OCULAR BIOTRIBOLOGY AND CONTACT LENS LUBRICATION MECHANISMS

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THESIS SUMMARY

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The work described in this thesis is concerned with mechanisms of contact lens lubrication. There are three major driving forces in contact lens design and development; cost, convenience, and comfort. Lubrication, as reflected in the coefficient of friction, is becoming recognised as one of the major factors affecting the comfort of the current generation of contact lenses, which have benefited from several decades of design and production improvements.

This work started with the study of the in-eye release of soluble macromolecules from a contact lens matrix. The vehicle for the study was the family of CIBA Vision Focus® DAILIES® daily disposable contact lenses which is based on polyvinyl alcohol (PVA). The effective release of linear soluble PVA from DAILIES on the surface of the lens was shown to be beneficial in terms of patient comfort. There was a need to develop a novel characterisation technique in order to study these effects at surfaces; this led to the study of a novel tribological technique, which allowed the friction coefficients of different types of contact lenses to be measured reproducibly at genuinely low values. The tribometer needed the ability to accommodate the following features: (a) an approximation to eye lid load, (b) both new and *ex-vivo* lenses, (c) variations in substrate, (d) different ocular lubricants (including tears).

The tribometer and measuring technique developed in this way was used to examine the surface friction and lubrication mechanisms of two different types of contact lenses: daily disposables and silicone hydrogels. The results from the tribometer in terms of both mean friction coefficient and the friction profiles obtained allowed various mechanisms used for surface enhancement now seen in the daily disposable contact lens sector to be evaluated. The three major methods used are: release of soluble macromolecules (such as PVA) from the lens matrix, irreversible surface binding of a macromolecule (such as polyvinyl pyrrolidone) by charge transfer and the simple polymer adsorption (e.g. Pluoronic) at the lens surface. The tribological technique was also used to examine the trends in the development of silicone hydrogel contact lenses. The focus of the principles in the design of silicone hydrogels has now shifted from oxygen permeability, to the improvement of surface properties.

Presently, tribological studies reflect the most effective *in vitro* method of surface evaluation in relation to the in-eye comfort.

Keywords: Contact lenses, Hydrogels, Tribology, Lubrication, Surface Modification

For My Family

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Chapter 1

Introduction

1.1: Hydrogels

1.1.1: Introduction

Hydrogels, by definition, are water-swollen polymer networks of either natural or synthetic origin. They possess the ability to imbibe large quantities of water or biological fluids without dissolving (Peppas., 2004). Hydrophilicity of these gels is attributed to the presence of group such as hydroxy, carbonyl, amide or sulfonic, along the polymer chain. Cross-links are formed by covalent bonds, electrostatic, hydrophobic or dipole-dipole interactions, which prevent the gel from dissolving fully. The structural and physical integrity of the gels are a result of these interactions.

Research on hydrogels started in 1960 with a landmark hydrogel paper based on poly (2-hydroxyethylmethacrylate) known as polyHEMA developed by Professor Otto Wichterle and his co-workers in Czechoslovakia. Wichterle and Lim suggested that it was a biocompatible synthetic material. This resulted in the development of the various applications of hydrogels for example biocompatible polymers and novel drug delivery systems (Wichterle et al., 1960). Ratner and Hoffman suggested that the physical properties of hydrogels resembled those of living tissue more than other classes of synthetic biomaterial. Their relatively high water content and soft rubbery consistency give a strong superficial resemblance to soft living tissue (Hoffman., 2002).

The great advantage of this material over others is that the gel can be stable over varying conditions such as pH, temperature and tonicity, which are commonly encountered in biomedical uses (Corkhill et al., 1990).

1.1.2 Water in Hydrogels

The property that makes these materials favourable for use in the body is the water within the polymer. Water has numerous roles within a hydrogel; such as a plasticiser, a transport medium within the polymer matrix (for dissolved species such as oxygen) and a "bridge" between the different surface energies of synthetic polymers. Water absorbed by a hydrogel network structure contributes to the mechanical and physical properties of the gel (Corkhill et al., 1987). The water in hydrogels is thought to exist in more than one state and the state the water is in influences the properties of the hydrogel. In fact, water exists in a range of states between two extremes. Water strongly associated with the structure of the polymer through hydrogen bonding, which is known as non-freezing or as sometimes referred to "bound" water and water with an amount of freedom and mobility, which is unaffected by the polymer known as freezing or as sometimes called "free" water. The properties of hydrogels are strongly affected by the ratio of non-freezing to freezing water present in the polymeric network as well as the equilibrium water content.

A water starved hydrogel will absorb water until it reaches equilibrium. This is known as the equilibrium water content (EWC). The EWC can be defined using the equation below:

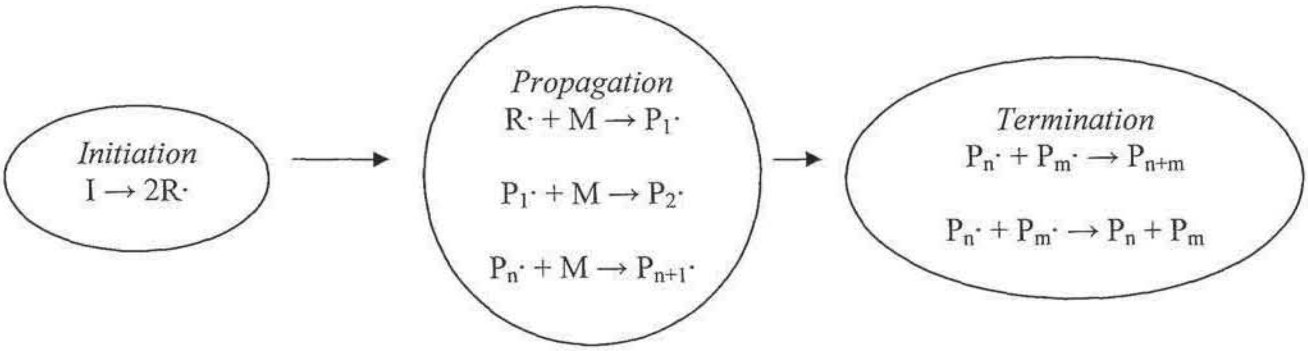
$$\textbf{EWC} = \frac{\textbf{Weight of water in gel}}{\textbf{Total weight of hydrated gel}} \times 100\ \%$$

Equation 1.1: The Equation for Equilibrium Water Content

The EWC can be determined by immersing the hydrogel in water for several days and then weighing the hydrogel. The hydrogel is then allowed to dehydrate in a vacuum oven and reweighed. These values can then be substituted into equation 1.1 to evaluate the EWC. Water in the hydrogel can be seen to act as a plasticiser giving the gel more flexibility, a bridge between the very different surface energies of the biological and synthetic systems, and allows for transport of water soluble species, such as oxygen, through the polymer network. It may therefore be used to transfer polar drugs from the polymer (e.g. contact lens) to the target area (e.g. tear layer).

1.1.2 Hydrogel synthesis

Hydrogels are commonly synthesised by the addition of initiator to monomer and cross-linking agent, which are required to polymerise, this polymer is then allowed to absorb water to become a hydrogel. The polymer can be initiated in a variety of ways, such as ultra violet light, redox pairs and thermal initiation. These methods although different have the same purpose, which is to create the initiating radicals. The radicals then react with the monomer to form propagating radicals, which then continue to react with more monomer forming large propagating species, these continue to propagate until they are terminated or they run out of monomer. See figure 1.1 a for schematic of the polymerization.



KEY: I = initiator, R· = Radical, M = Monomer, $P_1\cdot$ = First propagating radical, $P_2\cdot$ = Second propagating radical, $P_n\cdot$ + $P_m\cdot$ = Propagating radicals with n and m number of monomers respectively.

Figure 1.1: A schematic to show the addition polymerisation of a monomer

Most work on hydrogels is done with lightly cross-linked hydrogels that are polymerised using one of the initiation methods previously stated, to produce glassy, transparent polymer matrices, which are very brittle. When immersed in water, the glassy matrices swell to become soft and flexible. Although these permit the transfer of water and some low-molecular-weight species, such hydrogels are considered to be essentially non-porous (Corkhill et al., 1990).

1.1.3 Applications of Hydrogels

Hydrogels can be synthesised for a wide range of applications. Adjusting the method of preparation and composition affects the level of swell or mechanical strength (Dumitriu., 2002). Some examples of the applications for hydrogels are given below:

Contact Lenses Hydrogels are used for a range of ophthalmic applications for example as soft contact lenses (see section 1.3 for further information). Another ophthalmic application is for intraocular lenses. The integral part of most cataract operations is the substitution of the crystalline lens for a transparent intraocular lens. Foldable lenses composed of hydrophilic polymers (polyHEMA or HEMA copolymers) were specifically designed to accommodate the small incision procedure used to replace the lens. These polymeric materials are compatible with the eye and produced low-level anti-inflammatory responses (Dumitriu., 2002).

Tissue Prosthesis and Tissue Regeneration Millions of people suffer from degenerative tissue in their joints. Hydrogels can be used to replace articular cartilage or tissue. Model systems enable the parameters controlling the biomechanical properties of articular cartilage to be simulated (Dumitriu., 2002). A substantial amount of interest has been shown in the application of hydrogels as a tissue cell regenerator for the central nervous system (CNS).

Lubricants Biomaterial surfaces can be lubricated with hydrogels. The hydrogel helps to provide a lubricous coating for example latex gloves, catheters and drainage tubes. This enables ease of use when in contact with hydrophilic species (Dumitriu., 2002).

Dressings Hydrogels can be used for ulcerous and wound coverings. They act as barriers, preventing infection and moisten wounds, which promotes the healing process. Dressings absorb secretions and extrudate without adhering to the wound. Minimal trauma occurs when these dressings are removed (Dumitriu., 2002).

Drug Delivery Systems (dermal drug delivery) These drug delivery devices provide an alternative method to administer actives across the skin barrier. Gastrointestinal absorption is the traditional route for orally administered drugs. Patches contain a lower concentration compared to the oral doses. If any adverse symptoms begin to develop the gel can be removed, halting any further release (Tan., et al, 1999). An active within the polymer matrix is the simplest form of drug incorporation into the hydrogel. The components used within the hydrogel play a major role in the rate of release and can be modified by using different types of monomers.

1.2: The Eye

1.2.1: Structure of the Eye

The eye is a round structure, which has a wall that consists of three layers: the outer sclera, the middle choroid layer and the inner retina (napa.ufl.edu). As shown in figure 1.2.

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Figure 1.2: Schematic cross section through the human eye

The sclera, is a strong fibrous coating, which protects the inner layers of the eye; it is white except for the area in front of the cornea, which is the part of the eye that allows light to enter.

The middle layer of the structure is the ***choroid***, which contains blood vessels and is modified at the front of the eye to form the colour of the iris.

The lens, which lies behind the pupil, has a biconvex shape; the chamber behind the lens is filled with a gelatinous substance that takes up 80 % of the total eye. The chambers between the cornea and iris, and iris and lens are filled with an aqueous humour. The inner part of the eye is the light-detecting ***retina.***

The part of the eye that is of most concern to drug delivery is the front of the eye as this is where the contact lens sits upon. Hence the cornea, the conjunctiva and the naso-lacrimal drainage system are examined more closely.

The Structure of the Cornea

The cornea is an optically transparent tissue that conveys images to the retina at the back of the eye, the cornea covers almost 1/6 of the eyeball's total surface area. The cornea receives nutrients and oxygen via the lacrimal fluid and aqueous humour as well as from blood vessels that line the junction between the cornea and the sclera.
The cornea is approximately 0.5 mm thick in the central region, and is 0.7 mm at the periphery (napa.ufl.edu).
The cornea is comprised of five layers:

1. The Epithelium consists of 5-6 layers of cells (increasing to 8-10 at the periphery), and has a total thickness of between 50 – 100 μm. A layer of cells is replaced everyday. The tight junctions and the hydrophobic regions of this layer makes it the most important barrier the drug will come up against in the eye.
2. Bowman's membrane is a thin sheet 8-14 μm thick that is positioned between the epithelium and the stroma. The membrane itself is a cellular homogenous sheet.
3. The Stroma or substantia propria accounts for approximately 90 % of the cornea. It is made up of mostly water (85 %), and contains 200-250 collagenous lamellae that are superimposed onto each other and run parallel to the surface. The lamellae provide the physical strength while allowing the cornea to remain optically transparent. The stroma's structure is relatively open and this allows the diffusion of hydrophilic solutes.
4. Descemet's membrane is secreted by the endothelium, and lies between the stroma and the corneal endothelium.
5. Corneal endothelium is responsible for keeping the normal hydration of the cornea. It consists of a single layer of hexagonal cells 5 μm high and 20 μm wide. The endothelium is in contact with the chamber of aqueous humour that lies between the cornea and the iris, and is subject to the passing of water from the chamber to the stroma.

The Conjunctiva

The conjunctiva is a thin, vascularised mucous membrane that lines the posterior surface of the eyelids and outer regions of the cornea, (shown in figure 1.3) as it is involved in the formation and maintaining of the precorneal tear film. This is a highly specialised fluid layer that covers the corneal epithelium, conjunctiva, and the walls of the conjunctival sac. Tears are necessary for the nutrition of the cornea, the removal of unwanted materials, for example bacteria, and the lubrication of the eyelids to allow them to move freely over the globe of the eye. At the present time drugs for the eye are delivered to the tear layer in the form of eye drops.

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Figure 1.3: The conjunctiva

The Naso-lacrimal Drainage System

This is the system for the removal of tears from the eye and therefore drugs from the tear film. The naso-lacrimal drainage system is made up of three parts: the secretory system, the distributive system, and the excretory system.

The secretory system consists of basic secretors that are set off by blinking and temperature changes due to the evaporation of tears, and reflex secretors that respond to physical or emotional stimulation.

The distributive system consists of the eyelids and tear meniscus around the edge of the lid. This works by spreading tears over the ocular surface by blinking, this prevents the development of dry patches appearing.

The excretory system consists of: the lacrimal puncta, the superior, inferior and common canaliculi; the lachrymal sac; and the naso-lacrimal duct. In humans, the two puncta are the openings of the lachrymal canaliculi and are situated on the lachrymal papilla (see figure 3). The tears are largely absorbed by the mucous membrane that lines the ducts and lachrymal sac; only a small volume of tears reaches the nasal passages. The normal tear flow rate is 1.5 µl min^{-1} (Larke., 1997).

Figure 1.4: The Naso-lacrimal Drainage System

1.2.2: Eye Disorders

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Figure 1.5: The targets for major eye disease

Below are some diseases of the eye that are treated by drugs:

- **Glaucoma** is the build up of pressure in the two chambers between the cornea, iris, and lens of the choroid layer that happens when the aqueous humour does not drain properly.
- **Retinitis pigmentosa, RP** is a general term for a number of diseases that affect the retina. These diseases are usually hereditary and affect individuals earlier in life.

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Figure 1.6: Example of Retinitis pigmentosa

- **Age related macular degeneration, AMD** refers to a degenerative condition that occurs most frequently in the elderly. AMD is a disease that progressively decreases the function of specific cellular layers of the retina's macula. The affected areas within the macula are the outer retina and inner retina photoreceptor layer (optobionics.com).

