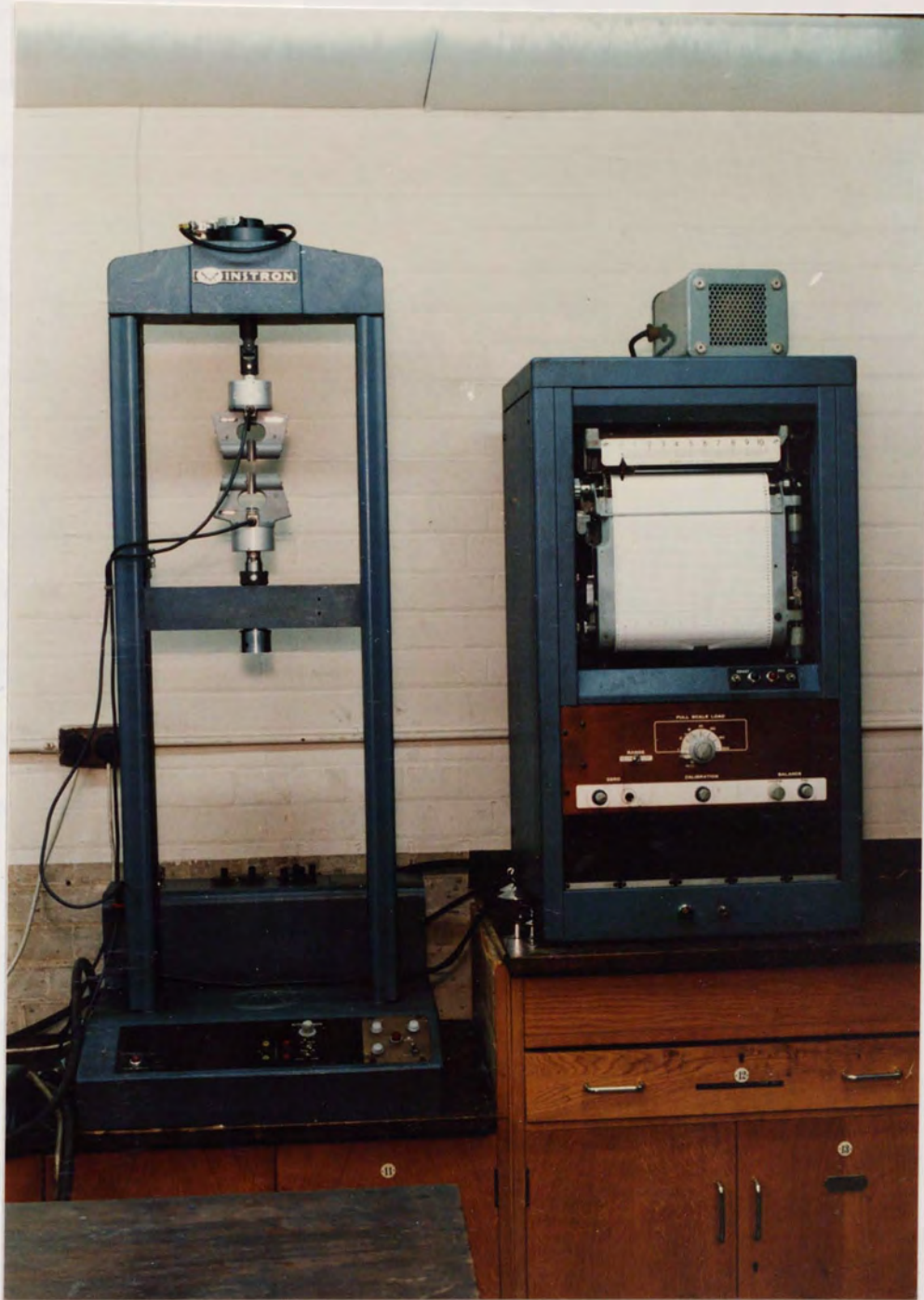


Figure 3.9 The set-up of tensile apparatus and a chart recorder

features on the tensometer; the tensile apparatus and a chart recorder (Figure 3.9). A small load cell i.e. range 100g to 2kg was used in this work. The cross-head speed of the jaw separation and the chart speed of the recorder were determined by 'trial and error' until a suitable speed ratio of 1:25 was determined.

The sample to be tested is clamped in the jaws by means of hydropneumatic pressure supplied from an air cylinder. For hard contact lens materials, pressure is in the range of 50 - 80 psi; for soft hydrogels 5 - 20 psi is adequate. This pressure was adjusted depending on the grip of the jaws on the sample i.e. if during the course of an experiment, a specimen was observed to be slipping from the jaws, the pressure was increased until a firm grip was achieved. After the primary setting, the apparatus is calibrated using different weight loads. Test specimens were made by dividing a hard contact lens into halves by splitting at the centre. The thickness of the sample at the edge and centre was measured using a Nissel thickness gauge. Width measurement was made using a similar technique; these two dimensions are required to calculate the cross-sectional area of the sample. As the sample is so small in size, the gauge length was decided to be 1mm, to minimise any errors. The chart recorder plots the force of tension against the elongation of the specimen; from the plot of each specimen, % elongation at break, tensile strength, and maximum load at break were determined.

If the original specimen had length l_0 and a cross-sectional area A ; a tensile force F increases the length of the specimen by an increase of Δl to give a stretched length of l . Then, for a material obeying Hooke's law, Young's Modulus E is defined as the ratio of stress to strain (both in tensile) or

$$E = \frac{\text{tensile stress } \sigma}{\text{tensile strain } \epsilon}$$

where

tensile stress = force per unit area

$$\sigma = F/A$$

and

tensile strain = change per unit length

$$\epsilon = \frac{\Delta l}{l_0} = \frac{(l - l_0)}{l_0}$$

Young's modulus (E) may be calculated from the slope of the initial straight line portion of the stress-strain curve. The broad objective in the use of tensile testing relevant to the contact lens application was to make use of it as a means of statistical evaluation. The tensile stress-strain plot can be related to the fracture profile of the polymer sample and is useful for a quick quality control of the technique and the sample material.

3.4.(4.2) Compression Testing

A modified ICI Pneumatic Microindentation Hardness Apparatus was used to study the deformation and recovery characteristics of the materials under constant load and to determine their rigidity modulus under compression. The instrument allows the indentation of any small test sample in a form of a thin film or coating, by a small sphere under a small constant load to be measured as a function of time. The recovery subsequent to load removal can also be recorded.

The ICI Pneumatic Microindentation Hardness Apparatus was originally developed in the paints industry to correlate deformation properties of surface coatings (such as paint films) with their ageing properties. Ng in his work modified this basic instrument to study the deformational properties of contact lens materials and the details

of his work can be found in his thesis and in published papers (115, 116). The apparatus is shown in Figure 3.10. The descriptions of the construction of this Microindentation apparatus are beyond the scope of this project; they can be found in the original article of Monk and Wright,⁽¹¹⁷⁾ as well as in Ng's thesis⁽¹¹⁵⁾ in which he also describes the modification adopted in measuring the response of contact lens materials under eye-lid load.

The measurement of deformation on the test sample under varying loads is carried out using a pneumatic method. The principle is that the primary displacement of the indenter probe caused by the deformation of the test sample under the load, alters the gap between a flapper and a small nozzle fed with a restricted air supply. The changes in pressure resulting from these movements are amplified and applied to a pneumatic recorder.

Calibration and Testing Procedure

The ICI Microindentation Apparatus is provided with various loads and indentors, and was originally set up to give a full scale deflection of 6 μm on the recorder. For the purpose of this work only the 1/16" spherical indenter was used together with a range of loads (in studying the deformational behaviour of materials under eye-lid pressure ($\sim 2.6 \times 10^3 \text{ Nm}^{-2}$) a flat ended indenter (0.063cm radius) and a weight of 0.34g was used). The calibration was carried out as suggested in the instruction manual using the specimen stage as a base. The sensitivity of the instrument was pre-set and the counter-balance was adjusted until a full scale deflection (about 9 μm on the strip chart) was obtained on the recorder. A load (e.g. 16g) was placed on the hook of the weight-lowering bellows and lowered on to the beam by switching the programmer to "TEST LOAD". The fine adjusting wheel was set at zero; the coarse adjusting wheel

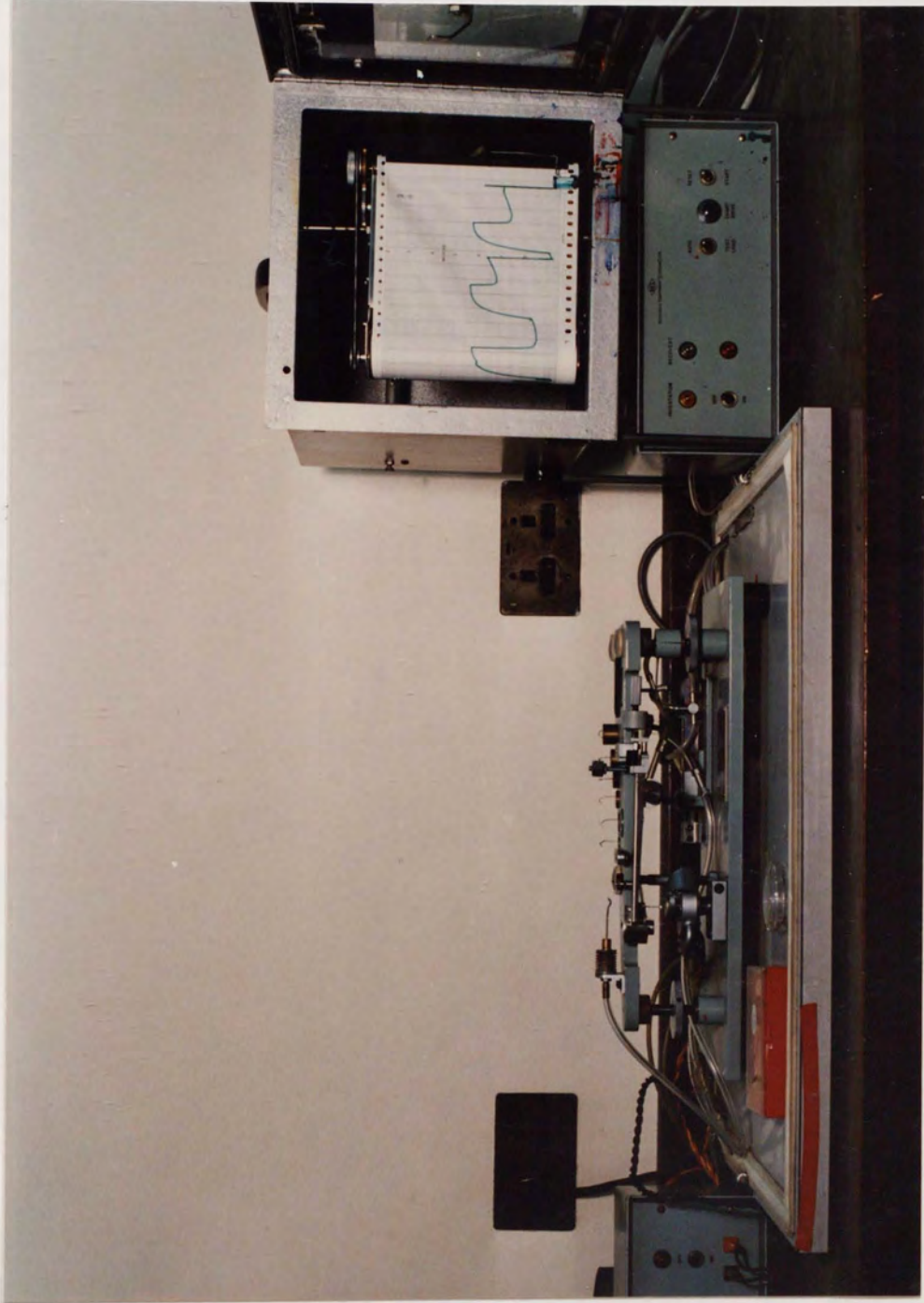


Figure 3.10 The ICI Pneumatic Microindentation Hardness Apparatus

was rotated clockwise to lower the top plate until the indenter probe touched the sample stage and the recorder indicated zero on the chart. The fine adjusting wheel was then rotated in an anti-clockwise direction at every interval of 1/2 micron, and the corresponding half micron reading on the recorder chart was taken. A calibration curve was then constructed. After the calibration, the fine adjusting wheel was returned to zero and the "TEST LOAD" was switched off. The indenter probe was raised by locking the adjusting knob. A test sample of known thickness (pre-determined using a Nissel thickness gauge) was placed on the sample stage and secured with the clip. Different mounting procedures have been devised in the work from time to time. Examples are to be found in the work of Ng and Middleton (115,118). The indentation and recovery curves for each material at a given load were recorded automatically at the time scale of 1 minute each. For each sample, three or four points on the specimen were tested for each set of deformation measurements, and an average depth of indentation in microns on the test specimen under a given load was calculated. The experiment was normally carried out at room temperature, although the temperature controlled sample stage of the instrument allowed work to be carried out between -50°C to 90°C. The principles of this technique in studying and evaluating the compression behaviour of a given polymer is related in the Hertz equation,

$$\frac{E}{1-\nu^2} = \frac{3}{4} \frac{mg}{r^{1/2}h^n}$$

where E = Young's modulus of elasticity

m = load in (g)

ν = Poisson's ratio

g = gravity

r = radius of indenter

h = depth of indentation (in μm)

A plot of $\log(m)$ against $\log(h)$ gives the slope n in the above equation.

(For a perfectly elastic material, n is $3/2$). Again the technique was employed primarily to compare the trend in behaviour of the polymers selected in this study to the compressive mode of stress, rather than to provide any definitive values.

CHAPTER IV

POLYMER PROPERTIES AND CONTACT LENS PERFORMANCE

In the context of biomedical research, it is appropriate to emphasise the fact that contact lenses represent an excellent example of the biomedical application of polymers. The problems encountered in applications such as hip and finger joints, kidney dialysis membranes, heart valve components and contact lenses (particularly in extended wear) are in many respects similar. Thus questions of mechanical properties (strength and stiffness), compatibility and in some cases permeability, frequently arise. Similarly, it is relevant to point out that in many respects the contact lens field has produced pioneer work of subsequent benefit in the broader biomedical field. This is particularly true of hydrogel polymers. A much more extensive range of these materials has been used in contact lenses than in other applications, which for some time utilised only polyHEMA, and this experience in the field of contact lenses has led to an increase in availability of hydrogels for other uses.

Although it is now well established that oxygen permeability, together with surface and mechanical properties constitute an important group of parameters in this, as in several other applications, further questions arise. These centre around the fact that each of these "properties" may subsume several aspects of the behavioural characteristics of polymers together with the problem of defining limits or ranges of 'in vitro' property measurements that correspond to acceptable 'in vivo' behaviour.

In Chapter 2, the development of rigid gas permeable contact lens materials as reflected in the growing number of specifications in the patent literature was reviewed. Although improved oxygen permeability was a key feature of the claims for improved performance, both surface and mechanical properties were described. In the same chapter, a range of commercially available contact lens materials was listed together with manufacturer's claims for the properties of the materials in comparison with those obtained in independent laboratories. In this chapter, comments on the measurement of properties that are believed to be relevant to both clinical performance and manufacture of rigid gas permeable contact lenses are made pointing out, where appropriate, such problems as irreproducibility and lack of standardisation.

4.2. OXYGEN PERMEABILITY

This is arguably the most important single property of this group of materials, since it was a desire to achieve an improvement in the permeability of PMMA that led to their development. Because PMMA has an extremely low permeability to oxygen, whereas the cornea has a continual requirement for oxygen, effective clinical use of this material requires a fitting technique that allows sufficient oxygen to pass under the lens. This so called 'tear pump' mechanism is achieved by fitting the lens slightly flatter than the cornea, thus causing it to 'rock' on the eye as a result of eyelid movement. Since in many cases, this tear pump mechanism is inadequate on its own, to supply the oxygen demand of the cornea, oxygen deprivation, resulting in a degree of corneal oedema, is not uncommon with PMMA lenses.

The initial requirement, therefore was for materials with sufficiently greater permeability than PMMA to allow part of the oxygen demand of the cornea to be met by direct passage of oxygen through the lens. This raises two questions. What level of oxygen permeability would be required to satisfy the cornea's demand for oxygen, and how can the permeability of the materials be reliably measured in a manner that reflects their use in the eye? The oxygen requirement of the cornea has been expressed in various ways, including a direct figure for oxygen consumption and, alternatively, the minimum partial pressure of oxygen required to maintain normal corneal metabolism. It must be pointed out that such quantities are impossible to measure in such a manner that the techniques used give unambiguous answers and do not influence corneal behaviour. Thus, the value widely accepted for many years as the minimum partial pressure of oxygen required to prevent corneal oedema (11-19 mm Hg (8)) has been progressively updated to 23-37 mm Hg (9), 40 mm Hg (10) and even 74 mm Hg (11). Since the work on which the latter figure is based also interpreted as showing an exponential decline in corneal thickness, and since the error bars on the relevant measurements that is used to demonstrate the requirement as 74 mm Hg, are equivalent to a partial pressure change of 60 mm Hg, the difficulty in obtaining an absolute correlation can be appreciated. These comments are not intended as a

criticism of the excellent work and contributions to scientific knowledge of the groups involved, but rather an indication of the problems in this difficult field. Before this information can be translated into a property requirement for contact lens materials, some consideration of the principles and definitions involved in oxygen permeability is required.

4.2.(1) Definitions of Oxygen Permeability

The important fundamental texts (119-122) in modern membrane science are agreed upon the use of the simple fundamental definition:

$$P = DS \quad (1)$$

for the transport of the gas through a polymer membrane. In this expression, P is the permeability coefficient for a given polymer-permeant (i.e. gas) system, D is the diffusion coefficient of the gas through the polymer, and S is the solubility in the polymer. In order to correlate the permeability coefficient (P) with the rate at which the gas passes through a membrane of given dimensions (area and thickness) for a given gas pressure, the equation:

$$j = \frac{PA}{L} \Delta P \quad (2)$$

is used. Here j is the flux of the gas (volume passing through in unit time), A is the membrane area, L is the membrane thickness, and ΔP is the pressure difference across the membrane. The flux j is sometimes expressed by the symbol Q, or its components

$\frac{V}{t}$ (volume per unit time). Since the oxygen passing through the contact lens is

consumed by the cornea, it is apparent that in principle, it should be possible to balance this consumption requirement with the oxygen flux through a contact lens of given dimensions and given conditions, and to define the required lens behaviour in terms of a permeability P. Amongst the people who have carried out this sort of analysis, Fatt's work (123) appears to have had the greatest long term influence. He re-presented

equations (1) and (2) as:

$$j = \frac{Dk}{L} (P_L - P_O) \quad (3)$$

as part of an analysis of contact lens behaviour, where P_L is defined as the oxygen pressure at the front surface of the lens, and P_O as the oxygen pressure behind the lens (i.e. at the corneal surface). It is apparent that P_O should correlate with the minimum oxygen tension for normal corneal function. Unfortunately, Fatt chose to use k to represent gas solubility instead of the more usual term S (equation (1)). For this reason, the contact lens literature favours the use of the term Dk whereas in membrane science, DS or more commonly P (equation (1)) is used. Thus Dk (or more simply P) is the permeability coefficient for a given material, whereas $\frac{P}{L}$ or $\frac{Dk}{L}$ refers specifically to the permeability of a sample of that material of a given thickness (such as a contact lens). The values of the permeability coefficient are frequently different when, on one hand, the membrane separates two gas phases and, on the other, when the membrane separates two liquid phases. The difference between these values, referred to as P_g and P_d respectively, is associated with the so-called 'barrier effect' and will now be discussed.

4.2.(2) Techniques to Measure Oxygen Permeability

The different experimental procedures for determining oxygen permeability are schematically shown in Figure 4.1. In each case, oxygen at a known concentration passes from the donor side of the cell through the membrane (of known thickness and cross-sectional area) to a receiver side, also of known volume, where it is sensed. In Figure 4.1a, which is a gas/gas transport system, the donor side is initially at a positive pressure with respect to the initially evacuated receiver side. The increase in pressure of the receiver side is monitored (usually manometrically) and the rate of transport of oxygen, and thus the permeability coefficient for the membrane, may be calculated. In Figure 4.1b, a liquid/liquid cell is shown. The cell is stirred on both sides

of the membrane, the concentration on the donor side is initially set at some positive level relative to the receiver side. The increase in concentration on the receiver side is monitored and since the volume of liquid on the receiver side is known, the permeability coefficient is again calculated. The difference between 4.1a and 4.1b is, of course, that 4.1a leads to the gaseous permeability coefficient P_g , whilst 4.1b leads to the dissolved oxygen permeability coefficient P_d . Since the sensitivity and accuracy of the measurement system used on the receiver side deteriorates as the receiver volume increases, attempts are made to minimise this. As a result, systems of the type shown in Figure 4.1c may advantageously be used in which the donor side is stirred and the receiver side is of minimal volume and contains a built-in detector.

It has been shown to be particularly important to stir the high concentration side of the membrane in order to minimise surface layer effects. Studies have shown that although failure to stir the low concentration side of the membrane produces a drop of only some 3% in the measured transport properties of the membrane, this figure increases to a minimum of 10%, together with a great deal of irreproducibility, if the high concentration side is not stirred (124, 125).

Thus, the least satisfactory, but in many ways most convenient system, is shown in Figure 4.1d. This is the basis of commercial systems frequently used to measure the permeability coefficient (expressed as Dk , see above) of contact lenses. The system has several shortcomings. Firstly, the donor side is unstirred, secondly the thickness of the contact lens normally shows a centre-to-edge variation, and thirdly, because the lenses vary in curvature, the volume of the receiver side is not fixed. In practice, this last point should be less important in this system, since the technique is not usually operated in the manner that measures rate of increase in oxygen concentration on the receiver side of the cell, but rather the resultant equilibrium oxygen consumption by the electrode. The ability to do this relies on the assumption that oxygen transported to the receiver side is efficiently consumed by the electrode sensor, and that, as a result, the partial pressure of oxygen on the receiver side is always effectively zero. With very permeable samples however, these assumptions are not justified. In all cell

configurations, it is important to have an oxygen-tight seal of the membrane in the cell, but this again is more difficult to achieve with the format and samples involved in the type 4.1d devices.

The nature of the barrier effect and its experimental isolation was first effectively described by Hwang and Kammermeyer (126). The past workers in these laboratories have (109, 127) pointed out its relevance to contact lens materials many years ago, a point which has subsequently been repeated by several workers (128, 129, 130). When measurements are made in the gas phase, oxygen dissolves directly in the polymer at the membrane-gas interface and the permeability coefficients show no dependence on thickness. When measurements are made in the condensed liquid phase, oxygen dissolved in this phase is hampered in its subsequent dissolution in the membrane by the presence of a structured water layer at the aqueous interface with the polymer membrane. The presence of a stagnant boundary layer in unstirred systems is well known, but the barrier effect described here is observed even when the liquid is agitated. As a result, when polymer membranes of progressively decreasing thickness are used, the relative contribution of this barrier becomes greater, a point illustrated by plotting inverse of the apparent permeability coefficient against inverse of the thickness. Extrapolating to infinite thickness ($1/L \rightarrow 0$) produces permeability coefficients similar to those obtained in the gas phase. This is shown in Figure 4.2, in which increased slope corresponds with increased barrier effect, and zero slope implies the absence of such effect (as in gas/gas measurements). The major consequence of this effect for rigid gas permeable contact lens materials is a function of the fact that improved oxygen permeability has only been achieved at the expense of some sacrifice in wetting properties. As a result, attempts to improve transport properties of a contact lens by reducing centre thickness are, with these materials faced with the law of diminishing returns. This is illustrated in Figure 4.3, in which oxygen flux (i.e. $\frac{Dk}{L}$, see equation (3)) is plotted against $1/L$ (i.e. decrease in thickness). It is therefore, apparent that the true value of $\frac{Dk}{L}$, may not be obtained simply by dividing Dk by thickness for materials

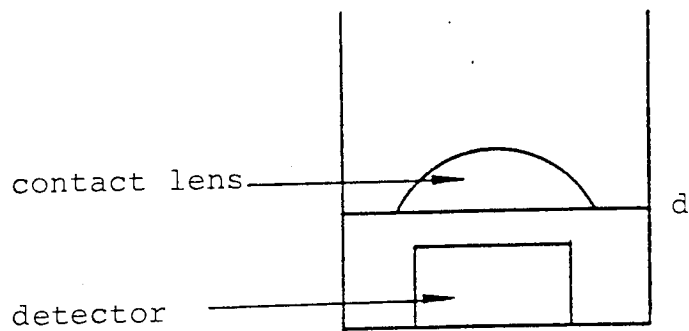
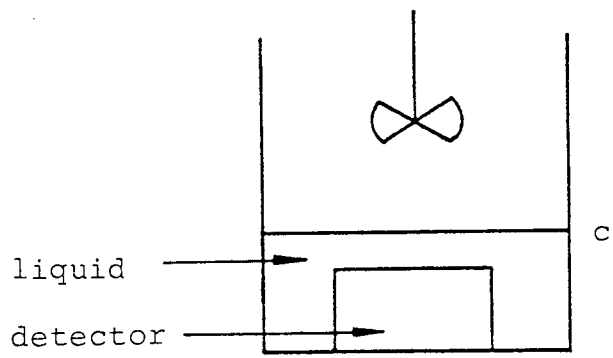
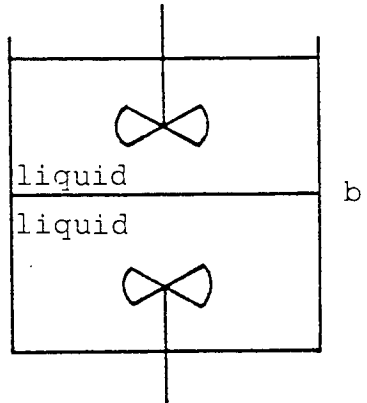
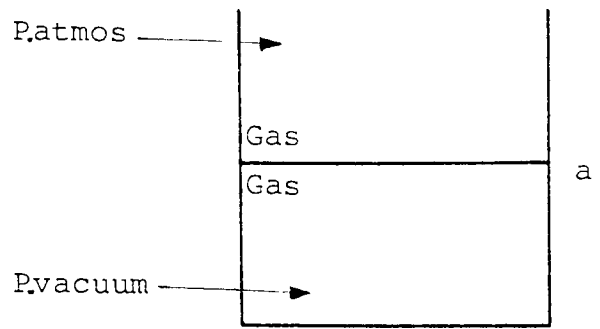


Figure 4.1 Schematic presentation of some experimental techniques for determining oxygen permeability

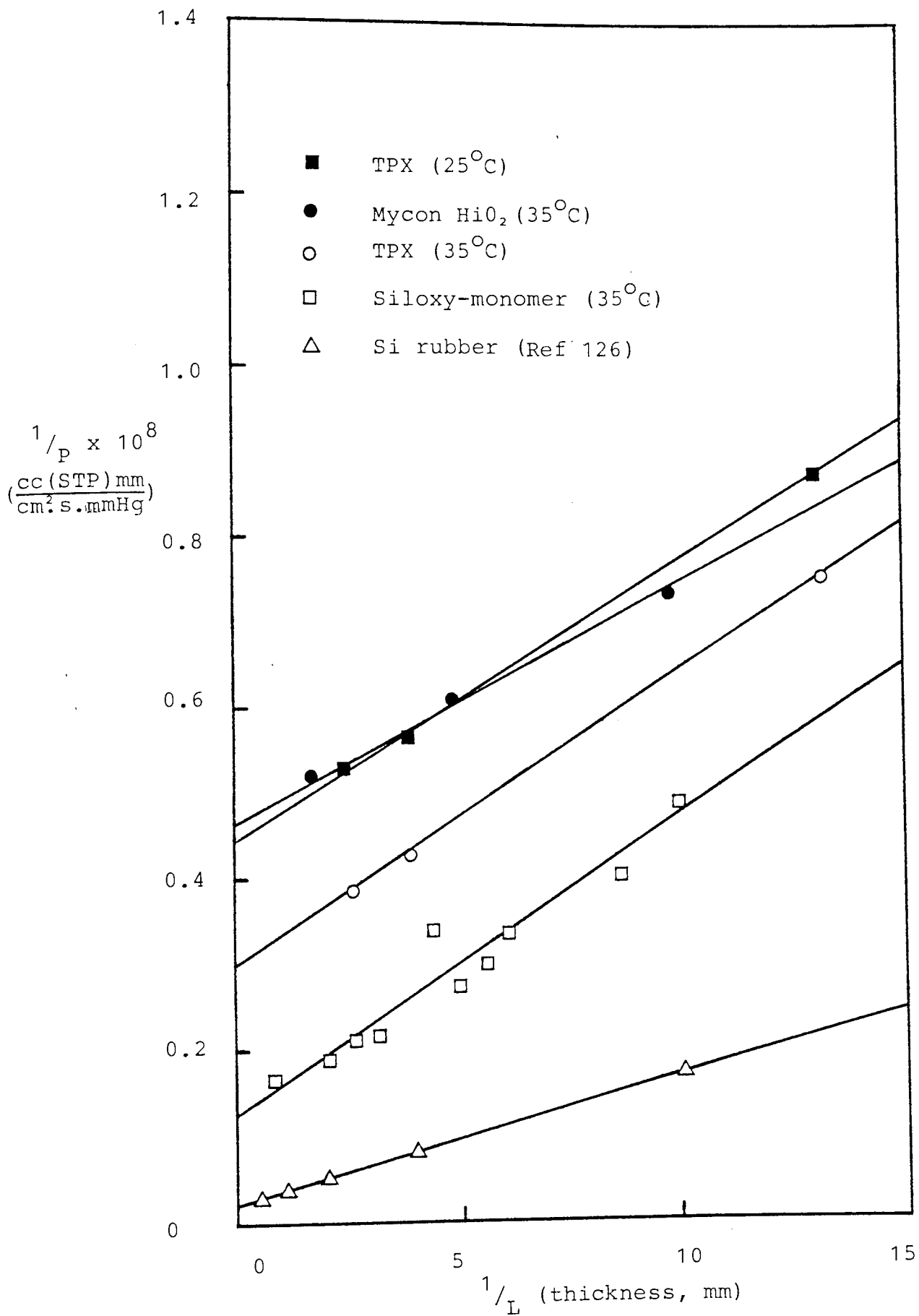


Figure 4.2 Plot of inverse the apparent permeability coefficient against inverse of thickness

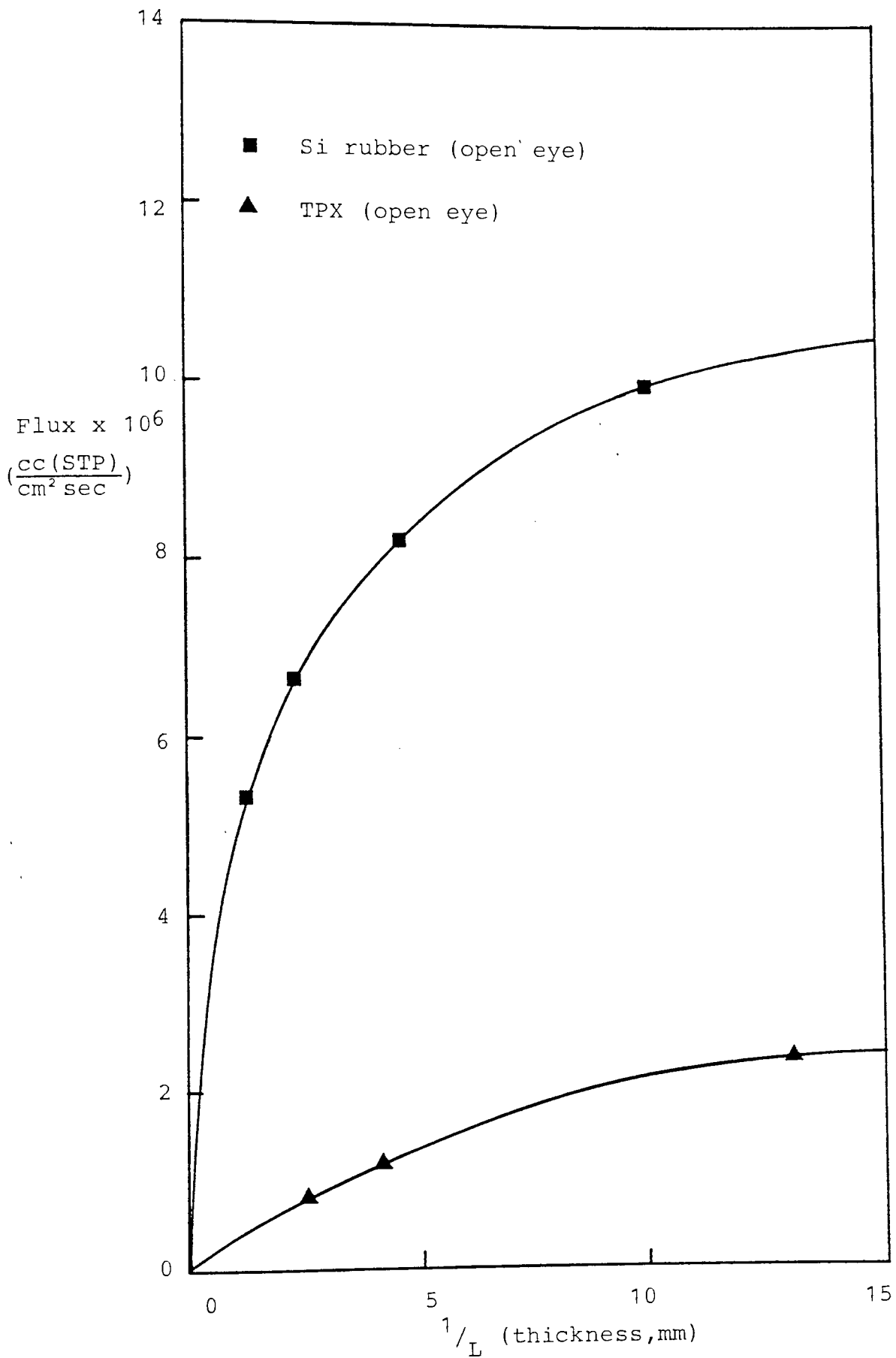


Figure 4.3 Oxygen flux against decrease in thickness

with an appreciable barrier effect (which includes most non-hydrogels).

4.2.(3) Comparisons of Oxygen Permeability Data

Having considered some of the principles and pitfalls of measurements of oxygen permeability in contact lens materials, it is appropriate to compare measurements that were made in this work with those of other workers and those published by manufacturers. A selection of these is contained in Table 4.1, together with two other useful experimental quantities (where these are available). The first of these is the "silicone rubber equivalent" which is the silicon content expressed as the (hypothetical) percentage of silicone rubber in the material to which this would be equivalent. The second is the ratio of permeability at 35°C to that of 20°C (P_{35}/P_{20}). For materials as structurally similar as these siloxymethacrylate copolymers, the energies of the activation for the transport process should be very similar, as should the ratios of P_{35}/P_{20} .