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Figure 1.7: Example of age related macular degeneration

- **Conjunctivitis** is the inflammation of the conjunctiva, which is caused by bacterial and viral infections, or allergens to pollen, smoke, and pollutants.
- **Dry Eye Syndrome** is the inability to wet the ocular surface efficiently.
- **Keratitis** is the inflammation of the cornea, caused by bacterial, viral, and fungal infection.
- **Iritis or Uveitis** is the most common cause of painful red eye and inflammation of the iris (emedicine.com)
- **Other Conditions** include the ophthalmic complications of Rosacea (irritation of the ocular surfaces), blepharitis (inflammation of the lid margins) and chalazia (Meibormian cysts of the eye) (napa.ufl.edu).

1.2.3: Drug Delivery to the Eye

The drugs delivered to the eye mainly contain functional groups such as alcohol, carboxylic acid and phenol, which allow them to enter the eye.

Drug Delivery Vehicles

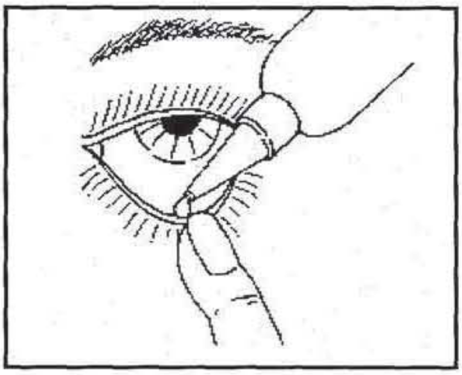

Figure 1.8: Eye drop administered in the lower conjunctival sac

The most common method for administering ocular drugs is the placement of drops into the lower conjunctival sac of the eye. These drops are usually drained away quickly, aided by the automatic reflex of blinking. The precorneal region then returns to the normal volume of about 7 μl (Larke., 1997). The concentration of the drug in this region drives the drug across the cornea via passive diffusion. Hence, for a drug to be effective it needs to have good corneal penetration and needs to be in prolonged contact with the cornea tissue.

There are a variety of drug delivery systems on the market today, however, around 70 % of drugs prescribed for eye medication is in the form of eye drops. This is mainly due to cost, ease of manufacturing, patient compliance, efficacy and stability.

Current Issues with Drug Delivery

In this section each type of drug delivery will be outlined.

- ***Liquids (eye drops / lotions)*** are solutions or suspensions, which are relatively safe, convenient and take immediate effect. When eye drops are applied to the lower conjunctival sac there is initially a high concentration of the drug present. This declines rapidly with kinetics close to first order, therefore patients receive either a higher dose or lower dose than required.

Figure 1.9: An example of commercially available eye drops

- ***Eye ointments*** are semi-solids that are applied to the exterior regions of the eye. They are usually produced with a mixture of semi-solids and solid hydrocarbons (e.g. paraffins) which have a melting or softening point close to the temperature of the body, and must be non–irritating to the eye. Upon administration the ointment breaks up into small droplets that remain in the lower conjunctival sac of the eye for longer periods than eye drops. However, ointments have poor patient compliance due to the fact that they cause blurred vision for several hours.

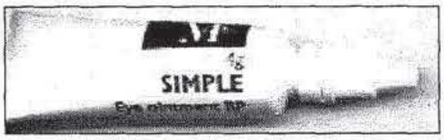

Figure 1.10: An example of commercially available eye ointments

- ***Hydrogels*** are administered to the patient as a liquid, which then polymerizes to form a gel in-situ in the eye. This process may take several hours; therefore, some of the initial liquid may be lost due to the naso-lacrimal drainage system.

Figure 1.11: An example of commercially available hydrogels

- ***Solid matrices and devices*** are relatively new vehicles for drug delivery. They are solid polymeric inserts and discs and are more efficient than eye drops and ointments because they are less affected by the naso-lacrimal drainage and, therefore, stay in the conjunctival sac for longer periods of time and can deliver a controlled dose. These discs can be, degradable or non – degradable. The non-degradable inserts have been shown to have a more predictable release rate than degradable ones. Issue with these solid devices is that patients are very reluctant to place solid objects into their eyes. Also as some of the discs are non – degradable they must be removed.

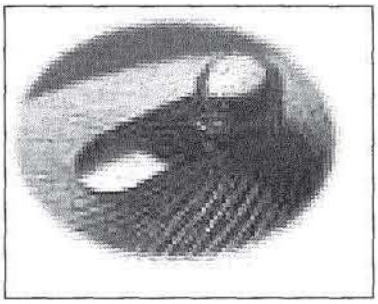

Figure 1.12: An ocular insert

1.3: Contact lenses

1.3.1: Brief History

One of the earliest references of relevance to the history of contact lenses can be dated back to 1508 with Leonardo da Vinci in his Codex D, folio 3, which relates to the basic theories of sight. It was over 100 years later that the first work involving the eye and a potential lens was published. Theories and experiments about neutralisation of the cornea continued into the 17th and 18th century, however, it was not until 1845 that the theoretical ideas began developing into clinical experiments. Sir John F. W. Herschel in his dissertation of light described how the optical correction could be done using transparent animal jelly (Herschel 1845). Between 1887 and 1889 the forerunners of modern lenses evolved, lenses were being developed simultaneously in multiple centres across Europe. By 1892 the potential uses of contact lenses were being realised; correction of refractive error, the protection of exposed cornea, remolding the corneal shape and neutralisation of corneal irregularities. Lenses could be used for either cosmetic or prosthetic purposes.

Although the reasons of contact lens failure had been recognized, it took over 40 years before these reasons were better understood and overcome for successful lens wear to be achieved. In the early 20th century, the lens choice lay between blown glass lenses produced by Müllers of Wiesbaden and the ground glass contact lenses such as those made by Carl Zeiss.

The ability of reproducing the exact corneal shape was a major factor in the successful wear of contact lens. Since 1880 there had been many attempts to accurately replicate the surface of the cornea, after 1930, more information on ocular topography began to emerge. A lot of this work was down to Dr Josef Dallos and other workers such as Dr Newton Wesley and George Jessen from Chicago.

Up until the mid 1930s, all contact lenses had been made of blown or ground glass. Since the mid 20th century, new materials called plastics had been developing. One new polymer developed by John Crawford and Rowland Hill for ICI was methyl methacrylate (MMA), which went by the trade name 'Perspex'. In 1938 Theodore E. Obrig working together with Mullen made the first plastic contact lens using the new Perspex material. The material was lightweight, optically clear, non-reactive, easily moulded, ground and polished, and inexpensive. Lenses made from PMMA could be made thinner than the glass lenses saving about 60% in the weight.

Up until this point contact lenses had been scleral lenses, however, with the new plastic lenses being made available lathe-cut from solid blocks of material. This allowed numerous new lens designs to be developed, searching for the optimum in comfort and wearability. The first corneal contact lens made was produced by accident by Kevin Tuohy (1946), when a high negative power scleral lens, cracked forming a perfect disc. Tuohy polished the edges of the lens and took it home to try on his wife. He then designed, manufactured and patented the corneal lens (patent granted in 1950). The performance and comfort of a corneal lens depended on the upper lid to raise the lens on the cornea after each blink. As PMMA was much lighter than glass, this led to the success of the corneal lens.

The development of contact lenses as we know them today came with the invention of soft contact lenses, which were first developed by Professor Otto Wichterle from his work on cross-linked hydrophilic gels (later known as hydrogels). Wichterle and his co-worker Lim had prepared a cross-linked gel of 2-hydroxyethylmethacrylate (HEMA). It was transparent, absorbed up to 40% of water and exhibited good mechanical properties. In December 1961, Wichterle continued his experiments at home transforming polyHEMA into the shape of a contact lens using a homemade centrifugal casting device, with which he cast his first four lenses. Otto Wichterle took on a patent on his lenses, which was purchased by Bausch & Lomb. In 1968 the United States Government decided that a soft lens should be regarded as a drug and needed the Food and Drug Administration (FDA) approval before its general clinical use. It wasn't until 1971 that Bausch & Lomb were granted FDA approval for the polyHEMA lens, and began producing Soflens® using the spin-casting technique. Although use of extended wear lenses to correct refractive error was not granted until 1981.

Over the next few years, as soft contact lenses were developed using copolymers of HEMA and other polymers such vinyl pyrrolidone (NVP). The soft contact lenses were now becoming available in a wide range of water contents; low (38%), medium (50 – 65%) and high (68 – 80%) that were manufactured by either spin casting or lathe-cut.
Another method of manufacture soon emerged this was injection or cast moulding. Where a measured amount of lens material is injected into the space between two dies, the polymerisation takes place when the mould is full. Although the initial set-up cost was large, no lens material was wasted and lens production was significantly faster. This method eventually led to the production of disposable contact lenses.

In 1982 the first disposable contact lens to be manufactured and marketed as disposable was invented by Michael Bay, who was a Danish ophthalmologist. Michael Bay sold this technology to Johnson & Johnson. In 1988 Vistakon (the optical section of Johnson & Johnson) launched the 'Acuvue' disposable lens (HEMA/methacrylic acid (MA)). The lens from Michael Bay and the original Acuvue lenses were weekly extended wear lenses that were worn continuously for a one-week period then discarded.

It was not until 1995 that daily disposable contact lenses were released into the market, with Vistakon's 1-Day Acuvue®. The next major evolution was in the release of silicone hydrogel contact lenses in 1998, with both CIBA Vision and Bausch and Lomb releasing silicone hydrogel contact lenses within months of each other (Lamb et al., 2007)

1.3.2: Contact lens Materials

The following section will only deal with conventional soft hydrogel contact lenses as silicone hydrogel contact lenses are discussed in more detail in chapter 6 of this thesis. Water present in the hydrogels dominates the properties of soft conventional hydrogel contact lenses. It is possible to alter the water content, and therefore, the hydrogel contact lens properties by changing the monomer hydrophilicity and also the monomer ratios. The most important properties required for successful contact lens wear are listed below with a brief indication of each property.

- **Swell factor and dimensional stability** Linear and volume swell that occur with hydration of the hydrogel material this is a direct consequence of the volume of water absorbed by the hydrogel. The swell and stability of hydrogels can vary with temperature, pH and tonicity (osmolality or salt concentration). The stability of the lens is important to maintain the correct refractive correction and lens fit.

- **Mechanical properties** are a key feature of contact lenses and play a vital role in lens comfort and handling performance. In their dehydrated state most hydrogels are hard and brittle. However, when swollen in water they become soft and rubber-like with very low tear and tensile strengths.

- **Refractive index** is an important property that provides the lens with the correct refractive power. Refractive index (RI) decreases progressively with increased water content, hydrogels at 20% water have a RI of 1.46-1.48, whereas, at a water content of 75% the RI is 1.37-1.38.

- **Oxygen permeability** is a very important property in contact lens wear, indeed many earlier lens failures can be put down to the prevention of oxygen to the cornea. This was first recognised in 1889 by August Müller (Pearson 1978), in that the cornea needs oxygen dissolved in the tears. In order for extended wear, a certain value of oxygen permeability (Dk) was needed to prevent hypoxia of the eye during the hours spent asleep. Holden and Mertz proposed the value of 87 barrers (Holden et al., 1984). The Dk of water is 100 barrers, therefore, conventional hydrogels of ~75% water content have a Dk of 40 barrers as the water present in the hydrogel provides the lenses with oxygen permeability. The need to improve oxygen permeability led to the development of hydrogels with siloxy or silicone groups incorporated into the lens matrix (silicone hydrogels).

- **Surface properties** of the lens affect the performance of the contact lens during wear. Surface properties play a vital role in the comfort of the lens and also the surface deposition of lipids and proteins. The main surface probing techniques that can be used in order to study the surface properties of hydrogels are surface energy (Wettability) and coefficient of friction.

The properties that are becoming more and more relevant in contact lens design are the surface properties of the lens. Comfort that the lens supplies the wearer is still the number one area for improvement. The discomfort of the lens is still the major reason given for contact lenses wearer dropout. (Tighe., 2007)

1.3.3: Classification of Contact lenses

The first basic principle of hydrogel design is fairly simple; to achieve a particular water content, a mixture of monomers is chosen such that there is a specific balance of more hydrophilic and less hydrophilic. A cross-linking agent (usually about 1% of the total monomer mix) is added to produce a network.

A particular combination of monomers and cross-linking agent is classified in the United States in two ways. The hydrogel is given a United States Adopted Name (USAN) identity. For example Focus® DAILIES® has the USAN identity of nelfilcon A. The USAN identity is unique to the specific monomer composition.

The FDA also has a classification system in which lenses are split into four groups. These allow the lenses to be subdivided, by the water content and the ionic character of the lens.

The lens groups plus an example in each case are shown below:

I. **Low water content non-ionic** – (<50% EWC <0.2% Ionic content)
   E.g. Soflens 38, Bausch & Lomb, 38% EWC, USAN – Polmacon A

II. **High water content non-ionic** – (>50% EWC <0.2% Ionic Content)
   E.g. Focus® DAILIES®, CIBA Vision, 69% EWC, USAN – Nelfilcon A

III. **Low water content ionic** – (<50% EWC >0.2% Ionic Content)
   E.g. Soft Mate II, WJ/PBH, 45% EWC, USAN – Bufilcon A

IV. **High water content ionic** – (>50% EWC >0.2% Ionic Content)
   E.g. Acuvue, Vistakon, 58% EWC, USAN – Etafilcon A

1.3.4: Applications of Contact Lenses

Contact lenses can have a variety of applications, but are generally separated into two distinct groups: cosmetic and therapeutic. Cosmetic contact lenses are lenses that are used instead of spectacles to correct refractive error. Therefore, cosmetic contact lenses are for the vision correction of the eye caused by ocular irregularities such as; myopia, hypermetropia, presbyopia and astigmatism.

Other examples of cosmetic contact lenses are coloured contact lenses that are used to change the appearance of the eye. Cosmetic lenses are also used in the entertainment industry to make the eye appear more unusual or unnatural. For example in horror movies contact lenses are used to make the eye appear demonic, cloudy or lifeless.

Therapeutic contact lenses are used to protect, relieve pain and aid healing of the eye and cornea, they can also be used to deliver drugs to the eye. An example of therapeutic contact lenses is the use as a bandage after refractive surgery (Lattimore et al., 2000).

1.4: Lubrication

1.4.1 Introduction

When the coefficient of friction between two solid surfaces is decreased in the presence of a liquid, the liquid is described as a lubricant. This lowering of the friction or lubrication takes place through three different modes: boundary, fluid-film and solid film lubrication. The term fluid-film lubrication also includes hydrodynamic lubrication. Differentiation between the various types of lubrication can be made using a Stribeck curve. In this the variation in the coefficient of friction is plotted as a function of the Sommerfeld number.

The coefficient of friction during lubrication is potentially influenced by sliding speed (v), normal force (N), and solution viscosity (η). In lubrication theory, these three factors often appear as a single quantity called the Sommerfeld number.

$$S = \frac{\eta v}{NL}$$

where L is a function of the sample dimensions

Equation 1.2: The Sommerfeld Number (Nairn et al., 1995)

Boundary lubrication is defined as that in which a very thin film of lubricant separates the sliding surfaces, so that the chemical and physical nature of the surfaces and the lubricant are of major importance. In such cases, the thin film between the solid surfaces usually contains only one or two layers of lubricant molecules. In contrast in fluid-film lubrication the opposing two solid materials are completely separated by fluid. As a result, the friction becomes very low and the wear of the solid materials is often negligible. Solid-film lubrication arises with the use of extreme pressure additives in the boundary lubrication situation. PTFE is a commonly used solid-film lubricant which exhibits uniquely low friction under almost any environmental conditions because of its inertness to chemical reagents and its high temperature resistance.