The "equivalent" silicone rubber content has been obtained by elemental analysis and conversion of the result of this to the poly(dimethyl siloxane) repeat units. The interesting feature here is the large number of materials whose silicone rubber equivalent is in the region of 20-25%. These are what might be regarded as "first generation" siloxymethacrylate polymers with oxygen permeabilities (measured at 20°C)

lying in the region of 7 to 10 Dk units i.e. $\times 10^{-11} \frac{\text{cc O}_2 \text{ (STP) cm.}}{\text{cm}^2 \text{ sec. mm Hg}}$. The

competitive demand for increased oxygen permeability is reflected in the review of the patent literature related to those materials. In the siloxymethacrylate based polymers, increased oxygen permeability has frequently been achieved by one or both of the two strategies. The first is to increase the siloxymethacrylate content of the materials (with concurrent increase in crosslink density and added hydrophilic monomer to minimise deterioration in wettability and mechanical properties). The second is the use of siloxymethacrylates with larger, longer and more branched siloxanyl substituents. Neither approach is without some disadvantage in terms of mechanical and surface

TABLE 4.1 TABLE OF OXYGEN PERMEABILITY FOR VARIOUS CONTACT LENS MATERIALS

Name of Material & Manufacturer	Polymer Type	Si rubber equivalent %	DK x 10 ⁻¹¹ ($\frac{\text{cc O}_2 (\text{STP}) \text{ cm}}{\text{cm}^2 \text{ sec. mmHg}}$)	Ratio
			20°C 35°C	P35°C P20°C
PMMA	Methyl methacrylate	0	0.1(a)	
CAB	Cellulose acetate butyrate	0	12(a)	
Silicone rubber	Dimethyl siloxane	100	350	
TPX	4-methyl pent-1-ene	0	20(a)	
Alberta XL30 (Calgary)	Siloxymethacrylate	25	12.8(a) 8.73(c)	
Boston I)) (Poly-Tech.) Boston IV)	Siloxymethacrylate	26	10.1(a) 7.9(b) 11.1(e)	(d/a) (d/b) (d/c) 1.188/1.519/1.081
Fluorofacon A (3M)	Siloxymethacrylate	35	14(a) 26.3(c)	
Hyperm (Hydron Europe)	Perfluoroether		70+(c)	1.286(d/c)
London (Contact Lens Mfg)	Siloxymethacrylate	21	12.2(a)	1.148(d/c)
Lamda X (Polymer Labs)	Siloxymethacrylate	26	8.5(a)	
Optacryl 60 (Optacryl)	Siloxymethacrylate	27	3(a)	
		21	9.1(a) 7.4(b) 6.9(e)	10.8(b) 12(d)

continued overleaf

TABLE 4.1 - continued

Name of Material & Manufacturer	Polymer Type	Si rubber equivalent %	DK x 10 ⁻¹¹ (cc O ₂ (STP) cm ⁻¹) cm ² sec. mmHg	Ratio P35°C P200°C
			20°C 35°C	
Oxyflex (Polymer Labs)	Siloxymethacrylate	10	7.2(a) 10.5(d)	1.458(d/a)
Oxyflow (Contact Lens Supp)	Siloxymethacrylate		20.1(a)	
Oxford (Contact Lens Mfg)	Siloxymethacrylate	22.5	5.5(a)	
Paraperm O ₂ (Paraperm)	Siloxymethacrylate		7.9(b) 12.2(c) 12.9(b) 15(d)	1.633(b) 1.229(d/c) (d/a) (d/b) (d/c)
Polycon I)) (Syntex)		19	6.5(a) 3.1(b) 5(c)	0.092/1.452/0.9
Polycon II)			6.5(b)	1.354(b/d)/1.846(d/b)
Silcon (Dow Corning)	Silicone		12(b, c)	1.792(b/b)
SM-38 (Contact Lens Co Calgary)			9.2(a) 12-14(d)	1.413(d/a)

Footnote

a) Results from Aston at 20°C, b) Results from Fitzgerald at 20°C c) Manufacturer's results at 20°C d) Manufacturer's results at 35°C e) Other

properties. A series of other strategies is described in patent literature including, principally, the incorporation of fluorine into the polymers.

The lack of uniformity and reliability amongst measured and quoted oxygen permeability is reflected in the deviations from the 'normal' or predicted values of P_{35}/P_{20} (the ratio of permeabilities at 35°C and 20°C). One source of deviation obviously arises from genuine experimental disagreement between workers. The fact that few values presented by manufacturers, or indeed in the scientific literature, were measured against internal standards (i.e. polymers of known structure and permeability), obviously limits the reliability of these figures. A more difficult problem, however, lies in the inherent variability of the material produced. Because of the nature of the polymerization reactions involved, it is common to find structural and compositional variation in different samples of materials from the same manufacturer. The underlying problem in this, and in other areas of contact lens technology is thus one of standardisation.

4.3. SURFACE PROPERTIES

It is clear that the transport of oxygen across the water-polymer interface is a factor of great importance in considering the oxygen permeability of materials in biological environments.

4.3.(1) Definitions of Surface Properties

A fundamental basis for understanding the nature of interfacial phenomena at a polymer surface is important, since these phenomena are related to various aspects of the compatibility of materials with the host environment.

The primary feature of importance in contact lenses is the necessity to maintain a coherent tear film at the lens surface (131). The underlying forces that interact at a solid/liquid interface are conveniently, and most commonly, considered in terms of contact angle, (Figure 4.4a). It was Thomas Young who first indicated that forces acting on the droplet, when it has reached equilibrium may be resolved and expressed by the

relationship:

$$\gamma_{sv} - \gamma_{sl} = \gamma_{lv} \cos\theta \quad (4)$$

where γ_{sv} is the free energy or surface tension at the interface of solid and vapour, γ_{sl} is the free energy or surface tension at the interface of solid and liquid, γ_{lv} is the free energy or surface tension at the interface of liquid and vapour, and θ is known as the contact angle (being the internal angle between the surface and the tangent to the droplet surface interface). This provides a basis for the quantitative description of wettability of the substrate, together with the spreading of a liquid on that substrate, and their relation to the contact angle. As θ diminishes and approaches zero, the liquid approaches the condition where it will spread on the surface. This condition is referred to as spontaneous wetting of the surface (in contrast to the situation where a mechanical force is used to induce spreading) and leads to the simplest relationship between the wettability of the surface and the ability of liquids of different surface tension to wet it. Figure 4.5 shows such a relationship, which illustrates the concept of "critical surface tension" of the substrate. Figures of this type are obtained by measuring the contact angle of a series of liquids of known surface tension (by direct observation with a travelling microscope equipped with a goniometer eyepiece, for example) on the substrate in question. The results are plotted in the form $\cos\theta$ (y axis) against surface tension of the wetting liquid (x axis), a function which is, in many cases, linear. This enables a line to be extrapolated on the graph to a point corresponding to spontaneous wetting i.e. $\cos\theta = 1$. The value of the surface tension obtained in this way, which would correspond to that of a liquid just able to spontaneously wet the substrate, is known as the critical surface tension of the substrate. Liquids having surface tensions equal to, or less than, the critical surface tension of a given substrate would be expected to wet or spread on that surface.

A rather more precise description of surface properties arises from the works of Fowkes (132) and his analysis of the interaction of forces of different kinds

across interfaces. Fundamental to this philosophy is the concept of the free energy of a surface. It is convenient to regard this as the equivalent of a solid or liquid surface tension, but being composed of two components. The first of these components is characteristic of the relatively non-polar background forces in molecules of the Van der Waals type, and is known as the dispersive component. The second originates principally from molecular dipoles and is known as the polar component. Thus for a liquid:

$$\gamma_l \text{ (Total)} = \gamma_l \text{ (Dispersive)} + \gamma_l \text{ (Polar)} \quad (5)$$

and for a solid:

$$\gamma_s \text{ (Total)} = \gamma_s \text{ (Dispersive)} + \gamma_s \text{ (Polar)} \quad (6)$$

The abbreviations γ_s^d , γ_s^p , γ_l^d and γ_l^p are normally used.

One very useful concept that arises from this treatment is that of interfacial tension between two liquids or between a liquid and a solid. The greater the interaction of forces of the same type across the interface, the lower will be the interfacial tension at that interface, and vice versa. For this reason, two liquids such as water and octane, which have very different balances of polar and dispersive forces, show little interaction at their interface and are thus immiscible. On the other hand, water and ethyl alcohol both have strong polar contributions which operate across an interface resulting in the miscibility of these two liquids. In the same way, the interfacial tension between a liquid and a solid is a measure of the interaction between these materials. Two important equations must be quoted, the first of these illustrates the way in which the operation of forces across the interfaces are calculated, the basis of which is the so-called geometric mean concept exploited by Fowkes. Thus, for a solid and a liquid, the interfacial tension is given by:

$$\gamma_{sl} = \gamma_s + \gamma_l - 2 (\gamma_s^d \gamma_l^d)^{1/2} - 2 (\gamma_s^p \gamma_l^p)^{1/2} \quad (7)$$

The second equation which was developed by Owens and Wendt (133) utilizes this principle in such a manner that measurements of contact angles of two different liquids enables the unknown polar and dispersive components of a given solid to be determined. This assumes that two liquids of known polar and dispersive components have been chosen. Owens and Wendt's expression in the general form is shown below:

$$1 + \cos\theta = \frac{2}{\gamma_l} [(\gamma_s^d \gamma_l^d)^{1/2} + (\gamma_s^p \gamma_l^p)^{1/2}] \quad (8)$$

re-arrangement enables two readily solved simultaneous equations to be generated and γ_s^d and γ_s^p thereby determined.

There are certain aspects of this theoretical consideration that produce problems in reproducible characterisation of polymer surfaces. Most of these are well recognised and compensated for by scientists working in this area, but unfortunately, as a result of inadequate standardisation, have led to misconceptions and the generation of inaccurate and ill-characterised data by contact lens manufacturers.

4.3.(2) Techniques to Measure Surface Properties

Some comments on the types of measurements that are made, the results that they yield, and the problems associated with their measurement and interpretation will illustrate this point. The most common method for measuring surface properties involves the use of a sessile droplet of liquid, introduced onto the surface of the material by a hypodermic syringe. The introduction and measurement are carried out in air, which means that the liquid will be in equilibrium with its vapour. This is essentially the condition described in Thomas Young's relation (equation (4)). Before considering the use that can be made of such information, some comments on factors that affect the form of the droplet and its contact angle on the material substrate are necessary.

In the first place, the liquid is responding to the surface forces in the polymer, emphasising that this leads to the measurement of surface properties. The liquid-solid interaction is thus greatly influenced by minute traces of surface impurities, such as are caused by accidental handling, and accumulated during storage. Careful

cleaning of the surface (using dilute surfactant followed by rigorous washing with pure water and careful drying under vacuum), is therefore essential. The techniques developed by Zisman (134) in his extensive work on surface energetics provide a sound basis, for studies of this type.

Secondly, there is normally a difference between a contact angle produced as a droplet advances over the surface, on being dispensed from the hypodermic syringe, and the contact angle made with the surface as the droplet recedes if it is drawn back into the syringe. These two angles, the so-called "advancing" and "receding" contact angles are often conceptually regarded as the advancing angle over a dry or unwetted surface and the receding angle as liquid withdraws over a previously wetted surface. The difference between them is referred to as contact angle hysteresis. Its magnitude is illustrated by the difference between Figure 4.4b and 4.4c. The measurement normally used, is referred to as the equilibrium advancing contact angle, and is taken immediately after the advancing droplet has been allowed to come to rest.

Other factors that can influence the experimentally determined contact angle are droplet size and surface roughness (or rugosity). These factors were again considered in detail by Zisman in his important early work (134). The rule of thumb with respect to droplet size is that it is important to be consistent and not to use too large a droplet, otherwise distortion of the idealised droplet shape occurs. The effect of rugosity is rather more complex, and is summarised by Wenzel's equation (135),

$$r = \frac{\cos\theta'}{\cos\theta}$$

where r is the surface roughness factor (the true area of the solid to the apparent area), θ' is the apparent or measured contact angle, and θ is the true contact angle. In essence, this means that a roughened surface will give a lower contact angle than on the smooth surface of the same material. This emphasises the necessity of ensuring that equally smooth surfaces are used when making comparisons between two surfaces. This can be quite difficult with fabricated articles such as contact lenses.

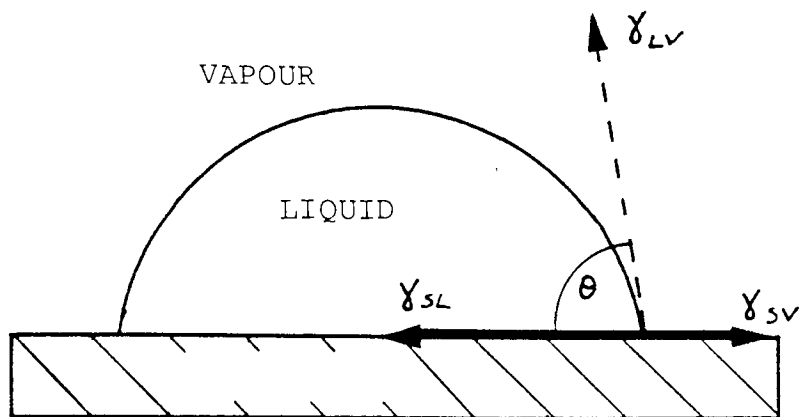


Figure 4.4a Profile of sessile drop resting on solid surface, exhibiting the equilibrium contact angle (θ).

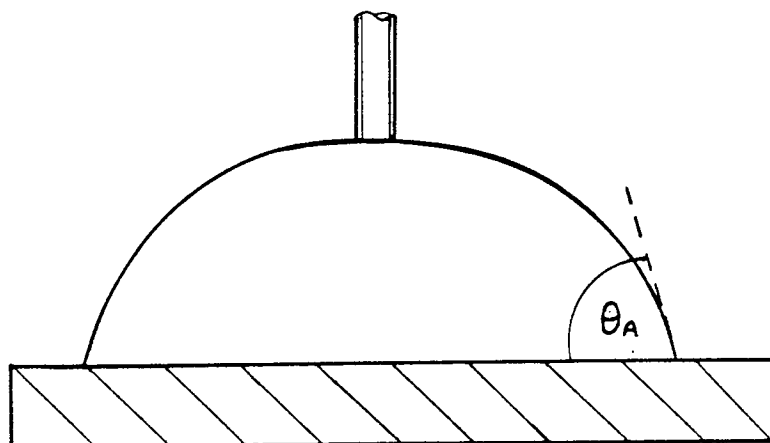


Figure 4.4b Projected image of water droplet on plane surface showing advancing contact angle (θ_A).

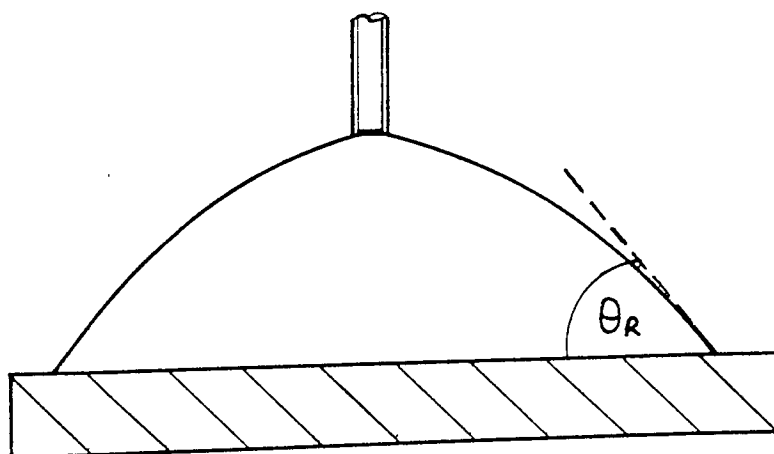


Figure 4.4c Projected image of water droplet on plane surface showing receding contact angle (θ_R).

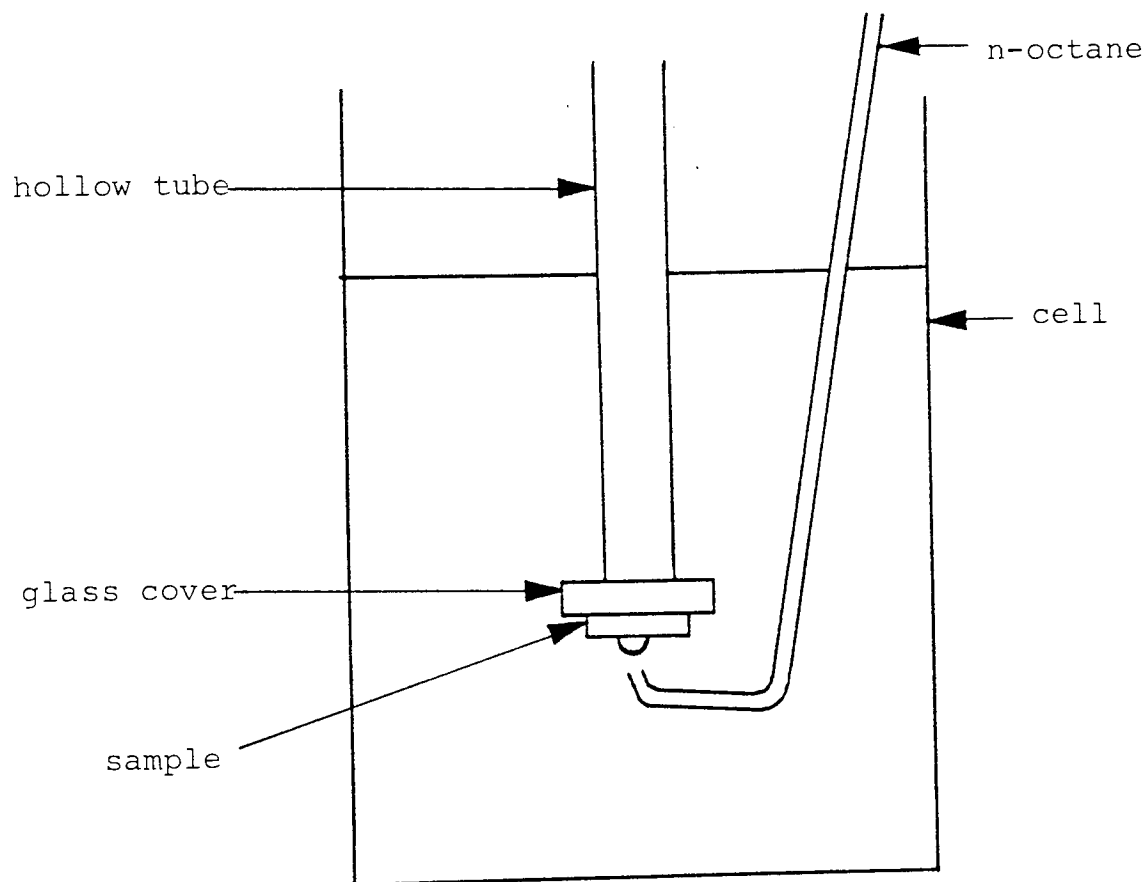
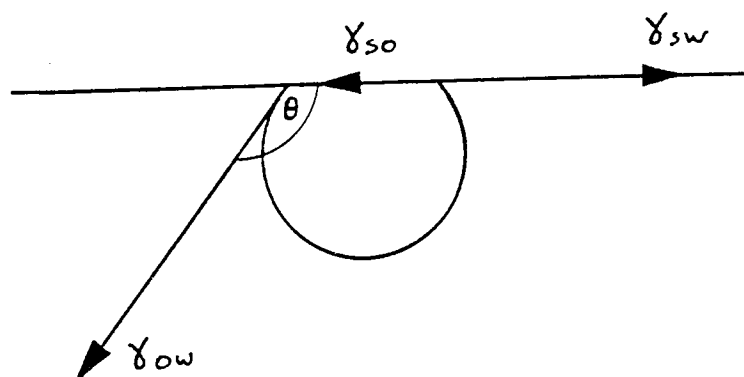


Figure 4.4d Hamilton's apparatus



where-

γ_{ow} = free energy of the octane - water interface

γ_{sw} = free energy of the solid - water interface

γ_{so} = free energy of the solid - octane interface

Figure 4.4e Samples held underwater wetted by a drop of n-octane

Inverted bubble or droplet measurement techniques are fundamentally different from those involving the measurement of a sessile drop in air. The inverted methods require the sample to be immersed in a liquid (usually water) which is displaced by a droplet of a second liquid (or air) introduced beneath the sample surface. The method is illustrated in Figure 4.4d. It is obviously essential that the droplet is of lower density than the immersion fluid. When the density difference is large, as in the case of air, the influence of droplet (i.e. bubble) distortion and the importance of droplet (bubble) size is much greater than in the case of the sessile drop experiment. The method is valuable in the study of hydrated surfaces, and has been cleverly adapted by Hamilton (136) to the study of polar components of surface energy of solids. This is achieved in principle by choosing a liquid whose dispersive component is the same as that of water (e.g. octane, $\gamma_d = 21.8$ dynes/cm), thus allowing a direct correlation to be made between contact angle and polar component of surface free energy. One of the greatest difficulties of this method is that of exact determination of the tangent to the droplet at its point of contact with the solid, and thus measurement of the contact angle. This is apparent from a comparison of Figures 4.4d and 4.4e with 4.4a, 4.4b and 4.4c. Measurement of contact angles of inverted droplets is particularly difficult with angles in the region of 140° and above.

The information that can be obtained from these relatively simple techniques, if used with care and precision, is considerable. In the first place, sessile drop measurement in air with liquids of different surface tension can be used in the form of a Zisman plot (e.g. Figure 4.5) to determine the critical surface tension of a solid. Ideally, 4 or 5 liquids should be used, none of which should interact strongly with the substrate. The critical surface tension gives an idea of the gross wettability of the substrate and is most useful in the case of solids that do not exhibit an appreciable polar component of total surface energy. A more precise description of surface properties may be obtained by using two or more liquids whose surface tensions have known polar and dispersive components. Sessile drop measurement in combination with Owens and

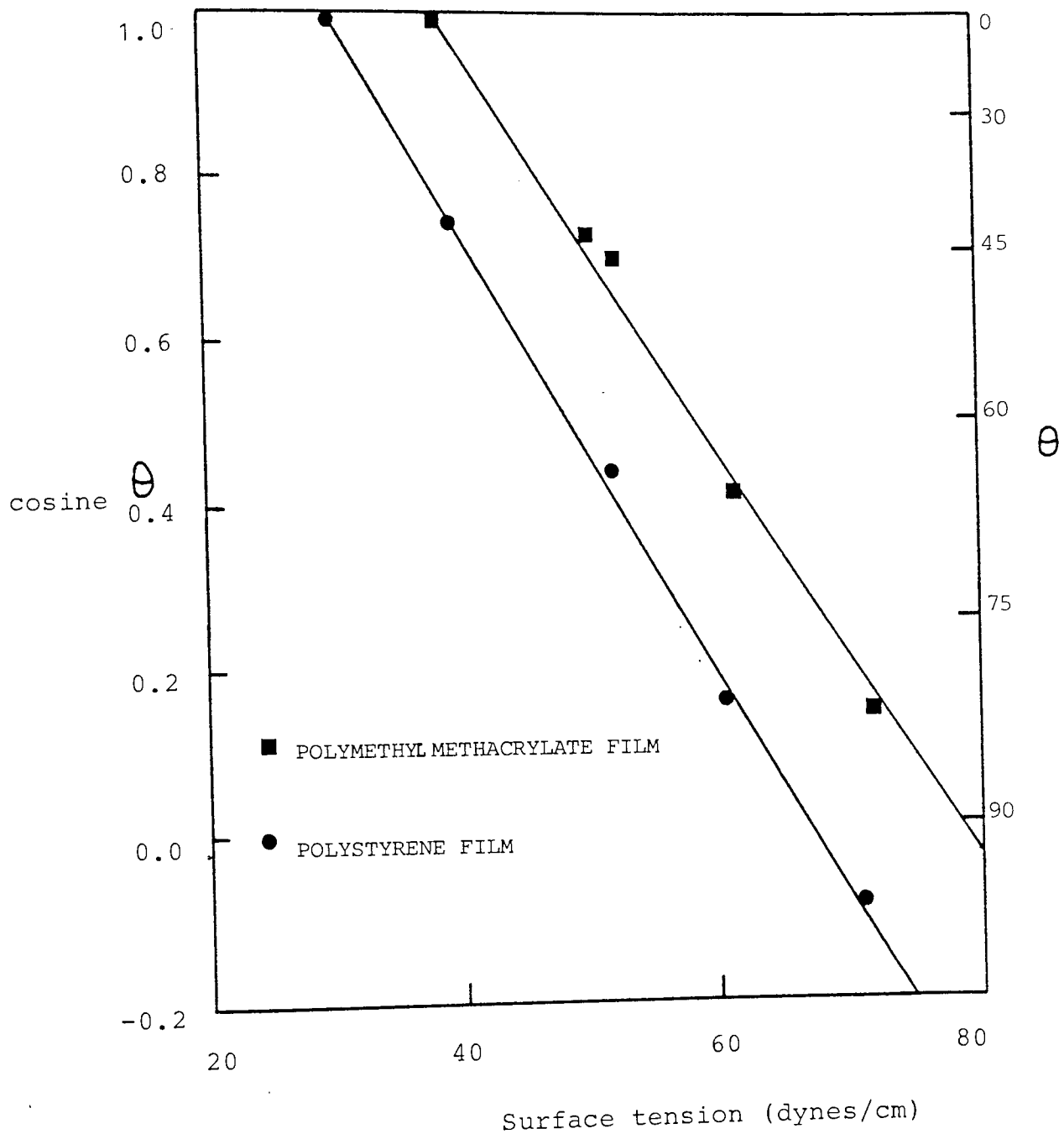


Figure 4.5 Relationship between equilibrium contact angle (θ) and surface tension of a liquid for solid surfaces having different critical surface tensions.

Wendt's analysis in (equation (8)) allows polar and dispersive components of surface energy to be determined. Water, methylene iodide and formamide are amongst the most commonly used liquids in this type of experiment. Inverted droplet measurements are very useful, but their interpretation is open to more debate. Even Hamilton's apparently straightforward correlation of contact angle with polar surface energy component has been the subject of some doubt. The principle reason for this is the effect of mutual solubility of the liquids on their surface tensions and the extent to which this is important in what are almost instantaneous measurements. A more general problem with these methods is their conceptual similarity to receding angle techniques. Thus, the impinging droplet or bubble displaces water from the hydrated surface, and the extent to which the resultant interface is dominated by a residual water layer is open to debate.

All these measurements have some part to play in the surface characterisation of contact lens materials. Although critical surface tension is a useful parameter, the fact that these materials need a degree of polarity in order to sustain the all important tear fluid layer suggests that it is not wholly adequate. Information obtained on dry gas permeable (non-hydrogel) materials is also valuable. Although it may be argued that lenses are soaked and thus, to a degree "hydrated" before use, the tendency of the front lens surface to become dryer in wear is well known. The 'dry' contact angle will give a useful guide to tear film stability under the least advantageous conditions. The effect of soaking in saline, and in proprietary wetting solutions illustrates the wettability of the lens under the most advantageous, but not necessarily representative, conditions. The least physiologically representative, but most effective method for measuring the "wettability" of the lens is to pre-soak the material and then measure a receding contact angle using not water but a low surface tension wetting solution to make the measurement. The equivalent of this is to immerse the sample in wetting solution and use the inverted air bubble technique. Measurements of this sort are unrepresentative of any clinical or physiological situation in which the lens is worn but are commonly used by manufacturers to demonstrate how wettable their own materials are. In all these methods of measurement a 2 degree "error bar" must be allowed, because

this is the limit of reproducible measurement. It is plainly nonsensical therefore, to quote values to an accuracy of 0.1 degree as is sometimes done, especially in commercial literature.

These points taken together illustrate the need for standardisation in measurement of contact lens properties by materials scientists and materials manufacturers. In particular, they illustrate the need to define the measurement conditions accurately when quoting results. It is, unfortunately, common to read manufacturer's literature claims for a particular wetting angle without any indication of the wetting liquid, the state of hydration or degree of pre-soaking of the material, or even the technique used to make the measurement. The difference between a sessile drop contact angle measured with water on a surface and a captive (inverted) air bubble contact angle measured in a proprietary wetting solution can be as much as 40° - 50° . Figures quoted in absence of any definition of measurement conditions are therefore meaningless as a basis of comparing the behaviour of competitive materials.

4.3.(3) Results of Surface Properties of Contact Lens Materials

Some comparison of experimentally determined surface properties using the types of techniques described here are shown in Table 4.2. These include manufacturer's values (conditions unspecified), values quoted in the literature, and work done in these laboratories. The effect of soaking under various conditions is illustrated in the table, which again show varying values from different sources. Characterisation work in these laboratories involves several techniques and procedures. The measurement of surface energy parameters provides the best way to compare the useful information in relation to the molecular nature of the surface. The effect of soaking on water contact angle gives a useful indication of the extensive change that may take place on storage of contact lenses in their soaking solutions (for example the dry contact angle of Boston drops from 65° to 42° after soaking).

The extensive baseline of clinical information on poly (methyl methacrylate) which does not change dramatically, coupled with the work on the surface

TABLE 4.2 CONTACT ANGLE AND SURFACE FREE ENERGIES OF VARIOUS CONTACT LENS MATERIALS

NAME OF MATERIAL AND MANUFACTURER	CONTACT ANGLE (degrees)		SURFACE FREE ENERGY (MN)		
	DRY	SOAKED	POLAR γ^p	DISPERSIVE γ^d	TOTAL γ^T
PMMA	63(a)	20(c)	10.9	40.3	51.2
CAB	64	25(c)			
Si Rubber	93				
AIRLENS	76(c)	19(c)			
ALBERTA XL30	63(a)	28(d)	11.6	37.4	49.0
BOSTON I	65(a) 80.8(b)	42(d) 33.3(e)	12.9	31.1	44.1
BOSTON IV	79(a) 90(c)	25(c)	3.6	40.5	44.1
EQUALENS	55.3(a) 30(c)		19.2	30.6	49.8
FLUOROFOCON A		44(d)			
HYPERM	71(a)		8.2	35.4	43.6
LAMDA X	67(a)		11.2	32.8	44.0
LONDON	75(a)		5.5	38.7	44.2
MENICON O ₂		16(d)			
OPTACRYL 60	65(a) 75.9(b)	25(e)	11.0	35.0	46.0
OPTACRYL K	82(c)	38(d) 12(c)			
OXYFLEX	66(a)	22(c)	10.2	37.0	47.2
OXYFLOW	72(a)		7.2	37.2	44.4
OXFORD	78(a)		4.1	39.8	43.9
PARAPERM O ₂	80(b) 23(c)	46(d) 23.1(e) 20(c)			
PARAPERM EW	68.3(a) 92(c)	22(c)	2.2	35.7	45.9
PARAPERM PLUS	91(c)				
POLYCON I	67(a) 76.6(b)	25(d) 30.4(e)	10.5	38.4	48.9
POLYCON II	82.7(b)	50(c)			
SILCON	92.8(b) 31.4(b)				
SILPERM	90(a)	50-55(d) 15(c)			
SM 38	70.5(a)		8.4	36.3	44.7

Footnote

- a) Aston
- b) Fitzgerald
- c) Others
- d) Japanese Paper
- e) P Honan

treatment of TPX⁽¹⁰⁹⁾ illustrates the value of the carefully and accurately determined sessile drop in air technique. The additional information from the surface energy measurement and soaking profiles again provide a useful guide to the nature of the material and hydration characteristics in clinical use.

The significance of contact angle and surface energy measurement as predictive techniques for clinical performance of clean homogeneous surfaces in the form of contact lenses is indisputable provided the characterisation work is adequate. Once a lens has been worn, however, biological deposits at the surface build up in a manner that is frequently heterogeneous. In a recent study ⁽¹³⁷⁾ carried out jointly between Judith Morris at the London Refraction Hospital and these laboratories, the lenses of the patient who was suffering from problems of poor lens wetting (premature tear film break-up) was studied. It was clear that although small, typically lipoidal droplets caused non-wetting of lenses by the thin structured tear film, their influence on the relatively large hemispherical droplets of water and methylene iodide was small. Essentially, the water droplet bridged the small non-wetting areas and indicated that macroscopic wettability of the lens surface was good (better even than the materials before wear). The study was complex involving analysis of lens spoilation and fitting the patients with lenses using a protocol in which lens material wear time and storage solutions were varied. The results are published elsewhere ⁽¹³⁷⁾. In summary, however, the work demonstrated clearly that the surface wettability is a necessary but not sufficient criteria for tear film stability. The additional factor that appears to be required is the surface homogeneity on a scale that correlates roughly with tear film thickness (5 - 15 μm).

4.4

MECHANICAL PROPERTIES

It is apparent that variations in mechanical properties of what are essentially polymers whose properties lie in a tough to glassy regime, will be less critical in relation to clinical performance than either oxygen permeability or surface properties. This does not mean to say that the mechanical properties are not important in this respect,

but they are more obviously related to problems associated with manufacturing and durability outside, rather than in, the eye. Perhaps for this reason, less attention has been given to determination of mechanical properties of gas permeable contact lens materials, than has been given to either permeability or wettability. It is important, however, to have some factual base on which to work when comparing materials. For this reason determination, with reasonable accuracy, of some fundamental mechanical properties of materials in the form of contact lenses is a desirable aim. This is in fact perhaps the major problem, for although many test procedures, techniques, and materials' characteristics are known in the field of mechanical properties they are not designed for small curved samples of changing cross-section. To provide a basis for discussion, the types of information obtained in conventional mechanical testing must first be outlined.

In general, mechanical property testing involves the application of some form of deforming force to a sample and a concurrent study of the way that the sample responds. The results are often expressed in the form of strength or modulus. The strength of a material is usually defined in terms of the force per unit area required to cause failure when the material is subjected to a particular type of test procedure (eg tensile, shear, impact, tear). The modulus, on the other hand, is defined as the true stress (i.e. force per unit area) required to produce a true unit strain (i.e. deformation) in the direction of the force (eg tensile modulus, rigidity modulus). The most common types of mechanical property tests are described below but first it is necessary to comment on the units used in quoting the results.

Several different units of stress are used (eg. tsi, tons weight per square inch; psi, pounds weight per square inch; kg or kgf mm⁻², kilogrammes weight per square millimetre and dyne cm⁻², dynes per square centimetre). The SI unit of stress is Nm⁻² (newtons per square metre), but this is an extremely small quantity and MNm⁻² (mega newtons per square metre, equal to 10⁶ Nm⁻²) is a more useful unit. The units are related in the following way:-

$$1 \text{ dyne cm}^{-2} = 0.1 \text{ Nm}^{-2} = 10^{-7} \text{ MNm}^{-2} = 1.45 \times 10^{-5} \text{ psi}$$

$$= 6.46 \times 10^{-9} \text{ tsi} = 1.02 \times 10^{-8} \text{ kg mm}^{-2}$$

Some of the ways in which this information is obtained are outlined below.

4.4 (1) Examination of Materials Under Tension

A polymer specimen is stretched if a tensile stress is applied to it. The tensile test is normally carried out with a tensometer (which measures the extension produced as the load is applied), the schematic form of a tensometer is shown in Figure 3.9 and a typical tensile stress-strain relationship is shown in Figure 4.6. A stress-strain curve of this type provides wide-ranging mechanical data of the material under test:

- (i) how strong it is (ie. the ultimate tensile strength of the material which is determined by the magnitude of YS in the graph),
- (ii) how much it can be deformed before fracture (ie. the elongation at break of the material which is determined by EB),
- (iii) how stiff it is (ie. the elastic modulus [Young's modulus] of the material which is determined by the initial slope TM), and
- (iv) how tough it is which can be determined from the area under the whole curve.

$$\text{Yield Strength (YS)} = \frac{\text{Load at Yield (N)}}{\text{Cross Sectional Area (m}^2\text{)}} \quad \begin{array}{l} \text{UNITS} \\ \text{Nm}^{-2} \end{array}$$

$$\text{Tensile Modulus (TM)} = \frac{\text{Stress (Nm}^{-2}\text{)}}{\text{Strain}} \quad \text{Nm}^{-2}$$

$$\% \text{ Elongation at Yield} = \frac{\text{Extension at Yield (m)}}{\text{Original Length (m)}} \times 100\%$$

$$\% \text{ Elongation at Break} = \frac{\text{Extension at Break (m)}}{\text{Original length (m)}} \times 100\%$$

mechanism of failure of the specimen.