Experiments on lubrication of metal surfaces as a function of the Sommerfeld number produces a Stribeck curve, as shown in figure 1.13. At a high Sommerfeld number, the surfaces are lubricated by hydrodynamic lubrication and there is no contact between the surfaces. As the Sommerfeld number reduces the surfaces get closer and the coefficient of friction increases. If the lubricant is itself capable of adsorbing on the surfaces, or contains additives that adsorb on the surface, the Stribeck curve makes a transition to boundary lubrication. In boundary lubrication, the coefficient of friction is lower than for dry friction alone. The lubrication is provided by molecular monolayers adsorbed to the surfaces.

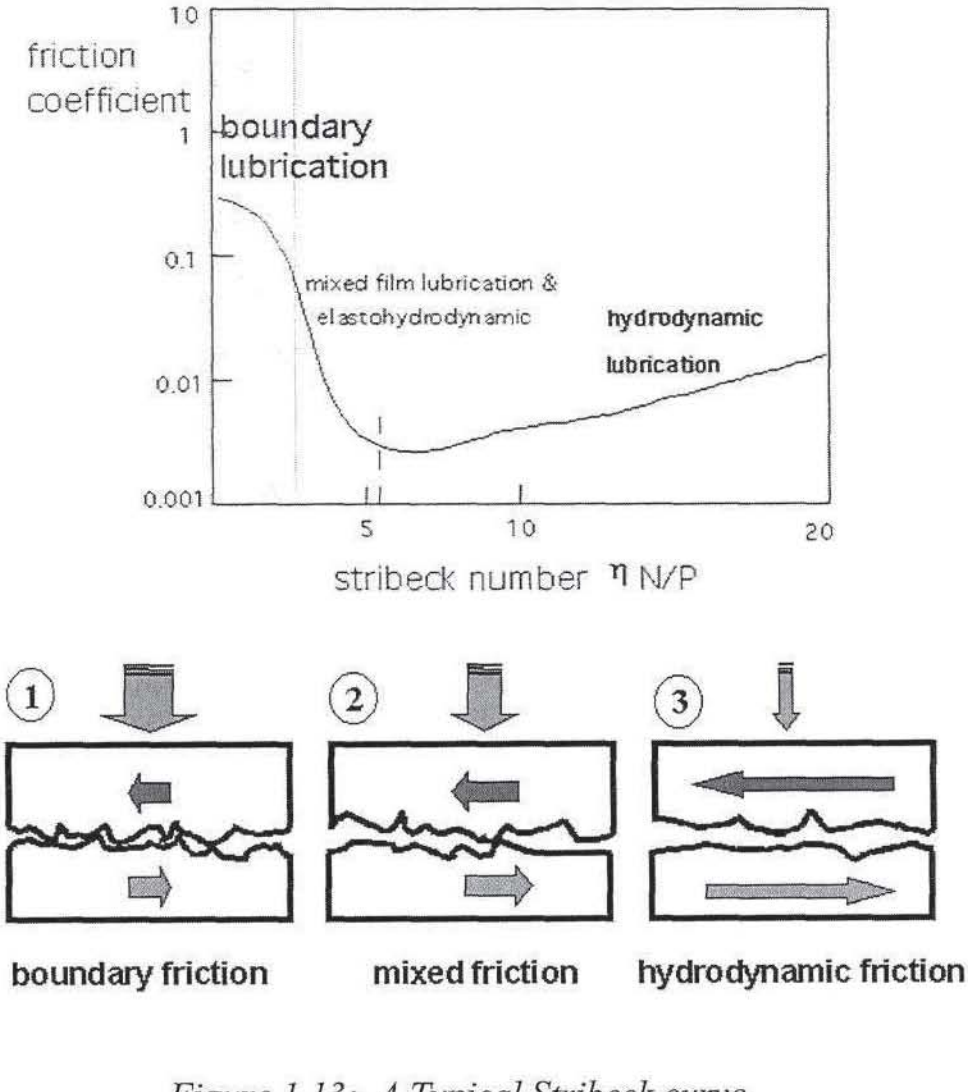

Figure 1.13: A Typical Stribeck curve.

1.4.2: Polymer Lubrication

Hydrophilic polymers are presently incorporated in the design of a rich variety of biomedical and pharmaceutical products. Contact lenses, ocular implants, biological adhesives, anti-thrombogenic coatings, soft tissue replacement and permanent implants are some of the current commercial applications that incorporate hydrophilic polymers. They are used at the surface of such devices to augment biocompatibility and reduce trauma to surrounding tissue. Lubrication has been widely considered to be important in biomedical technology. For instance, biomaterials used for catheters or endoscopes should have a surface with good handling characteristics when dry, becoming slippery upon contact with bodily fluids. This enables easy use of the device and prevents mechanical injury to the mucous membranes, minimising discomfort felt by the patient.

Until recently, lubrication was considered to be applicable to metals and ceramics, but not to polymers. This is because lubrication always accompanies wear, against which polymers are weak, especially under large normal loads. The poor wear resistance of polymers is due to their low modulus and rigidity compared to metals and ceramics. The smallest units of the constituents of metals and ceramics are associated with each other through primary and secondary bonding at high densities, which results in high melting temperatures. However, the repeat units of polymers are constructed through primary bonds only in one direction with very weak lateral bonding. As a result, the constituent units of polymers have a much higher mobility than those of metals and ceramics even when they are cross-linked.

In a typical polymer any surface segment is able to change its position as a result of environmental factors. As rotation along the main chain is not restricted as it is in metals and ceramics. However, this high degree of mobility results in poor resistance against wear since these segments may be readily deformed and stripped off from the surface when it is subjected to high mechanical stress. The motion also allows liquid molecules to enter the interstices of the polymer segments, resulting in polymer swelling even though the density of chemical or physical cross-linking is high. The characteristics of the polymer surface are therefore greatly influenced by the liquid that is used to swell the polymer.

Although very few man-made materials are known that have slippery surfaces, it is not difficult to find such surfaces occurring naturally. These include slippery surfaces on mucous tissues and organs in animal bodies. The purpose of these surfaces in nature has not yet been fully understood, but it is obvious that the slippery surface greatly reduces the frictional resistance occurring when the surface slides on another solid object. These surfaces contain a large amount of water, and when this water is squeezed out by fingertip touch it acts as a lubricant making the surface slippery. Another feature of such surfaces is to prevent the surface from adhering to other objects with which it is in contact. All of the naturally occurring slippery surfaces are extremely hydrophilic, synthetic materials such as polyHEMA are not nearly as slippery although they are known as hydrophilic polymers.

When the coefficients of friction of various polymers are determined against a glass plate in pure water, it was found that both a very hydrophobic and a strongly hydrophilic surface exhibited very low values. In these extreme cases, the work of adhesion between the polymer and the glass surface is very low. Since the work of adhesion is directly related to the molecular interactions between the surfaces of both substances, low adhesion values mean there are no strong interactions. An example of this is hydrophilic or hydrophobic surfaces in water. This seems reasonable because a very hydrophobic polymer such as PTFE has low coefficient of friction. Thus, a surface has a low coefficient of friction if its surface energy is either extremely high or low, i.e., if the water contact angle is either very high or low. From a practical point of view, it is easier to achieve an extremely hydrophilic polymer surface than it is to achieve an extremely hydrophobic one. This is because the water contact angle of even the most hydrophobic surface currently available is no larger than about 120 degrees. Thus hydrophilic materials or coatings are the easiest routes for the production of lubricating polymer surfaces. (Ikada., 1993)

1.4.3: The Lubrication of living tissues

Animals, including humans, possess a wide variety of sliding and frictional interfaces, the most important interface being the contact between the skin and external objects. The body secretes sebum onto the skin, an oily substance that reduces the friction and wear of the skin. Inside the body, lubrication is also essential, such as in the lungs where lubrication is needed so that the bronchioles can freely dilate during breathing. There are other lubricating films in the body that separate other organs in the body such as the liver and intestines. During the delivery of a baby, a white flaky layer, known as vernix caseosa covers the baby to help reduce the friction between the skin of the baby and the birth canal.

Human movements such as walking, running, flexing of the limbs and the back, gripping of the hands all require articulating joints. Articulating joints consist of a synovial joint where closely conformal cartilaginous surfaces slide past each other. The cartilage is immersed in synovial fluid and a membrane encloses the articulating joint.

It is reasonable to summarise that any living tissue needs protection from high levels of friction and wear by an evolved lubricating film or system. One of these lubricating systems will be discussed next in more detail. In healthy synovial joints, a range of lubrication mechanisms are in operation; some of these correspond to the classic lubrication mechanisms found in machines, while other lubrication mechanisms are specific to living organisms. The mechanisms of synovial lubrication are not yet fully understood. Hydrodynamic lubrication is effective in healthy synovial joints, where the synovial fluid has sufficient viscosity and contact speeds are sufficient for the hydrodynamic film to form. In rheumatoid joints, the viscosity of the synovial fluid is greatly reduced, the cartilage is porous and an ionic mechanism inside the cartilage prevents leakage of synovial fluid into the cartilage. The cartilage or cells beneath the cartilage secrete phospholipids to cover the surface with a lubricating film. These films are thought to act as boundary lubricating films in moving joints, providing a low coefficient of friction and protecting the articular cartilage against damage at low velocities. In common with other bodily fluids, the synovial fluid contains proteins. Proteins are high molecular weight substances composed of amino acids. It is known that synovial proteins are effective in controlling friction and wear, yet the tribology is poorly understood. Proteins are entirely different from the much smaller molecules typical of lubricant additives. Another specialised series of proteins, known as mucins, provide not only lubrication but also exhibit stickiness, a useful property to trap bacteria and dust in the respiratory tract. The lubrication mechanism of mucins, like other human proteins, is still not fully understood.

Current findings from the research on polymers and metals in wet sliding tests suggest that absorbed films of proteins tend to raise friction coefficients while lowing wear rates. This is probably because the thick adsorbed film of tangled proteins shield the surface while the protein molecules from the opposing surfaces become entangled.

1.3.4: Lubrication of the eye

The natural lubricant of the eye is the tear film, which governs the lubrication. The complex multi-component structure of the tear can be split into three distinct layers.

- The outer layer is referred to as the lipid layer, which is produced by the meibomian oil glands of the margins of the eyelid. The main function of this layer is to prevent evaporation of the tears. This lipid layer is around 0.1μm in thickness.
- The middle layer is known as the aqueous, or watery, layer and is manly produced by the lacrimal gland. This layer rinses away debris, and contains nutrients and antimicrobial agents that nourish the eye and protect it from harm. This makes the majority of the tear film and is approximately 8-10μm in thickness.
- The innermost layer is the viscous mucin layer, which is produced by the surface of the eye. Mucin allows the watery components of the tears to 'wet' the surface of the eye.

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Figure 1.14: A Proposed Model of the Tear Film

There are many contradicts in the proposed mechanism of lubrication of the eye, some researchers believe the outer layer lipids are the chief lubricant during blinking,

whereas, Dr Frank Holly of the Dry Eye Institute in Lubbock, Texas, believes that the watery layer bounded either side by mucus is the lubricating layer for blinking, therefore, the lubrication of the eye is hydrodynamic lubrication. Therefore, mucins also play a key role in the lubrication of the eye (Jacobson., 2003, Kaura., 1986).
The lipid and mucins are also vital in providing lubrication when tear break up occurs. Figure 1.15 shows the mechanism of tear break up.

Figure 1.15: The Mechanism of Tear Break up.

When the tear film has broken up there is no aqueous layer to provide hydrodynamic lubrication. Thus, the lipid and mucin must provide adequate lubrication for the lid. Therefore, the mechanism of lubrication in the areas of dry spots is boundary lubrication. It is therefore safe to assume that the mechanism of lubrication in the eye is not yet fully understood; in a similar way to the lubrication mechanism of synovial joints.

Lubrication is also very important in contact lens wear. From a clinical point of view lubrication is important in the interactions between contact lenses, the upper eyelid, and the surface of the cornea. Contact lens disturbs the tear film and therefore the natural lubrication mechanism. The contact lens divides the tear film into two layers, the pre- and post lens tear film. Pre-lens tear film is thought to consist of a superficial lipid layer anteriorly, with a base layer that is aqueous. Post-lens tear film likely consists of aqueous with a mucins gradient near the cornea epithelium (Nichols., 2007). However, this is still yet to be fully understood.

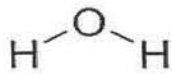
Chapter 2

Materials and Methods

2.1 Materials

2.1.1: Reagents

Distilled Water - Water is boiled and then the stream is condensed into a clean container, this leaves the solid contaminants behind producing very pure water.

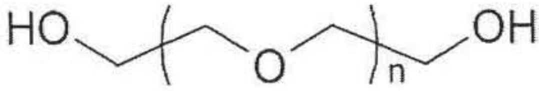


Water

Saline – Saline is the general term used for a solution of sodium chloride in water. It is used for many medical applications such as intravenous infusion, rising of contact lenses, and nasal irrigation. Physiological saline is comprised of 0.9% w/v NaCl, equivalent to 300mOsm/l.

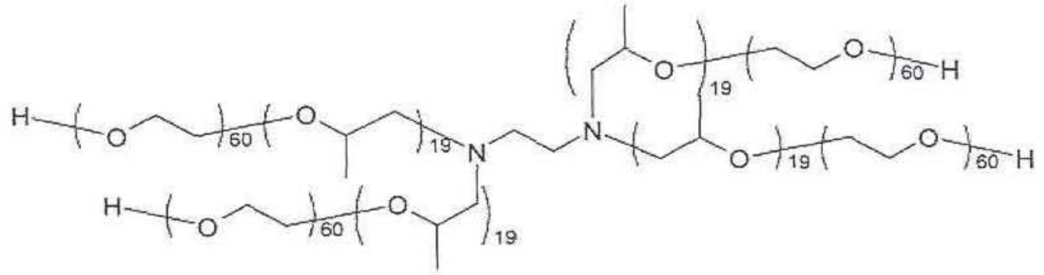
HypoTears™ - HypoTears is an artificial tears product, indicated for temporary relief of burning and irritation due to dryness of the eye or to exposure to wind or sun. HypoTears contain the active ingredients: 1% polyvinyl alcohol and 1% polyethylene glycol 400.

Polyethylene Glycol – Polyethylene glycol (PEG)



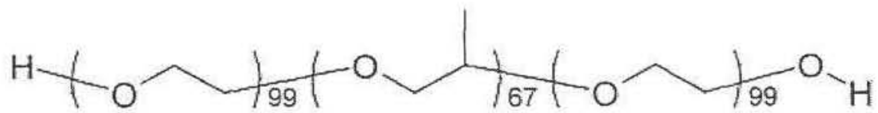
Poly (ethylene glycol)

Poloxamine – An example of a poloxamine structure is Tetronic 1107, the structure of which is shown below.



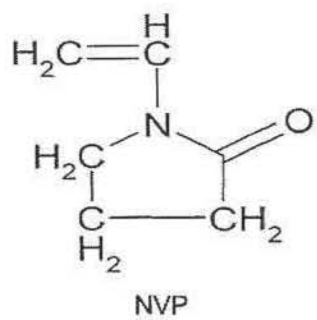
Poloxamine - Tetronic 1107

Poloxamer – An example of a poloxamer structure is Pluronic F127, the structure of Pluronic F127 is shown below.