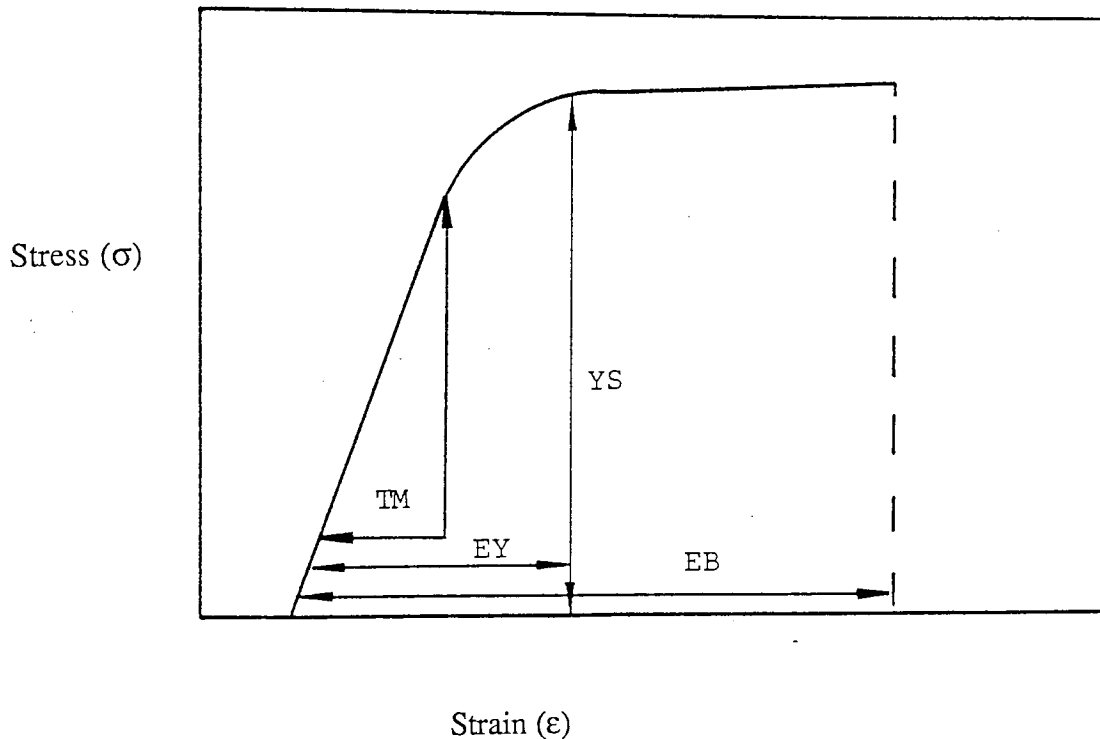


Figure 4.6 Idealised polymer stress-strain curve showing tensile modulus (TM), yield strength (YS), elongation at yield (EY) and elongation at break (EB)

4.4 (2) Examination of Materials Under Compression

The type of test carried out on any polymeric material should depend on what stresses it will experience in service and there are other tests for specific properties in this respect (eg. impact strength). Simulating the actual service conditions of the polymer in experimental tests may provide many difficulties since no single commercially available technique can provide all the experimental conditions for testing polymers in different applications. The nearer the experimental conditions are to the service conditions, the more significant will be the results obtained from the experimental tests. One of the more important and significant tests is the time-dependent deformation

tests. One of the more important and significant tests is the time-dependent deformation and recovery of the materials under successive periods of load application and removal (ie. eyelid movement). Unlike perfectly elastic rubbers, plastic materials are viscoelastic, (ie. they deform time-dependently when a load is applied to them and recover time dependently when the load is removed) and this may result in a permanent deformation of the materials. This must be taken into account when attempting to correlate mechanical property measurements with clinical behaviour.

The instrument used in this laboratory to study deformational properties is a modified Pneumatic Microindentation Hardness Apparatus whose layout is shown in Figure 4.7. Basically the instrument allows the indentation of any test sample in a form of a thin film or coating, by a small sphere under a small constant load, to be measured as a function of time. The recovery after the load has been removed can also be measured as a function of time. Both the indentation and recovery curves are recorded automatically and the time scales (less than 2 minutes) of each can be set separately. Because wide variation of both magnitude of load and indenter diameter or form is possible, a wide range of materials properties can be monitored with this technique.

This type of microindentation hardness apparatus was originally used by the paint industry to assess changes in mechanical properties of paint coatings caused by ageing and weathering. For polymers in contact lens applications, this instrument not only enables the deformation and recovery characteristics of the materials to be measured under a small, constant load (eg. a load equivalent to the eyelid pressure, $\sim 2.6 \times 10^3$ N/m²) but also enables rigidity moduli of the materials to be evaluated. A typical load/recovery curve for an elastomeric material such as silicone rubber is shown in Figure 4.8, and typical equations which inter-relate load (m), equilibrium depth of indentation (h), indenter radius (r), sample thickness (t), with Young's Modulus (E), Rigidity modulus (G) and Poisson's ratio (ν) are shown in equations 9 to 12.

$$\frac{E}{1-\nu^2} = \frac{3 mg}{4 r^{1/2} h^{3/2}} \quad (9)$$

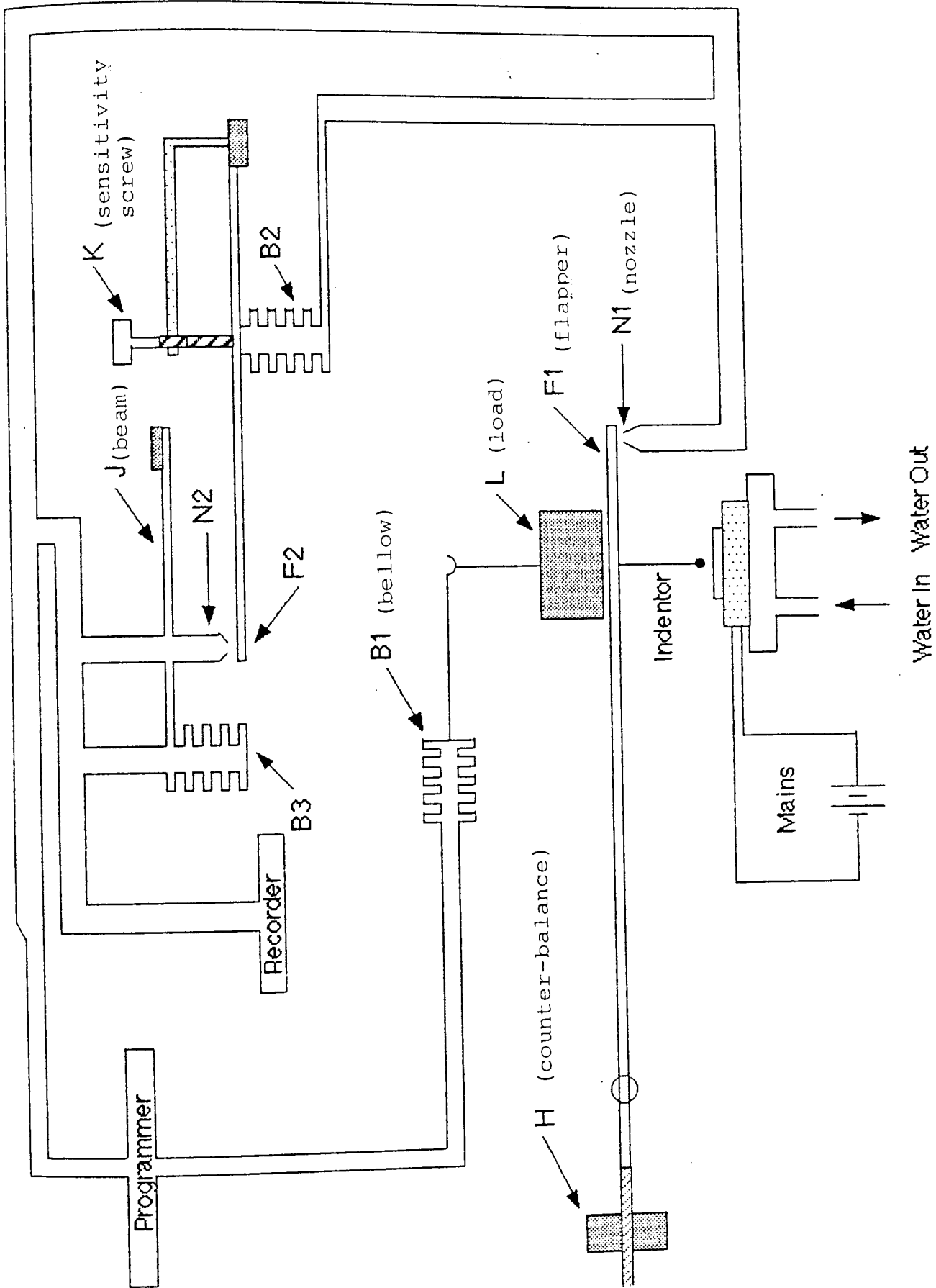


Figure 4.7 Pneumatic Microindentation Hardness Apparatus

$$G = 0.36 \frac{mg}{r^2} \left(\frac{t-h}{h} \right)^{3/2} \quad (10)$$

$$G = \frac{mg}{2\pi r^2} \left(\frac{t}{h} \right)^3 \quad (11)$$

$$G = \frac{3}{16} \frac{mg}{r^{1/2} h^{3/2}} \quad (12)$$

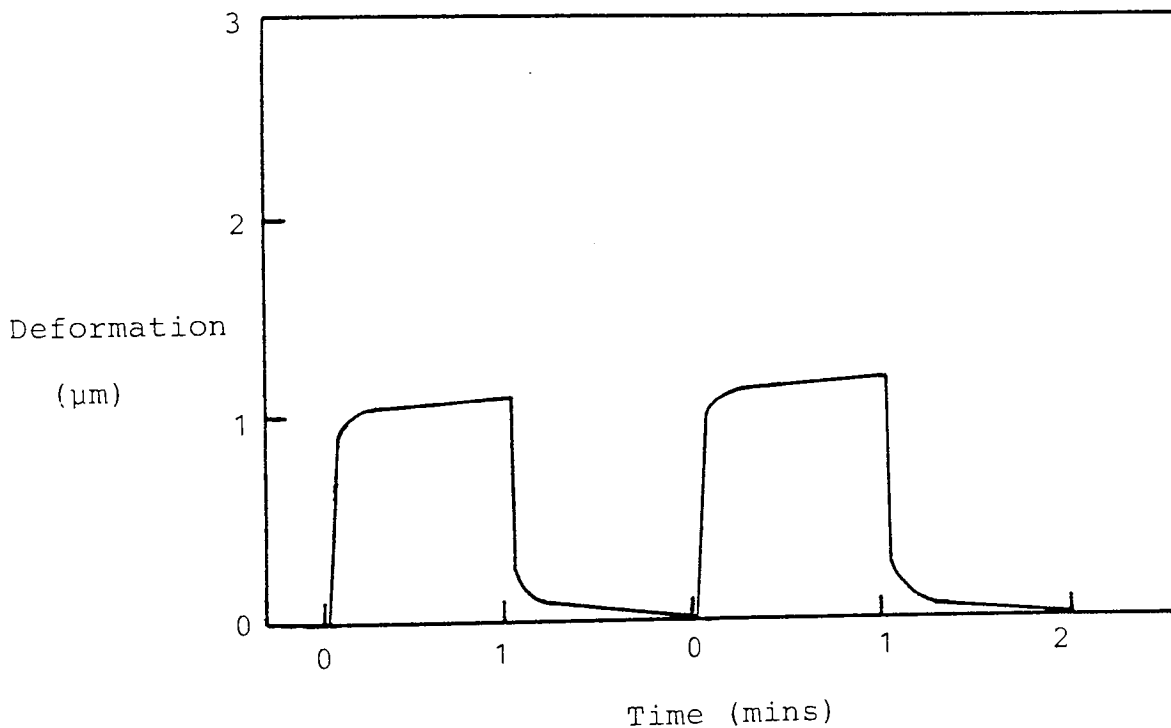


Figure 4.8 Typical deformation properties of an elastomeric material (eg. silicone rubber) under eye-lid pressure.

The technique has the following advantages for testing polymers in contact lens applications:

- (i) only a small sample (eg. 0.5cm diameter flat disc of thickness 0.1mm) is required (alternatively a contact lens of known centre thickness can be used),

- (ii) the deformation and recovery characteristics are recorded automatically and the timescale of each can be separately varied,
- (iii) unlike other commercially available hardness testers which are designed for comparison purposes, this instrument measures indentation in microns, which can then be converted to % elongation for a wide range of loads and indentors,
- (iv) unlike most commercially available creep testers which employ tensile forces, this instrument measures creep under compression, simulating more effectively the service conditions of a lens,
- (v) the test is non-destructive.

Although some of these aspects of behaviour are more important for soft than for hard lenses, the technique is applicable to both types of materials.

4.4 (3) Hardness Test

Hardness can be defined as resistance to penetration. In a hardness test, an indenter made of a hard material is pressed on the surface of the material under test and the extent to which it sinks in for a given pressure and time is an inverse measure of the hardness. There are many hardness testers available commercially for plastics and rubbers, such as the Vickers indenter, the Rockwell hardness tester and the Shore durometers. Gouza (138) classifies hardness tests into three categories:

- (i) Hardness tests that measure the resistance of a material to indentation by an indenting probe (eg. Brinell, Vickers, and Shore Durometers). Some tests measure the indentation with the load applied and some measure the residual indentation after the load is removed.
- (ii) Hardness tests that measure the resistance of a material to scratching by another material (eg. the Bierbaum scratch test, the Moh hardness test; similar techniques are commonly used in paint testing and involve pulling the sample beneath a loaded indenter).

- (iii) Hardness tests which measure rebound efficiency or resilience (eg. various Rockwell testers). Many of the hardness tests are a combination of (i) and (iii).

The Rockwell α scale hardness test measures the depth of penetration with the load applied; R, L, M and E scale tests measure depth caused by a spherical indenter after most of the load has been removed. Thus the amount of rebound or recoverable deformation is important in these hardness tests. In the Vickers Microhardness test, a microscope is used to measure the diagonals of the pits left by a diamond-shaped indenter (being a 136° pyramid diamond) on a square base. There is a linear relationship between the depth of impression and the hardness number. Each of these methods uses an arbitrary scale satisfactory for comparison purposes and the scales can be approximately compared.

Although hardness testing using these various instruments is a fairly convenient method for comparing the relative hardness of any given materials, we believe that the micropenetrometry technique used in our work (q.v.) is a more sensitive and versatile technique. It provides direct indentation results and can also be used to calculate rigidity modulus.

4.4 (4) Other Mechanical Tests: Tear, Flex, Creep

Variations and additional types of mechanical test may be used but in general, they are less readily adapted to contact lens studies; some of these are briefly described here.

Tear Strength Test: Tear strength is the force required to propagate a tear in a notched specimen and is expressed as force per unit length of the resultant tear. The result depends on many factors such as depth of notch, mode of applying the tearing force, thickness of specimen and temperature of test.

Flexural Test: A specimen is flexed repeatedly until it fractures. The number of flex cycles to break measures the flexural ability of the material. The flex can be repeated in linear extension, or repeated bending without tension, or a combination of bending and

extension.

Creep Test: Plastics often tend to become distorted if they are constantly loaded. Creep tests are therefore important for plastic materials in service. A creep test records deformation against time for a constant stress. When a load is applied to a polymer specimen, there is an instantaneous elastic deformation, followed by the time-dependent deformation or creep. A creep test is normally carried out in tension rather than compression.

4.4 (5) Relevance of Mechanical Testing to Contact Lens Performance

Given the assembly of testing techniques outlined above, it is important at this point to assess their relevance to the behaviour of contact lens materials. This question can be approached from two stand points. The first is what do we need to know about the behaviour of contact lens materials in laboratory tests, in order to predict their behaviour in fabrication and use? The second is how can we adapt the most appropriate of the foregoing techniques to give us this information? Given that the deformation of rigid gas permeable contact lenses in the eye is infinitesimal compared to that of soft hydrogel lenses, the most relevant areas of mechanical performance of these materials lie in fabrication, handling and durability.

Amongst the problems that arise in these respects are brittleness of materials (manifested during fabrication and handling), softness of materials (which produces problems in lens polishing during manufacture, and poor scratch resistance in handling), and creep (which causes dimensional instability of the lens). These various aspects of mechanical behaviour can be broadly related to the molecular response of the materials to the applied loads. As a result, the most useful information can be obtained from carefully controlled tensile and compressive tests. Although hardness and creep testing is, in principle, valuable in evaluating the potential performance of contact lens materials, the lack of adequately sensitive and reproducible tests that are able to discriminate between polymers presented in the form of lenses make direct measurement of these properties a limited present value.

There are obviously problems in adapting contact lens specimens to tensile stress-strain testing and to micropenetrometry. The problems may be summarised in each case as below:

Tensile Test	Micropenetrometry
Non-uniform cross-sectional area	Base-line drift commonly due to poor contact between sample and mounting stage.
Small sample size (causes problems in mounting)	Aggravated by curvature of the lenses.
Slippage in the jaw during testing	
Fracture of sample during mounting	

Given these problems, however, fairly sophisticated and valuable information related to material performance can be obtained by these techniques. Thus, the initial modulus and elongation at break of the tensile test curve indicates the stiffness and flexibility of the material together with the degree of deformation before fracture. The precise profile of the stress-strain curve indicates the nature of the yield process, and any tendency of, for example the siloxane component to undergo phase separation will become apparent. The difference between tensile stress-strain curves of dry and soaked lenses gives a good indication to the dimensional stability of the material and is a useful substitute for short-term creep tests in this sense.

Some guidance in interpreting the profile of a stress-strain curve comes from the work of Carswell and Nason⁽¹³⁹⁾ who have divided the types of stress-strain curves obtained with polymers into three classes.

i) Hard, Brittle

Poly(methyl methacrylate) at room temperature shows hard, brittle behaviour having a simplified stress-strain curve as shown in Figure 4.9. Brittle materials generally break at the yield point. They have a high Young's modulus, and quite a high tensile strength but have very small elongations at break.

ii) Soft, Weak

A soft polymer gel-like polyHEMA shows soft, weak characteristics having a low modulus, a low tensile strength and only moderate elongations at break. Figure 4.9 shows this type of behaviour.

iii) Soft, Tough

Elastomers show soft, tough behaviour having low modulus, very high elongations and moderately high breaking strength. Figure 4.9 indicates this behaviour.

4.4 (6) Tensile Testing of Rigid Gas Permeable Contact Lens Materials

In routine tensile testing of contact lenses, (see experimental chapter), the % elongation at break, the maximum load at break, and the tensile strength were recorded. These are summarised in Table 4.3. Broad comparison of the tensile properties of these commercial rigid gas permeable materials shows, not surprisingly, that they have similar but not superior properties to PMMA. Thus PMMA can be taken as a yardstick to provide a reasonable base line for these groups of materials. The typical tensile stress-strain curve (load against extension) of PMMA is of the hard brittle type as shown in Figure 4.9. As the proportion of siloxy monomer incorporated, and as the bulk size of the siloxy side chain used is increased, the profile of the curve moves towards the soft tough form shown in Figure 4.9. Separation of the siloxy and methyl methacrylate block also becomes apparent. It is important to note that tensile testing readily picks up batch to batch variation and variation within individual batches of materials. Unlike compression testing, tensile testing is very molecular weight dependent and, even though the polymers are cross-linked, changes in the perfection of

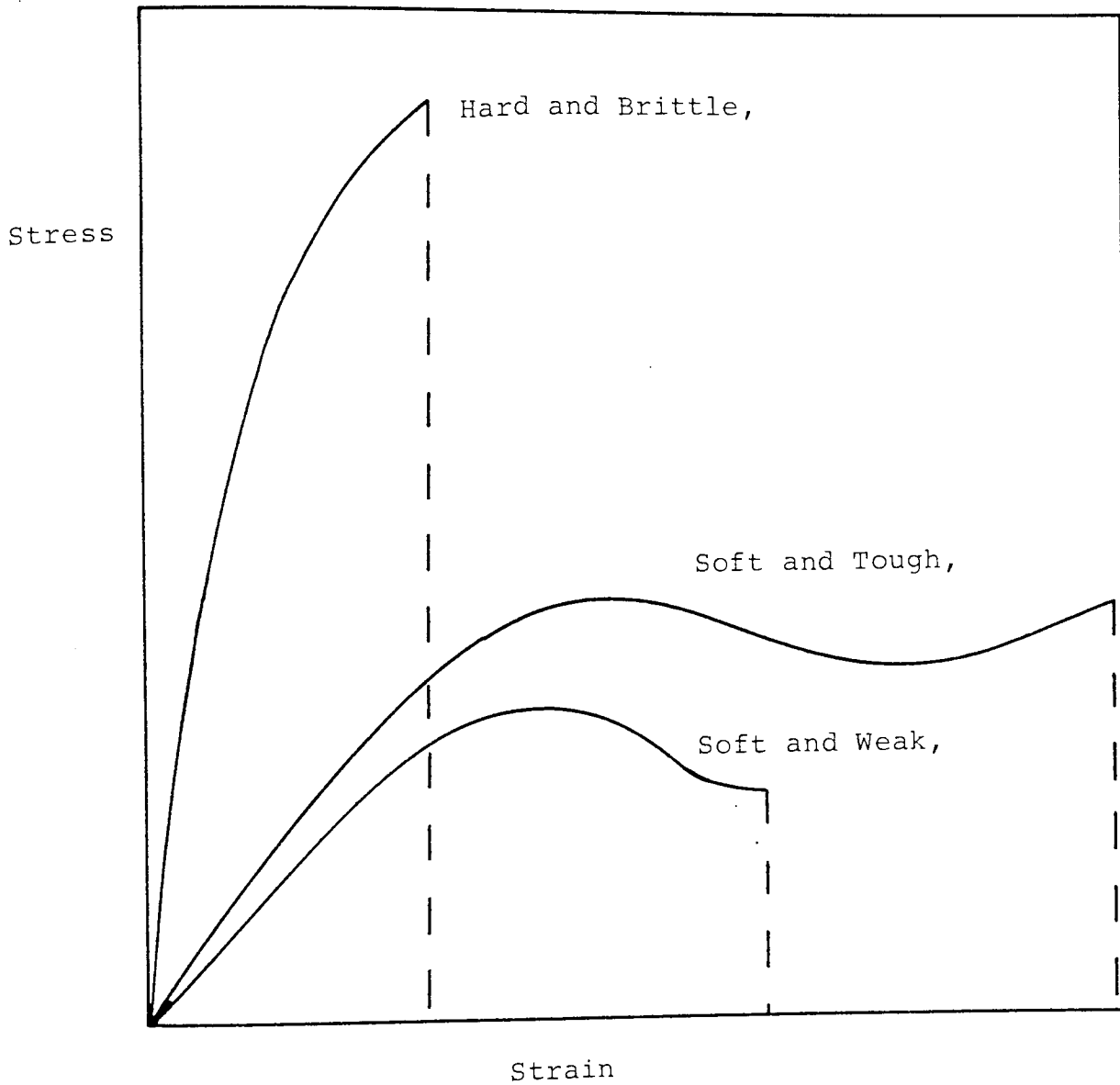


Figure 4.9 Stress-strain relationships of polymers and their mechanical characteristics

the network will produce changes in tensile properties. It is, therefore, a good quality control technique for hard gas permeable contact lens materials.

4.4 (7) Compression Testing of Gas Permeable Contact Lens Materials

Using the procedure described in the experimental section, micropenetrometry with various indentors can be readily carried out on lens materials in different forms (button, lenses, lathe-cut or moulded discs).

The lack of elasticity in the materials is readily revealed by their behaviour in compression related to that of silicone rubber itself (compare with Figure 4.8). The rigidity modulus and Young's modulus of a material may both be calculated from the results of microindentation studies provided that a reasonably sound value of Poisson's ratio for the material may be estimated (see equation (9)). The data is best handled by rearranging the Hertz equation:

$$\frac{E}{1 - \nu^2} = \frac{3 \text{ mg}}{4 r^{1/2} h^{3/2}} \quad (9)$$

where E = Young's modulus

ν = Poisson's ratio

m = load

g = gravity

r = indenter radius

h = depth of indentation

to the form

$$\log m = n \log h + \log \frac{4}{3gr^{1/2}} \cdot \frac{E}{1 - \nu^2} \cdot \frac{1}{10^{4n}} \quad (13)$$

TABLE 4.3 TENSILE RESULTS OF SOME COMMERCIAL CONTACT LENSES

Lens name	% elongation at break	Maximum load at break (N)	Tensile Strength (N/mm ²)
a) Alberta XL 30	56%	3.9	5.95
b) Hyperm	89%	3.6	6.0
c) Oxyflex	96%	0.6	0.7
d) Oxyflow	36%	0.4	0.6
e) Optacryl 60	60%	3.8	6.5
f) Polycon	94%	5.9	6.8
g) SM-38	61%	0.7	0.6
h) Boston 1	77%	3.7	5.5
i) PMMA	90%	6.7	6.0
j) Boston 4	41%	0.9	1.2
k) London	53%	1.3	1.7
l) Oxford	52%	2.2	2.2
m) Lamda X	58%	1.2	3.0

which enables a plot of $\log m$ (load) against $\log h$ (depth of indentation) to give a gradient n . The load-indentation results for a group of gas permeable contact lens materials are shown in the form of the log-log plot in Figure 4.10.

It is clear that the PMMA based material (Paragon 18) is more rigid than Paraperm O₂, Equalens and Oxyflow (in that order). This method of visual presentation of the results has the advantage that the response to increasing loads can be assessed. In this context it is apparent that some departure from the theoretical value of 3/2 for the slope of the line occurs. The value of Shore hardness for PMMA (Paragon 18) and Paraperm O₂ (86.5 and 85, respectively) produces the same hardness ranking for these materials, but gives no information about the deformation/load characteristics. Values of Young's modulus for these two materials (derived from the microindentation work) were $2.126 \times 10^3 \text{ Nm}^{-2}$ and $0.901 \times 10^3 \text{ Nm}^{-2}$ respectively.

The technique is versatile and can be extended by a conical rather than a spherical probe to produce a procedure that is very similar to the various hardness methods referred to in a preceding section.

4.5 CONCLUSIONS

The underlying problem that has bedevilled the field of contact lens materials has been the lack of adequate standardisation. Whereas legislation and common scientific practice have made it possible to compare most pharmaceutical products, one with another, no such situation exists with contact lenses. Given the relative explosion in the number and types of material that have become available in the last 15 years, this is a serious problem. Even the activities of the FDA in America have failed to produce a satisfactory and generally observed basis for the assessment and comparison of different lens materials of the same type. Thus, it is quite common to see so called 'wetting' angle results quoted with no detail of wetting liquid or technique used. As comments in an earlier section have shown without such information, it is impossible to make any comparative judgement of one material against another.

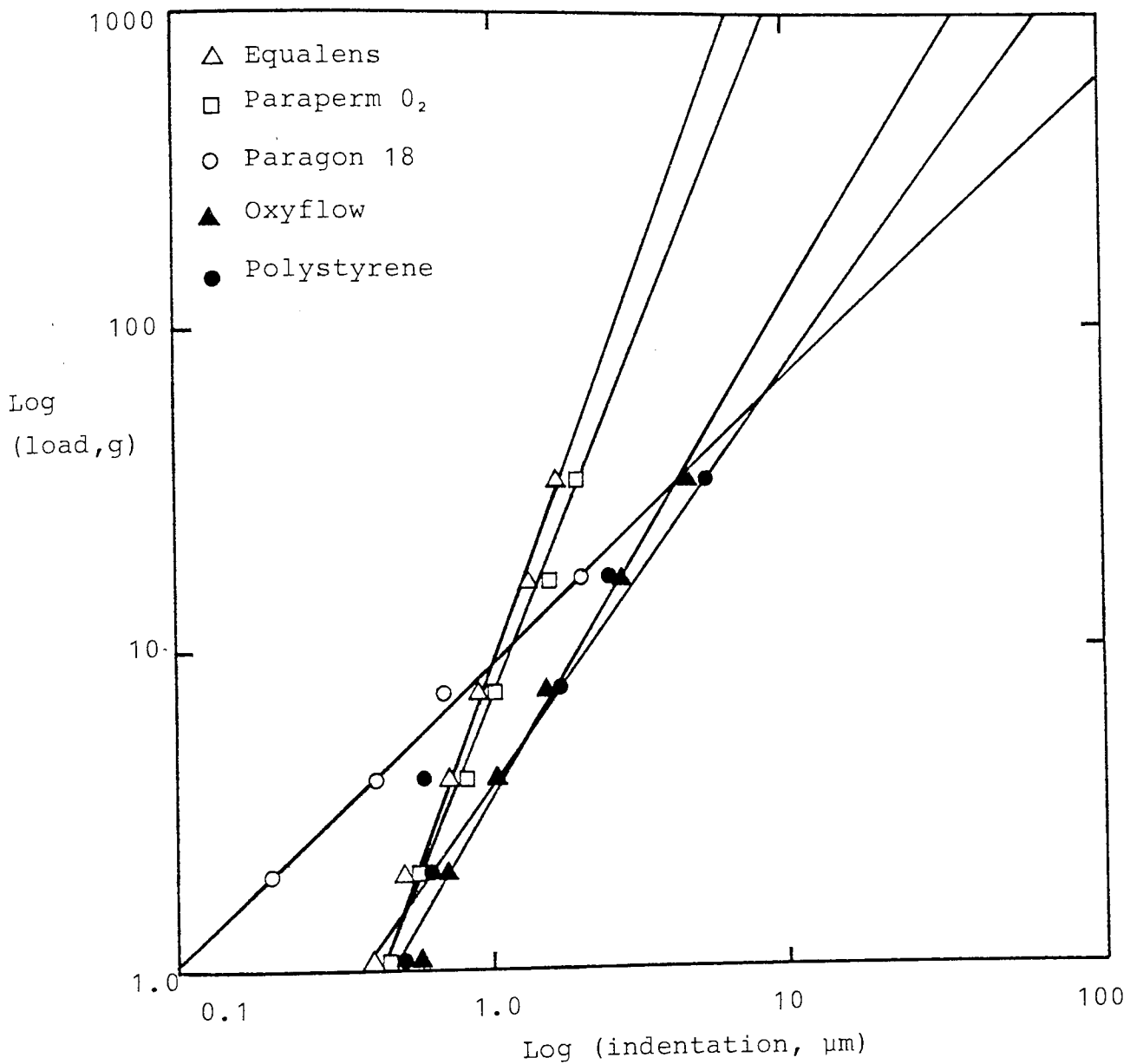


Figure 4.10 Variation in log indentation (h) with log load (m) for some gas permeable contact lens materials

In this chapter, the problems and pitfalls associated with measurement of surface, mechanical and permeability properties of contact lens materials were highlighted. Although there is no substitute for carefully controlled wearer trials in order to assess utility and performance of a lens material, good 'in vitro' test data both helps to focus attention on good candidate materials in the material development programmes and aids the ophthalmic practitioner's task in selecting from the large number of commercial materials presently available.

CHAPTER V
ROLE OF ALKYL METHACRYLATES IN DESIGN OF RIGID GAS
PERMEABLE MATERIALS

5.1 INTRODUCTION

The previous chapters have described ways in which the oxygen permeability of rigid gas permeable contact lens materials has been improved commercially, and ways in which the properties of such materials can realistically be assessed outside the eye. It is a feature of this area, that progress has not resulted from the publication of fundamental studies describing the relationships between polymer structure and performance, which have then been adapted to produce commercial products. Indeed such structure-property work as has been done forms the basis of the patent specifications and commercial products with virtually no conventionally published experimental results being available. In this chapter, some attempt is made to remedy this, by examining some of the more fundamental aspects of the effect of polymer structure on performance relevant to this type of application.

In particular, the approach of using the least permeable methacrylate (methyl) in combination with monomers that are structurally and dramatically different in order to induce oxygen permeability needs critical consideration. It is possible, and a strategy that is certainly worth considering, that the use of higher alkyl methacrylates (more permeable than methyl methacrylate) would entail the use of lower proportions of siloxanyl groups in order to produce a physiologically acceptable level of oxygen transport in the resultant contact lens material. Such copolymers will be less structurally heterogeneous than existing commercial gas permeable contact lens materials and might well be cheaper, more controllably polymerized, and possess better ocular compatibility. An assessment of this strategy is presented in this chapter.

Polymethyl methacrylate (PMMA) has long been established as a hard contact lens material. This is due to its excellent combination of optical properties, toughness, lightness, and most importantly, its balance of polar and dispersive surface free energy components which enables a coherent tear film to wet the lens surface.

Unfortunately, PMMA has very low oxygen permeability. This is compensated for, however, by fitting the PMMA lens to 'rock' on the cornea, thereby pumping oxygen to the anterior tear film. As mentioned in the previous chapters, PMMA may be taken as having 'base line' mechanical properties in terms of hardness, tensile and compression properties.

The majority of patents covering the rigid gas permeable contact lens materials are based on the extension of the Gaylord organosiloxo monomers⁽³⁸⁾, such as those of Ellis, Novicky and Tanaka in the 1970's, followed by Hoya, Toyo, Paragon, and Syntex in the 1980's. In order to maintain the delicate balance between oxygen permeability, surface wettability and mechanical properties, the practical upper limit of siloxo monomers appears to be around 60 - 70 weight % in total monomer contents. This restricts the quantity of other monomers incorporated to within certain limits and hence there is a narrow range in overall properties of the material. Often the surface and mechanical properties are sacrificed in order to produce materials of high oxygen permeability. The usual remedy for improving the surface wettability of these hydrophobic siloxo monomers is by the incorporation of polar, hydrophilic monomers which in turn reduce permeation of oxygen and other gases through the bulk of the polymer. The incorporation of large siloxo groups leads to an inevitable deterioration in the mechanical properties by increased phase separation, decreased scratch resistance etc. The most widely applied method of improvement is to increase the crosslink density of the polymer in an attempt to counteract this trend.

This chapter is concerned with the study of the effect of replacement of the methyl group by other related simple alkyl groups, and the use of such materials in copolymers. Part of the original aims and objectives of this work (carried out in conjunction with Dr P J Skelly (140)) was to produce gas permeable contact lens materials that would be susceptible to conventional melt processing; which

conventional commercial contact lens materials are not. This thesis does not deal with the melt processing technique and its use, since that was the area dealt with by Dr Skelly. The work described here is treated sequentially: firstly the factors affecting oxygen permeability (since this is an important requisite for any replacement of PMMA), secondly the factors affecting surface properties (since these are related to the general question of ocular compatibility), and finally the factors affecting mechanical properties (which are related principally to fabrication and handling).

5.2 GAS/GAS PERMEABILITY OF SIMPLE ALKYL METHACRYLATES

5.2 (1) Davenport Gas Permeability Apparatus

The Davenport Gas Permeability Apparatus is designed to measure gas permeability of polymer films in gas/gas conditions (i.e. P_g values, see Chapter 4) for a range of gas permeants (such as oxygen, nitrogen and carbon dioxide). The use of this technique has the advantage of providing sound fundamental information upon which a copolymerization strategy can be based. Perhaps surprisingly, the literature does not contain adequate comparative permeability data for polymers of alkyl methacrylates. Cast films of a range of methacrylates (ethyl, n-butyl, isobutyl and isopropyl) were therefore prepared and the permeability to oxygen, nitrogen and carbon dioxide determined. The experiments were carried out at a temperature of 22°C ($\pm 1^\circ\text{C}$).

5.2 (2) Results and Discussion

Figure 5.1 illustrates the form of the primary gas permeability results for PEMA and PIBMA. From these experimental data, the permeability coefficient (P_g) of the materials may be calculated using the following equation:

$$P_g = \left(\frac{273}{273+T} \times \frac{\Delta P_2}{\Delta t} \times \frac{1}{76} \times V_2 \right) \times \frac{1}{A} \times \frac{1}{(P_1 - P_2)} \times L$$

where

T is the test temperature (°C)

$\frac{\Delta P_2}{\Delta t}$ is the pressure change in the capillary (cmHg sec⁻¹)

Δt

A is the area of test specimen (23.77cm²)

(P₁ - P₂) is the pressure difference across the sample (cmHg)

V₂ is the total volume (ml) of vacuum between the test specimen and

the mercury level. It is the sum of the volume (V₁) of the cavity

(5,10,15 or 20ml); the volume of (0.018 y) of the capillary above the

mercury level half way through the experiment (where y is the length of

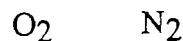
the capillary above the mercury; and 0.018 cm² is the cross sectional area

of the capillary); and the free space volume (0.24ml) in the filter paper,

$$\therefore V_2 = (V_1 + 0.018y + 0.24)$$

Table 5.1 lists the results for the alkyl methacrylates studied.

A useful general validation of the results is obtained by comparing the permeability ratios of $\frac{CO_2}{O_2}$ and $\frac{O_2}{N_2}$ for each polymer; since these should be broadly



similar for the different methacrylates. Similarly, in general, it would be expected that as the chain length in the alkyl methacrylate increases, the permeability to the three gases would increase. These broad principles allow grossly erroneous results arising from, for example, flawed membranes, to be excluded.