Poloxamer - Pluronic F127

Polyvinyl Pyrrolidone – The polymer polyvinyl pyrrolidone (PVP) is polymerised from *N*-vinyl pyrrolidone (NVP), it has many trade names including Povidone (See 1-Day Acuvue® Moist™). The structure of the monomer unit for PVP is shown below.



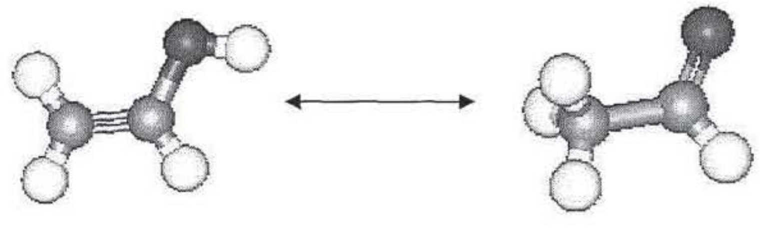
NVP

Polyvinyl Alcohol – PVA

The polymer polyvinyl alcohol is discussed in more detail below, as this is the polymer studied in detail in chapter 3 of this thesis.

The Production of polyvinyl alcohol

Unlike conventional polymers (polyvinyl alcohol) (PVA) is not formed by the free radical polymerisation of vinyl alcohol (because vinyl alcohol monomer is not stable and tends to form a tautomer). The vinyl alcohol undergoes keto–enol tautomerism whereby the COH group stabilises to C=O group, as shown in figure 14.



Vinyl Alcohol **Acetaldehyde**

Key: Carbon, Oxygen, Hydrogen

Figure 2.1: The tautomerism of vinyl alcohol

PVA is, therefore, produced by the hydrolysis of poly (vinyl acetate) as shown in figure 2.2.

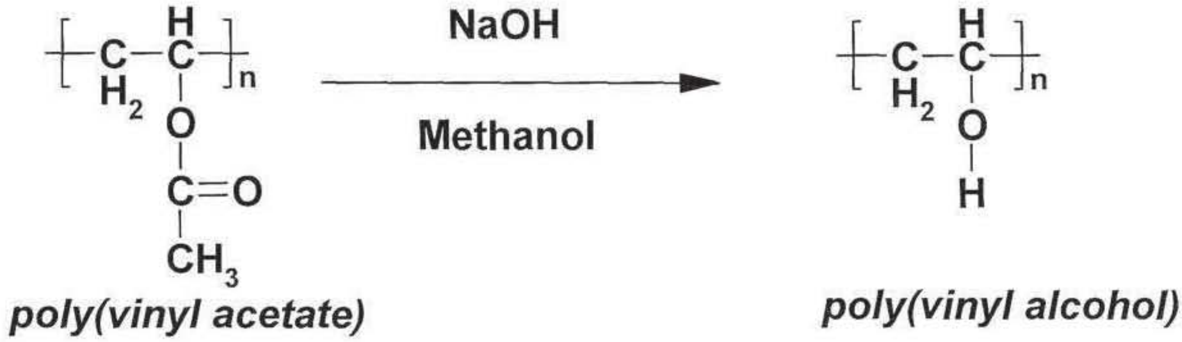


Figure 2.2: The hydrolysis of poly (vinyl acetate)

Poly (vinyl acetate) is made by the free radical vinyl polymerisation (the polymerisation of a double bond) of vinyl acetate, which is synthesised by the oxidation of ethylene in the presence of acetic acid, as shown in figure 2.3 and 2.4. This is done on a large industrial scale and is a relatively cheap process.

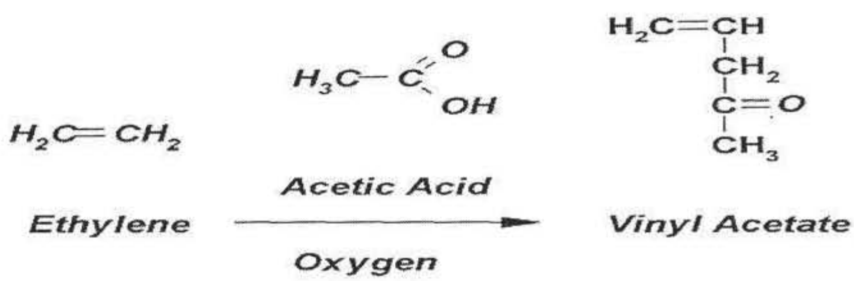
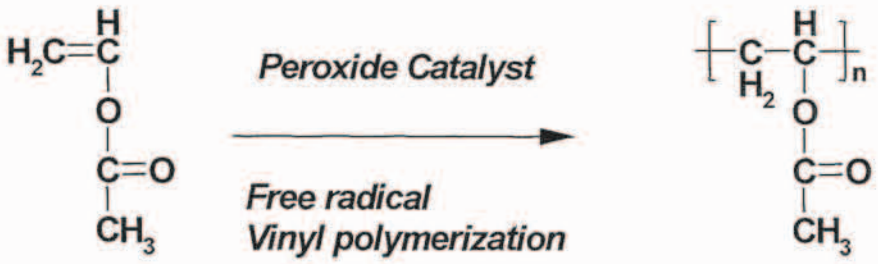


Figure 2.3: The production of vinyl acetate

Vinyl acetate is easily polymerised to poly (vinyl acetate) in the presence of heat and a small amount of peroxide catalyst.



Vinyl acetate ***poly(vinyl acetate)***

Figure 2.4: The production of poly (vinyl acetate)

The poly (vinyl acetate) is then modified into polyvinyl alcohol by hydrolysis using sodium hydroxide (NaOH) and methanol as demonstrated in figure 2.2.

Properties and Applications of PVA

Table 2.1 shows the main properties of granular and powder poly (vinyl alcohol) (Molyneux., 1983).

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Table 2.1: A Table Showing the Main Properties of PVA.

Examples of the commerial uses of poly (vinyl alcohol) are listed below.

- Coatings in the paper and textile industry to make them shiny.
- Manufacture of wood glues and other adhesives.
- An emulsifier in paints, as a copolymer of itself and polyvinyl acetate.

PVA's wide range of applications is due to the ease of chemically modifying the backbone to give the polymer its different properties. Commercial PVA has molecular weights, which span from 14000 to 200000. In 1974, the worldwide production of PVA was 500000 tons, hence, PVA is readily available (Bühler et al., 1999).

2.1.2: Contact Lens Materials

This section will present information on contact lens materials with the majority of the information coming from the U.S. Food and Drug Administration (FDA) website, particular the information submitted for the lenses approved use as a medical device. Before medical devices, such as contact lenses are sold in the U.S., the FDA reviews the marketing application from the medical device companies and determines whether the companies can release the device into the marketplace.

Daily Disposables Contact Lenses

Focus® DAILIES® - CIBA Vision (nelfilcon A)

Focus® DAILIES® was the first daily disposable contact lens launched from CIBA Vision. CIBA Vision is a company under the Novartis umbrella. The lens has nelfilcon A for the lens matrix. Nelfilcon A polymer is a modified polyvinyl alcohol (PVA) structure. The lens is 69% water and 31% polymer, the lens received FDA approval in November 1996. The structure of nelfilcon A is shown in figure 2.5 (510k – FDA K963487)

Figure 2.5: Nelfilcon A (Bühler et al 1999)

1-Day Acuvue® - Johnson & Johnson Vision Care (etafilcon A)

In 1995 1-Day Acuvue® became the first daily disposable contact lens released into the market. The lens polymer is comprised of 2-hydroxyethyl methacrylate (HEMA) and methacrylic acid (MA). The lens is 58% water and 42% polymer, figure 2.6 shows the structures of the main constituents of etafilcon A (510k FDA K962804)

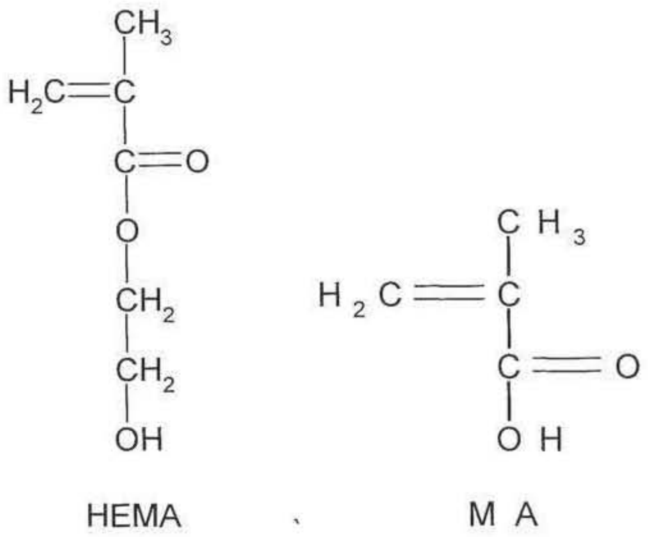


Figure 2.6: Monomers of 1-Day Acuvue®

1-Day Acuvue® Moist™ - Johnson & Johnson Vision Care (etafilcon A)

This lens was granted FDA approval in November 2006, the lens polymer (HEMA and MA) and water content is identical to that of 1-Day Acuvue®. The major difference between 1-Day Acuvue® and 1-Day Acuvue® Moist™ is that the 1-Day Acuvue® Moist™ is packaged in buffered saline containing Povidone (See poly (vinyl pyrrolidone). (510k – FDA K062614)

Soflens® One Day – Bausch & Lomb (hilafilcon A)

The Soflens® One Day contact lens gained FDA approval in March 1998, the lens is 70% water and 30% polymer. Hilafilcon A is a copolymer of HEMA and *N*-vinyl pyrrolidone (NVP), the structures of the two materials are shown in figure 2.7. (510k – FDA K974780)

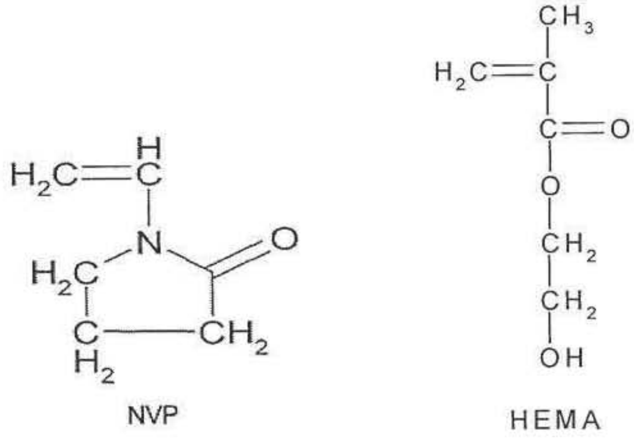


Figure 2.7: The monomers of Hilafilcon.

Soflens® 59– Bausch & Lomb (hilafilcon B)

Soflens® 59 is a two week replacement daily wear contact lens that gained FDA approval in March 2000; the lens is 59% water and 41% polymer. Hilafilcon B is a copolymer of HEMA and *N*-vinyl pyrrolidone (NVP) (510k - FDA K994125).

Soflens® Daily Disposable– Bausch & Lomb (hilafilcon B)

Soflens® Daily Disposable is the newest daily disposable contact lens launched by Bausch & Lomb the lens gained FDA approval in June 2006, the lens is 59% water and 41% polymer. Hilafilcon B is a copolymer of HEMA and *N*-vinyl pyrrolidone (NVP) (510k – FDA K061157).

Silicone Hydrogel Contact Lenses

Focus® Night & Day™ - CIBA Vision (lotrafilcon A)

The lens material is 24% water and 76% lotrafilcon A, which is a silicone-containing hydrogel with a plasma coating (510k – FDA K970746). The lens received FDA approval for daily wear in May 1997, and gained approval for 30 days extended wear on 12th October 2001 (FDA website 2001).

PureVision® - Bausch & Lomb (balafilcon A)

The lens material is 36% water and 64% balafilcon A, which is a copolymer of silicone vinylcarbamate, *N*-vinyl pyrrolidone, a siloxane crosslinker and vinyl alanine wetting monomer. The lens first received FDA approval in August 1997 (510k – FDA K972454) and gained approval for extended wear in February 1999 (FDA website, premarket approval (PMA) database).

Acuvue® Advance™ - Johnson & Johnson Vision Care (galyfilcon A)

The lenses are composed of 47% water and 53% galyfilcon A, packaged in a buffered saline solution with up 0.01% methyl ether cellulose. The galyfilcon A material is a copolymer of 2-hydroxyethyl methacrylate, (3-methacryloxy-2-hydroxypropyloxy) propylbis(trimethylsiloxy)methylsilane, N,N-dimethylacrylamide, polyvinyl pyrrolidone, mPDMS-monomethacrylate (n=11), 2-propenoic acid, and 2-methyl-,1,2-ethandiyl ester (510k – FDA K032340).

Acuvue® Oasys™ - Johnson & Johnson Vision Care (senofilcon A)

The lenses are made of a silicone hydrogel material that is approximately 38% water and 62% senofilcon A, and contains an internal wetting agent. (FDA website - P040045b). The lens is supplied in a sterile state, packaged in a buffered saline solution with 0.005% methyl ether cellulose. (510k – FDA K042275)

AIR OPTIX™ – CIBA Vision (lotrafilcon B)

The lens received FDA approval in March 2004, the lens material is 33% water and 67% lotrafilcon B, a fluoro-silicone containing hydrogel which is surface treated (510k – FDA K033919).

Biofinity™ - CooperVision (comfilcon A)

Biofinity™ is a soft contact lens in group I, it is a daily wear silicone hydrogel contact lens that is not surface treated and characterised by high oxygen permeability (Dk). The lens material, comfilcon A, is composed of silicone macromers cross-linked with other monomers. The lens is 48% water and 52% comfilcon A (510k – FDA K0502560).

AIR OPTIX™ AQUA – CIBA Vision (lotrafilcon B)

The lens received FDA approval in December 2007, the lens material is 33% water and 67% lotrafilcon B, a fluoro-silicone containing hydrogel which is surface treated. Lenses are supplied in sterile sealed blister packs containing isotonic phosphate buffered saline solution (PBS), or PBS with 1% copolymer 845 (510k – FDA K073459). Copolymer 845 has the IUPAC name of poly (1-vinylpyrrolidone-co-2-dimethylaminoethyl methacrylate). The copolymer is used in the hair care industry in styling gels and mousses.

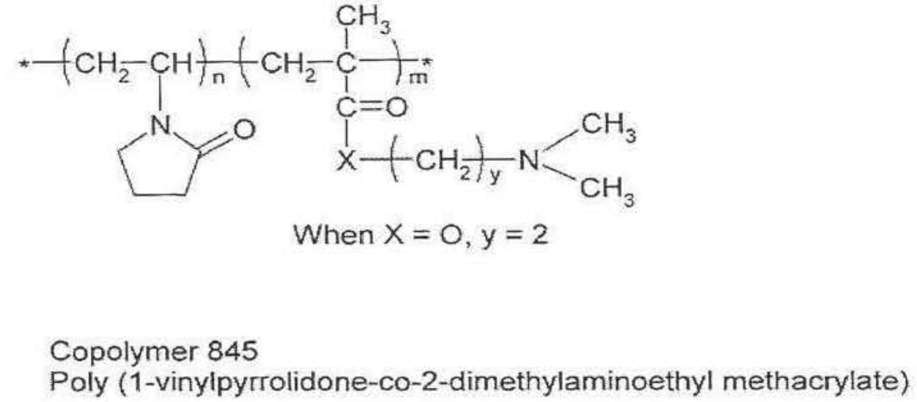


Figure 2.8: The structure of Copolymer 845.