The Davenport Gas Permeability Apparatus was used to study the gas permeability behaviour of simple alkyl methacrylates and provided a fundamental basis for further work, although absolute values are not readily adapted to experimental contact lens materials for the following reasons: the small diameter of the fabricated lens material in the button form for lathe cutting and in particular melt processing is not

TABLE 5.1 DAVENPORT PERMEABILITY OF ALKYL METHACRYLATES

<u>POLY ALKYL METHACRYLATE</u>	<u>GAS PERMEABILITY</u> (ccO ₂ (STP) cm _____) (cm ² sec mmHg)			<u>GAS/GAS RATIO</u>	
	O ₂	N ₂	CO ₂	O ₂	CO ₂
				N ₂	O ₂
Ethyl Meth.	0.5	0.2	0.9	~2.5	~1.9
N-butyl Meth.	5.3	1.7	28.8	~3.6	~4.8
Isobutyl Meth.	4.6	0.8	15	~5.8	~3.3
Isopropyl Meth.	3.5	0.8	11.7	~4.4	~3.3
SMI	174.2	68.4	989	~2.5	~5.7
MMA (60) SMI (40)	10.4	4.5	47.6	~2.2	~4.6

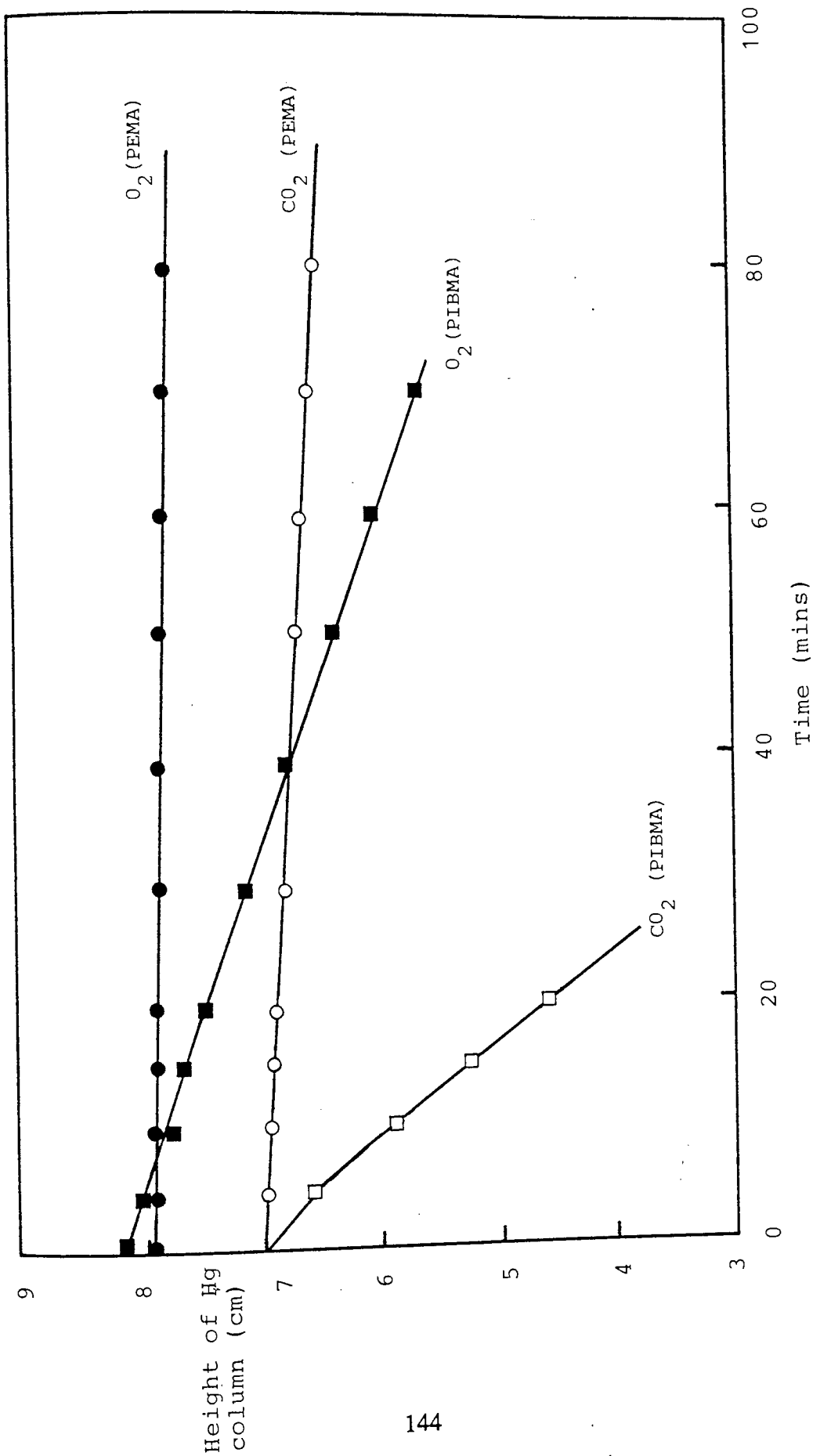


Figure 5.1 Comparison of oxygen and carbon dioxide permeabilities of PIBMA and PEMA using a Davenport gas permeability apparatus

applicable and the final lens form may require some types of surface treatments as a part of subsequent finishing. Therefore the Davenport technique is used to make comparative results of experimental samples based on this information. The technique required must be adaptable to the contact lens form. Such a technique is the Schema Versatae and details of a comparison between these two techniques may be found in Chapter 4.

5.3 OXYGEN PERMEABILITY AND THE EFFECT OF STRUCTURAL VARIATIONS IN METHACRYLATE

5.3 (1) Glass Transition Temperature (T_g) and Density (ρ) on Oxygen Permeability

In the course of work originated by Dr P J Skelly, the importance of the glass transition temperature (T_g) and the density (ρ) of the polymer used in contact lens applications, were highlighted. In commercial fabrication processes that involve latheing and polishing techniques, the T_g should be above 40°C. Moreover, his work together with the literature data (112) on permeability (i.e. diffusion and solubility factors) indicated a possible method of using density as a selection principle in polymers. The relationship between permeability coefficient (P), solubility coefficient (S) and diffusion coefficient (D) (i.e. $P = DS$), has been discussed in Chapter 4. The fundamental factors to be taken into account are:

- a) For hydrocarbon polymers, the oxygen permeability rises dramatically as density is lowered.
- b) The diffusion coefficient is strongly affected by density.
- c) The solubility of a gas can be strongly influenced by density.

Clearly, several factors can now be related in the design and selection of new contact lens materials. Firstly, the knowledge that the simple alkyl methacrylates produce oxygen permeabilities some 10, or even 40 to 50 times, greater than methyl methacrylate. Secondly, the minimum T_g requirement for lathe cutting and polishing is around 40°C. Thirdly, the broad guidelines relating changes of density with permeability.

Some of the densities of polymers were determined experimentally to complete the list of densities available from the literature. It is apparent from these studies that the methacrylates with branched side groups (eg PIBMA) have low densities (1.03), whereas those with cyclic side groups (eg PCHMA) lead to higher density (1.10) polymers. In addition to PIBMA, there were several other possible monomers which could be considered in making low density methacrylates; however most would be ruled out on cost grounds. Figure 5.2 shows the T_g against density (ρ) for polymethacrylates, indicating the region of interest when T_g (of above 40°C) and low density are considered. This figure, however, gives no actual permeability values for the polymers.

5.3 (2) Synthetic Strategy for Modified Methacrylates

In an attempt to produce polymers of low density methacrylates, copolymerisation of branched and long chained monomers have been tried. The idea behind the production of copolymers is to attain better oxygen permeability than can be achieved by single homopolymers based on methacrylates (such as PIBMA, which appeared to have a reasonable oxygen permeability value of around 6 Dk units). The density of a polymer may be regarded as the "looseness" of the polymer structure to packing; linear side chains, branched side chains or cyclic side chains will contribute to

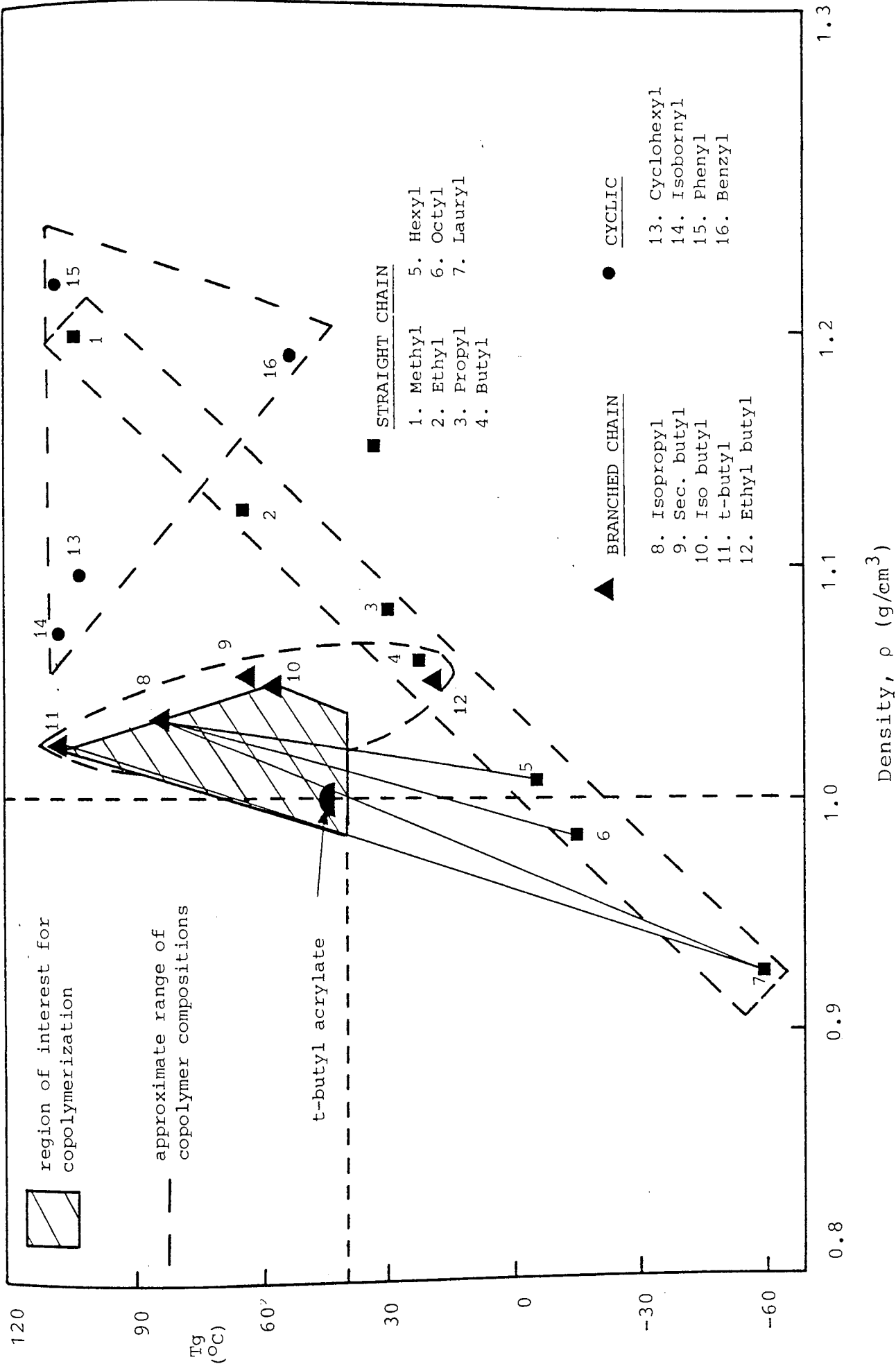


Figure 5.2 Tg and density of polymethacrylate derivatives

lowering of density. The Tg of any given copolymer can be predicted with a reasonable degree of accuracy using the following equation:

$$\frac{1}{T_g} = \frac{W_1}{T_{g1}} + \frac{W_2}{T_{g2}} + \frac{W_3}{T_{g3}} + \dots + \frac{W_n}{T_{gn}}$$

in which T_{gn} is the Tg of the given homopolymer

W_n is the weight % of the monomer

T_g is the calculated Tg of the co/terpolymer

The hypothesis of "low density - high permeability" was observed to hold for a series of copolymers based on branched methacrylates together with long-chained methacrylates. A selection of these results are shown in Table 5.2, and a graph of log of permeability against density is shown in Figure 5.3. The plot clearly shows a general relationship between the log P and density (ρ). It was found that by increasing the number of carbon atoms in the side chain, the general decrease of density has resulted in an increase in the permeability. This is partly due to the increase in side chain length which causes polymer molecules to be spaced apart, so reducing the intermolecular interaction. Additionally, it is expected that increase in the chain length results in an increase in its bulkiness (as a free volume effect) together with an increase in chain flexibility. The exception to the rule occurs when the number of carbon atoms in the methacrylate side chain is 12 or more (i.e. lauryl methacrylate upwards). It is reported that the properties closely related to Tg rise with increase in chain length due to side chain crystallization and possible formation of block copolymers⁽¹⁴¹⁾. Although the high oxygen permeability seen among the linear bulky side groups is useful, it has been observed⁽¹⁴⁰⁾ that they can only be used in small quantities due to

TABLE 5.2 OXYGEN PERMEABILITY, T_g AND DENSITY OF POLYMERS

<u>POLYMERS</u>	<u>T_g(K)</u>	<u>DENSITY</u> <u>(ρ)</u> <u>(gcm⁻³)</u>	<u>OXYGEN</u> <u>PERMEABILITY(P)</u> <u>(X10⁻¹¹ cc(STP)cm cm² sec mmHg)</u>
PMMA	432	1.19	0.1
PEMA	338	1.10	1.0
PIBMA	326	1.02	6.8
PtBMA		1.02	too brittle/fragile
PtBA	251	0.99	7.0
PIPMA	354	1.03	4.0

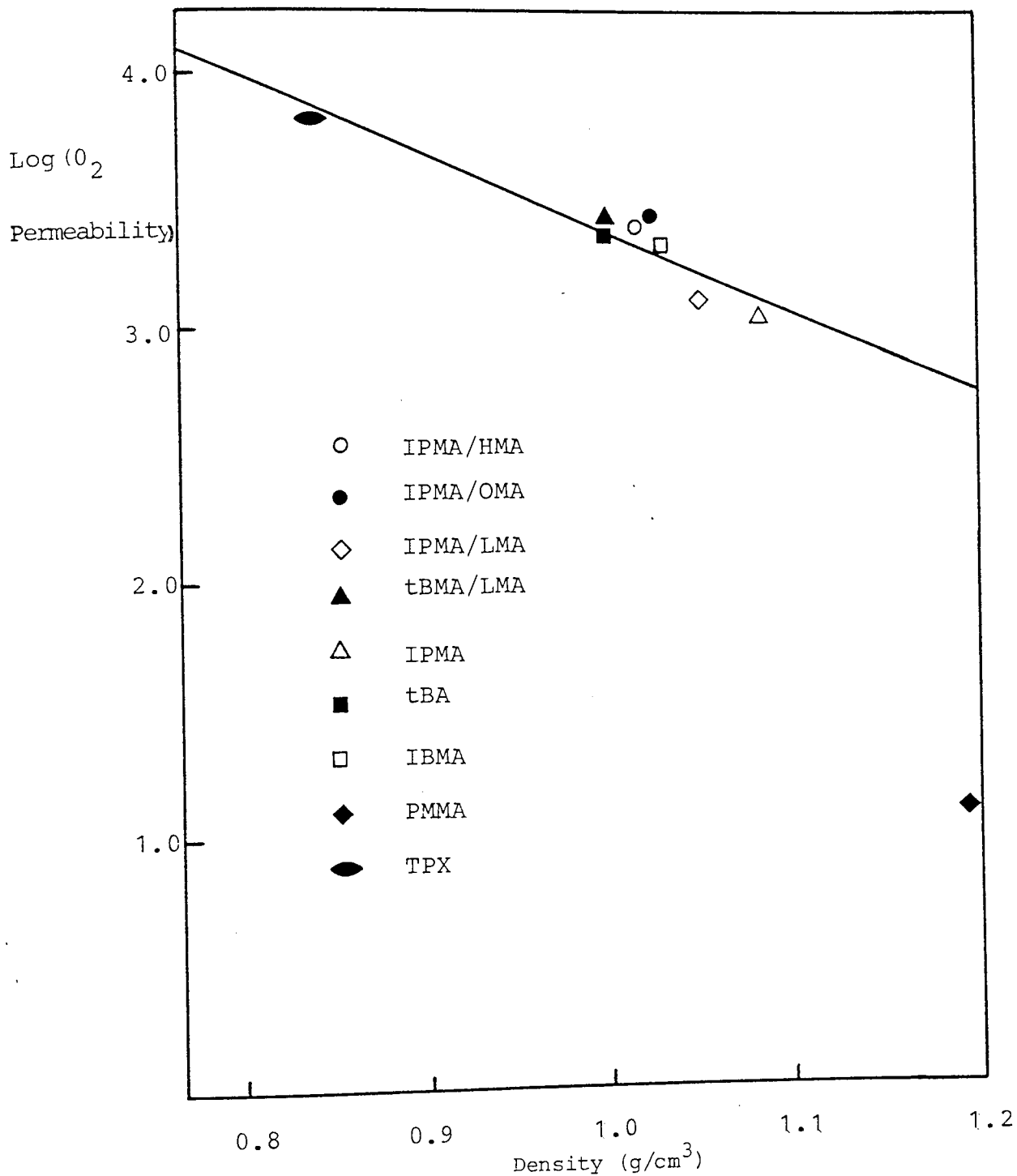


Figure 5.3 Effect of density on the oxygen permeability ($\times 10^{-11}$, ccO₂(STP) cm/cm² sec.mmHg) of various polymers.

their lowering of T_g (see Figure 5.2), which leads to the material being too flexible at room temperature. Initially, oxygen permeabilities of homopolymers of alkyl methacrylates were investigated with Schema Versatae (Table 5.2); the results are quoted from project students working in the laboratories, and show interesting results. Starting from methyl methacrylate to the ethyl substituent leads to lowering of density and T_g together with an increase in the permeability. This is to be expected by prediction from the earlier argument of "low density and high permeability". Moving further into branched side groups, such as isobutyl methacrylate, brings about a further decrease in the T_g and density with considerable increase in its oxygen permeability. These results indicate the effect of bulky side groups on increasing the free volume of the chain structure. Hence, branched side groups appear to be more effective in raising the permeability than does an increase in chain length. This is further shown by the increase in oxygen permeability from PEMA to PIPMA.

The effect of chain flexibility can be seen from the results of PIPMA and PIBMA in that the extra CH_2 in PIBMA appears to contribute to higher permeability in this methacrylate. PtBA and PtBMA were examined to further elucidate the effect of branched side groups on the permeability. PtBA appears to have an ideal balance of T_g , density and permeability, although the high cost of this monomer (£435/100g) does not justify its pursuit in the search for a high oxygen permeable material. PIBMA on the other hand gives equally acceptable oxygen permeability at much lower cost (£0.98/100g); PtBMA although it appeared promising in its density, was too fragile to be measured in the permeability apparatus.

These results on homopolymers on their own do not give any indication of the permeability of copolymers. Table 5.3 shows the density and oxygen permeability of assorted copolymers based on MMA. Figure 5.4 is a graph of oxygen permeabilities of copolymers plotted against molar % of MMA in the total composition.

TABLE 5.3 OXYGEN PERMEABILITY AND DENSITY OF COPOLYMERS WITH MMA

<u>POLYMER</u>	<u>DENSITY (ρ)</u> (gcm^{-3})	<u>OXYGEN PERMEABILITY (P)</u> ($\times 10^{-11} \frac{\text{cc (STP)cm}}{\text{cm}^2\text{sec mmHg}}$)
MMA	1.19	0.1
MMA(70) β -PEMA(30)	1.03	0.16
MMA(60)EHMA(40)	1.10	2.73
MMA(50)EHMA(50)	1.08	3.37
MMA(80)A174(20)	1.13	0.5
MMA(60)A174(40)	1.05	2.9
MMA(40)A174(60)	1.00	8.5
MMA(90)EEMA(10)	1.18	2.61
MMA(60)EEMA(40)	1.13	7.23
MMA(60)SMI(40)	1.065	15.2

Footnote: A174 is γ -methacryloxy propyl trimethoxysilane ($\rho = 1.045 \text{ gcm}^{-3}$)

SMI is tris(trimethylsiloxanyl) methacryloxy propylsilane ($\rho = 0.93 \text{ gcm}^{-3}$)

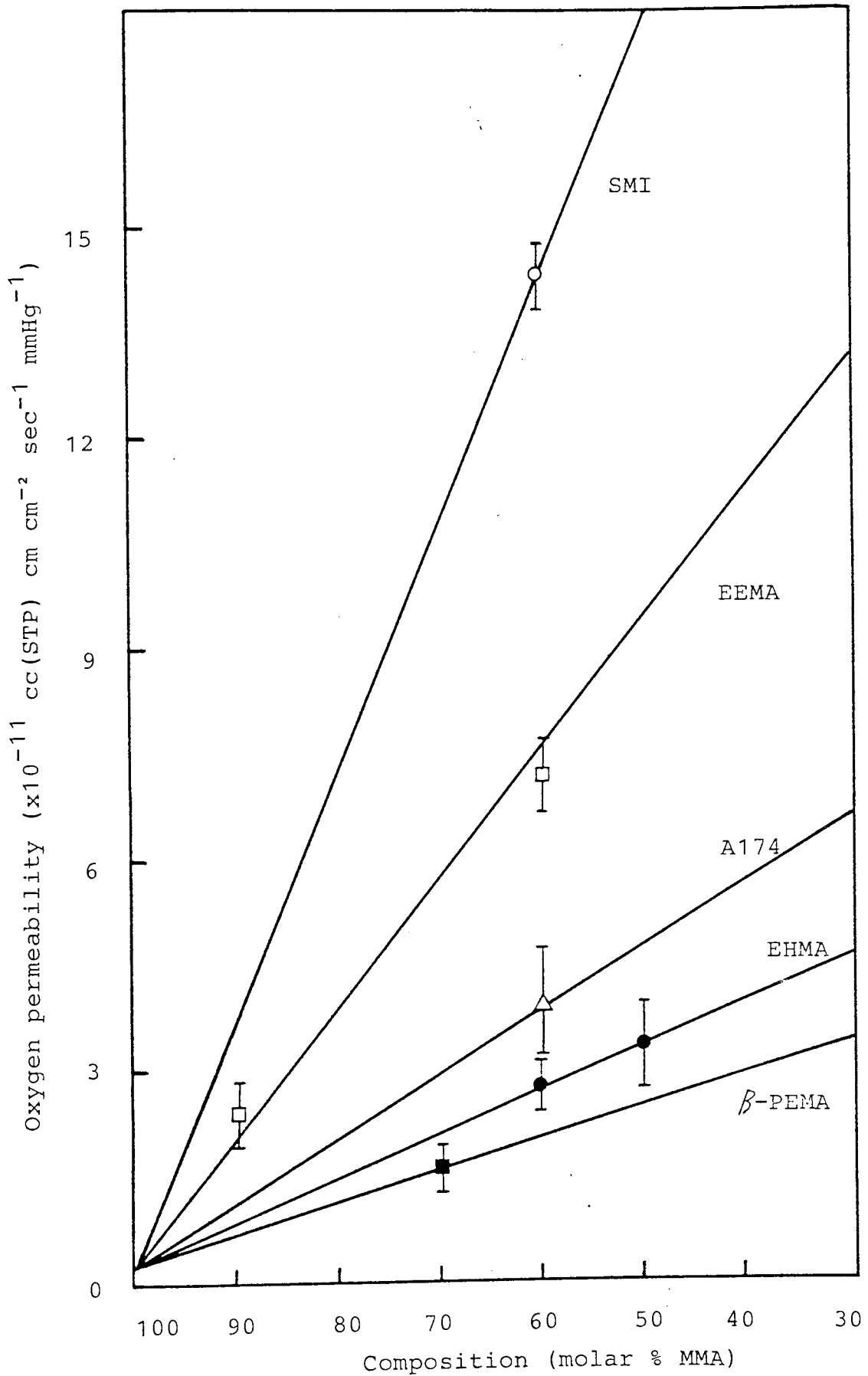


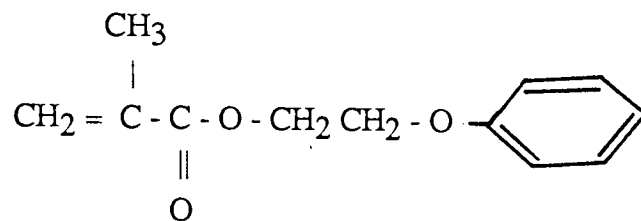
Figure 5.4

The effect of MMA composition of various copolymers on oxygen permeability

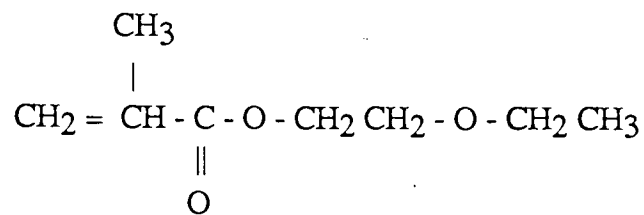
It was plotted to show comparative trends of these materials and the lines are based on average values rather than absolute composition - permeability profiles. There is no intention therefore to imply linearity in the case of each composition-permeability profile. The plot clearly shows the interesting effect of structural variation of comonomers on the permeability of MMA.

The oxygen permeability of MMA(70) β -PEMA(30) copolymer indicates that the presence of aromatic rings on a flexible side chain appears not to have any positive effect on oxygen permeability. Increasing the side chain length, as in EHMA, results in moderate improvement in the permeability but the branched chain has difficulty in free mobility. The presence of silicone (as in A174) in the methacrylate side chain appears to improve the permeability of the copolymer, although again the stiffness in the side chain counteracts other structural benefits. In contrast, the flexible ether bond in EEMA with no branching or aromatic substituent increases the chain mobility of the polymer molecules resulting in the greatly improved permeability. The further effect of siloxy substituents can be demonstrated by the more complex silane comonomer (SMI) whose permeability is 150 times greater than PMMA homopolymer. The structural variation of these comonomers are illustrated in Figure 5.5. The unexpected low permeability in A174/MMA copolymer is probably due to the A174 monomer being susceptible to exchange (transfer) reactions tending to cause crosslinking in the resulting polymer. Although A174 is volatile enough to be distilled, there is greater variability between the monomers supplied, the big error bars reflect for these variations in the results. These copolymers based on MMA indicate the effect of structural variation in comonomers quite clearly.

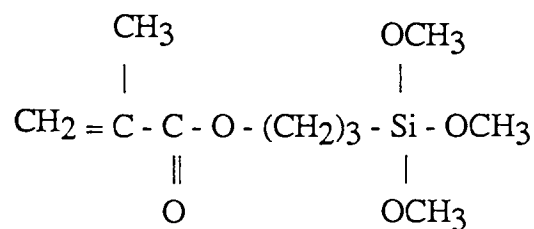
Table 5.4 shows the results of density and oxygen permeability of copolymers based on IBMA. As seen from Table 5.4, PIBMA appears to have acceptable permeability, however, here the attempts were made to show the structural



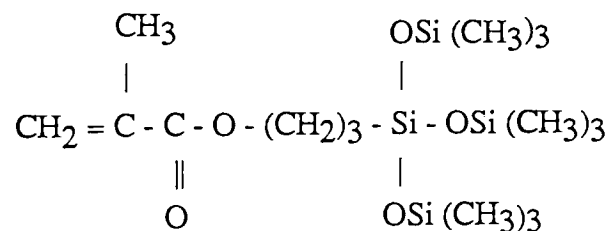
β - Phenoxy ethyl methacrylate (β PEMA)



Ethyl ethoxy methacrylate (EEMA)



γ-methacryloxy propyltrimethoxysilane (AI74)



Tris(trimethylsiloxanyl) methacryloxy propylsilane (SMI)

Figure 5.5 Structures of comonomers used with MMA

TABLE 5.4 OXYGEN PERMEABILITY AND DENSITY OF COPOLYMERS
WITH BRANCHED METHACRYLATES

<u>POLYMER</u>	<u>DENSITY</u> (ρ) (gcm^{-3})	<u>OXYGEN</u> <u>PERMEABILITY (P)</u> ($\times 10^{-11} \frac{\text{cc (STP) cm}}{\text{cm}^2 \text{ sec mmHg}}$)
PIBMA	1.03	6.8
P(IBMA(90)MMA(10))		7.8
P(tBMA(75)LMA(25))	0.99	7.8
P(IPMA(60)HMA(40))	1.02	7.5
P(IPMA(70)OMA(30))	1.02	7.8
P(IPMA(80)LMA(20))	1.04	4.5
P(IBMA(60)SMI(40))	0.995	18.4

effect on the existing permeability by copolymerization. Although there is an increase in the permeability of copolymers, there seems to be a limited effect of long chained comonomers on PIBMA based copolymers. Indeed by comparing with the permeability of PIBMA(90) MMA(10) copolymer, it is difficult to detect whether the improved value is due to the structural factors present in PIBMA (such as branched bulky side group) or the plasticizing effect of long straight chains.

5.3 (3) The Permeability Criteria and Their Influence on Surface Properties

As indicated by the improved permeability of siloxy-MMA copolymer, the presence of a silicone substituent contributes to high oxygen permeability. Indeed the literature based on the vast number of patents examined in Chapter 2 indicate the amount of interest concerning materials based on siloxy polymers. However, it is well known in the field of materials science that these siloxy-based polymers are very hydrophobic.

There is a strong clinical belief that suggests a Dk of around 7 to 8 units being quite acceptable for rigid gas permeable materials (taken at room temperature) in daily wear purposes. Indeed many main stream rigid gas permeable materials (such as Boston 4, Polycon) possess a permeability (Dk value) of around 8. By projecting the Dk of these materials at an eye temperature of 34° - 35°C, the indication is that the possible oxygen permeability will be around 10 to 12 units. The non-silicone based methacrylate materials were shown to have Dk of around 7 to 8 units at room temperature which is in keeping with the above case and should be quite acceptable as well as enabling a better compromise with other properties to be attached. Thus, in selecting clinically suitable rigid gas permeable materials, it is also necessary to consider their surface properties together with oxygen permeability. It is therefore appropriate at this stage to turn our attention to the attainment of surface properties of

these methacrylate based materials.

5.4 SURFACE PROPERTIES OF METHACRYLATE POLYMERS

For a material in contact lens applications to perform effectively, it is a necessary condition of the tear to wet the surface of the lens and that the surface remains free from any deposits or debris. Most of the commercially available rigid gas permeable materials have hydrophobic surfaces and to counteract this, various treatments have to be performed. Some specially prepared wetting solutions are commercially available, and these are reported to make contact lenses more comfortable (111). The most usual method is to incorporate comonomer into the polymer system to improve the surface property without unduly affecting the oxygen permeability.

5.4 (1) Wettability Studies of Alkyl Methacrylates

The initial work on surface wettability characteristics were made on copolymers with which oxygen permeability studies were made earlier on in this chapter. The most convenient way of assessing the wettability is by the sessile drop contact angle measurement. In this study the preliminary checks were made using distilled water, and for surface energy calculation, water and methylene iodide were used. It is expected that materials based upon simple alkyl methacrylates should reflect the acceptable water contact angle of PMMA, where the surface of this polymer is just wettable by the tear fluid. Any copolymerized substituent groups, including polar groups, should have reasonable wettability characteristics upon interaction with polar dominated water. However, for the material to perform effectively, it is essential to have a balance of polar and dispersive components; here again PMMA can be taken as a base line material.

Table 5.5 indicates the surface characteristics of MMA copolymers and Table 5.6 of IBMA based copolymers. A quick glance down the water contact angle

POLYMER	CONTACT ANGLE (°)		SURFACE FREE ENERGIES (dynes cm ⁻¹)		
	WATER	METHYLORIDE	TOTAL (γ _T)	POLAR (γ _p)	DISPERSIVE (γ _d)
MMA(70)β-PHEMA(30)	63°	36°	47.9	12.3	35.5
MMA(60)EHMA(40)	77°	37°	42.6	5.0	37.6
MMA(50)EHMA(50)	73°	41°	42.2	7.5	34.7
MMA(90)EEMA(10)	63°	27°	50.4	10.8	39.6
MMA(60)EEMA(40)	64°	32°	48.7	11.3	37.6
MMA(90)IBMA(10)	68.5°	26.5°	48.6	7.8	40.8
MMA(80)A174(20)	71°	37.5°	44.2	7.9	36.2
MMA(60)A174(40)	72°	42°	42.2	8.2	34.0
MMA(40)A174(60)	78°	45°	39.0	5.7	33.4
MMA(100)	62.5°	25°	51.2	10.9	40.3

TABLE 5.5 CONTACT ANGLES AND SURFACE FREE ENERGIES OF COPOLYMERS BASED ON MMA

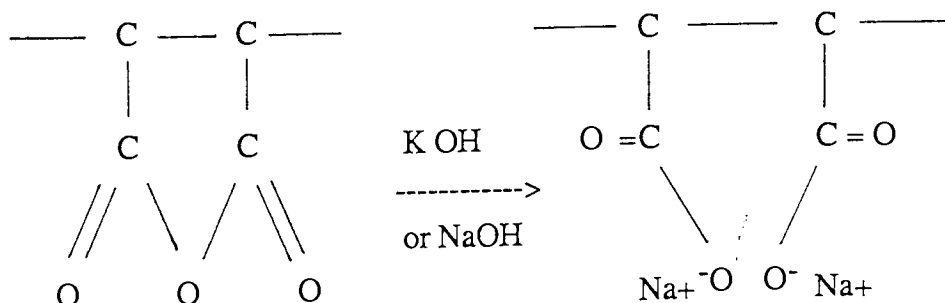
POLYMER	CONTACT ANGLE (°)		SURFACE FREE ENERGIES (dynes cm ⁻¹)		
	WATER	METHYL IODIDE	TOTAL (γT)	POLAR (γp)	DISPERSIVE (γd)
IBMA	64°	33°	48.4	11.2	37.2
IPMA	69.5°	33°	46.2	8.1	38.2
tBA	68.5°	31.5°	47.1	8.4	38.7
tBMA(75)LMA(25)	73°	37.5°	43.5	6.9	36.6
IBMA(90)MMA(10)	68.5°	26.5°	48.6	7.8	40.8
IPMA(60)HMA(40)	73°	26.5°	47.3	5.6	41.7
IPMA(70)OMA(30)	74°	32°	45.2	5.7	39.5
IPMA(80)LMA(20)	76.5°	37°	42.7	5.2	37.5

TABLE 5.6 CONTACT ANGLE AND SURFACE FREE ENERGY COMPONENT OF BRANCHED COPOLYMERS

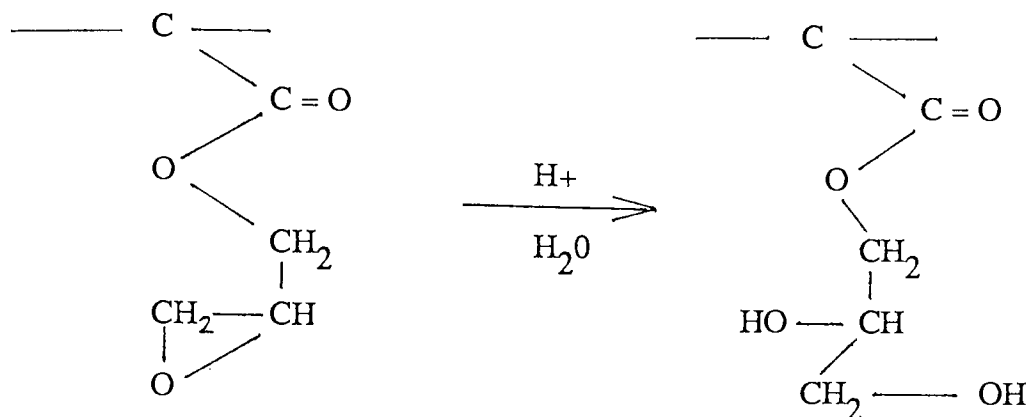
column shows that most of the copolymer systems do not have adequate wettability on their own. On the other hand, those with an equivalent degree of wetting as PMMA do not possess enough permeability (compare to Table 5.3). Therefore, it is essential to improve on the surface properties without affecting oxygen permeability. Based on the idea of copolymerization systems being more favourable than a single homopolymer to fulfill all the requirements, attempts were made to copolymerize those monomers which upon synthesis gave required results.