1-Day Acuvue® TRUeye™ - Johnson & Johnson Vision Care (narafilcon A)

The lens gained FDA approval on 3rd March 2008, the lens material is 46% and 54% narafilcon A, the lens is packaged in buffered saline solution with methyl ether cellulose. Narafilcon A is made of a silicone hydrogel containing an internal wetting agent (510k – FDA K073485).

2.2 Methods

2.2.1: Refractive Index

The micro-refractometer used for measuring the refractive index was an Index Instruments automatic refractometer GPR 11 – 37X. The refractometer water bath was turned on and allowed to reach steady temperature of 25 °C for about one hour. Two or three drops of HPLC water were placed onto the refractometer's synthetic sapphire prism, the instrument detected and scanned the HPLC water, after the refractive index had stabilised the instrument was tared. The instrument was then clean and dried and two or three drops of the sample to be analysed was placed upon the sapphire prism, the refractometer automatically scanned the sample giving the refractive index of the sample to five decimal places, the refractometer also gave the temperature that the sample was at, to one decimal place.

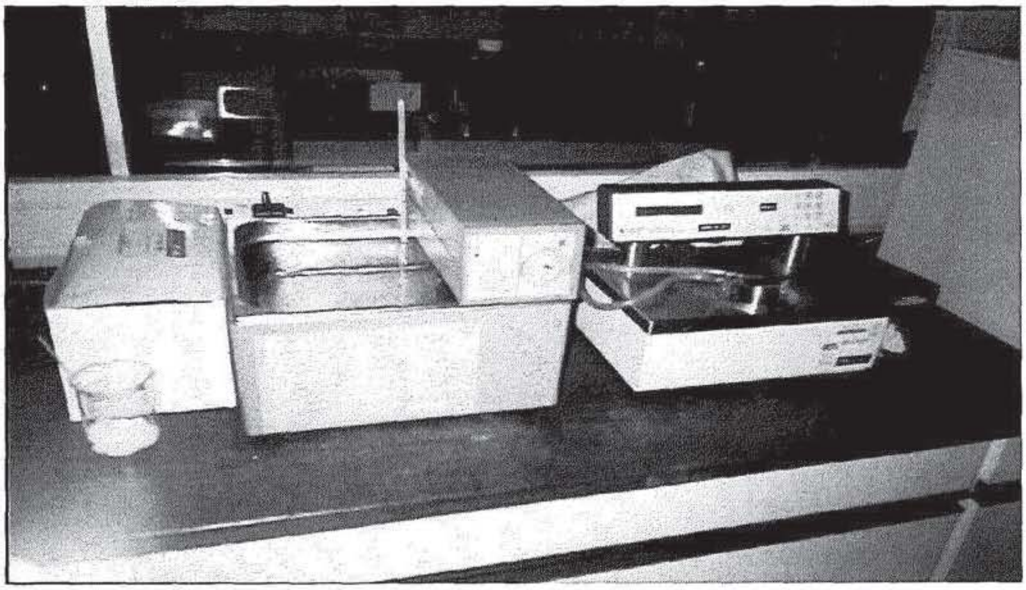


Figure 2.9: The Refractometer Instrument

2.2.2: Eppendorf Extraction Model

The ability to measure the amount of soluble polyvinyl alcohol (PVA) released from a lens matrix containing residual linear PVA is key to this project. In addition it was necessary to develop a laboratory method that gave some indication of the release action of the eye (e.g. mechanical agitation of the eyelid). The most successful method involves vortex agitation in conjunction with a volume of extraction medium equivalent to the tear volume per hour encountered in the eye. This is approximately 1.5 μl / min which was converted to 100 μl per hour for this experiment.
This extraction process was used in conjunction with a highly sensitive refractometer the use of which is described in the chapter 3 'Macromolecular Entrapment and Release of Hydrophilic Polymer from Contact Lenses'.

The volume of medium used in the *in vitro* model was 100 μl per hour. 100 μl of media was placed into 500 μl Eppendorfs microtube. The contact lens was then blotted on filter paper and placed in the Eppendorf microtube, making sure not to tear the lens as this would increase the release surface area of the lens and, therefore, the release rate. The Eppendorf microtube was then vortexed for 30 seconds and subsequently left for one hour, after which the extraction media was removed and replaced with a fresh medium. The same extraction procedure was followed. Effort was made to remove all the liquid off the contact lens between transfers. The procedure was repeated so that the lens was extracted for six hours.

2.2.3: Fluorescence Spectroscopy

Fluorescence is defined as the emission of radiation by molecules brought into an excited state after absorption of UV, visible or IR radiation. Because only small amounts of material are required, fluorescence spectroscopy is useful for the looking at the very small volumes of medium used in this work.
Although fluorescent studies are conventionally carried out in aqueous liquid in a square cell it is possible to obtain excellent fluorescent spectra of fluorescent agents attached to or entrapped in a hydrogel. This is because the RI of the hydrogel is close to that of the aqueous medium in which it is placed and does not produce surface scattering instead, by using a cylinder cell and allowing light to impinge on the front curved surface of the lens, good fluorescent spectra can be obtained of the first 1-2 microns. The figures 2.10 and 211 show spectra, which illustrate the two types of scans that are usually done.

A Hitachi F4500 Spectrophotofluorimeter was used, this machine is capable of four methods of sampling only two were used and these are described in further detail:

3D scan

This produces contour maps of the sample that allows the maximum excitation and emission wavelengths to be determined, and allow the second method of sampling to have the maximum effect (single wavelength).

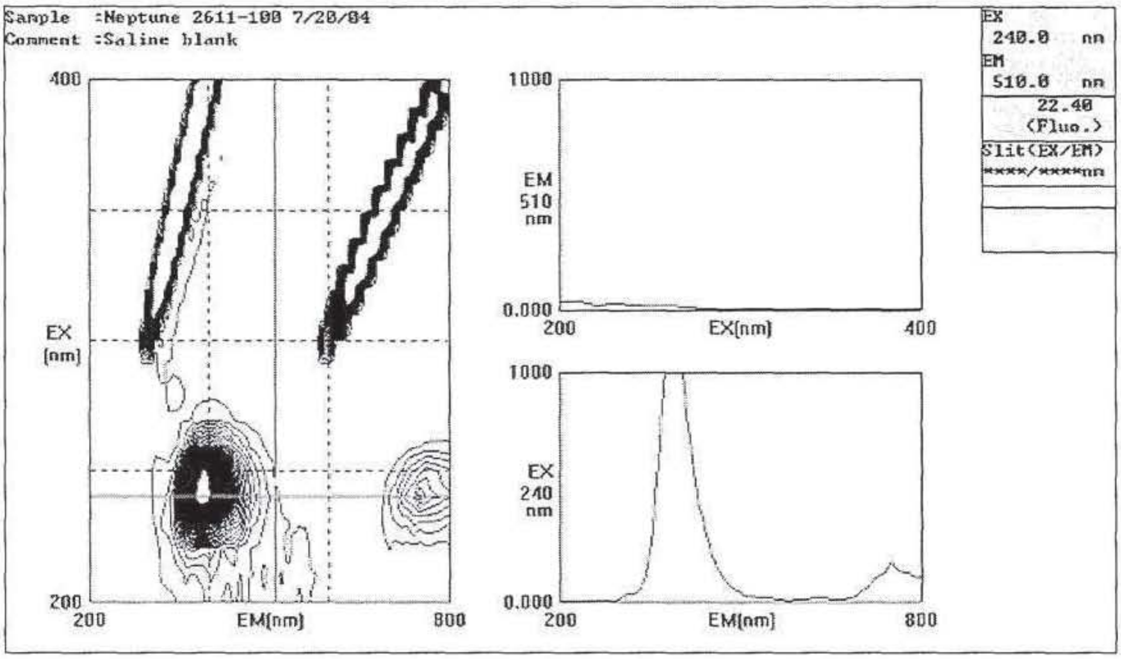


Figure 2.10: An Example of 3D Fluorescence Scan

Single Wavelength

This is a 2D scan at a single wavelength, which was determined using the 3D scan; it allows the peak height to be seen more clearly and values to be compared by overlaying spectra.

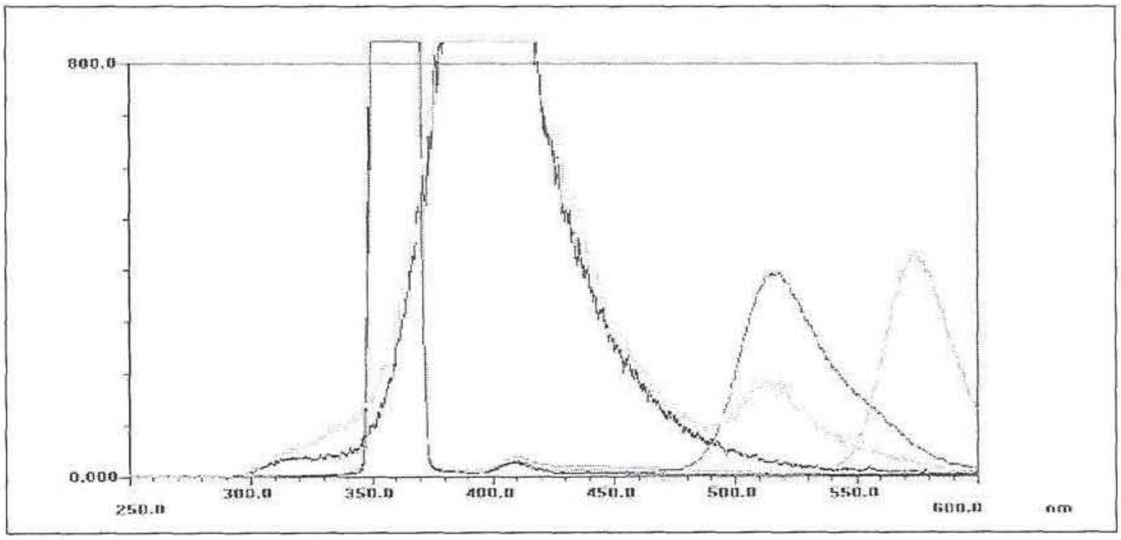


Figure 2.11: An Example of a 2D Fluorescence Scan

Chapter 3

Macromolecular Entrapment and Release of Hydrophilic Polymer From Contact Lenses

3.1: Introduction

The central theme of this work is the understanding and measurement of ocular lubrication of contact lenses; in particular the role of soluble macromolecules incorporated in-solutions or associated either by adsorption from solution or by incorporation into the lens matrix during manufacture. In each case the aim is to immobilise the macromolecule at the surface of the lens as a means of improving surface hydration, reducing friction and enhancing comfort.

There are numerous contact lenses and solutions benefiting from the presences of hydrophilic macromolecules. The industry has moved in this direction during the length of this PhD course. In particular, daily disposable contact lenses; chapter 5 of this thesis looks in more detail at the friction benefits that have arisen from the incorporation of macromolecules.

3.1.1: The Release of Poly Vinyl Alcohol (PVA) from CIBA Visions Focus® DAILIES®

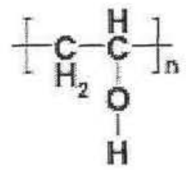
In 1998, B. J. Tighe et al, presented work at the British Contact Lens Association conference comparing the properties of daily disposable contact lenses packing solutions. Observations were made that the packing solution of CIBA Visions Focus® DAILIES® had an unexpected surface tension of 61.4 mN/M. Water has a surface tension of 72 mN/M with the addition of sodium (saline solution) this increases to ~73 mN/M (Tighe B. J. et al., 1998)

Polyvinyl alcohol (PVA) is known to reduce the surface tension of solutions; CIBA's Focus® DAILIES® contact lens is made from a cross-linked modified PVA macromer. (See chapter 2 - PVA) and it was demonstrated that the packing solution did indeed contain PVA.

These observations highlighted an apparent paradox. CIBA scientists (Bühler, N., 1999) claimed that Focus® DAILIES® was a fully cross-linked matrix, however, the packing solution contained soluble PVA. It was confirmed that no PVA or other surfactant was added to the lens packing solution. Another aspect of this paradox is the general observation that solid PVA in not well tolerated as a long lasting implanted biomaterial or repeated temporary supports. However, PVA containing lenses are generally accepted and have reasonable comfort, except for a significant number of wearers experiencing end of day dryness. Could these facts be connected and the paradox resolved?

An experimental program was undertaken to try to resolve this paradox. The first problem to be addressed was the method of detection and quantification of the PVA in the packing solution.

3.2: The Detection of Polyvinyl Alcohol



poly(vinyl alcohol)

Figure 3.1: The structure of Poly (vinyl Alcohol)

From the structure in figure 3.1 it can been seen that PVA has only one functional group, an alcohol unit (OH) on alternate carbon atoms along the backbone of the polymer.

In chemistry there tends to be four classic spectroscopic methods of analysis: Infra Red (IR), NMR, UV-vis, and Mass spectroscopy.
Unfortunately we were using very small volumes at low sample concentrations. All the classic methods fail for one or more of the following reasons:

- Volume needed too large
- Lack of sensitivity for such low concentrations
- Not sensitive to the structure of polyvinyl alcohol

Another technique was needed that is sensitive to small concentrations and uses a very small volume (~100 μl). Refractive Index is a universal detector for gel permeation chromatography (GPC) and is affective to study the concentrations of polymer solution; it therefore, was a logic choice to investigate.

3.2.1: Refractive Index as a Potential Quantifiable Technique

One of the main applications of refractive index (Cowie., 1991) is to measure the concentration of a solute in an aqueous (or organic) solution. It is this capability that underpins its use as a detector in GPC.

Access to a micro-refractometer was obtained that uses very small volumes of solution (<100μl). This refractometer was investigated to see if it could solve the problem of detection and quantification of PVA.

Some initial experiments were set up to see if the micro refractometer:

(a) Was accurate and reproducible.

(b) Was able to distinguish between different PVA concentration standards.

(c) Was able to determine very low concentrations.

Initially the error associated with the refractometer was evaluated by measuring the refractive index of 100 μl of saline obtained from CIBA Vision.

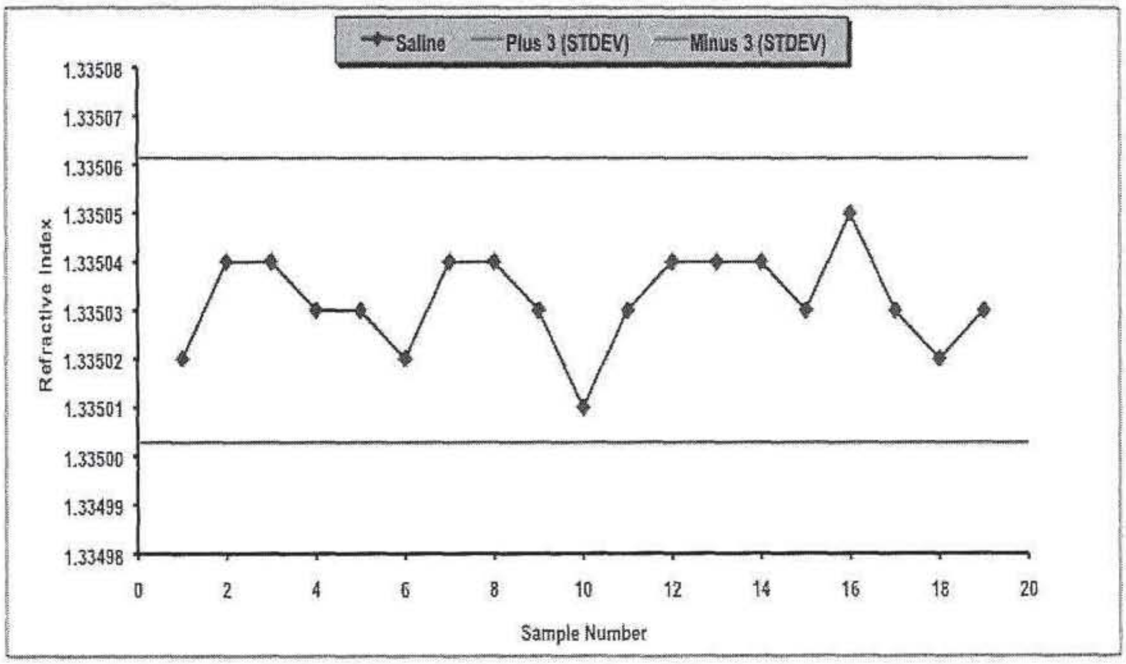


Figure 3.2: The refractive index of Saline

The mean of the saline was 1.33503 with the majority of the points falling within 0.00001 of this figure.