5.4 (2) Surface Modification by Copolymerization

Initially, incorporation of polar hydrophilic monomers such as 2(hydroxyethyl methacrylate) (HEMA) and methacrylic acid (MAA) were tried. This serves to increase the overall bulk hydrophilicity of the copolymer as well as surface properties. Then, secondly, comonomers with side groups which can be made hydrophilic by chemical reactions such as maleic anhydride (Ma) and glycidyl methacrylate (GMA) were attempted. This occurs at the surface of the copolymer rather than throughout the bulk. The outline of the relevant reactions are as shown below schematically. The ionized groups at the surface upon hydrolysis create more surface wettability with maleic anhydride copolymers. The hydrolysis reaction is:



In glycidyl methacrylate copolymers, the ring opening of the epoxide side groups leads to the improved surface wettability. The reaction is:



Results of both strategies are listed in Table 5.7 where copolymers were produced primarily to find a comonomer which will provide the best balance of oxygen permeability and surface wettability (indicated roughly by water contact angle). Contact angles of distilled water on dry untreated copolymer discs were determined, then to bring forth the chemical treatment on the second type of comonomers, 10% and 20% potassium hydroxide (KOH) were used by soaking the polymer in the solution at room temperature, followed by thorough rinsing with distilled water. The oxygen permeabilities of the copolymers incorporating hydrophilic monomers were investigated at the same time to evaluate the possible effect of these monomers on the permeability property; they are also listed in Table 5.7. The scatter of results was thought to be due to the presence of a surfactant or residual monomer layer; effective removal of the layers was performed by soaking briefly in distilled water or ethanol. Water uptake, on the other hand, at the surface of the polymer by the hydrophilic monomers was not contributory to the scatter of results.

The simple addition of hydrophilic polar monomer such as HEMA (in small amount) did not bring about any substantial increase in the surface wettability as expected. Furthermore, oxygen permeability is observed to decrease when polar monomer is added to the bulk. A higher proportion of polar groups present in the bulk leads to more molecular interaction (e.g. dipole attractions) thus increasing the overall chain stiffness and resultant fall in oxygen permeability. There was little effect

TABLE 5.7 CONTACT ANGLE AND OXYGEN PERMEABILITY OF
"WETTABLE" COPOLYMERS

POLYMER	DRY	SOAKED IN KOH FOR 24hrs(1)		O ₂ PERMEABILITY (X10 ⁻¹¹ Dkunit)
	CONTACT ANGLE	10%	20%	
PMMA	62.5°			0.1
PIBMA	75°	78°	60°	6.8
PIBMA/HEMA 2.5	68.5°	72.3°		5.5
PIBMA/HEMA 5	74°	72°		7.4
PIBMA/Ma 5	79°	77°	71°	3.2
PIBMA/Ma 10	77°	66°	65°	4.8
PIBMA/Ma 15	62°	64°	65°	4.4
PIBMA/GMA 5	74°	71°	70.5°	4.6
PIBMA/GMA 10	77°	76°	73°	6.0
PIBMA/GMA 15	63°	67°	64.5°	5.0

Footnote

(1) Washed, dried, and contact angle measured with distilled water.

on HEMA copolymers when they were soaked in potassium hydroxide for 24 hours. However, prolonged soaking is known to produce progressive water absorption in the case of polymers containing 2-hydroxyethyl methacrylate or methacrylic acid⁽¹³⁵⁾.

The second strategy of polymerization of monomers with surface modification by surface hydration was shown to be more beneficial in improving the wettability of these copolymer systems. Although at 5% molar incorporation, there is no appreciable effect on contact angle, at 15% molar incorporation, these copolymers were comparable to PMMA homopolymer. Unfortunately, again, the oxygen permeabilities were reduced in both Ma and GMA copolymers due to the existence of polar groups. As discussed earlier, polar groups lead to increased molecular interactions with subsequent stiffness in the chain and reduced free volume as molecules are attracted closely within polymer network. The combined decrease in the free volume and increased chain stiffness leads to reduction of the gas permeability due to the hindering in diffusion of gas. In glycidyl methacrylate's case, the permeability is slightly better because of flexibility in the ester linkage.

The effect of soaking in potassium hydroxide showed instant results upon ring opening comonomers even after a short period of soaking, in contrast to the negligible effect upon HEMA. The effect on the increase of surface wettability in soaking is such that in maleic anhydride it is related to the progressively opened carboxylate (COO^-) substituent, therefore it is expected that there is continuous hydrophilic modification. In the case of glycidyl methacrylate, the presence of two hydroxy groups incur moderate hydrophilicity. The main interest here is in studying the surface properties of unsoaked materials, and the effect upon these properties following relatively short periods of surface treatment.

Table 5.8 shows the water contact angles of simple alkyl methacrylate homopolymers, indicating the broad similarities between them. PMMA is shown to

TABLE 5.8 WATER CONTACT ANGLE OF HOMOPOLYMERS BASED ON
SIMPLE ALKYL METHACRYLATES

<u>POLYMER</u>	<u>WATER CONTACT ANGLE (°)</u>
MMA	62.5°
EMA	66.5°
IBMA	64°
tBMA	66.5°
nBMA	68.0°
IPMA	69.5°
tBA	68.5°

have the lowest water contact angle. As the methacrylate chain grows with the addition of -CH₂ groups, the polar ester linkage is distanced further from water molecules making the resultant wettability drop as the series goes up in chain length. Simple chemical reactions such as with potassium hydroxide solution give better wettability than untreated surfaces, although its clinical implication is debatable. Many proprietary wetting solutions induce progressive hydrophilicity in alkaline solutions (though these are tested for its short-term effect and not its long-term effect).

Thus judicious adjustment in the choice of the comonomer and the quantity of comonomer is necessary in order to achieve adequate surface wettability in accordance with the required oxygen permeability. One solution to this problem may lie in treating the most outer surface structure of otherwise permeable polymer by an effective surface treatment such as plasma etching or plasma grafting. This avenue of thought is dealt with in more detail in Chapter 6.

5.5 MECHANICAL PROPERTIES OF METHACRYLATE COPOLYMERS

The consideration of mechanical properties, at first, may appear to be the least important aspect in the choice of materials to be used in contact lens applications. Unlike the other previously discussed properties of oxygen permeability and surface property, where the consideration is based on the clinical implications, the mechanical aspects are more related to processing, fabrication and handling. Although it is important for the material to withstand the constant blinking action, problems arise more often in processing stages and handling than in the eye. Here again, PMMA has a balance of properties which forms the basis in choosing the mechanically acceptable material.

The work was tackled in two main streams; one was to characterise the polymers used in contact lens applications using the micropenetrometry technique with

spherical indentors, then the second approach by comparison of the appropriate materials with commercially available materials by tensile testing. The effect of crosslinking (in commercial materials, agents are added to increase the crosslink density to improve mechanical properties) upon oxygen permeability was also studied.

5.5 (1) Compression Properties of Methacrylates

In order to investigate the effect of structural variation upon the mechanical properties of alkyl methacrylates, micropenetrometry (see Chapter 4) by indentation was performed on alkyl methacrylate homopolymers. Table 5.9 shows the results by means of 1 minute deformation for varying loads. Figures 5.6 and 5.7 show the correlation of log (load) with log (indentation) for various types of methacrylate. Quite clearly these methacrylates fall into a broad band having similar slopes. The slope corresponds to n in the Hertz equation:

$$\frac{E}{1 - \nu^2} = \frac{3}{4} \frac{mg}{r^{1/2} h^n}$$

where E is Young's modulus of elasticity, ν the Poisson's ratio of the material, m the load, g the gravity, r the radius of the spherical indenter, and h the depth of indentation.

5.5 (2) Tensile Properties of Methacrylates

Tensile tests were carried out on selected methacrylate copolymers to compare with the tensile behaviour of some commercial rigid contact lens materials. Table 5.10 indicates the selection of results. The indication is that these synthesized methacrylate polymers have similar tensile properties comparable to commercial contact

TABLE 5.9 1 MINUTE DEFORMATION (h) in MICRONS (μm)

<u>POLYMER</u>	<u>LOAD (m) (gm)</u>						
	<u>0.6</u>	<u>1</u>	<u>2</u>	<u>4</u>	<u>8</u>	<u>16</u>	<u>32</u>
PMMA (t=1.05mm)		0.1	0.19	0.4	0.66	1.78	4.08
PBMA (t=0.92mm)	0.11	0.19	0.3	0.6			
PIBMA (t=0.87mm)		0.1	0.15	0.32	0.75	1.88	2.65
PIPMA (t=0.4mm)		0.18	0.67	0.9	1.75	3.83	5.37
PtBA (t=0.21mm)		0.74	1.32	2.89	4.33		

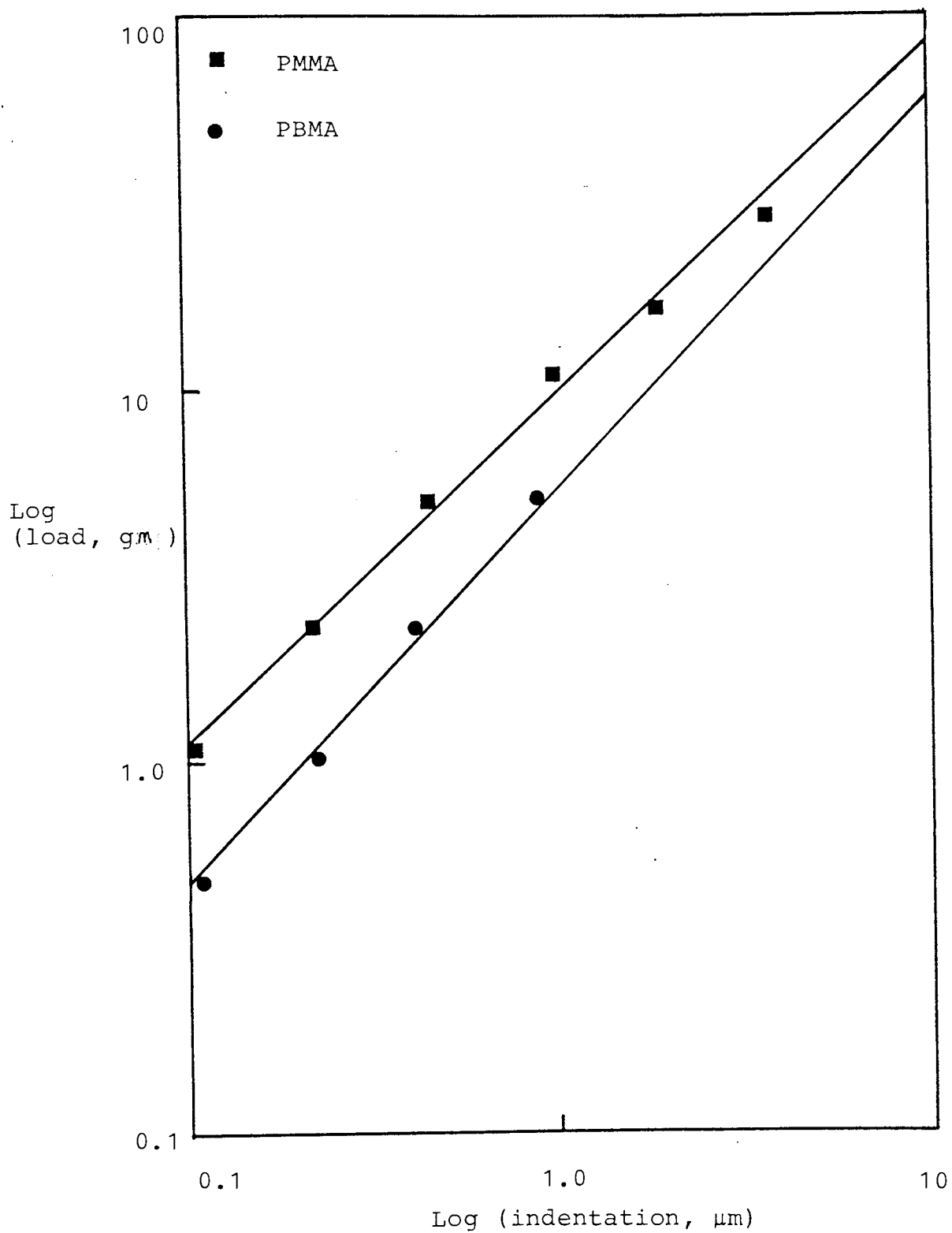


Figure 5.6 Correlation of log indentation (h) and log load (m) for straight chain methacrylates

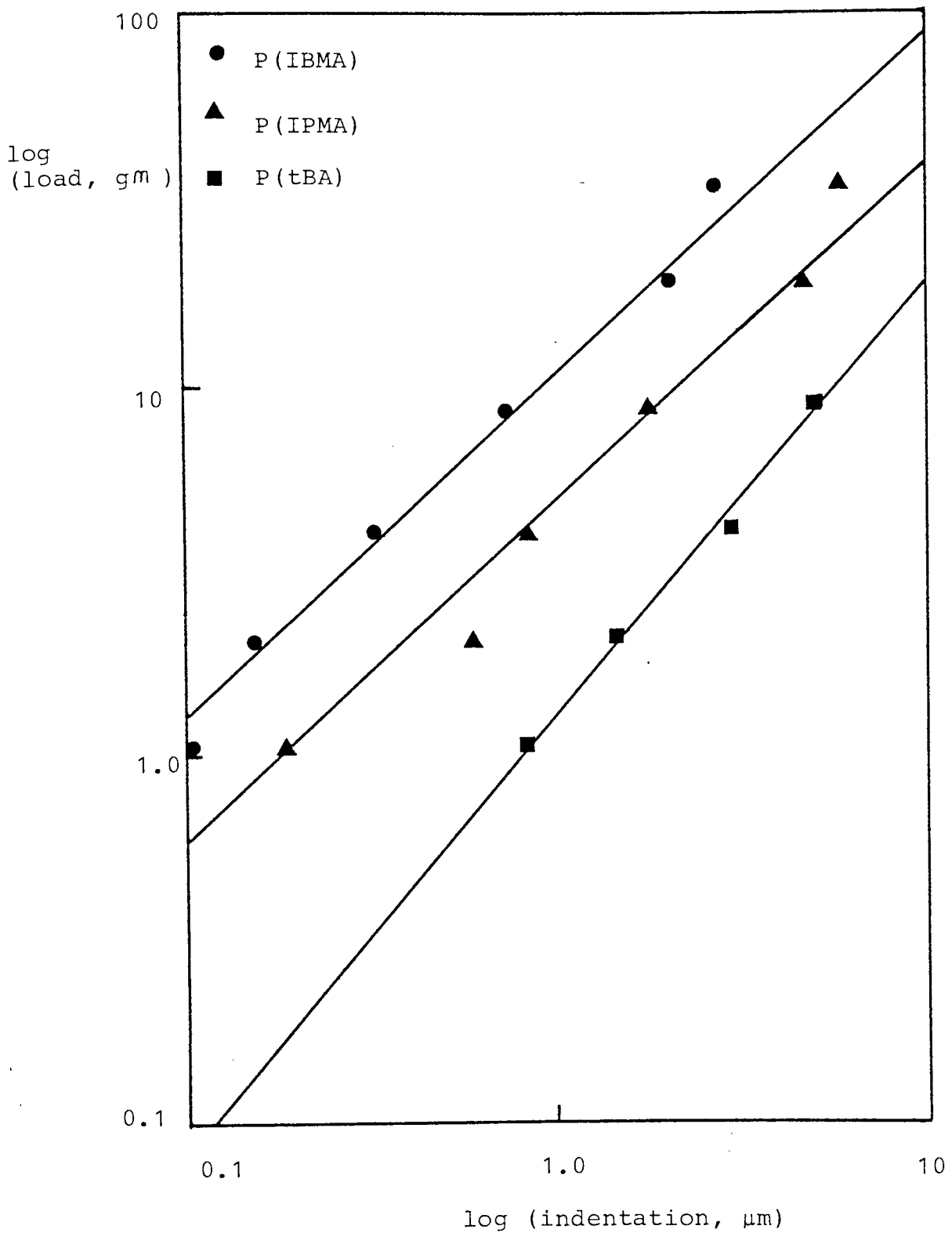


Figure 5.7 Correlation of log indentation (h) with log load (m) for branched methacrylates

lens materials. An experimental material with % elongation at break between 30 and 50% is thought to be adequate for a material to be used as a contact lens. The strong nature of PMMA is thought to be related to the inter-molecular polar attractions of ester groups in the methacrylate chain and also the close packing afforded by the methyl group being compact. As branching or bulky cyclic groups interfere with close packing and reduce the chance of interaction between molecules, the tensile strength is shown to deteriorate dramatically in copolymers of MMA with IBMA and CHMA. Low molecular weight polymers are associated with a reduction in tensile strength and increase in the general brittleness of the polymer. This is because of shorter chain length leading to less entanglement of polymer chains which gives the polymer its viscoelastic nature. Presence of impurities or chain transfer reaction causing shorter polymer chains also reduces the tensile strength through lowering of the molecular weight.

5.5 (3) Crosslinking and Oxygen Permeability

A small amount of crosslinking agent is often added to commercial contact lens materials to improve their mechanical properties. In organo-siloxo materials of the type originated by Gaylord, there is tendency for phase separation to occur between dissimilar siloxo and methacrylate components. Also siloxo substituents increase flexibility and decrease strength. Crosslinking provides anchoring points for the chains and those anchor points restrain excessive movement and maintain the position of the chain in the network; thus dimensional stability is improved. Here, the effect of the crosslinking agent was determined by measuring the properties of crosslinked polymers. Table 5.11 shows the results as an increase in contact angle coupled with lowered permeability.

TABLE 5.10 TENSILE PROPERTIES OF GAS PERMEABLE MATERIALS

MATERIAL	ELONGATION AT BREAK (%)	TENSILE STRENGTH (N.mm ⁻²)	MAXIMUM LOAD AT BREAK (N)
<u>Commercial</u>			
BOSTON 1	70	5.5	3.71
POLYCON	80	7.5	5.95
OXYFLOW	40	0.6	0.37
OPTACRYL 60	60	6.5	3.81
PMMA	85	9.34	9.25
<u>Experimental</u>			
PIBMA	52	3.45	3.61
IBMA(90)MMA(10)	46	0.82	0.71
PMMA(50)CHMA(50)	33	0.2	0.15

TABLE 5.11 PROPERTIES OF UNCROSSLINKED PIBMA AND
CROSSLINKED PIBMA -EDG

<u>POLYMER</u>	<u>DENSITY</u> (gcm ⁻³)	<u>O₂ PERMEABILITY</u> (P) cc (STP) cm cm ² sec mmHg	<u>CONTACT</u> <u>ANGLE</u>
PIBMA(100)	1.02	6.8 x 10 ⁻¹¹	64°
PIBMA(99)EGD(1)	1.04	5.8 x 10 ⁻¹¹	66°

5.6 CONCLUSIONS

In this chapter, attempts were made to elucidate the effect of replacing the methyl group by other related alkyl groups on the property requirements of gas permeable contact lens materials. The work provided some interesting points in comparing these materials with the basic hard contact lens material PMMA.

The gas permeability phenomena of simple alkyl methacrylates were investigated initially using a Davenport Permeability Apparatus. Table 5.1 shows a fifty fold increase in gas permeability from methyl methacrylate to branched alkyl methacrylates. This apparatus, though useful for providing results of the fundamental work, was not applicable to direct measurement on contact lenses.

The relationship between density and permeability of these groups of methacrylates were examined from literature and empirical values (see Figure 5.3). There is a general relationship between the log of permeability and density; linear side chains, branched side chains or cyclic side chains contribute to lowering of density and

a resultant increase in the permeability. Together with the literature values of glass transition temperature (T_g) and densities, a group of alkyl methacrylates were selected to form copolymers having T_g s of around 40°C with low density ($SG < 1.00$) in order to provide copolymers having higher oxygen permeability than the respective homopolymers. The copolymerization strategies were set by choosing comonomers of varying structures and the effect of such copolymerization on PMMA and PIBMA as base monomers were examined. The presence of bulky silicone substituents contributed to attainment of higher oxygen permeability. However, there is clinical belief that a Dk of around 7 to 8 units is acceptable for daily wear purposes. The non-silicone based alkyl methacrylate copolymers had shown Dk of around 7 units (see Table 5.4) with scope of better compromise with other properties such as surface wettability. The mechanical properties of these methacrylates were not significantly different to commercial rigid gas permeable materials.

The first copolymerization strategy to improve surface wettability involved the incorporation of hydrophilic polar monomers at low levels of 2.5% to 5%. This method did not produce any significant increase in the surface wettability (Table 5.7). On the other hand, copolymerization of reactive side group monomers (such as maleic anhydride) together with surface modification has demonstrated a reasonable improvement in the surface wettability (Table 5.7). Unfortunately 5%, 10%, and 15% molar incorporation of such comonomers caused problems due to polar interactions at molecular chains causing the oxygen permeability to fall. There is scope for improvement of surface wettability by soaking in alkaline solutions such as potassium hydroxide to induce progressive hydrophilicity provided the treatment causes no physiological effect in the eye. Difficulty exists in producing copolymers having both requirements of oxygen permeability and surface wettability to suffice clinical and physiological compatibility by the simple synthetic strategies. Another

method of surface improvement involves plasma oxidation and is dealt with in the next Chapter.

CHAPTER VI
SURFACE MODIFICATION OF POLYMER MATERIALS
BY AN OXYGEN PLASMA

6.1 INTRODUCTION

The last chapter described attempts to achieve a balance of oxygen permeability, surface wettability and mechanical properties by copolymerization of an appropriate combination of monomers. Individual objectives of attaining acceptable levels in each property were obtained. However, it was difficult to achieve adequate surface wettability by the synthetic means of incorporating hydrophilic reactive monomers without affecting oxygen permeability. The introduction of polar side-chains has a favourable effect on improving the surface wettability of a copolymer, but unfortunately it also causes an increase in the intermolecular attraction within the polymer network, reducing the diffusivity of gases through the polymer bulk. The polar hydrophilic monomers are thus observed to interfere with the bulk oxygen permeability. This is so even when the effect was limited to surface layers by ring opening, described in the previous chapter.

As the two objectives of balancing oxygen permeability and mechanical properties were achieved by the copolymerization of suitable monomers, the next aim was concentrated upon achieving the surface wettability improvement by means of external surface modification without impairing the bulk oxygen permeability. Much research has been conducted to investigate the modification of the hydrophilicity of synthetic polymers through various chemical, thermal and radiation treatments. In recent years, for example, glow discharge plasmas have been utilized in surface modification, surface coating, etching and photoresist development. The advantages of using plasma treatment are that:

- a) the modification of surface takes place at depth of a few μm ,
therefore the bulk properties are not affected.
- b) being a dry gaseous process, it does not require solvent washing and

drying, thus saving in terms of raw material with reduced danger of pollution,

c) it is fairly economical as operating temperatures are low.

A glow discharge plasma involves chemical reactions in a partially ionized gas composed of ions, electrons, and neutral species. In a discharge, free electrons gain energy from an imposed electric field and lose this energy through collisions with neutral gas molecules. The transfer of energy to the molecules leads to the formation of a variety of new species including metastable atoms, free radicals, and ions. These products are all chemically active and thus can serve as precursors to the formation of new stable compounds. The unique surface modifications which can be achieved by a plasma are due to the effects of ultraviolet radiation and chemically active species.

The surface modifications by plasma may be broadly divided into areas depending on the gases used and the techniques employed. They are:

- 1) surface modification by inorganic gases,
- 2) coating of thin films by plasma polymerization with organic gases,
- 3) surface graft polymerization of vinyl monomers using the free radicals in the plasma.

The use of glow discharge plasmas in the surface modification of materials used in the design of contact lenses is not an area extensively covered in the commercial or patent literature. The topic is conveniently divided into two sections. Firstly, surface modification using gaseous media, and secondly surface grafting of hydrophilic monomers, which has been discussed in Chapter 2. It is sufficient to say that the patent literature does not provide any fundamental data for understanding the processes involved in achieving the desired effect.

It seems inappropriate to investigate the effect of gaseous plasma treatment

at the polymer surfaces related to the contact lens materials, before studying particular groups that are present without determining whether specific groups were more susceptible than others to treatment of this type, bearing in mind both the effectiveness and durability of the treatment. The three basic questions that were therefore asked were:-

- 1) What groups are affected at the surface ?
- 2) How are they affected ?
- 3) What subsequently happens to the plasma treated surfaces ?

As there were only a few papers available which presented information on the stability of the treated surfaces, other than the observation that treated surfaces lose their reactivity after a period of time, the bulk of the work centred around the study of plasma susceptibility and stability of standard polymers such as polymethyl methacrylate and polystyrene. Just as it was necessary to study the oxygen permeability, surface and mechanical properties of the simple alkyl derivatives from MMA, it is equally logical to examine the plasma treatment of alkyl methacrylates to find the particular susceptibility of structural variations to this treatment. For comparison, polystyrene was chosen as a model substrate to represent aromatic polymers, where the benzene ring is known to affect the plasma oxidation susceptibility. The initial investigation was carried out on alkyl methacrylate polymers to establish the plasma treatment protocol in terms of r.f. power, duration of treatment and post-plasma handling. The various groups of polymers were plasma treated to examine the susceptibility of a given polymer structure in sustaining the surface wettability. The study was extended to other materials used in contact lens applications. Finally attempts were made to suggest possible reaction mechanisms in order to explain the observed reversion of wettability following plasma treatment.

Polymer membranes in the form of thin films were cleaned using a commercial surfactant (such as Boston contact lens cleaner) and dried in air by wiping the excess surface water with filter paper. The prepared membranes were placed in a vacuum oven at 40°C overnight to ensure thorough drying. Dried polymer membranes were subjected to plasma oxidation by Nanotech plasma equipment.

Nanotech plasma process equipment including a P1C2 plasma process control, an ATC1 automatic tuning controller and a NRF1 radio frequency supply with a parallel plate reactor were used. After the polymer samples were cleaned, they were cut into different shapes for ease of identification and placed in the reactor chamber. The chamber was evacuated to a pressure of 0.4 torr with an oxygen flow rate of 15 cc min⁻¹ using a flow control system. After 30 seconds, the timer and radio frequency source were switched on simultaneously, the r.f. forward power was 100W with the reflected signal, less than 1W. The pressure in the chamber fell immediately to less than 1 millitorr and remained at this level for the duration of the process. After the allotted time, the radio frequency was immediately switched off and the vacuum released. The samples were removed from the process chamber as soon as the pressure had reached one atmosphere.

The samples taken out of the reactor were placed on a mounting table and the contact angle measurement using distilled water was performed immediately afterwards. In most instances, the water droplet spreads on the surface spontaneously on the treated surface which caused difficulty in measuring the contact angle immediately following treatment. The normal protocol of contact angle measurement as set out in earlier chapters are followed here. In order to provide information on surface energies of

the treated polymer samples, contact angles with methylene iodide were also determined. The measurements were subsequently taken at intervals in order to study the decay process. In between measurements, samples were kept under cover in bottles to avoid contamination. In the temperature controlled tests, the treated samples were wrapped in aluminium foil and stored in the oven at 80°C or stored in the refrigerator at 0°C between measurements.

A quick check on the substrate surface was done by eye to note any physical changes at the surface of the treated polymers. No obvious changes in the appearance of the polymer samples were observed.

6.3 INITIAL INVESTIGATIONS

Preliminary investigations were carried out in order to establish the protocol of the effective treatment conditions in terms of (a) r.f. power, (b) duration of treatment in the plasma, (c) sample handling following plasma exposure. Discs of polymethyl methacrylate containing a small amount of ethylene glycol dimethacrylate (EGD) were plasma treated for various times and various post-reaction protocols followed. The contact angle measurement on discs immediately after the plasma treatment was extremely difficult to perform due to the very wettable surface produced at the onset of the treatment. Table 6.1 lists the contact angles with water at 100W and range of treatment times. Figures 6.1 and 6.2 indicate the general trend observed in the decay of wettability as a function of time, by gradual reversion towards the original wetting angle. Table 6.2 lists the contact angles of discs treated for 3 mins at 100W, and shows the variation of post-plasma handling effect after 24hrs. Figure 6.1 shows the slow and continuous reversion to the higher contact angle region of PMMA with a very small quantity of crosslinking agent. On the other hand Figure 6.2 shows the initial decay and

the plateau region of PMMA(85) EGD(15) copolymer where EGD contributes as a comonomer rather than a crosslinking agent.

A surfactant was used to clean the treated surface of the discs in an attempt to mechanically remove the superficial readily detachable dust layers. The results obtained did not differ markedly from the results of discs left untouched after the plasma treatment. At 24 hours after the plasma treatment, the contribution of the dust layer is probably quite small to the surface wettability decay process.

The treated discs stored under water immediately following the plasma treatment sustained marginally better wettability than discs stored in air although the decay still occurs in this post-treatment. Although there is no direct evidence it may be said that water is acting as a protective environment for the newly treated hydrophilic surfaces. This environment could act in several ways, of which possibilities include water acting as solvation shells for activated species, a low oxygen concentration pool, and perhaps as an ultraviolet light screen. It must be stressed again that these are speculative suggestions and not derived from any direct experimental evidence.

The longer treatment period of ten minutes did not necessarily cause a significant improvement in the surface wettability compared to 3 minutes exposure. Although the surface wettability of the discs was improved by only 30 seconds treatment, 3 minutes duration showed more favourable results. Hsieh and Chen (142) in the study of improvement of hydrophilicity of poly (ethylene terephthalate) by gaseous glow discharge report that, drastic improvement in wettability was achieved during the initial 2 minutes of exposure. They suggested that oxidation of the surface reached equilibrium at about 2 minutes. The results in this study appears to support this observation.

Polystyrene discs were treated at vastly different exposure times to further elucidate the effect of the treatment conditions. Figure 6.3 clearly shows that initial

TABLE 6.1

CHANGE IN CONTACT ANGLES AT VARIOUS TREATMENT TIMES

IMMEDIATELY UPON REMOVAL OF PLASMA

<u>MATERIAL</u>	<u>CONTACT ANGLE WITH DISTILLED WATER (°)</u>			
	<u>INITIAL</u>	<u>30 SEC</u>	<u>3 MINS</u>	<u>10 MINS</u>
PMMA(99)EGD(1)	65°	49°	31°	34°
PMMA(95)EGD(5)	63.5°	47°	35°	38°
PMMA(90)EGD(10)	62.5°	53°	30°	40°
PMMA(85)EGD(15)	63.5°	47°	37°	37°
PMMA(75)EGD(25)	65°	37°	34°	37°

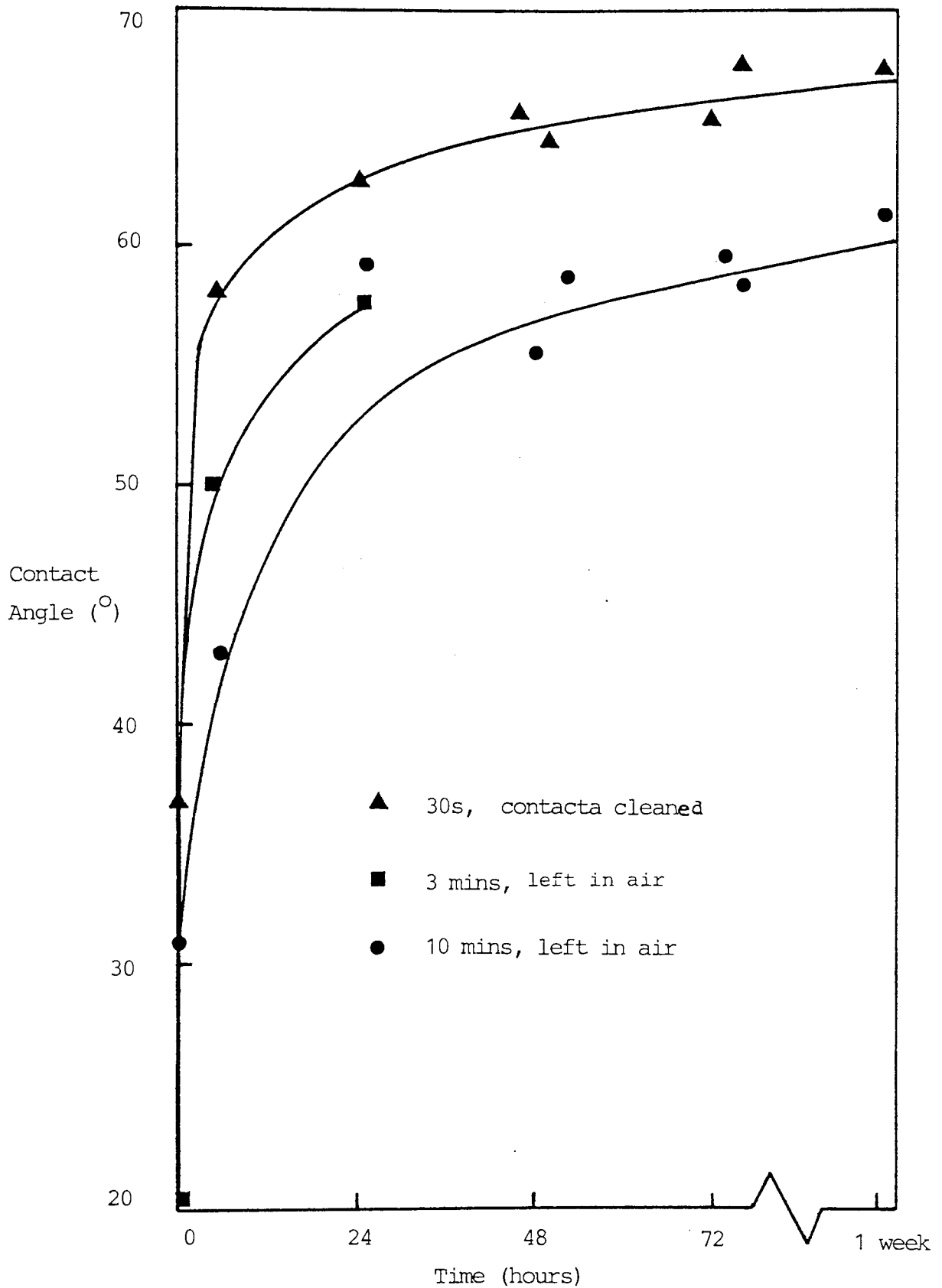


Figure 6.1 Surface wettability decay of plasmatreated PMMA containing 1% EGD (Legends; two experimental points refer to plasma exposure time and subsequent treatment of the samples)

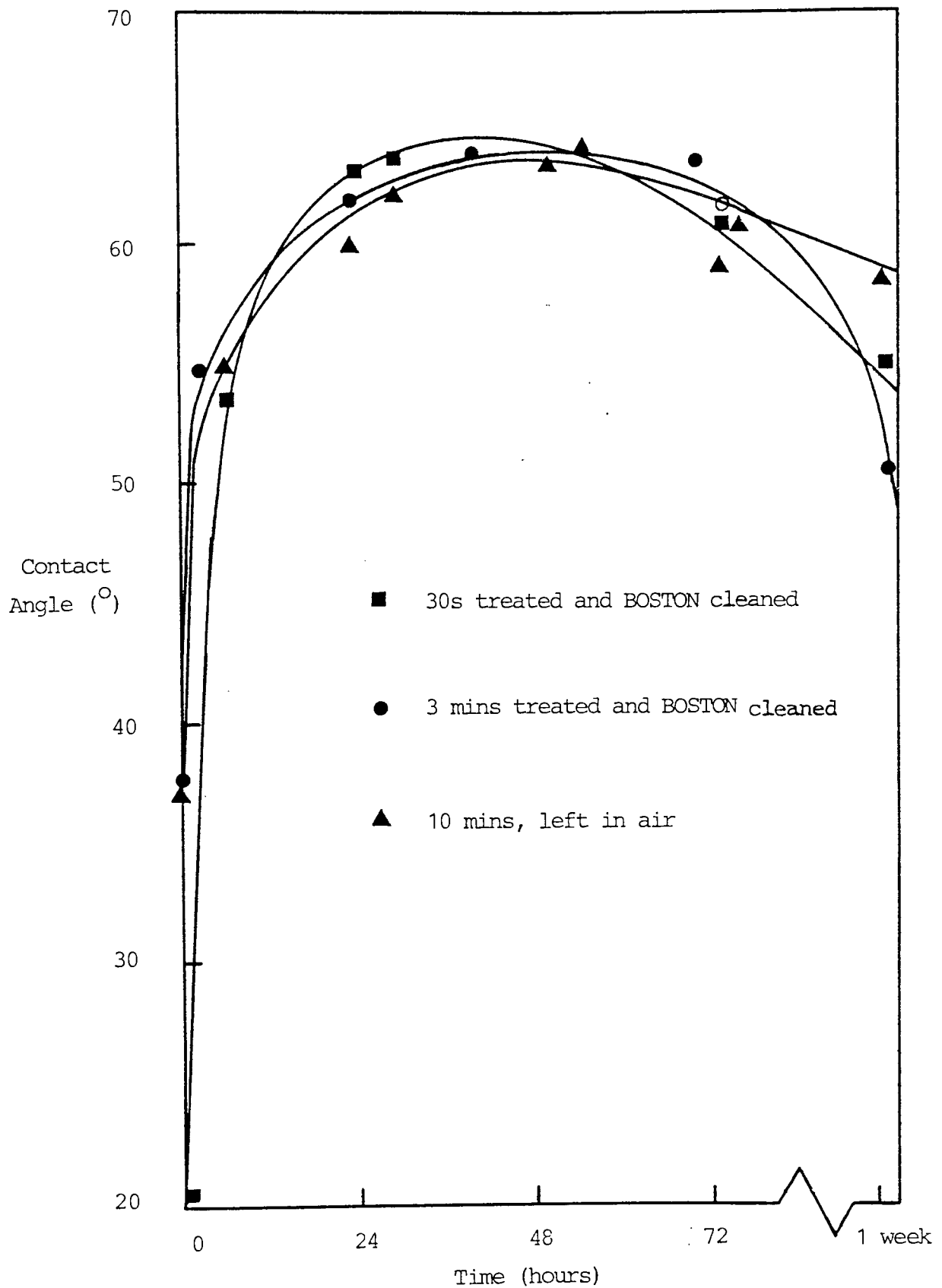


Figure 6.2 Surface wettability decay of plasma treated PMMA containing 15% EGD (Legend; two experimental points refer to plasma exposure time and subsequent treatment of sample)

TABLE 6.2

SURFACE WETTABILITY OF DISCS TREATED FOR 3 MINUTES STORED IN
VARIOUS WAYS (MEASUREMENT AFTER 24 HOURS)

<u>MATERIAL</u>	<u>Immediately</u> <u>after treat-</u> <u>ment</u>	<u>Stored in</u> <u>air at room</u> <u>temp.</u>	<u>Surfactant</u> <u>cleaned and</u> <u>stored in air</u>	<u>Stored under</u> <u>water</u>
PMMA(99)EGD(1)	31°	60°		58°
PMMA(95)EGD(5)	35°		60.5°	56°
PMMA(90)EGD(10)	30°	60°		52°
PMMA(85)EGD(15)	37°		61°	53°
PMMA(75)EGD(25)	34°	52°		51°

improvement of surface wettability after 75 minutes treatment is sustained for longer than after 3 minutes exposure. At this period of 75 minutes, polymer etching becomes more evident and physical removal of surface layers takes place.

After establishing that 3 minutes exposure time is sufficient for equilibrium to be reached, the next variable to be altered was the power supply of the plasma. For this work, polystyrene was treated at powers of 20W, 40W and 100W and Figure 6.4 shows the contact angle decay over a period of hours and then weeks; the increasing r.f. power appears to produce progressively increased surface wettability.

6.4 STABILITY OF PLASMA TREATMENT

After establishing the treatment conditions that would produce the desired change in the surface treatment on the polymer surfaces, the objectives of the next investigation centred on the stability of the plasma treatment. Here the emphasis is placed upon finding a) the type of polymer structure that is most susceptible to plasma treatment; b) the way these groups are affected; and c) the stability of treated surfaces.

6.4 (1) Plasma Treatment of Alkyl Methacrylates

As most of the synthetic work described in this thesis was based around alkyl methacrylate groups of polymers, the initial study was performed on these simple methacrylates. Figures 6.5 and 6.6 show the wettability decay of straight chain methacrylates and branched methacrylates over a period of 1 week, treated for 3 minutes at the r.f. power of 100W. The first polymer in this series is PMMA and its wettability stability is shown to hold by slower increase in its water contact angle compared with PEMA and P_nBMA. As the CH₂ group is added onto the ester chain,

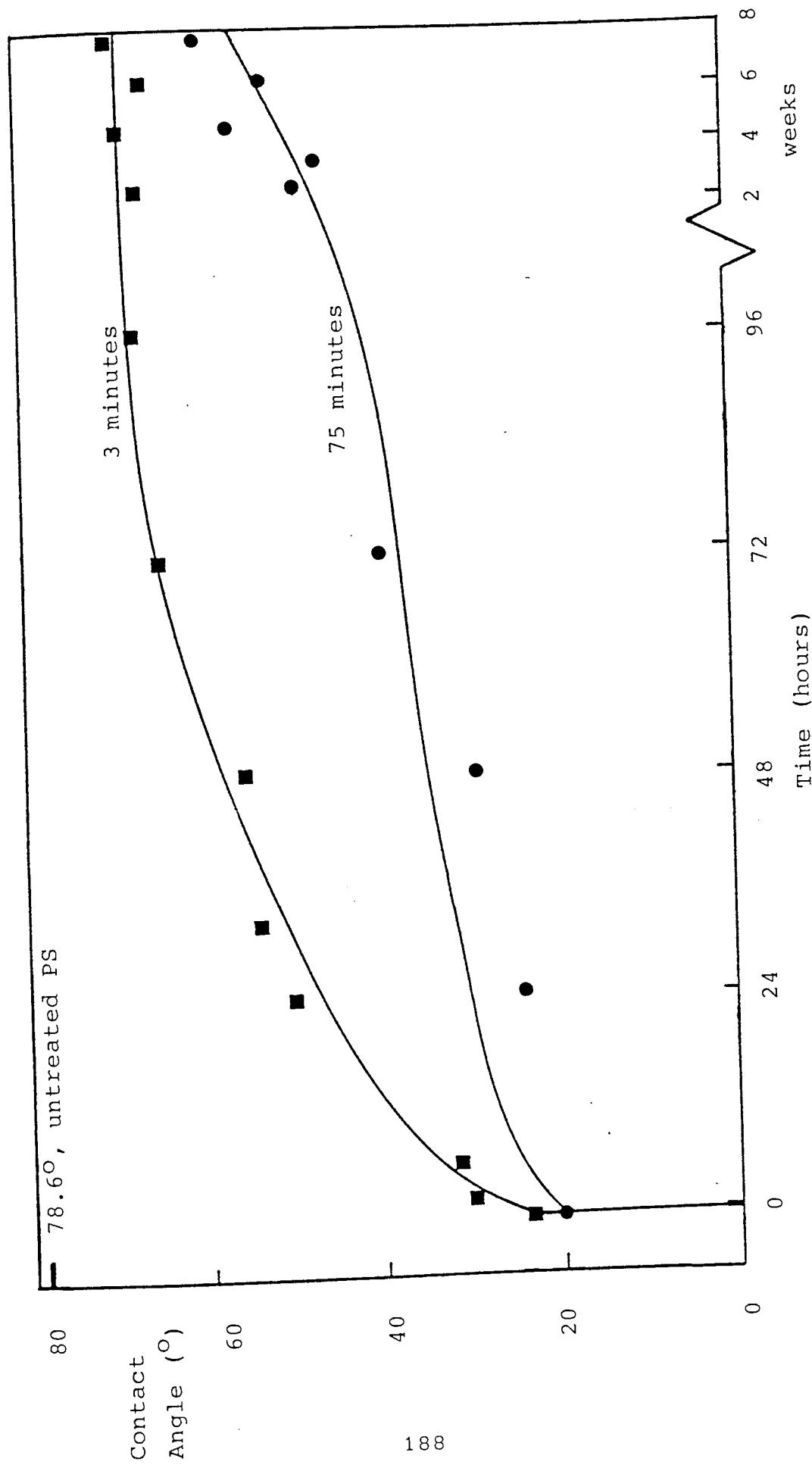


Figure 6.3 Surface wettability decay of PS subjected to plasma treatment of 3 and 75 minutes.

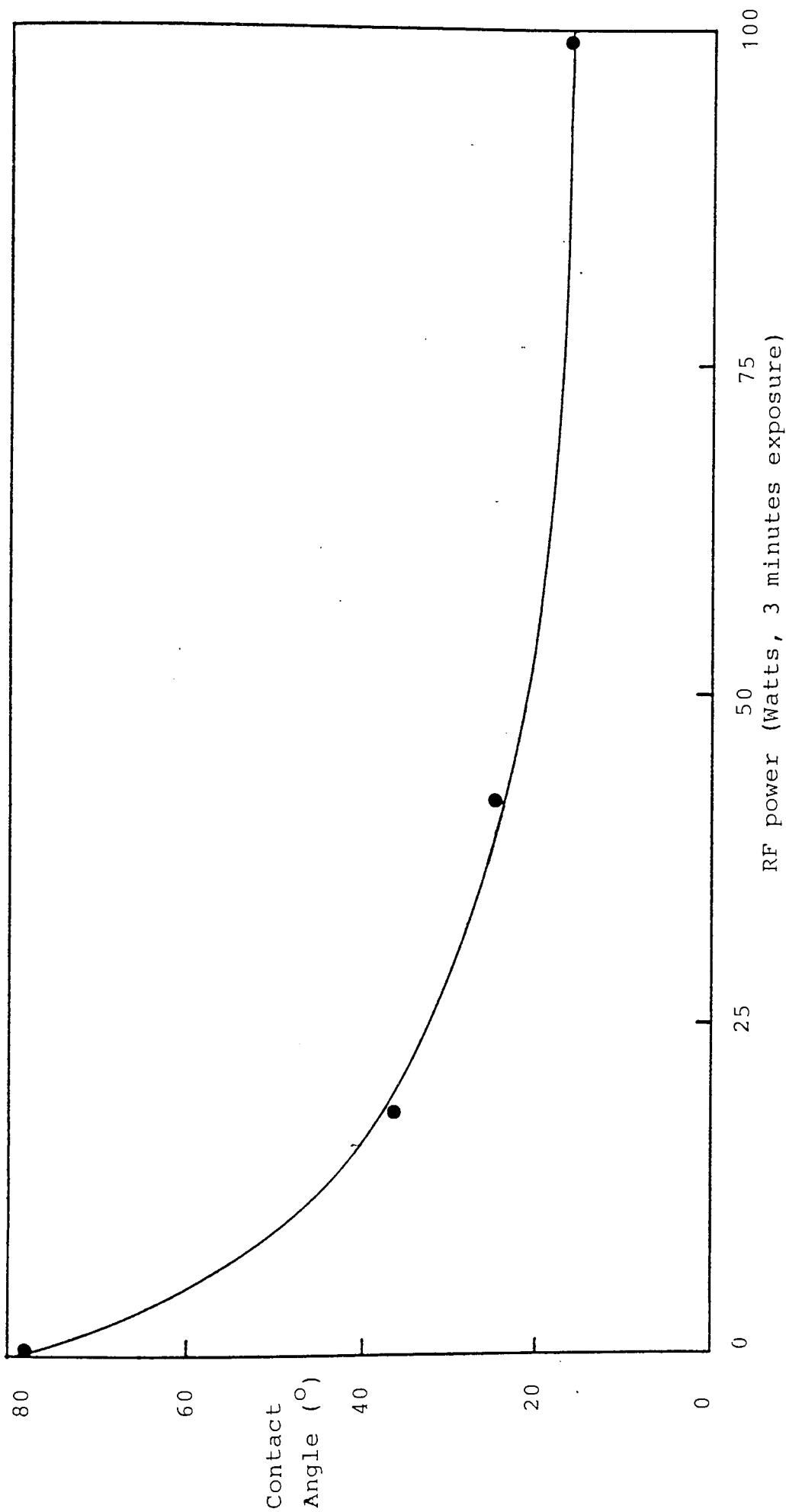


Figure 6.4 Contact angle of PS immediately after plasma treatment

the decay of wettability was observed to be more pronounced (Figure 6.5).

Figure 6.6, clearly indicates that branched methacrylates lose their initial wettability much faster than straight chain methacrylates in Figure 6.5. Again, as the number of CH₂ groups increases, so does the decay of wettability i.e. the original more hydrophobic state returns at a faster rate. Overall comparison between straight chain methacrylates and branched methacrylates show that branched materials are more hydrophobic in nature than straight chained methacrylates, even after the plasma exposure.

6.4 (2) Plasma Treatment on Aromatic Polymers

The second group of materials to be tested were polymers containing varying concentrations of aromatic groups in different environments, e.g. polystyrene, poly (ethylene terephthalate). The presence of an aromatic component in the polymer is known to convey increased resistance to plasma oxidation (143).

The materials were tested by contact angle measurement after plasma treatment at a power of 100W for 3 minutes. Figure 6.7 shows the results are shown as decay in the wettability. With the exception of polystyrene (PS), these aromatic materials are observed to return to their original contact angles after 1 week; and have polar groups on their back-bone (having different initial surface energy components). The schematic diagram of the structures of aromatic polymers studied here are drawn in Figure 6.8, the repeating units are indicated in brackets.

By comparing these two groups of materials i.e. polymers with methacrylate substituents and polymers with aromatic components, two differences are noticed. Firstly, the initial susceptibility of aromatic polymers to the treatment shown by a lower initial contact angle. Secondly the slower rate of reversion to its original state

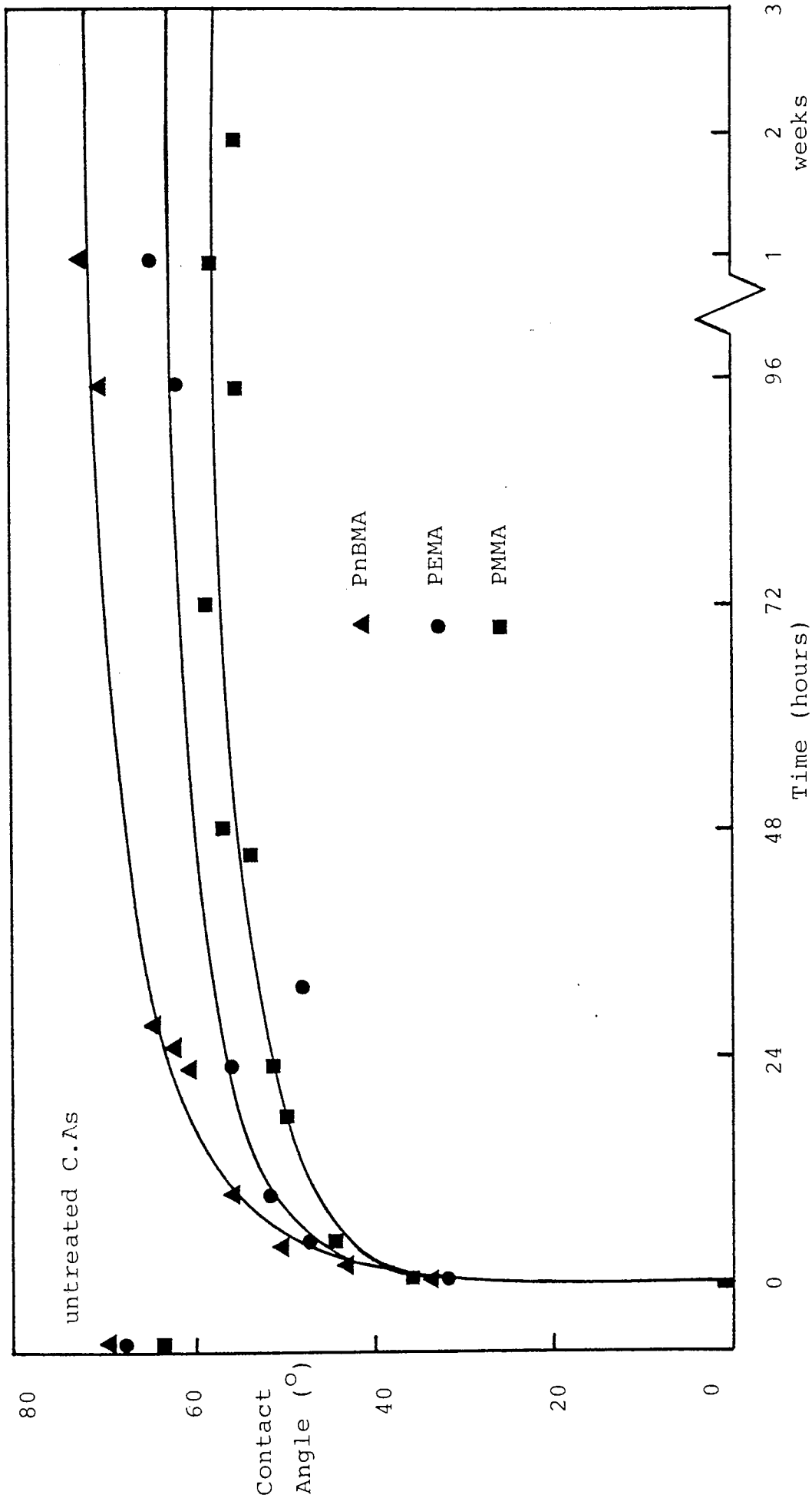


Figure 6.5 Surface wettability decay of plasma treated straight chain alkylmethacrylates

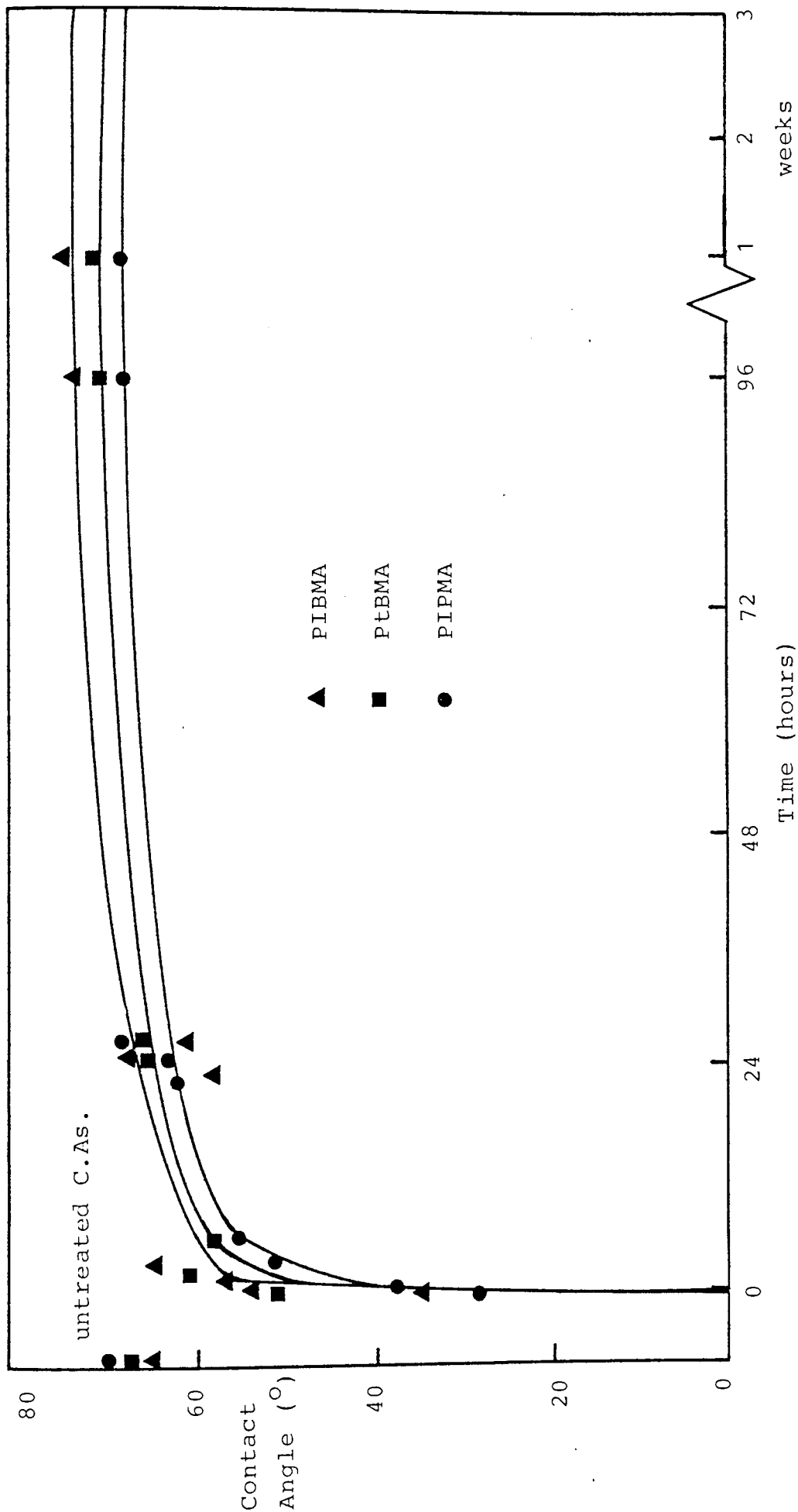


Figure 6.6 Surface wettability decay of plasma treated branched methacrylates

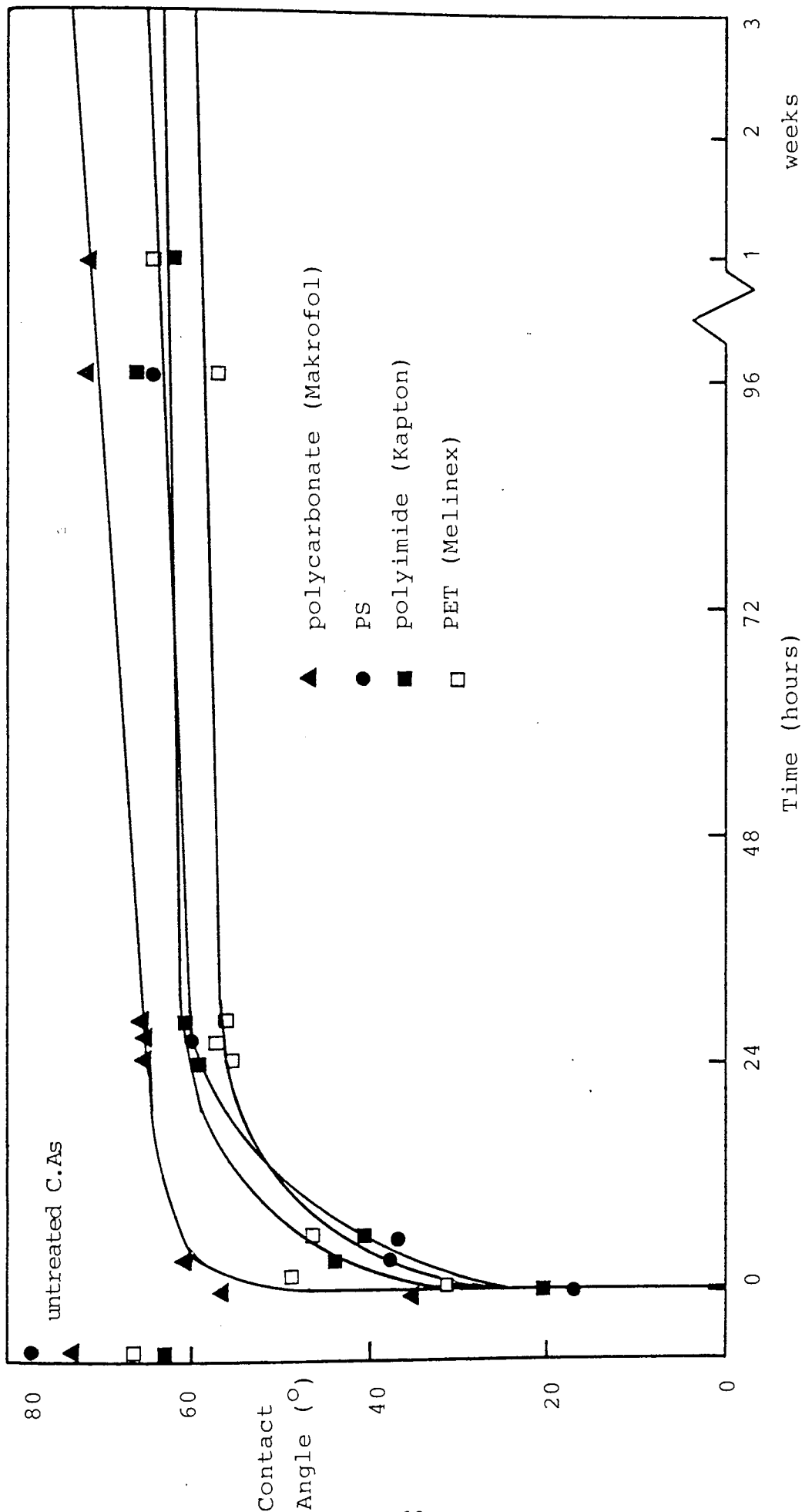


Figure 6.7 Surface wettability decay of plasma treated aromatic polymers

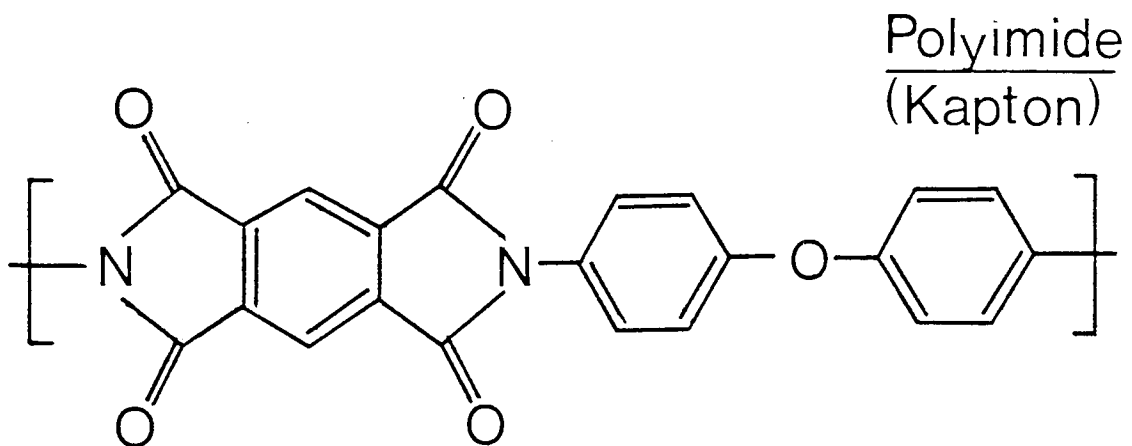
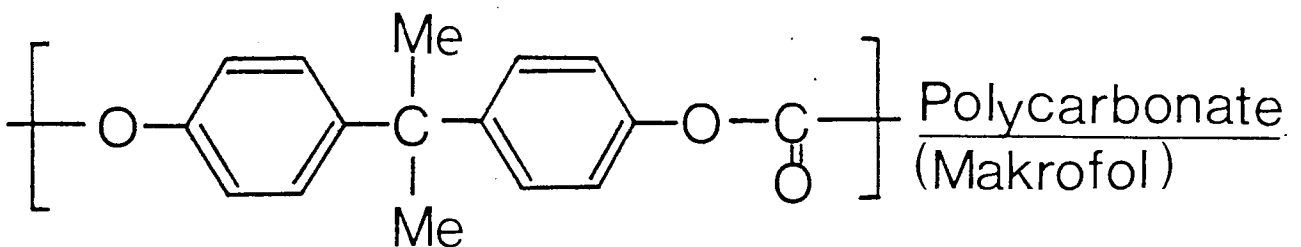
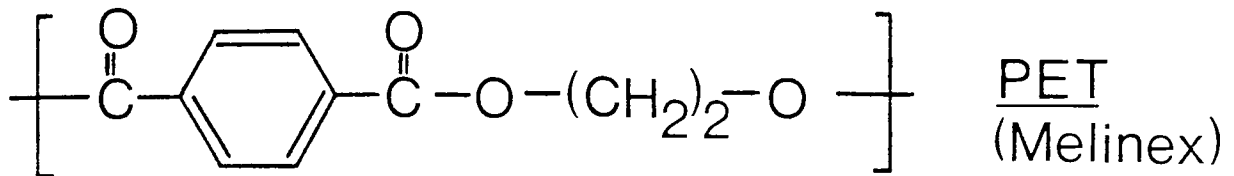
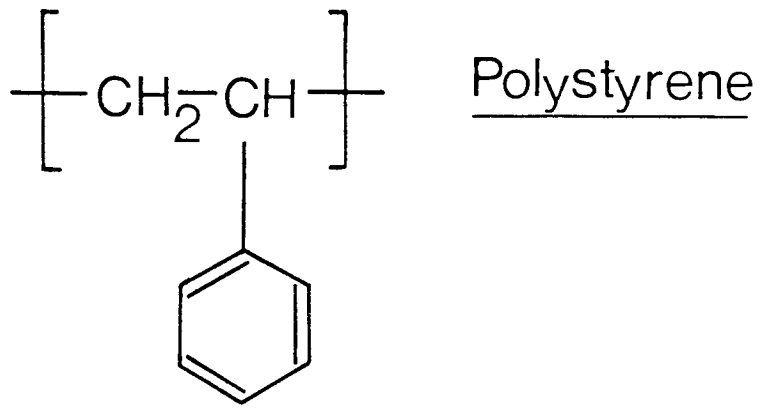


Figure 6.8

Schematic diagram to show the repeat units of aromatic polymers.

shown by aromatic materials (i.e. methacrylates return to the half the original value by 6 hours, whereas in aromatics, this is achieved in 9 hours). In all cases, with the exception of polystyrene, the wettability of the polymer 1 week after treatment is shown to return to its original state (within the experimental error).

6.5 SURFACE FREE ENERGIES OF TREATED POLYMER SURFACES

What causes the difference in the plasma treatment stability and what and how is it affected? These were the major questions then asked in the course of this work. In order to elucidate the possible process in which these hydrophobic materials were made more hydrophilic by plasma treatment, attempts were made to evaluate the surface free energies. Contact angles with water and methylene iodide were measured on the polymer surfaces before and after plasma treatment. The results are best shown as histograms for before and after treatment. Figure 6.9 shows the surface free energies of polymer surfaces prior to and 10 weeks after the treatment. PMMA and PS were chosen to represent polymers containing methacrylate and aromatic groups respectively. In both cases, it is interesting to note that the polar component of surface energy after the plasma exposure is higher than before the plasma exposure whereas the dispersive component is lowered. These changes are particularly noticeable in the case of PS. The rise in the polar component of surface energy for PS indicates that there must be some polar groups introduced at the surface of this normally hydrophobic polymer.

6.6 EFFECT OF PLASMA TREATMENT ON COPOLYMERS

The studies on the effect of plasma treatment have so far been confined to homopolymers of varying structures. This section aims to investigate the effect of

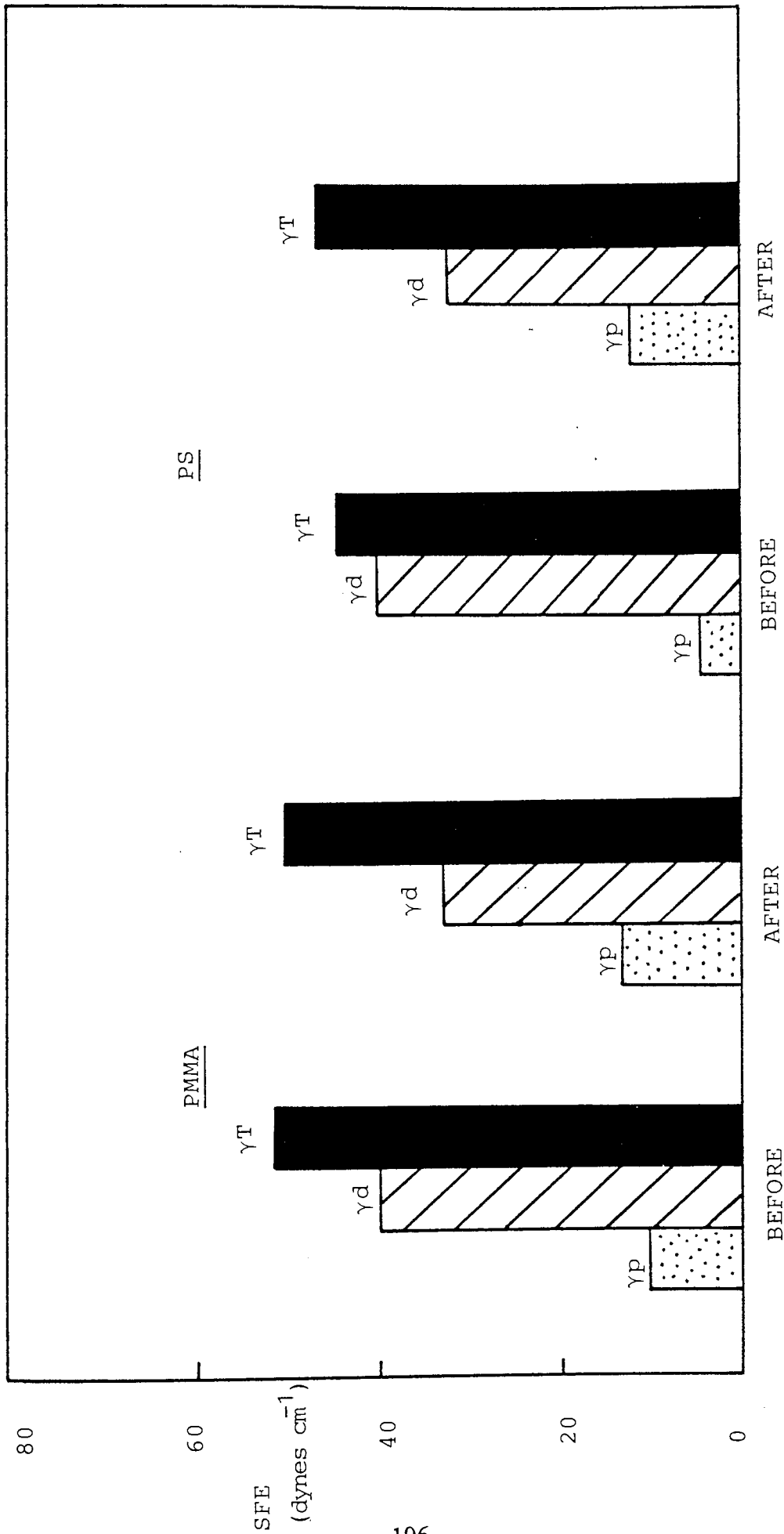


Figure 6.9 Change in surface free energies (SFE) before and (10 weeks) after plasma treatment for PMMA and PS.

plasma oxidation on copolymers studied in Chapter 5. The copolymer systems studied were based on PIBMA with long chain methacrylates; these copolymers incorporate branched groups of an IBMA component with straight long chain methacrylates. The decay curves of the copolymers are shown in Figure 6.10. The reversion to the original contact angle appears to be established within 12 hours of plasma treatment; thereafter the process proceeds at much slower speed. The reversion behaviour of these copolymers lies between those of the straight and branched chain homopolymers (Figures 6.5 and 6.6 respectively).

6.7 EFFECT OF PLASMA TREATMENT ON POLYMERS RELEVANT TO CONTACT LENS DESIGN

As the overall objective of this work is to modify surface wettability of a material without impairing its oxygen permeability, it became important to understand the effect of plasma treatment on groups of materials frequently encountered in contact lens applications. The study was conducted to investigate the relative plasma susceptibility and stability of the treated surfaces and arises from an interest in finding out the resultant effect rather than an in-depth analysis of the fundamental processes involved.