The standard deviation of the saline was 0.00000976 to 3 S.F, so in conclusion the refractometer is an accurate and reliable piece of equipment.

As the refractometer was proven to be accurate and reliable the next step was to investigate if PVA could be measured quantitatively.

A known amount of solid PVA was dissolved in a known volume of media by heating and stirring the mixture. This produced a 1% weight to volume (w/v) concentration of PVA stock solution. The stock solution was then diluted with more media to form 0.1, 0.2, 0.3, 0.4 and 0.5% w/v PVA solutions. The chosen media was saline, with the PVA used having a molecular weight average (M_n) of 47000. Commercial Focus® DAILIES® lenses use PVA with a molecular weight of around 47000.

The refractive indices of the PVA standard solutions were measured using the method described in chapter 2, which needs only 100µL of solution.

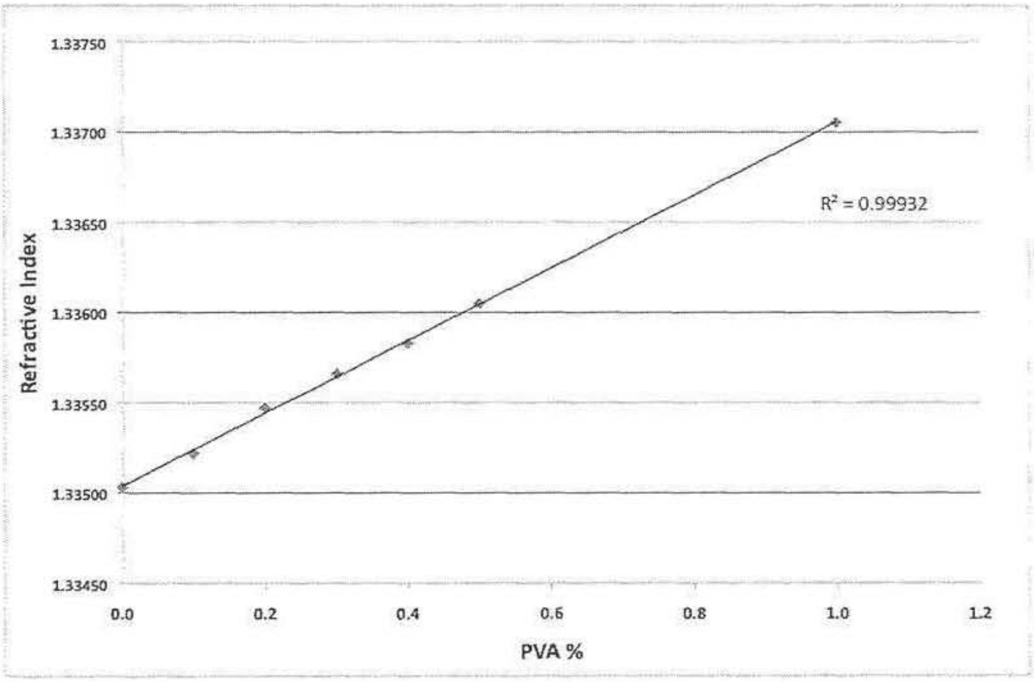


Figure 3.3: Concentration Curve for Polyvinyl Alcohol Solutions

Figure 3.3 shows the refractive indices of the PVA standard solutions with concentrations varying from 0.1% to 1% wt/v. The graph shows a linear dependence of refractive index with PVA concentration. It is important to note that the y-axis intercept is the value obtained for saline in section 3.2.2 this value was 1.33503. The results from figures 3.2 and 3.3 show that the refractive index can be used to detect polyvinyl alcohol at a sufficiently low sensitivity.

3.3: Investigation of the Focus® DAILIES® Paradox

The paradox faced was that a supposedly fully crossed-link PVA matrix was showing sign that PVA was being released out into the packing solution. Thus lowering the surface tension of the packing solution. Now that a detection method was available to use the first experimental steps were to:

(A) - Test the packing solutions of Focus® DAILIES® lenses of different ages (shown by their different expiry dates)

(B) - Try to release PVA from a new lens straight from the packing solution.

The refractive indices of the packing solutions of commercial contact lenses with different expiry dates, and therefore having different ages, were recorded and plotted. The experiment was undertaken to see if there was a difference in RI of packing solution of the new and old commercial lenses. The results showed a negative linear relationship between RI and expiry year with newer lenses having a lower refractive index than older lenses, as shown in figure 3.4.

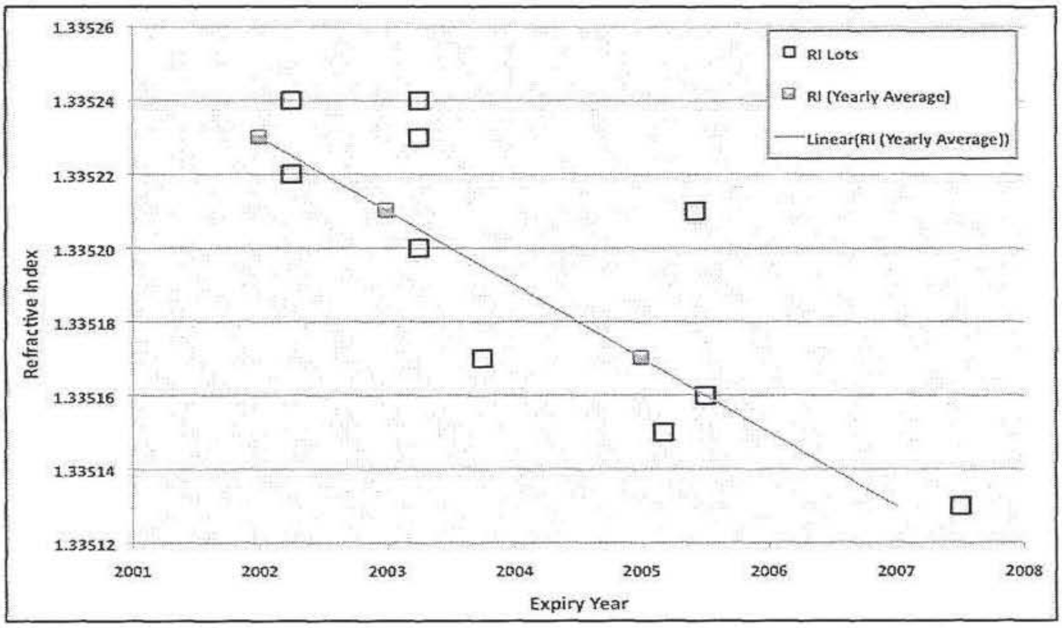


Figure 3.4: The packing solutions of commercial contact lenses

The graph in figure 3.4 demonstrates that the packing solutions of older lenses appear to have a higher refractive index than newer lenses. This suggests that the older lenses have released more PVA into the packing solution, as they have been in the packing solution for a longer period than the newer lenses.

The next step was to investigate the short-term release of PVA from Focus® DAILIES®. This was carried out by placing contact lenses into contact lens cases, with 2ml of saline for 250 hours under constant gentle agitation. The refractive index of the solution was taken periodically and the amount of PVA released was calculated from the concentration curve.

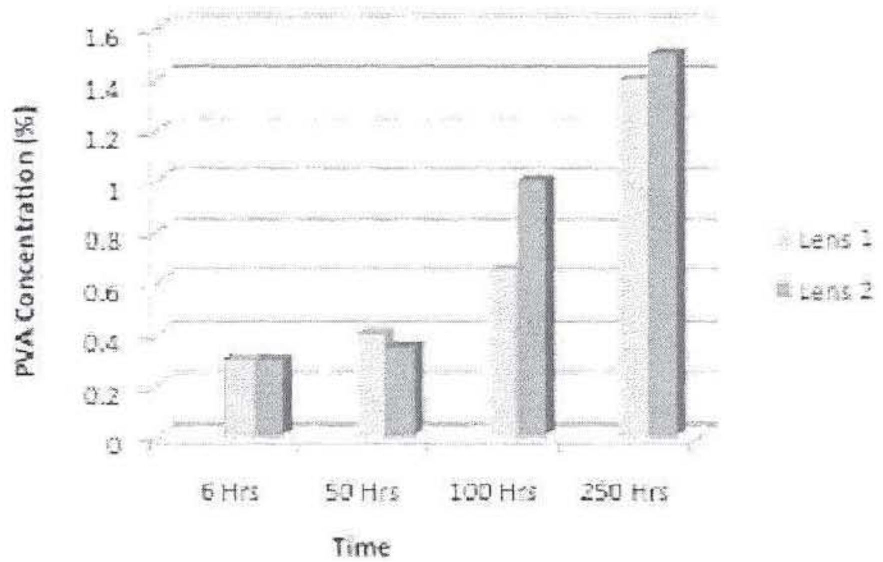


Figure 3.5: The Long Term Release of PVA from DAILIES

Figure 3.5 shows that PVA is released over a period of 250 hours with continuous gentle agitation. This fact and the fact that older lenses have more soluble PVA present in the lens packing solution suggests that soluble PVA is progressively released over a period of time.

Results so far have only indicated that PVA is released from the Focus® DAILIES® lens matrix. The next logic to step is whether or not PVA is released during wear. This would be extremely difficult to do *in vivo*; therefore, a new *in vitro* model was developed that closely mimicked the conditions of wear.

3.4: The Development of a Novel "in-eye" Mimic Release Model

Results from the packing solution refractive indices and the short-term release into 2 ml of saline showed that there was plenty of PVA available for release from the lens matrix. Results so far, however, do not represent the conditions of the lens in the eye. Conditions the model attempts to mimic is the mechanical conditions that the lenses undergo and the tear flow rate of the eye.

The eye has a tear flow rate of ~1.5 μl / min (Larke., 1997), which equates to 90 μl / hr. The model was developed around the hourly figure of tear film turnover in the final model, a flow rate 100 μl / min was used. The extraction media used was the same as the previous *in vitro* lens extractions and also the same as the PVA concentration standards, which was saline provided by CIBA Vision.

The procedure for the model is to place a contact lens into an Eppendorf to which 100μL of extraction media (saline) is added. The Eppendorf is then agitated by vortexing for 1 minute at the start of each hour. At the end of each hour, the extraction media is removed into a new Eppendorf and new media placed into the Eppendorf containing the lens. This is repeated for the entirety of the desired time of the model. Figure 3.6 is a schematic representation of the release model described above.

The developed release model had to be able to measure the release from Focus® DAILIES® lenses that had been taken straight from the packing solution and also lenses that had been worn previously.

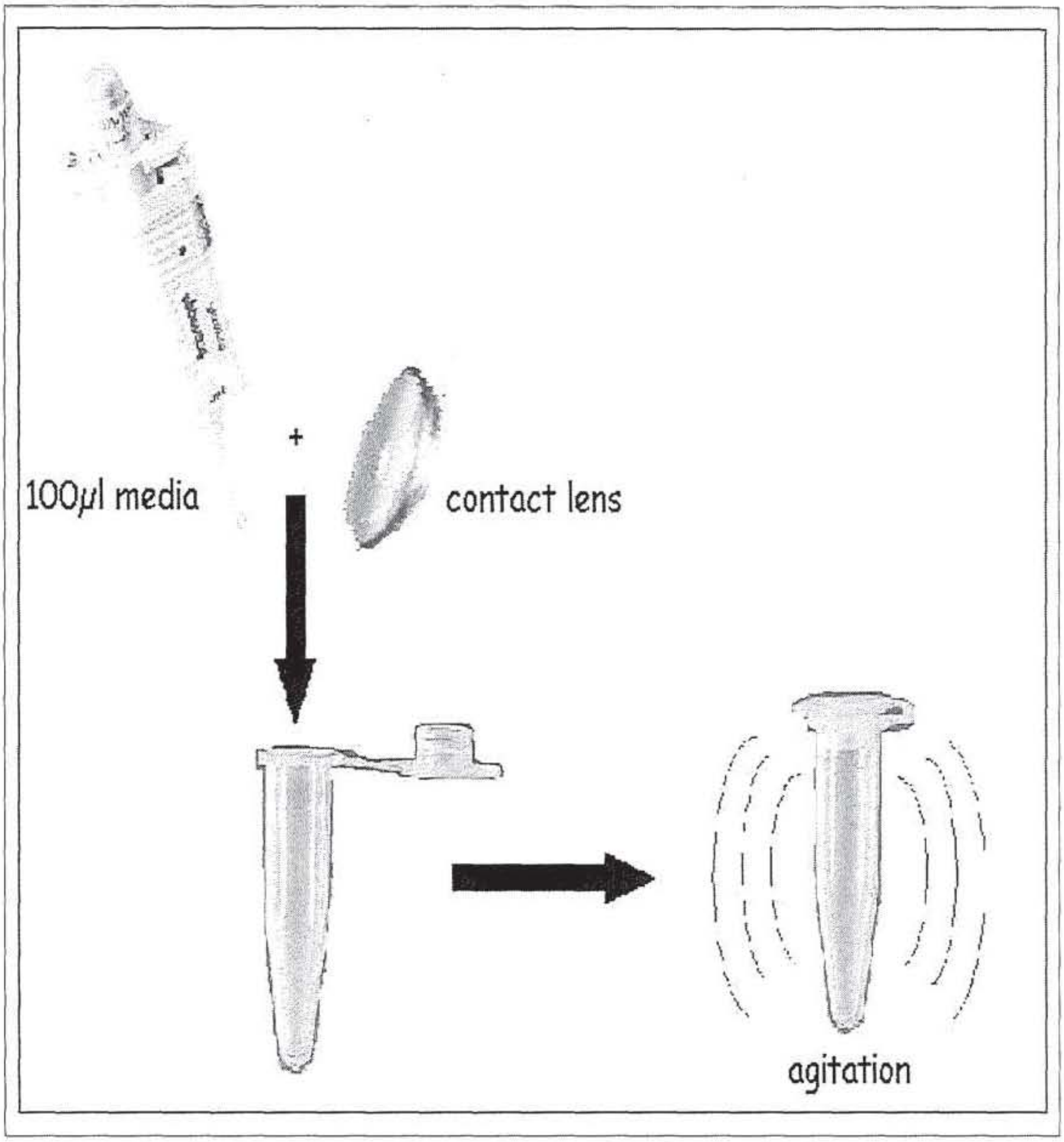


Figure 3.6: The Eppendorf in-vitro model for Release

The developed in-eye mimic release model was tested using Focus® DAILIES® contact lenses, for a period of six-hours. Therefore, six separate 100μl extracts were obtained, each extract was analysed using the micro-refractometer method discussed earlier in this chapter. For ease of use the section from 0 to 0.1% of the RI vs PVA concentration curve was expanded from Figure 3.3.

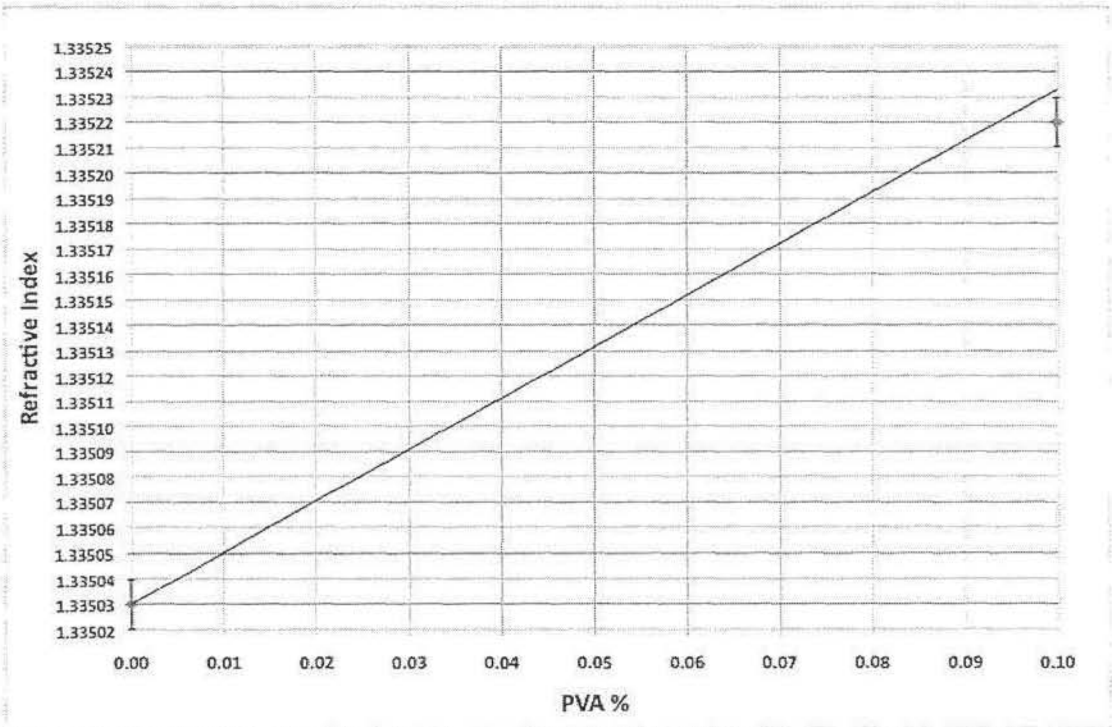


Figure 3.7: PVA standard at low concentrations

Figure 3.7 shows the expanded calibration graph of the lower refractive indices, for concentrations of PVA below 0.1%, which is where most of the refractive indices that we measured lie.

To convert the refractive index back to PVA concentration the equation of the line is needed, which is:

$$Y = 0.0019X + 1.33503$$

Therefore, $X = (Y/0.0019) - (1.33503/0.0019)$

Where: X = PVA Concentration (%)

Y = Refractive Index

Figure 3.8 shows the amount of PVA released from three different commercial Focus® DAILIES® Basic contact lenses using the in-eye mimic release model.

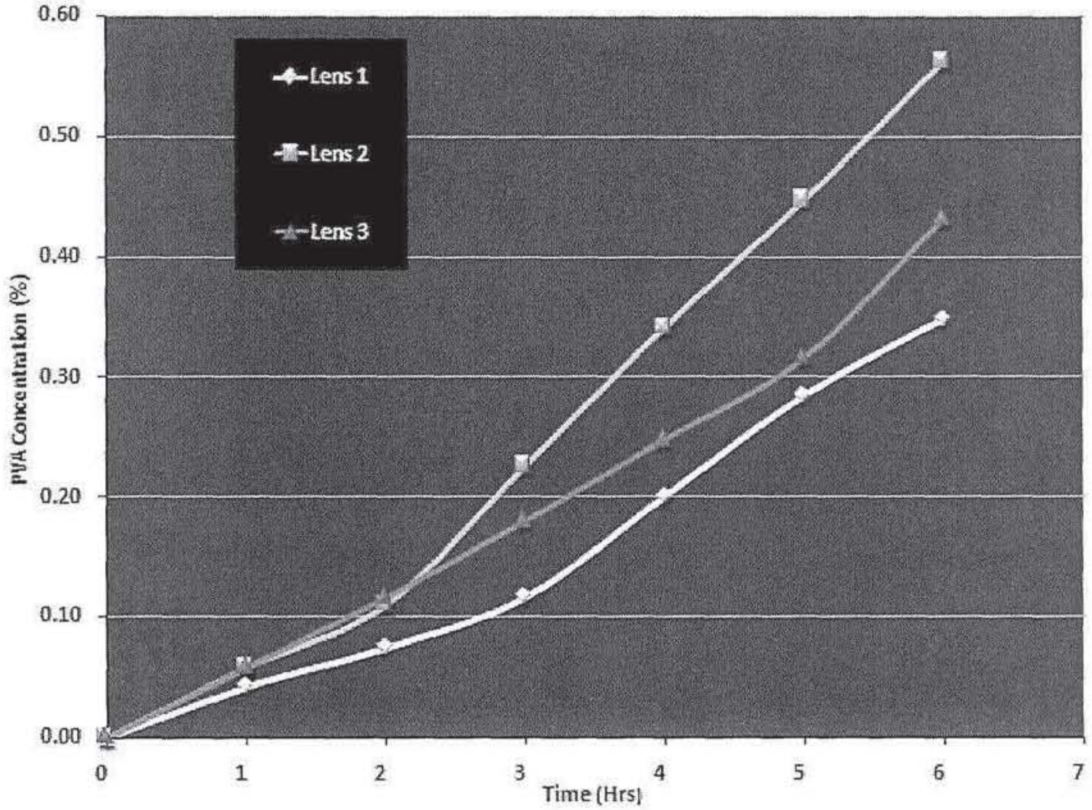


Figure 3.8: Testing of the Release Model (fig 3.6) using Three Focus® DAILIES® Basic Contact Lenses.

The above figure shows the release of PVA obtained for Focus® DAILIES® Basic lenses using the release model developed in this section. Some of the lenses were released over 0.5 mg of PVA during the 6-hour release process. On average a Focus® DAILIES® Basic contact lens weighs 35 mg, thus, the lens is releasing ~1.5% of the total lens weight during the 6-hour release.

This demonstrates that the developed model can be used in conjunction with measuring the refractive index to detect PVA at sufficiently low levels to further study the Focus® DAILIES® lenses.

The figure 3.8 showed that Focus® DAILIES® Basic releases PVA during the *in vitro* release model. However, this still does not give any information on the release of PVA during the wearing day. A lens that was worn the previous day for 8 hours was subjected to the *in vitro* release model, this was to attain if PVA was available for release from the lens.

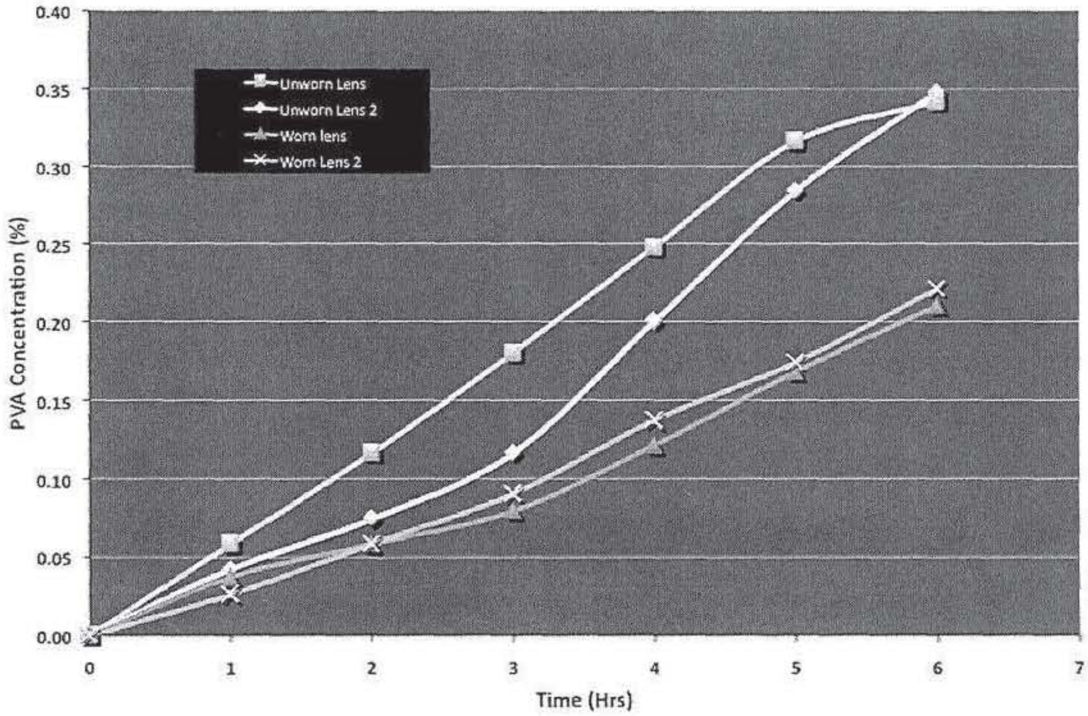


Figure 3.9: The PVA Concentrations Released from Worn and Unworn Focus® DAILIES® Contact Lenses.

Figure 3.9 shows the release curves for lenses straight from the packing solution against lenses that were worn for 8 hours the previous day. The worn lenses were stored in a small amount of saline to help maintain sufficient hydration overnight.

The curves show the amount of PVA released from an unworn commercial Focus® DAILIES® lens (unworn lens 1, unworn lens 2) and lenses that had been worn for 8 hours (worn lens 1, worn lens 2). The release of PVA is greater for the lenses taken straight from the packing solution when compared to the worn lenses.

This suggests that the worn lenses had released some of their PVA during the course of wear the previous day.

3.5: The Effect of Cross-Link Density on the Release of PVA from Focus® DAILIES®.

This section investigates the release of PVA when the cross-link density of the lens matrix is altered. The cross-linked density of the lenses was changed by the use of one of the following techniques:

1. The lens was exposed to gamma ray radiation for a set period of time.
2. The lens was placed into a solution of sodium periodate for a short period.

Gamma Rays (often denoted by the Greek letter gamma, γ) are an energetic form of electromagnetic radiation produced by radioactive decay or other nuclear / subatomic processes such as electron-positron annihilation.
Gamma ray sources are used for a range of applications in both medicine and industry. One of the industrial uses is in polymerisation; the energy release from the gamma ray provides free radicals that initiate polymerisation processes, most notably radical abstraction and cross-linking. (Alexander et al., 1957)
The gamma ray exposure in this instance was used to increase the cross-link density of the Focus® DAILIES® lenses, by enabling any uncross-linked PVA in the matrix to cross-link.

Focus® DAILIES® lenses that had been subjected to gamma ray exposure and restored in packing solution had the in-eye mimic release model carried out on them. These lenses were then compared to Focus® DAILIES® lenses taken straight from the packing solutions and subjected to the same release model.

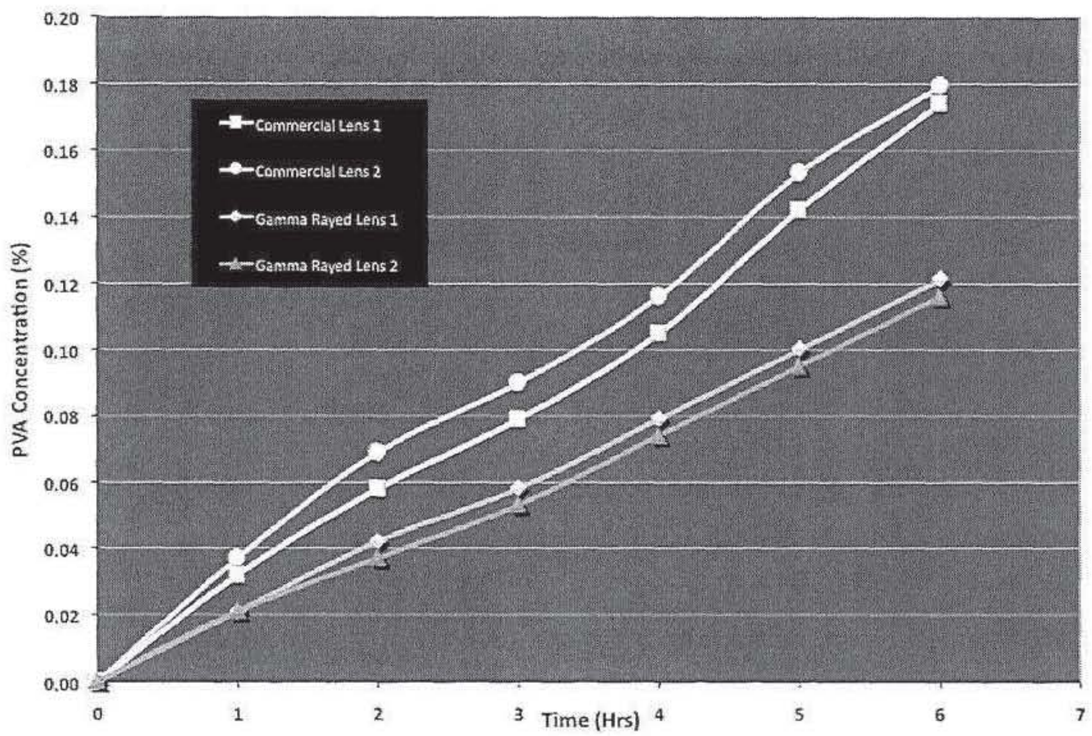


Figure 3.10: The Release Curves of the Gamma Ray Radiation Treated DAILIES vs Non-Treated DAILIES

Figure 3.10 shows the release curves for gamma ray treated Focus® DAILIES® lenses compared to normal Focus® DAILIES® lenses. All the lenses shown in figure 3.10 show PVA release. However, the gamma ray-treated lenses released less PVA than the lenses that were not exposed to gamma ray radiation.

Sodium periodate is known to cleave the head to head hydroxy groups in polyvinyl Alcohol. Thus, the cleavage of the PVA chain would increase the amount of free PVA, therefore, reducing the cross-link density.

The method addition of the sodium periodate, was to exposed the fluorescent tagged Focus® DAILIES® contact lenses to 100 μl of 0.01 % sodium periodate solution for a 10 minute period. This was then repeated for 1 hour, (6 x 10mins) the six 10 minute 100 μl extracts were then diluted down 4:1 with HPLC water and the fluorescence measured at 260nm on a Hitachi F-4500 fluorescence spectrometer using the method described in chapter 2 of this thesis.