To this aim, poly (4-methylpent-1-ene) (TPX) and a siloxy monomer (SM1) were plasma treated for 3 minutes at 100W and their surface characteristics investigated. Figure 6.11 shows the decay profile is broadly similar to branched methacrylates in Figure 6.6. This is a very interesting result as these two polymers have superior oxygen permeabilities in comparison to other polymers studied here, partly because of the bulky substituents and especially with the siloxy monomer, high oxygen solubility. The high oxygen permeability is related to the flexibility of the molecular chains. Yasuda and

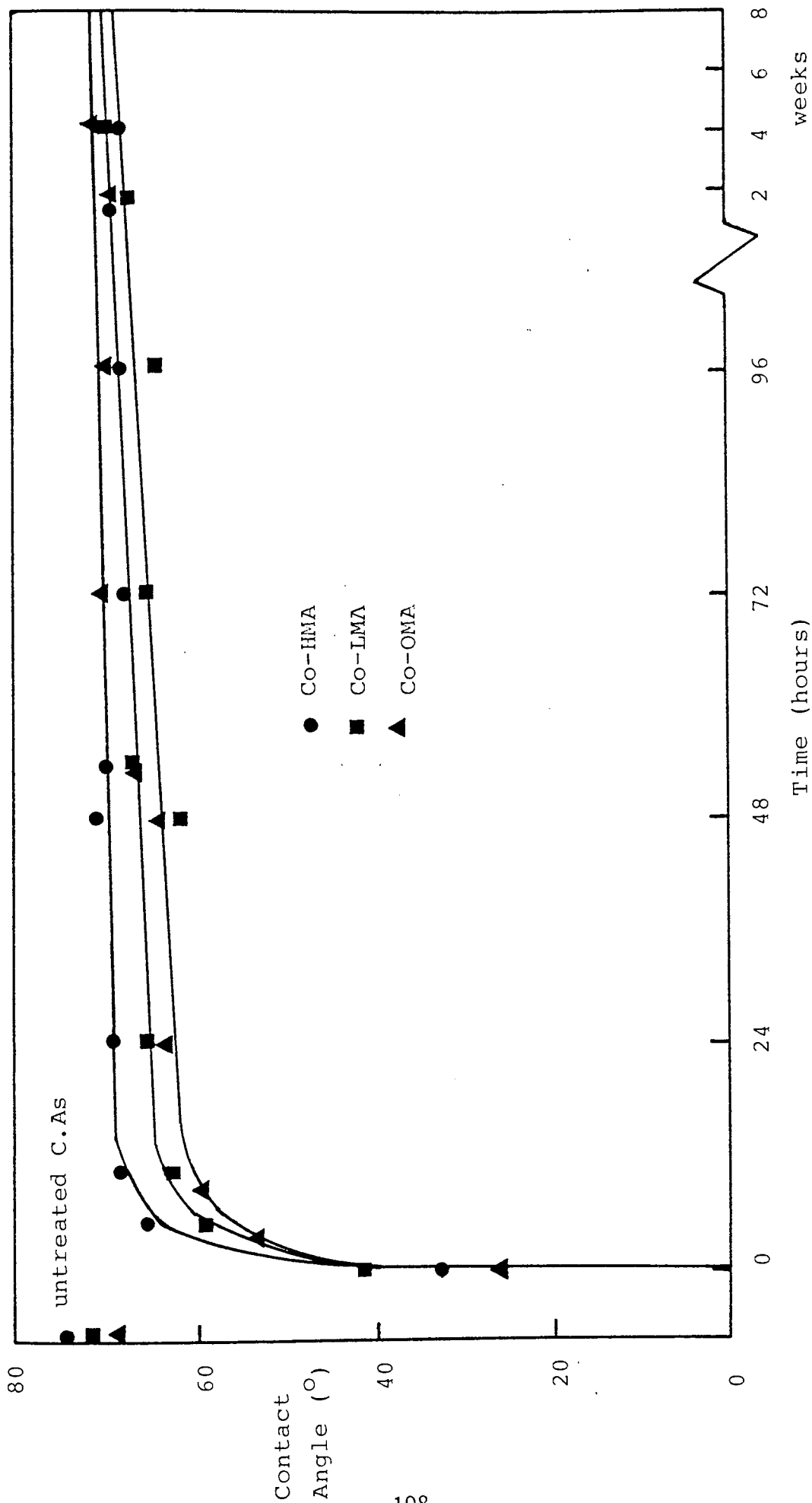


Figure 6.10 Surface wettability decay plasma treated PIBMA copolymers

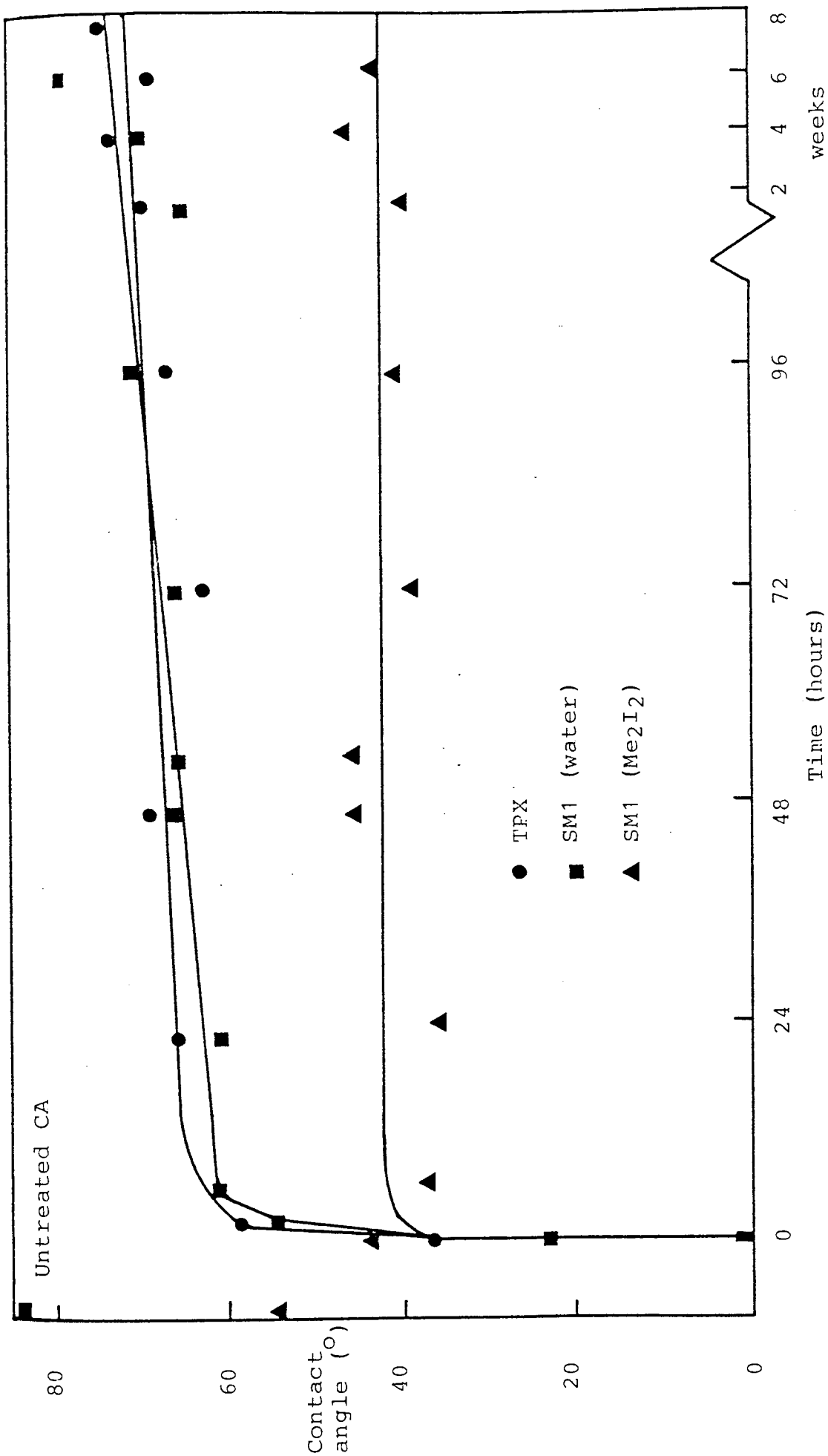


Figure 6.11 Wettability decay of plasma treated TPX and SM1

Sharma (144) reported that the loss of surface wettability in plasma treated polymers is due to the embedding of hydrophilic species to form energetically stable surfaces (i.e. minimising the interfacial tension). If this is the case, then materials with more flexible bonding would have less stable surface characteristics and return to their original state much more quickly than more stiff rigid materials i.e. siloxy polymer versus methacrylates. From these results, it can be deduced that aromatic chains are more stable than alkyl methacrylates which in turn are more stable than siloxy monomer.

Poly(siloxanes) are known to have greater resistance to oxygen plasma by the formation of a thin crust of silicon dioxide on the surface during the initial stages (145). The siloxy monomer examined in this study has along its molecular backbone, alkyl chains with siloxy side groups. Although the local siloxy linkage is flexible, the sheer bulk of the side silicone substituent does not readily allow rotational chain mobility. Consequently it is anticipated that the decay in wettability characteristics of this monomer would show features of both alkyl methacrylate backbone and silicone side chain. An indication of the susceptibility to the plasma treatment of a typical siloxy monomer relevant in the design of contact lens materials, allows predictions to be made on the resultant stability of a treated contact lens material incorporating organosiloxo monomers.

6.8 PROPOSED PROCESS IN THE DECAY OF PLASMA TREATED SURFACES

The earlier sections show that the plasma treated surfaces have a proportionally higher value of polar surface energy component compared to untreated surfaces. This is true for polymer surfaces with relatively high initial polar components (such as PMMA), and for surfaces with initially low polar components (eg PS).

This suggests the possible introduction of polar species present at the surface of the

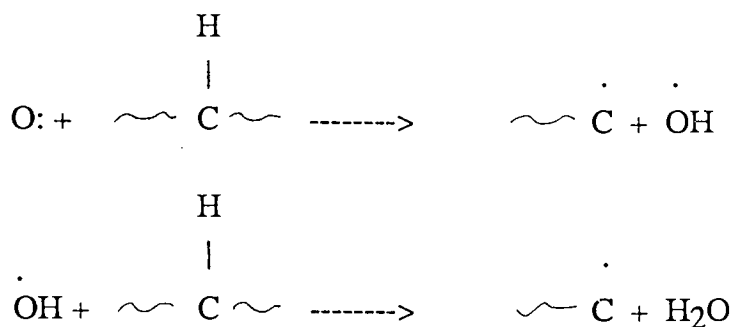
oxygen plasma treated substrate. Carbonyl, hydroperoxide and other oxygen - containing products may have been formed at the surface upon plasma oxidation. In the course of wettability decay, these species found at the onset of plasma treatment may decompose into stable molecules.

In order to study the feasibility of this theory, PIBMA and PS were treated for 3 minutes at 100W, then stored at 0° C in a refrigerator to retard the decomposition process, and at 80° C to accelerate the reaction. The wettability decay was monitored by contact angle measurements over a period of time. Figures 6.12 and 6.13 show the effect of storage temperature upon the stability of plasma treated substrates for PIBMA and PS respectively. In both cases, the higher temperature of 80° C is shown to cause a much faster return to the original hydrophobic state than at 0° C. In the case of PIBMA, the reversion is shown to occur sharply at around 6 - 8 hours after plasma treatment for 80° C storage. Again, the aromatic PS is observed to have better stability of treatment than PIBMA. This simple experiment shows the effect of storage temperature upon the wettability decay of plasma treated substrate, indicating a possibility of some decomposition reaction occurring during the oxidation decay process. Clark et al (146) have used ESCA techniques to examine polymer surfaces after brief exposure to different plasmas. Such studies on oxygen plasma of PS show the presence of C - O, C = O, - (C = O)-O, and O - (C = O) - O structural features with evidence for transformations of the pendant phenyl groups.

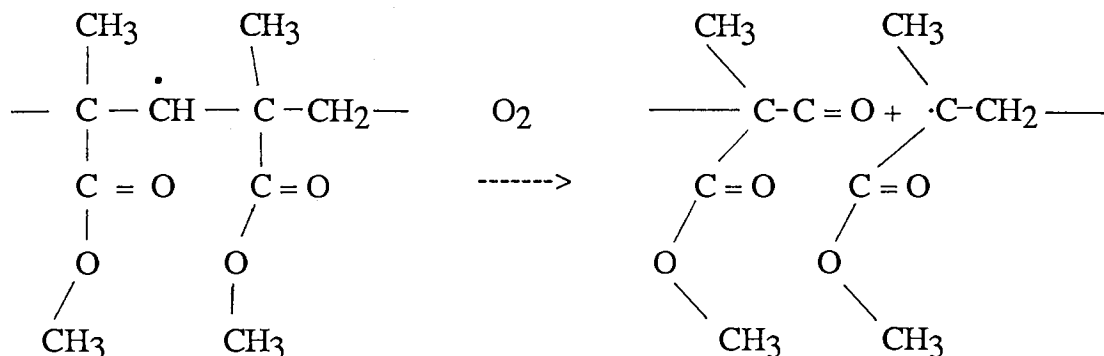
6.9 PLASMA OXIDATION PROCESS OF POLYMER

The interaction between an oxygen plasma and a polymer is a complex process in which the main primary reactants are oxygen atoms. The primary reaction of

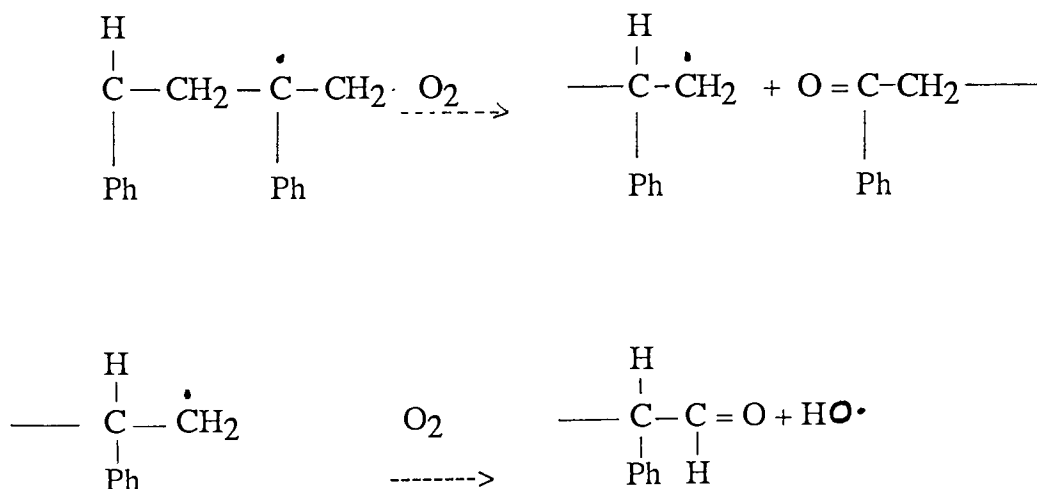
oxygen atoms with the polymer backbone is likely to be hydrogen abstraction:



This reaction should proceed much more readily at the tertiary C - H bond in PS rather than the primary and secondary C - H bonds in PMMA. With PMMA, the backbone secondary H atom would be preferentially abstracted leading to auto-oxidative cleavage:



With PS, the tertiary C - H bond will be the preferred site for attack on the chain so that the reaction will be:



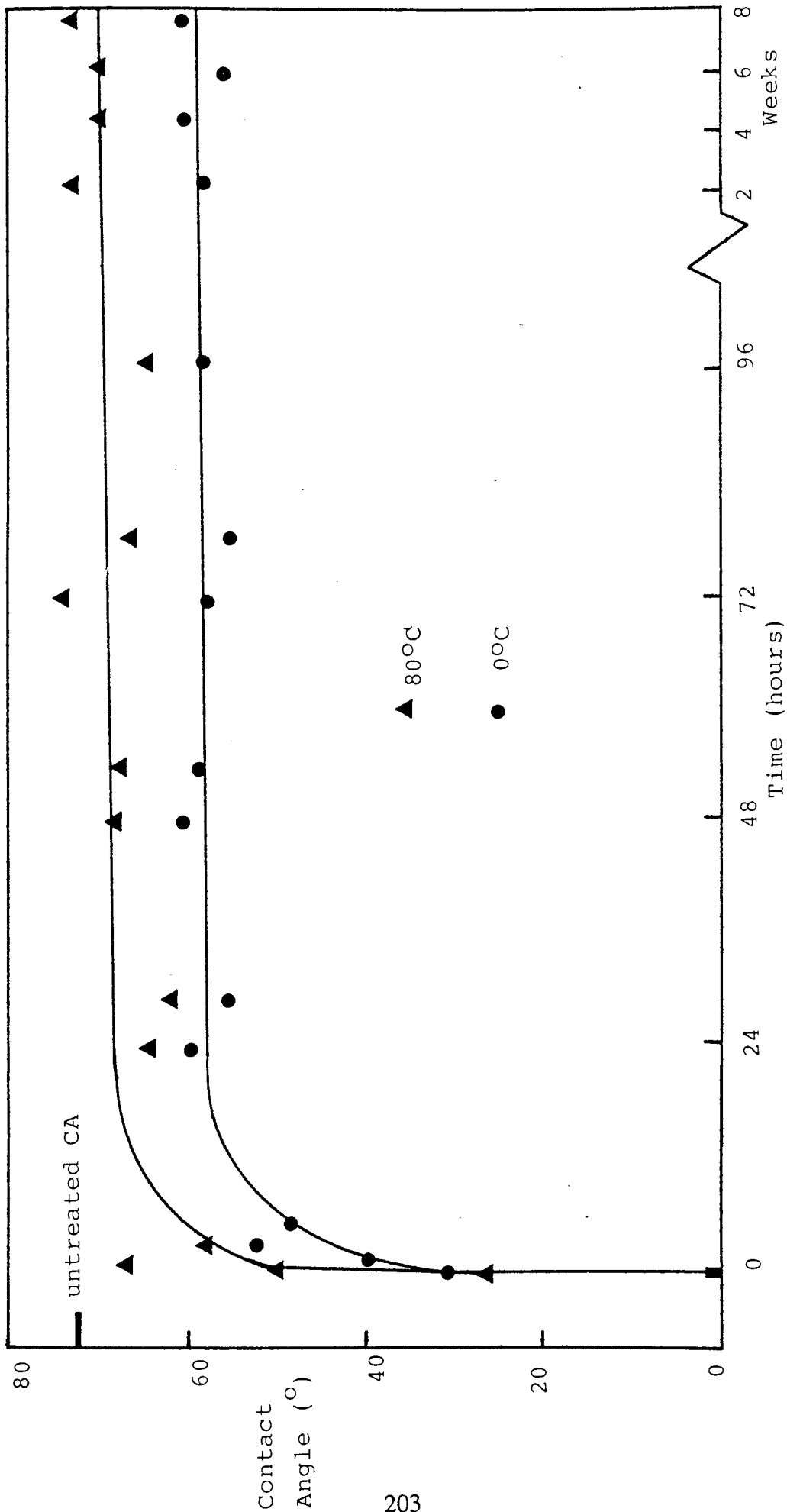


Figure 6.12 Effect of storage temperature on surface wettability decay of plasma treated PIBMA

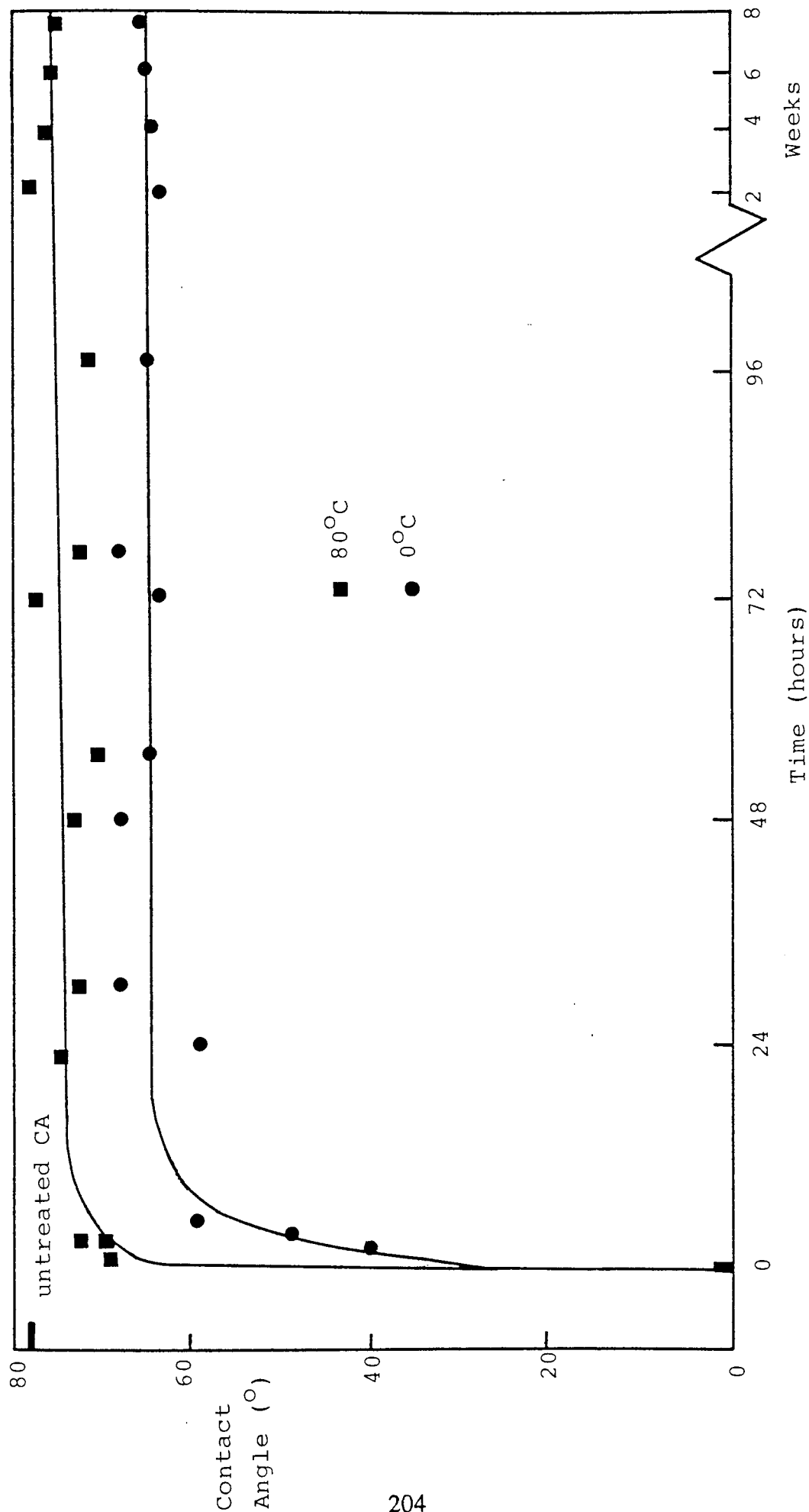


Figure 6.13 Effect of storage temperature on surface wettability decay of plasma treated PS

The stability of aromatic polymers seems to be dependent on some property of the benzene ring which is substantially independent of its position in relation to the polymer backbone. Moss, Jolly and Tighe⁽¹⁴³⁾ suggest that the formation of phenols by the reaction of ground-state oxygen atoms, contributing to a blocking process in the initiation stage of plasma oxidation. This causes loss of oxygen atoms without forming free radicals or products which could be expected to assist in the degradation of polymer surfaces.

A relatively crude evaluation of kinetic aspects of the underlying process was attempted by plotting the change in contact angle on a semi-logarithmic basis. This involved the assumption, suggested by inspection of the contact angle decay curves, that the change in contact angle is related to some approximate first order process. By plotting $\log(\text{final contact angle} - \text{contact angle at time, } t)$ against time, half lives for the decay processes at two temperatures were obtained; these were found to correspond to an activation energy of 35 KJ mol^{-1} and a frequency factor of around 10^7 sec^{-1} in conjunction with a rate constant of around order of 10^{-5} sec^{-1} . Although this procedure is very imprecise and involves several assumptions, the result is consistent with an energetically favoured decomposition process taking place at an isolated site at the polymer surface. In simplistic terms of collision theory, the anchored isolation of the groups deprives them of the collisional activation.

6.10 CONCLUSIONS

Fundamental data has been gathered on the effect of plasma surface modification on methacrylate and aromatic polymers. It was important to investigate if there were any characteristics specific to plasma treatment such as susceptibility and

stability upon the surface of polymers often encountered in contact lens applications. The interaction between an oxygen plasma and a polymer is a complex process in which the following four stages may be distinguished:

- Stage i) Surface bombardment by photons, electrons, ions, atoms and excited species creating free radical sites.
- Stage ii) Reactions of free radical sites on the polymer with molecular oxygen, leading to peroxides, alkoxy, and hydroxyl radicals.
- Stage iii) Chain cleavage leading to loss of the primary volatile species.
- Stage iv) Gas-phase reactions of the primary volatile products in the plasma.

The oxidation process produces reaction products with oxygen-containing functional groups (carbonyl - C = O, hydroperoxide - OOH, hydroxyl - OH) which are attached to the polymer surface. The changes in surface wettability caused by plasma treatment appears to be reached within a 3 minutes exposure time, although cases have been reported where longer plasma exposures cause a decrease in wettability (147). The wettability was shown to decay over a period of hours rather than weeks in all of the polymers which were plasma treated. There appears to be a relationship between polymer structure and the susceptibility and stability to plasma treatment. Aromatic polymers, such as polystyrene were observed to sustain their initial wettability over longer periods followed by slow reversion to their initially hydrophobic state. Polymers containing methacrylates were observed to be less stable than aromatics and it is suggested that they in turn are more stable to plasma treatment than siloxy-type polymer materials. The evaluation of surface free energies of plasma treated polystyrene indicated a net small change in the polar component from its initially uniform non-polar surface to the final polar state whose polar component is comparable to PMMA's polar component.

In contrast, there was a less marked change in the polar component of surface energy in PMMA. The decay of surface wettability is reported ⁽¹⁴⁴⁾ to be related to the burying of hydrophilic species into the bulk of the polymer to energetically stable states. The more flexible and rotational the molecules, the more likely this will happen. If this were true then the less plasma stable nature of siloxy polymers could be explained by their flexible molecular chains which allows hydrophilic groups to rotate easily, and in the case of polystyrene where the presence of aromatic rings does not readily permit chain rotation. The ease of chain rotation and flexibility is also related to gas transport phenomena by the diffusion component of P=DS.

The loss of initial surface wettability may also be related to decomposition of surface species e.g. hydroperoxide into smaller more stable molecules. The decay profile of PIBMA and PS at 80°C and 0°C revealed the temperature dependence of the wettability decay process. It is feasible that in the case of 80°C where the decomposition is accelerated, more rapid reversion occurs than where the decomposition was retarded by being stored at 0°C. In siloxy material, the oxidation product Si - COOH may be more unstable than CH₂ - COOH in methacrylates, giving Si - H and carbon dioxide as by-products. An I.R. spectrum of a treated sample should detect any decomposition products.

These findings have important consequences in the application of plasma treatment to contact lens materials. Plasma oxidation is believed to be confined to a thin surface layer (around few μm) and therefore the bulk properties should be unaffected. The use of plasma treatment in surface modification as found in the patent literature centred at the plasma grafting of hydrophilic monomers such as N-vinyl pyrrolidone and 2-hydroxyethyl methacrylate^(98, 99, 100). Because of difficulty in treating siloxy surfaces by gaseous plasma⁽¹⁴⁵⁾, it is suggested that incorporation of a low concentration of aromatic polymer (eg polystyrene) as a comonomer to sustain the effect

of plasma oxidation may be useful. The suggested synthetic copolymer comprises t-butyl acrylate to obtain oxygen permeability, maleic anhydride to give crosslinking with surface hydrophilicity and styrene to give susceptibility to oxygen plasma to produce improved surface properties.

CHAPTER VII
HYDROGELS AS EXTENDED WEAR CONTACT LENS MATERIALS

7.1. INTRODUCTION

Although the main part of the thesis is devoted to the design and development of rigid gas permeable contact lens materials, there was an opportunity to apply similar principles to extended wear hydrogel lenses to overcome some clinical and practical problems that arose with a particular material.

Hydrogels consist of a polymeric network swollen by an aqueous fluid. Though diverse kinds of hydrogels were known for a long time (e.g. gelatin, agar, the vitreous humour of the eye), it was the pioneering work of Wichterle and Lim⁽⁵⁾ with acrylic hydrogels that has revolutionized the contact lens industry. The first hydrogel contact lenses were made from cross-linked poly(2-hydroxyethyl methacrylate), (pHEMA), which is one of the most commonly used polymers for soft contact lenses. Since the introduction of pHEMA contact lenses, there has been continuous effort to develop other hydrogel contact lenses with improved properties. There have been many workers involved in different aspects of the use of hydrogels in biomedical applications in these laboratories. One of the topics related to hydrogels in extended wear application, which was initiated in early 1970s, has led to commercial products in the market. The material was based on the use of three acrylamides in combination with other monomers to give high water content for adequate oxygen permeability during overnight wear, coupled with high strength and a protein resistant surface. The rationale behind the selection of these monomers and design of the polymer is based on in vitro studies described by Middleton⁽¹¹⁸⁾. The long-term effects of extended wear on these materials, unfortunately manifested themselves in some cases as curling of the lens. This section of the thesis is related to attempts being made in overcoming these problems by refining the chemical compositions of the resultant polymeric material to achieve the required chemical and physical stability.

7.2. PROPERTIES OF HYDROGELS

Soft hydrogel contact lenses behave quite differently from hard lenses in the eye. The motion of the lens and tear fluid is much less and the oxygen permeability of

the material must be high enough for adequate oxygen to be transported through the lens to enable the cornea to function normally. This is particularly true in overnight wear when the lens acts as a fairly static extension of the cornea. The most important property of the hydrogel is its equilibrium water content, which is the percentage by weight of water in the swollen gel. Since the oxygen permeability of the gel can be shown to be dependent on passage through the water phase, it is possible to predict fairly accurately the way in which corneal oxygen consumption requirements can be met. In general an equilibrium water content of 30-50% is needed for successful use of the lens in daily wear, whereas, a figure of 70% or more is required for wear during sleep⁽¹⁴⁸⁾. These figures are for lenses of conventional design, having centre thickness in the region of 0.15 - 0.20 mm.

The presence of water as an internal plasticiser induces softness and thus comfort. On the other hand, it makes the lens more prone to damage during handling and produces visual instability. Also, although hydrogels present no problems in meeting the minimum wettability requirements in order to maintain a coherent tear film, surface spoilation of these materials has been a major problem, arising because of the longer periods of wear that their advantageous balance of properties permits.

7.3 EXTENDED WEAR HYDROGELS

As mentioned earlier, the permeability of oxygen through hydrogel lenses is predominantly determined by the equilibrium water content. Since the introduction of pHEMA lenses, efforts have been channelled principally towards developing hydrogel lenses capable of transmitting greater amounts of oxygen through the lens to the cornea thus enabling the lenses to be worn for longer periods of time. There are two ways to accomplish this; increasing the water content of the hydrogel lens, or decrease the thickness of the hydrogel lens. Most hydrogel lenses cannot be made very thin, because the frailability of them increases chances of lens breakage, most thin soft lenses tend to cling to the cornea making removal of epithelial debris by tear fluid difficult, and there is a tendency to ripple with each blink causing unstable vision. So far, the majority of efforts

in achieving higher oxygen permeability in hydrogel lenses have used those of high water content. Unfortunately, hydrogels of high water content suffer from problems including fragility and reproducibility.

Much of the work concerning biomedical applications of hydrogels goes back to the early 70's when fundamental correlations between hydrogel structure and physical properties were first studied in detail. As part of this continuing work one family of hydrogel materials based on the acrylamide group of monomers has been studied. The materials are based upon the combination of acrylamide and its derivatives with hydroxy alkyl acrylates (such as methacrylic acid). Figure 3.1b shows the structures of the main acrylamide monomers used. The acrylamides counteract the natural weakness of the hydrogel by virtue of their ability to form hydrogen bonding which gives a higher degree of interaction between polymer chains. In the accelerated 'in vitro' experiments on these types of material presented no apparent problems⁽¹¹⁸⁾. However, in the 'in vivo' applications, the changes in physical dimensions which sometimes manifest themselves as a curling of the lens are particularly puzzling and, as yet, are not possible to reproduce in the 'in vitro' state. This portion of the thesis is related to attempts in the investigation of possible cause and cure of these physical changes by using structural variations of component monomers. The cause of these physical changes may be due to several factors, for example, the difference between physiological and chemical environments in the laboratory and eye conditions, factors such as pH, tonicity, and temperature may be involved, as well as changes in anion and buffer in moving from the lens storage solution to the eye. These changes in the material may be brought about by the amide groups undergoing unfavourable reactions, particularly hydrolysis. This point is also important when considering the cleaning procedure of these amide based contact lenses. In elderly aphakic patients whose eyes often are fitted with extended wear contact lenses, it is common for these lenses to be removed by the ophthalmologist at intervals (say 3 to 6 months) and cleaned with a strong oxidative cleaner (e.g. sodium perborate). Therefore, the combined effect of the chemical reaction (such as hydrolysis) of the functional groups in the eye, and the degradation by an oxidative cleaner of these amide based hydrophilic

polymers form a potentially important role in controlling the dimensional stability of these materials in use.

7.4 NATURE OF THE PROBLEM AND EXPERIMENTAL APPROACH

It is fairly clear that the lens distortion observed arises from a relatively small extent of chemical reaction within the lens matrix. Amides hydrolyse under suitable conditions (e.g. in aqueous alkaline solutions) to regenerate the parent carboxylic acid and amine. It is also apparent that centre to edge "stretching" of the front surface of the lens occurs in the eye and that this produces lens distortion when the lens is removed from the support of the cornea. If extensive hydrolysis (say) were occurring, the water content of the lens would change and the lens parameters would be noticeably altered. It is perhaps likely that some enzymatic hydrolysis of the surface of the lens coupled with the centre to edge tension produced in the eye is responsible for permanent lens distortion.

Apart from obvious strategies such as increase in crosslink density, steps were taken to produce a more hydrolysis-resistant combination of acrylamides. The strategy is outlined below.

It is logical to think that greater protection can be afforded to the amide group by increasing the degree of substitution at the amide terminus. Three such strategies were considered:

- 1) Use of diacetone acrylamide (DAAc) as a main amide monomer; this has an advantage that DAAc is already a component of the hydrogel. This is the preferred strategy.
- 2) Use of N-alkyl acrylamides in place of the acrylamide itself (e.g. N-isopropyl acrylamide).
- 3) Use of N,N-dimethyl acrylamide. This has the advantage of being a liquid.

In compositional terms, there is need to be as close to the original composition of the lens material so that the physical properties criteria is not altered drastically i.e. in terms of EWC, machineability etc. It can be said that the work carried

out in this chapter serves to provide refinement of composition in order to overcome problems encountered in the long-term wear of this type of hydrogel. Since the EWC is the most important property of a hydrogel, it will be the limiting factor in deciding the new composition. The degree of substitution at the vinyl or amide terminal of the acrylamide will influence the final EWC, thus a small degree of compositional change is preferred.

7.5 EXPERIMENTAL METHODS

7.5.(1) Synthetic Procedure

Several compositions were produced based on the molar ratio of reagents used. In a typical preparation, a comonomer mixture of diacetone acrylamide, N-vinyl pyrrolidone, 2-hydroxyethyl methacrylate, and cyclohexyl methacrylate in a molar ratio of 20:55:20:5 were weighed into bottles. Ethylene glycol dimethacrylate (EGD) was used as a crosslinking agent, and t-butyl peroctoate (0.14% by weight) as an initiator. After each monomer was weighed in separate sample bottles the two methacrylates were mixed in a flask, slowly dissolving small quantities of diacetone acrylamide. Each bottle was washed with NVP ensuring complete dissolution of diacetone acrylamide. The comonomer mixture was filtered to remove any undissolved monomer before it was bulk polymerized in membrane, rod or button forms.

The production of thin membranes, rods, and buttons are as described in Chapter 3. After postcuring, polymer sheets were removed from the glass plates and placed with the Melinex attached in a container full of water to hydrate. For complete hydration to take place, it took at least 10 days, and most cases for 2 to 3 weeks. After hydration, the dry polymer sheets become hydrogel sheets which are easily separated from the Melinex. It is important to change the hydrating distilled water at frequent intervals to remove any trace of residual monomers. Discs of hydrogel were cut using a cork borer, stored under water, and were subsequently used to determine equilibrium water content. The completed rods were sent to Kelvin Lens Research Laboratories and lathe-cut into lens form. The lenses in the dehydrated state must be hydrated in distilled

water until equilibrium is reached. This can be done by placing the dry lens in a water-filled bottle and left for 5 - 7 days. The polymerized buttons were again sent to Kelvin Lenses Research Laboratories to be lathe-cut into lens form as in rods and hydrated like-wise.

7.5.(2) Physical Characterisation Methods

a) Equilibrium Water Content

The equilibrium water content (EWC) of a hydrogel is one of the most important properties in the physical characterisation of hydrated hydrogel materials.

The EWC of a hydrogel was measured after allowing the membrane to hydrate in distilled water for at least two weeks, enough time for the disc or lens to reach equilibrium hydration. No less than three samples were cut with a cork-borer (of diameter 10mm) from the hydrated film. The excess water on the surface was carefully removed by patting with clean filter paper, 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. The final weight was noted and the EWC was calculated according to the equation:

$$\text{Equilibrium Water Content (EWC)} = \frac{\text{Weight of hydrated sample} - \text{Weight of dehydrated sample}}{\text{Weight of hydrated sample}} \times 100\%$$

An average EWC of at least 3 samples was determined.

b) Cleaning Treatment

One of the strongest oxidative cleaners (sodium perborate) used to clean hydrogel contact lenses is Liprofin. It has a high alkali pH of 10 and thus it is necessary to neutralise treated lenses, before insertion in the eye (whose tear pH is 7.2). A sachet of Liprofin was dissolved in 25 ml of distilled water in a small bottle; the lenses are then placed in plastic vials which are placed subsequently into the bottle with Liprofin. It was warmed to 60°C, held for 2-3 hours then cooled to room temperature. The treated disc or

lens is then washed in distilled water and left to equilibrate for at least 1 week in distilled water and in saline solution. The final EWC was determined and compared to the original EWC prior to the Liprofin treatment.

c) Tensile Testing

The new composition hydrogels were tested with tensile equipment as described in Chapter 3 to compare their mechanical properties to the previous acrylamide hydrogels. Tensile testing was chosen because of its relative simplicity and its relevance to daily handling of the lens. For hydrogels, the ratio of the chart recorder to the crosshead jaw separation of 10:1 was used, with low jaw pressure of 10-20 psi, for example. It is most important to keep the hydrogel sample hydrated until it is required, to prevent any unnecessary dehydration during mounting and testing. A cutter of ~6 mm width was used to cut out dumb-bell shaped sample pieces and the sample thickness measured using a thickness gauge. Extra care is necessary when handling the hydrogel samples due to their fragile nature. At least three tests were performed per material.

d) Lens Parameter Measurement

An Optimec instrument is designed to measure the three essential parameters of soft contact lenses; namely, Back Curvature Optical Radius (BCOR), Central Thickness (CT), and Overall Diameter (OD) in saline. (149) The wet cell was filled to within ~5 mm of the top with fresh unpreserved 0.9% saline; the room temperature was recorded. A hydrogel sample was placed concave side down on the lens support. The centring device within the cell was used to centre the lens prior to measurement. The lens was left to equilibrate for one minute or so, then BCOR, OD and CT were determined. Before starting and after finishing any measurements, the cell was rinsed with clean distilled water to remove any dirt and stale solutions.

7.6 RESULTS AND DISCUSSION

The series of experimental work carried out in this chapter was done at the early stages of the project, which served to show and reflect the effect of chemical and structural modification on the physiological requirements and limitations imposed upon

the resultant material. The results will be presented accordingly as the strategies set out in section 7.4.

7.6.(1) Use of Diacetone Acrylamide

Diacetone acrylamide is already established as one of the components in the hydrogel material and is thus the most favourable option; several compositions were made based on different molar ratio of comonomers, to give resultant EWC of about 70%.

<u>Monomer</u>	<u>Composition</u>					
	A	B	C	D	E	F
Diacetone acrylamide (DAAcr)	20	30	30	40	25	30
N-vinyl pyrrolidone (NVP)	55	45	55	45	55	55
2-hydroxyethyl methacrylate (HEMA)	20	20	10	10	15	15
Cyclohexyl methacrylate (CHMA)	5	5	5	5	5	5

As diacetone acrylamide is the only solid comonomer in the system, it was anticipated to have problems of solubility in the liquid monomers such as N-vinyl pyrrolidone. By careful mixing to ensure complete dissolving of DAAcr, it was possible to incorporate a fairly large quantity of this monomer. Table 7.1 summarises the results of EWC of DAAcr hydrogels in various situations. EWC of the hydrogel was examined after 6 months to check the drift in the water content and to ensure complete hydration and removal of residual monomers.

Taking into consideration the experimental errors involved in evaluation of EWC, the overall results from diacetone acrylamide hydrogels were lower (around 60-65%) than expected to be useful for extended wear hydrogels. Middleton⁽¹¹⁸⁾ noted the depression of EWC for the copolymers of DAAcr and HEMA, and explains this by the methyl substituents within the 1.1 dimethyl 3 oxybutyl group giving rise to hydrophobic bonding with the methyl substituent of the HEMA units, together with the tendency to shield the hydrophilic amide group which would inhibit the attraction of water

molecules. It is particularly alarming that the EWC taken from hydrogels in button form is so much lower than the EWC value of membranes. Buttons were produced in order to combat a problem of exotherm reactions occurring in compositions with high NVP content, (such as C or E) in rod forms. The lower EWC in buttons may be due to the unreacted residual NVP monomer at the hydration stage with subsequent loss of hydrophilicity in the final hydrogel.

The effect of Liprofin treatment on diacetone acrylamide hydrogels are also shown in Table 7.1, as a slight change in EWC. For a single Liprofin treatment, it may be concluded that the treatment does not give large variations in EWC upon diacetone acrylamide hydrogels. However, in order to elucidate the long-term effect of Liprofin on these hydrogels, repeated treatment is required, as in reality, the contact lenses made of these hydrogels should undergo numerous cleaning procedures throughout its wearer period.

Modification of composition A was attempted by incorporating a small % of (2 mole %) methacrylic acid in an effort to increase the EWC. The results are shown in Table 7.2. The values, within experimental error, indicate an increase in water content, but this is still not acceptable for extended wear application.

7.6.(2) Use of N-alkyl Acrylamides

N-alkyl acrylamide monomers were also investigated as possible components to eradicate the problem of hydrolysis, since diacetone acrylamide turned out to be disappointingly low in EWC. The advantages of using N-alkyl acrylamides are better reactivity and hydrophilicity, with good intermolecular strength due to hydrogen bonding which implies better mechanical and chemical stability. Unfortunately, several problems were encountered during polymerization. N-tert-butyl acrylamide, which was the first N-alkyl acrylamide to be tested, had very low solubility in NVP (2.5g limit in 10g NVP). N-isopropyl acrylamide although sufficiently soluble in the liquid comonomers, produced a translucent polymer with some discolouration.

TABLE 7.1 EQUILIBRIUM WATER CONTENT (%) OF DAAcr HYDROGEL

<u>Composition</u>	<u>EWC (%)</u>				
	<u>Membrane</u>		<u>Lens from</u>	<u>After Liprofin</u>	
	<u>2 weeks</u>	<u>6 months</u>	<u>Buttons</u>	<u>Dist. Water</u>	<u>Saline</u>
A	57.6	59.4	59.5	60	60.2
B	63.4	64	53.1	68.3	58.6
C	70.1	75		73	71.2
D	67.4	73.3		55.4	66.2
E	65.5	71	59.9	75.5	66.3
F	66.7	70.7	59.2	69.6	70.3

TABLE 7.2 EQUILIBRIUM WATER CONTENT (%) OF MODIFIED COMPOSITION A

<u>Composition</u>	<u>EWC (%) of membrane</u>
A	57.6
A'	65.6

7.6.(3) Use of N, N-dimethyl Acrylamide

As the previous two strategies had difficulty in achieving EWC of 70% and above, together with solubility problems, other substituted acrylamides were considered. N, N-dimethyl acrylamide was chosen for being a disubstituted acrylamide; there should be improved resistance to hydrolysis with disubstitution owing to increased steric shielding. Kopecek et. al. (150) also reports that the substitution at the nitrogen atom enhances the hydrolytic stability much more than substitution at the α - carbon atom. They said, for reasons of comparison, that the hydrolytic stability of N,N-disubstituted acrylamides is higher than that of the glycol esters of methacrylic acid.

<u>Monomer</u>	<u>Composition (mole %)</u>		
	G	H	J
N, N-dimethylacrylamide (NNDMA)	30	25	30
N-vinyl pyrrolidone (NVP)	45	50	45
2-hydroxyethyl methacrylate (HEMA)	20	20	20
Cyclohexyl methacrylate (CHMA)	5	5	5
Methacrylic acid (MAA)	-	-	2
Ethylene glycol dimethacrylate (EGD)	1	1.5	1.5

NNDMA is a liquid which can be purified by reduced pressure distillation at a moderate temperature of around 40° - 50°C; additionally it should assist in better mixing with other liquid monomers. Table 7.3 shows the EWC of the above compositions. NNDMA is likely to yield high water content polymers as the hydrophilic groups on the nitrogen are quite small. The EWC results were comparable to the original extended wear hydrogels i.e. at around 70%. The rods however, were too fragile to be lathe-cut into lenses; this was attributed to the tendency of NNDMA to cause chain transfer reactions which are more prominent in this monomer than any other known alkyl acrylamide (151). However, stronger materials can be made by changing the polymerization conditions and/or initiator so that the chain transfer reactions are minimised.

Table 7.3 also includes the results of EWC after single Liprofin treatment; as can be seen, the hydrogels made of NNDMA exhibit stability of EWC. In order to investigate whether these NNDMA hydrogels would withstand repeated Liprofin treatment, the lens parameters were checked after each Liprofin cleaning using Optimec. There was no observable effect upon the lens parameters indicating improved hydrolytic stability.

7.6.(4) Other Modifications

Two further compositional changes were attempted to give an optimised

combination of monomers to satisfy clinical applications. Methacrylic acid is often to be found as a component of many extended wear hydrogel lenses; as a solvent to solid monomer and as a strengthener to weaker hydrogel backbones, and as such it would be useful to investigate whether it had any implication towards the mechanical instability i.e. curling. However, the removal of methacrylic acid from the original composition with the three acrylamides components produced hydrogels of lower EWC and thus this avenue of thought was stopped.

Variation of crosslink density in hydrogels has many effects on the resultant physical properties such as elasticity and mechanical strength. Also it can be expected to affect the EWC⁽¹¹⁸⁾. These two attempts, together with the earlier compositional modification upon the acrylamide derivatives indicate that the hydrolytic instability is strongly related to the susceptibility of the acrylamide to hydrolysis. Table 7.4 shows the summary of clinical observation as percentages showing physical distortion of these lenses, after periods of wear. It is clearly shown that hydrogels with the acrylamide component substituted by diacetone acrylamide or N,N-dimethyl acrylamide give much improved stability to the problem encountered in hydrogels with the acrylamide monomer. The shielding of the amide group of N-substituted acrylamide proved effective, as the hydrolytic stability of poly(N-substituted acrylamides) increases from N-monosubstituted to N,N-disubstituted.

7.7. CONCLUSIONS

This section of the thesis was related to hydrogel materials used in extended wear applications of contact lenses. The acrylamides based hydrogel in the original composition is strong and elastic; conferred by acrylamides and the presence of methacrylic acid which form intermolecular bonding. Also the resistance to proteinaceous spoilage has been acceptable in clinical applications. The restricting factors in refining work of this type is the ratio of the comonomers incorporated with changes in resultant property. The main problem encountered here is the hydrolysis of the acrylamide component. By removing the offending comonomer, and by structural modification with substitution e.g. (by DAAcr), the problem is eradicated. The combination of monomers

TABLE 7.3 EQUILIBRIUM WATER CONTENT (%) OF NNDMA HYDROGELS

<u>Composition</u>	<u>EWC (%)</u>	
	Rod	After Liprofin treatment
G	71.8	70.7
H	68.5	67.5
J	70.1	69.9

TABLE 7.4 SUMMARY OF CLINICAL OBSERVATION (AS % SHOWING LENS DISTORTION)

<u>Composition</u>	1 month	3 months	6 months
	Wear	Wear	Wear
Unmodified	10	20	50
α	0	10	10
β	0	0	0
γ	10	20	40
δ	10	20	50

Compositional Details

- α : Composition containing diacetone acrylamide (A)
- β : Composition containing N,N-dimethylacrylamide (G)
- γ : Composition with crosslink density varied
- δ : Composition without methacrylic acid.

used in the original hydrogel based on three acrylamides showed susceptibility to hydrolysis at the amide linkage of the acrylamide by a combination of the enzymatic influence of tears and oxidative cleaners.

A selection of compositions were made from hydrogels based on monomers with substitution at the amide terminus. The structural modification by the substitution demonstrated that disubstitution such as in N,N-dimethylacrylamide were effective in combating the mechanical instability, this is attributed to the shielding of the susceptible acrylamide group by disubstitution.

The repeated tests with oxidative cleaners such as Liprofin were also promising for disubstituted acrylamides, showing very small change in the EWC. The EWC of substituted acrylamides demonstrated that small substituents are preferred to large substituent, as shown by the EWC (about 70%) of the N,N-dimethylacrylamide and diacetone acrylamide (EWC about 62%).

The clinical observation of the modified acrylamides showed much promise in solving the original problem of lens distortion. Together with a further study on the lens spoilation should indicate the disubstituted acrylamide based comonomer such as N,N-dimethylacrylamide as potential replacement system in the extended wear application of this type of hydrogel.

CHAPTER VIII
SUMMARY AND CONCLUSIONS
SUGGESTIONS FOR FURTHER WORK

8.1 INTRODUCTION

This chapter summarises the results and discussions of the work described in this thesis, together with final conclusions. Additionally, suggestions are presented for further work which is designed to contribute to greater understanding of the underlying theme of structure - property relationships of materials in relation to ophthalmic applications.

8.2 FINAL DISCUSSION

The work presented in this thesis is designed to represent a contribution to the development of laboratory techniques to assess "in vitro" properties and behaviour of contact lens materials in such a way that their "in vivo" performance is predicted. An overview of the development of contact lens materials (with emphasis on the rigid gas permeable type) has been given on the basis of the published literature, especially the patent literature. Despite the lack of directly comparable scientific data in these publications, it is possible to discern trends in development of material structure and property relationships.

Development of patent literature : an overview

The search for materials with greater oxygen permeability stems from the desire to seek alternatives to the otherwise acceptable hard lens material PMMA, which has very low permeability to oxygen. Although several alternative thermoplastics and elastomers have been patented for contact lens applications, the majority of successfully marketed rigid gas permeable materials are based upon developments in 1974 by Gaylord⁽³⁸⁾ in which he described the use of tris-tri methylsiloxy, γ -methacryloxy propylsilane in rigid gas permeable contact lenses.

The subsequent development in the published patent literature (as reviewed in Chapter 2) are summarised in a flow chart in Figure 8.1. At around 1978

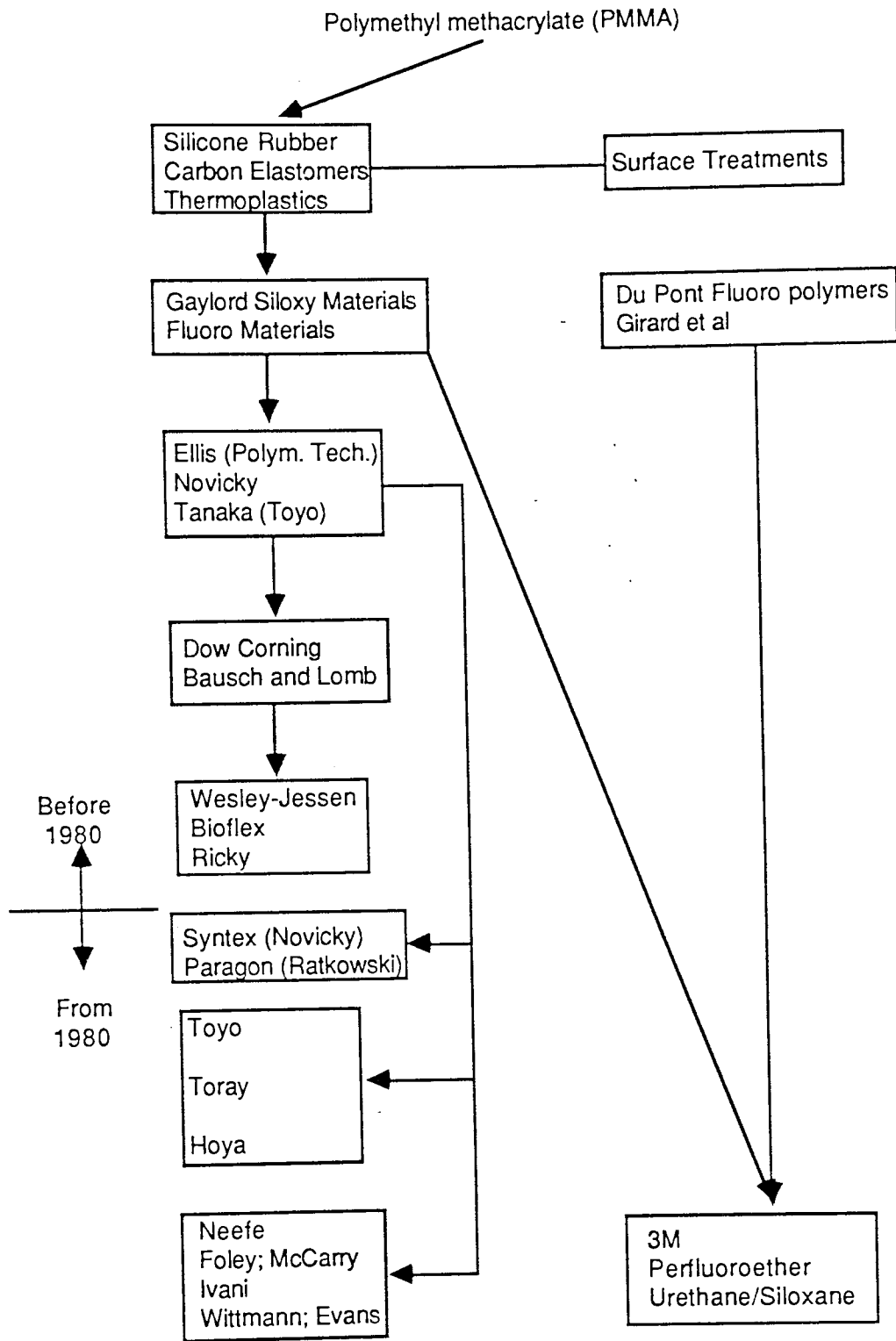


Figure 8.1 Contact lens material patent development

there were three workers Ellis, Novicky and Tanaka who began filing a series of separate patents related to siloxymethacrylate based contact lens materials. The Ellis and Novicky patents form a logical line of continuation from the early Gaylord's work whereas Tanaka's work is differentiated by the use of a group of monomers containing a hydroxyl group together with the branched siloxy and methacrylate units. Two similar pieces of work from Dow Corning and Bausch and Lomb also attempt to harness the high permeability of siloxy polymers. Further ideas emerging at the end of the 1970s also were; firstly the use of alkyl substituted polystyrenes and secondly the copolymerization of butyl methacrylate and acrylic acid.

The relatively recent patent publication from the 3M company described the use of fluoropolymers and at least one published review (104) points favourably towards this type of material, with respect to improved resistance to surface spoilation. The aforementioned hydrophobic siloxy materials have curiously similar ultimate spoilation problems to the more hydrophilic hydrogel materials, although the rate of spoilation is slower in the latter group of materials. The use of fluoropolymers is not new and again can be traced back to Gaylord(39) together with the earlier patent disclosures made by Du Pont (40, 41, 42) which are based on simple fluorinated methacrylate esters. They were apparently successful in preliminary clinical trials (94); however, because the siloxanyl methacrylates are claimed to give 15-20 times greater oxygen permeability, whereas the claims of the fluoroalkyl methacrylates patents are only some 3 to 4 times greater than PMMA, the former type of monomers have captured the efforts of manufacturers research and development interests.

The marked trend in the 1980s is the expansion of Japanese patent coverage, notably from Hoya Lens K.K. and Toyo Contact Lens Co. Ltd; with a curious feature of identical or very similar ideas patented by different companies within

a short space of time. Many of the U.S. patents appearing around this time are concerned with concepts of variations that have developed from the siloxymethacrylate patents literature. Some original ideas that have emerged around this period include silyl acetylene polymers, pentafluorostyrenes, urethane siloxanal acrylates.

Recent interest has concentrated upon achieving much higher oxygen permeability either by increasing the siloxy content or by incorporation of larger bulkier siloxanyl substituents. Despite the exaggerated claims made by some contact lens manufacturers for the so-called "super-permeable" contact lens materials, there is a certain lack of novelty and ingenuity of ideas in the underlying chemical approach.

Problems associated with the non-wetting of siloxy materials are yet to be satisfactorily solved. The copolymerization of hydrophilic monomers such as N-vinyl pyrrolidone are the most common technique to combat this problem. Gas plasma treatment of the lens surface and plasma polymerization have also been described in patent publications (98,100).

Characterisation of polymers: oxygen permeability, surface and mechanical properties

The physical properties of commercially available rigid gas permeable materials as compiled from, typically, manufacturer's literature, reviews and our own results, are summarised in Chapter 2, Table 2.1. Direct comparison of materials properties from patent disclosures is difficult due to the lack of standardisation of experimental procedures. The commercially available methods of measuring oxygen permeability, especially, are fraught with problems arising from the geometry of individual contact lens samples and lack of available standards for calibration of instruments. A recent report (152) suggests that as the value of the oxygen permeability increases, the probable error increases to the second power. This means, for example, that a given contact lens material claimed to have a Dk value of about 14

$\times 10^{-11} \text{cc(STP)cm cm}^{-2} \text{sec}^{-1} \text{mmHg}^{-1}$ at 25°C has a possible error of $\pm 55\%$. This theme is discussed in detail in Chapter 3.

Despite many efforts to improve the hydrophobic surfaces of siloxy methacrylates by various chemical and surface treatments, these coatings are only temporary and the treatment must be frequently repeated to be effective. Also such treatments are contra-indicated by their effect on oxygen permeability. With an increase in the quantity and bulk of the siloxanyl constituent, there is a related tendency for hydrophobic surfaces to prevail. Considerably less emphasis by manufacturers is placed upon the surface properties of gas permeable materials, and often there is little detail on techniques or procedures followed, making critical comparisons very difficult. The most convenient and popular method to measure the "wettability" of surfaces in the "in vitro" tests is the equilibrium sessile-drop technique.

Unfortunately, in most of the manufacturers literature and commercial publications, there is no clear indication of the surface characterisation technique employed, other than a "number" quoted as a contact angle. The presence of contact angle hysteresis (between advancing and receding angles), the difference between "dry" and "soaked" states of the lens substrate, various measurement protocols employed, and the use of different wetting solutions all contribute to vastly different values of a "contact angle" of a given lens surface. The search for a more "realistic" measurement of wettability has resulted in the equilibrium captive bubble technique, which is thought to be a simulation of an "in vivo" contact lens environment. This technique has been extensively used by many manufacturers for marketing purposes, because of low contact angle values so obtained.

The sessile drop measurement together with Owens and Wendt analysis (133) allows polar and dispersive components of surface energy to be determined for a given surface. The consideration of surface free energies and its relevance to the

surface properties of contact lens material has not appeared in any other work except in this thesis. The significance of such characterisation for clean homogeneous unworn contact lenses is important; however, after the lens is worn, the physiological interaction between the ocular secretions in tears and the lens leads to a chain of events resulting in heterogeneous surfaces. Clinical liaison work with Judith Morris of London Refraction Hospital indicated that tear wetting problems may be caused by the existence of small islands of lipoidal spoiliations. The most convenient method of surface characterisation, the contact angle technique, indicated good wetting on a macroscopic scale because the droplet covers the microscopic globular lipid deposits producing an apparently low contact angle. Recent studies by Benjamin et al (153) also showed rapid reductions of the "in vivo" contact angles after the first blink.

The incorporation of higher concentration of siloxy constituents increases the oxygen permeability but produces problems in mechanical stability, as their structures differ dramatically from the methacrylate comonomers, and there is a tendency for phase separation to occur. This leads to brittleness of the polymer and diminished durability. Short chain branching may occur during the polymerisation resulting in structures susceptible to mechanical distortion. This has led to a report of a case where a commercial gas permeable lens, of high quoted oxygen permeability, split on the eye during wear! These highly permeable materials are, also susceptible to damage during handling and are thus cause of great concern to the clinicians prescribing these types of contact lenses.

In published papers and patents, hardness is often quoted as a representation of the mechanical properties of a given material. However, these siloxy methacrylate polymers have rather similar hardness properties at around 85 Shore D hardness and this data cannot be used to directly compare materials in terms of

mechanical stability. Many of the difficulties in adapting the small contact lens samples to conventional mechanical testing techniques is due to the geometry and size of the samples.

Much of the information in the mechanical testing section are the results of original work carried out in these laboratories. Most of the pieces of apparatus employed are conventional instruments, but the techniques were adapted and designed to suit the contact lens samples. For example, using a conventional tensometer, samples of rigid materials were split into half-lens size and mounted in a small load crosshead jaw. Thus, tensile and compression testings are shown to give useful information indicating durability during handling as well as being a means of quality control. The interpretation of any claims and disclosures made by manufacturer's, must be carefully assessed in terms of their method of measurement and experimental conditions. The availability of standardised techniques described in this thesis is an essential element in making accurate and meaningful comparisons of available materials.

The use of alkyl methacrylates : an alternative strategy in the design of contact lens materials

The ideas of combining structurally dissimilar monomers containing methacrylate and siloxy groups have associated problems of heterogeneity in the resultant polymer network. In Chapter 5, the logic of synthesizing more homogeneous contact lens materials based on alkyl methacrylate copolymers was discussed. The variation in the structure of the alkyl substitution and the copolymers based upon them were studied in the light of the three essential physical properties to reflect their performance in contact lens application. A Davenport Gas Permeability Apparatus was used to study the effect of simple alkyl substituents on the gas permeability of the

homopolymer. The results, as shown in Table 5.1, indicate increased permeability to the three gases studied (O_2 , N_2 , and CO_2) as the substituent group became bulkier. This apparatus can be used to give absolute gas/gas permeability data, and as a means of validating other permeability measurement techniques. The favoured instrument to measure the oxygen permeability of a contact lens sample is the Schema Versatae Flux Meter where the permeability is measured polarographically. Although the accuracy of the data so obtained may be open to debate, it is the most convenient and adaptable technique for contact lens samples (being related to dissolved oxygen permeability).

The empirical results of density and oxygen permeability of alkyl methacrylate homopolymers (determined using the Schema Versatae Flux Meter), showed general relationships (Figure 5.3) which may be used in the primary selection procedure of these polymers in the pertinent application. Bulkier side groups in the network lower the density (by increasing steric hinderance and thus the difficulty of close packing) and result in a rise of oxygen permeability. The effect of copolymerising the appropriate comonomers with PMMA and PIBMA indicated a similar trend. (Tables 5.3 and 5.4 respectively). The bulky branched side groups showed promising results in terms of reduction in density with subsequent increase in oxygen permeability, indicating the effect of steric hinderance by branched groups being more effective in reducing the density and increasing oxygen permeability than either chain length or chain flexibility. The effect of copolymer structures upon the oxygen permeability was also investigated; Figure 5.4 clearly shows the result i.e. siloxy substituents give the highest increase in oxygen permeability. Although, the incorporation of siloxy substituents, as shown by the large number of patents, leads to high oxygen permeability; these groups have hydrophobic surfaces.

The modification of surface properties based on alkyl methacrylates by copolymerising with hydrophilic monomers or reactive side group monomers was

attempted as described in Chapter 5. Incorporation of polar hydrophilic comonomers led to moderate surface wettability together with a fall in oxygen permeability. The high proportion of polar groups in the bulk of the copolymer provides a high degree of molecular interaction leading to overall chain stiffness and subsequent decrease in oxygen permeability. Copolymerisation of monomers susceptible to surface modification by hydrolysis (such as maleic anhydride) showed promising improvements in surface wettability. Although satisfactory in vitro results were obtained with these materials the clinical assessment is required to determine long-term efficiency of this type of treatment.

The mechanical testing in tensile and compressive mode of the synthesized methacrylate copolymers showed comparable mechanical properties to those of commercial rigid contact lens materials. The compressive properties fell in bands. The synthetic work then produced homogeneous polymeric materials having adequate oxygen permeability and mechanical stability with marginally acceptable surface properties, showing the difficulty in achieving the ideal balance of properties with simple copolymerisation. It was particularly apparent in balancing oxygen permeability and surface wettability. The molecular structures beneficial in providing the required level of one property, for example surface behaviour, is often contrary to other requirements such as permeability.

The use of gas plasma in surface modification of polymers

In view of this, in Chapter 6, the application of gas plasma oxidation was considered in order to introduce surface hydrophilicity upon the synthesized polymers in which other properties may be considered adequate. The primary purpose of this type of surface treatment is to modify the surface property of polymers without affecting the bulk properties. Consulting the available patent literature on the use of gas

plasma in surface modification techniques of hydrophobic polymers, it became clear that there is a lack of fundamental knowledge relating the type of surface treatment to the susceptibility and stability to modification of different material types. Much of the work related to the use of glow discharge plasma (for example reference 146) is concerned with the chemistry of species present at the plasma surface.

The purpose of plasma work in this thesis is related to investigating the basic parameters controlling the treatment; the susceptibility and the stability of polymer substrates with particular reference to polymer materials used in contact lens application. The initial studies have established the experimental conditions suitable in order to attain the desired wettability; 3 minutes exposure time at r.f. power of 100W. The susceptibility of aromatic groups to treatment of this type were shown to be greater than methacrylate polymers. The bulkier and rigid aromatic ring structures may, after the initial surface wettability, be responsible for the subsequent slow loss of wettability in comparison to the flexible methacrylates. Yasuda and Sharma (144) postulate loss of surface wettability to embedding of reactive sites into the polymer bulk, hence more flexible structures show less tendency to sustain the induced hydrophilicity. The surface energy study of treated surfaces of polystyrene indicated the increased presence of polar groups thus improving the surface wettability. The introduction of species with a high degree of polarity such as carbonyl and hydroperoxide is reported (146) to be found at the plasma treated surfaces. Simple evaluation of kinetic aspects indicates that the loss of the surface wettability may be related to the decomposition of such products, especially hydroperoxide.

The effect of glow discharge plasma upon the polymer materials used in this thesis was observed to be, unfortunately, not permanent as reflected in the decay in the wettability. The decay process was found to be related to the structures of the treated polymer substrate; the presence of aromatic groups producing slower decay.

The plasma treatment carried out on poly(4 methylpent-1-ene) and a siloxy methacrylate monomer also indicated the effect of chain flexibility and ease of rotational mobility upon the wettability decaying process. The subsequent loss of the surface wettability was found to be related to two possible processes; one is the embedding of the reactive species and the other decompositional process of the polar species produced at the onset of the treatment. These fundamental studies are of relevance in choosing structures susceptible to plasma glow treatment for surface modification.

The principle of molecular design to achieve the desired combination of the physical properties of polymers, was applied also to hydrogel materials used in extended wear contact lens applications. The combination of three acrylamides in a complex copolymerization system indicated the instability of the acrylamide with respect to hydrolysis during long-term wear periods. This results in the stretching of the lens from the centre to edge (induced by the combination of blinking and the curvature of the cornea) which produces curling of the hydrogel lens. Additionally problems arise with the alkaline environment of a strong oxidative cleaner. Steric shielding in N-disubstituted acrylamides showed improved resistance of the amide group to the oxidative cleaners. Additionally by adjustment of the quantity of comonomers an improved copolymer which proved to be effective in overcoming the physical instability due to in vivo hydrolysis was developed.

8.3 CONCLUSION

The significance of contact lens materials as biomaterials has been established. The assessment of performance of a given material by in vitro techniques has been achieved through adapting and developing techniques with emphasis on choosing and standardising relevant experimental conditions and procedure. The goal

of producing more structurally homogeneous synthetic polymers was seen as desirable in order to develop materials with a finer balance of desired properties. This is particularly important in designing improvements in 'hard' lens materials to replace polymethyl methacrylate.

A critical assessment of published literature in this area was made, with the majority of information arising from patent publications. Thus by following the development of commercially available materials with an emphasis on rigid gas permeable materials, underlying chemical features based largely on bulky hydrophobic siloxy methacrylate were observed. The problems in assessing the potential value of each material through the patent literature stemmed from the lack of a fundamental basis or standard techniques which would allow direct comparisons. The need for such methodology has been fulfilled by developing and adapting conventional polymer testing methods, with great care for reproducibility, reliability and accuracy of the results. The laboratory techniques are also important in assessing the ultimate performance of materials prior to clinical tests involving, as they do, greater complexity and time. Comparisons have been made, wherever possible, between measurements made in these laboratories and those quoted elsewhere.

The common practice of incorporating bulky siloxy-methacrylates with methyl methacrylate to produce gas permeable materials is fraught with problems of hydrophobic surfaces and heterogeneous molecular structures. The use of various alkyl substituents in place of methyl in methyl methacrylate type of polymer have produced synthetic materials of more homogeneity. By copolymerizing structurally similar methacrylates with different functional groups to give desired physical properties, it was possible to synthesize a selection of materials of potential ophthalmic use. The main difficulty was found to lie in accomplishing the delicate balance of

oxygen permeability and surface properties using compatible structures.

The gas plasma glow discharge in modification of polymer substrate, enabled surface wettability to be attained without affecting the bulk properties of the polymer. An understanding of the possible mechanisms and the chemistry involved during the plasma treatment, was achieved by fundamental studies involving surface characterisation techniques. The further success of this treatment rests in attaining the permanence of the desired effects which unfortunately decay in time. The susceptibility and stability of the plasma treated aromatic structures were greater in comparison to straight chain methacrylates. The use of susceptible structure to this type of surface treatment may yield success in combination with branched methacrylates to produce enhanced oxygen permeability.

This reflects the importance of designing in vitro techniques to enable relevant properties to be accurately measured and studying those structural features that enable some control over each property to be exerted.

8.4 SUGGESTIONS FOR FURTHER WORK

It is hoped that the information contained in this thesis forms a basis from which other studies can proceed. The following are a few suggestions for such further work.

Extended work on alkyl methacrylates, particularly based on isobutyl methacrylate, by copolymerisation with functional monomers should be fruitful in ophthalmic applications. As was suggested in Chapter 6, a combination of monomers, for example, t-butyl methacrylate, maleic anhydride, methacrylic acid and branched styrene may well provide materials of greater potential. By further soaking the material in alkaline solution, the surface wettability may be improved; which brings the subject of clinical trial of potential material in vivo, following the in vitro assessment.

Ultimately, the spoilation studies upon the methacrylates material, after a wear period should provide further information for the usefulness of these materials in the ocular application.

It is anticipated that a great deal of information contained in this thesis extends beyond the contact lens application and to more general broader ocular applications such as intraocular lenses for aphakic patients. The physiological compatibility of the synthetic materials produced in this thesis may assist in considering the potential use of these types of polymers in intraocular application. Although, it is expected that the biocompatibility demand for such applications would be much greater than in contact lenses, the associated property requirements should be similar (such as the general question of transport and interfacial properties and mechanical stability).

As in parallel with the highly complex interfacial properties of biomaterials which come into contact with the human body, the materials used in ocular application require effective cleaners to remove spoilation and debris accumulated at the interface of biopolymer/bodysite. It would be of greater interest to study the spoilation and subsequent loss of wettability in rigid gas permeable type of materials as studied in this thesis. Hydrogels and their biocompatibility and subsequent spoilation problems have been studied in great detail in these laboratories and the wealth of information can be adapted and applied to the process in which the rigid materials are spoiled after wear.

There is a great deal of work to be done with plasma glow discharge treatment upon the surface of the polymer substrate. The results obtained in this thesis should provide a basis from which other studies can be made. Continuous monitoring of the plasma treated surface by surface chemical analysis techniques such as ESCA or I.R. spectroscopy in conjunction with the surface characterisation work as performed in this thesis, should give greater insight into the reaction processes taking place. The

greater degree of understanding in the process of the loss of surface wettability of plasma treated substrates should be useful in evaluating the susceptibility of particular structures to plasma surface modification.

As gas permeability P , is given by $P=D \times S$ (where D is diffusion coefficient and S is solubility coefficient) a further investigation upon their individual contribution with relation to structural variant may prove invaluable. Such studies may lead to the design of monomers with functionalities to provide the various desired physical properties, particularly improved oxygen permeability. Such improvements can be achieved with the combined effort of synthetic chemists and material scientists.

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