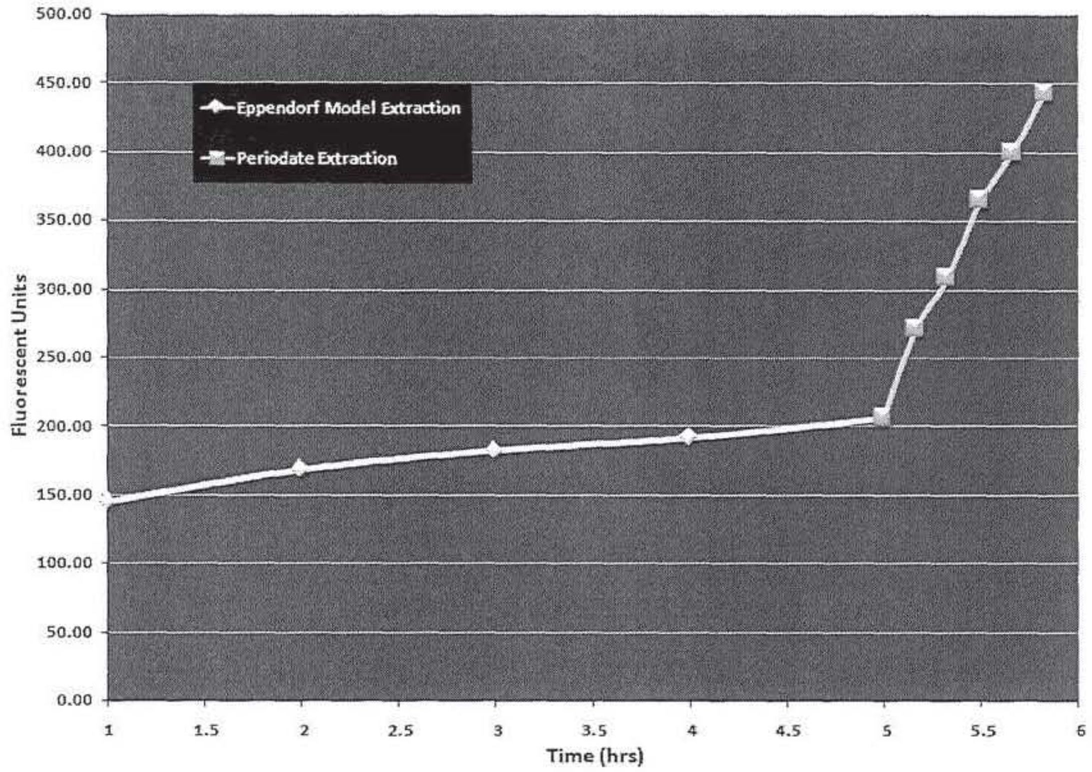


Figure 3.11: The Effect of Sodium Periodate on the Extraction of PVA from Focus® DAILIES® Lens.

Figure 3.11 shows the fluorescence obtained from the fluorescently tagged Focus® DAILIES® contact lens. The first part of the graph shows the amount of tagged soluble PVA released during five hours of the release model. The second section of the graph shows the amount of soluble PVA released after the sodium periodate solution is used as the extraction media.

The paradox that was mentioned earlier in this chapter said that the Focus® DAILIES® contact lens was a fully cross-linked PVA based matrix. The results from this section help to demonstrate that the released PVA detected, is PVA that has not be cross-linked or is weakly cross-linked in the lens matrix, thus, the paradox is starting to be resolved.

3.6: The Effect on Release of Adding Extra Non Cross-linked Soluble PVA to Focus® DAILIES® Lenses.

To further help solve the Focus® DAILIES® paradox and help to confirm the results obtained in the previous section (differing cross-link density). Focus® DAILIES® lenses were obtained from CIBA Vision that contained an extra 2% uncross-linked soluble PVA.

Lenses that had the extra uncross-linked soluble PVA were labeled and will be referred to as Neptune lenses (or Modified). Neptune lenses were subjected to the in-eye mimic release model along with control lenses (unmodified original Focus® DAILES® lenses taken straight from the packing solution).

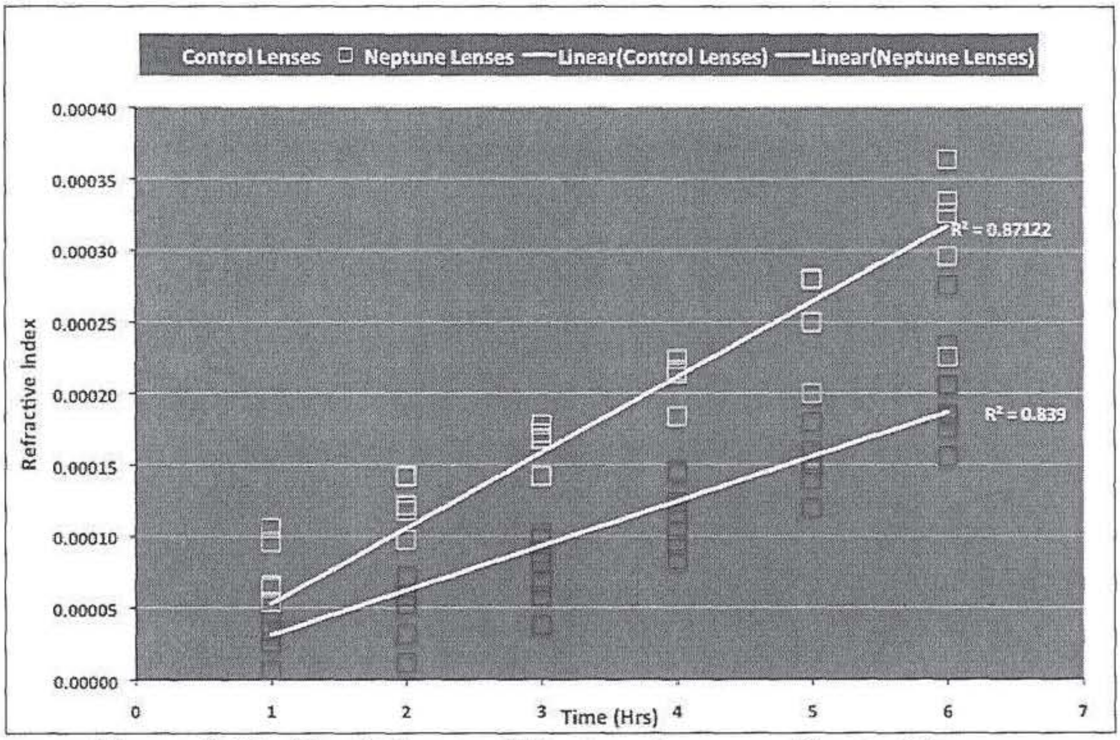


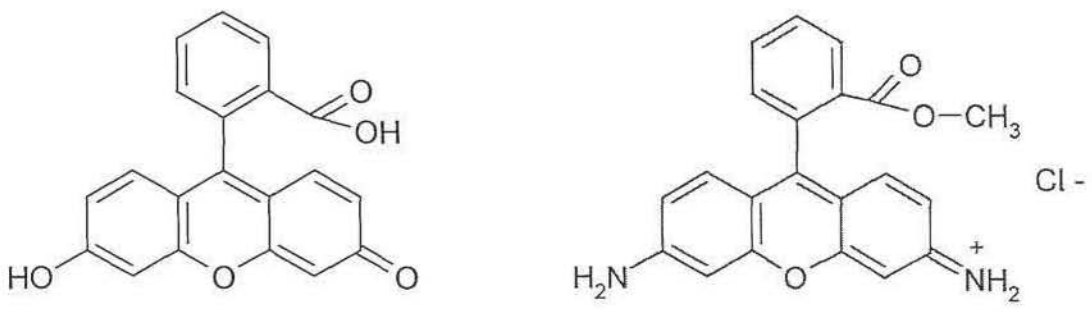
Figure 3.12: The Release of Neptune lenses vs Control Lenses.

Figure 3.12 shows the effect of the added uncross-linked soluble PVA. The graph shows the Neptune labeled lenses released more soluble PVA than the lenses without the added PVA. The majority of this extra release comes towards the end of the release period.

3.7: Using Fluorescence to Study the Release of PVA from Focus® DAILIES® Lenses.

Fluorescence is a useful investigative tool, particularly when identifying compounds that are difficult to detect in solutions.

A batch of modified Focus® DAILIES® contact lenses were obtained with fluorescently tagged chemicals attached to the polyvinyl alcohol contained in the lens. Two fluorescent tags were added to the lenses, Fluorescein and Rhodamine. The structures of which are shown in figure 3.13



Fluorescein Rhodamine

Figure 3.13: Structure of the Fluorescent Tags

The fluorescein tag was added to the extra uncross-linked soluble PVA with an M_n of 47000, and the rhodamine fluorescence tag was added to the uncross-linked soluble PVA with a M_n of 61000.

The following figures show the 3D spectra obtained from a Hitachi F-4500 fluorescence spectrometer using the method outlined in chapter 2 at a wavelength from 200 to 400 nm. The 3D spectra are of a saline standard, and samples of the fluorescein and rhodamine tagged PVA dissolved into saline.

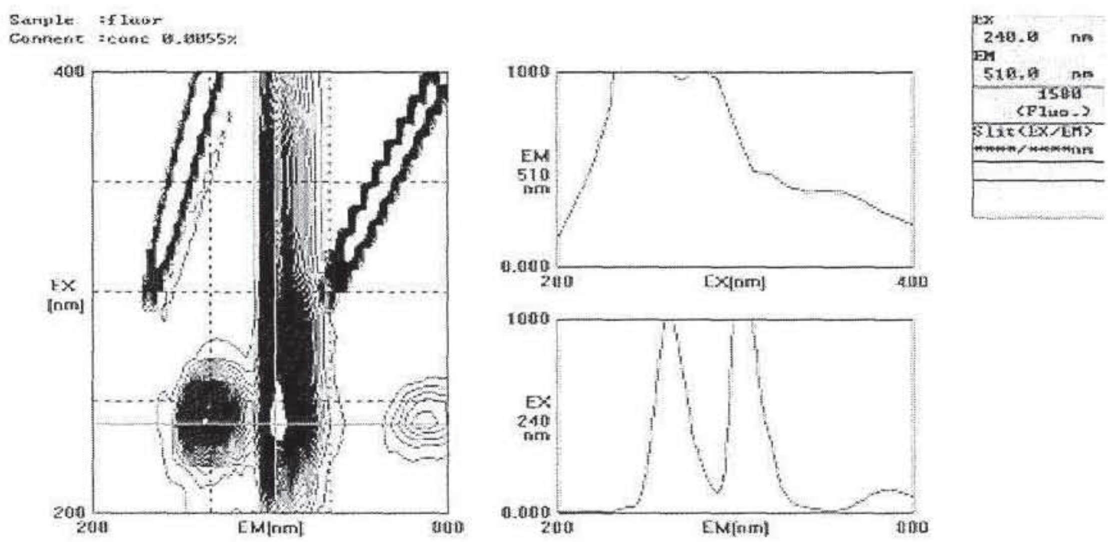


Figure 3.14: 3D Spectra of the Fluorescein Tag.

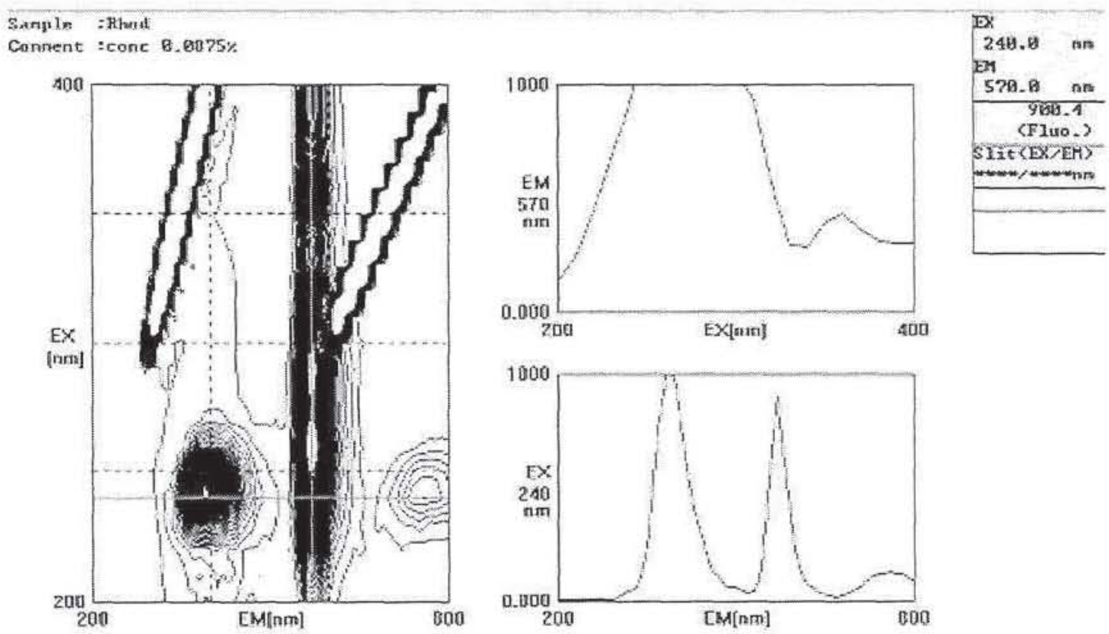


Figure 3.15: 3D Spectra of the Rhodamine Tag

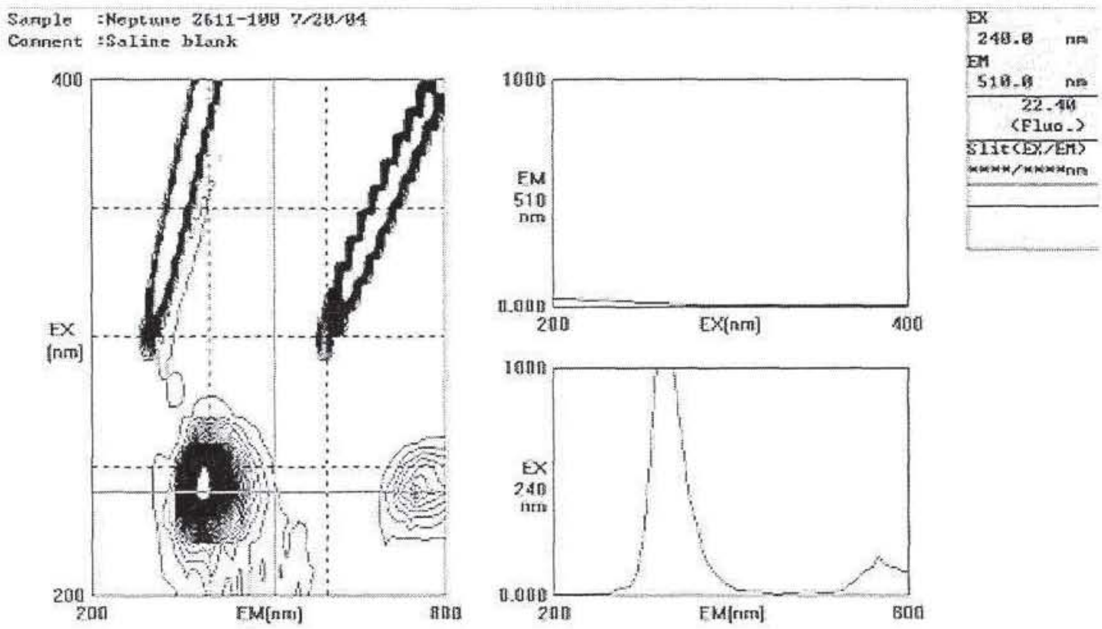


Figure 3.16: 3D Spectra of the Saline Blank

Figure 3.17 shows a 2D fluorescence of the fluorescent tags as well as the packing solution of the fluorescently tagged Focus® DAILIES® and saline blank.

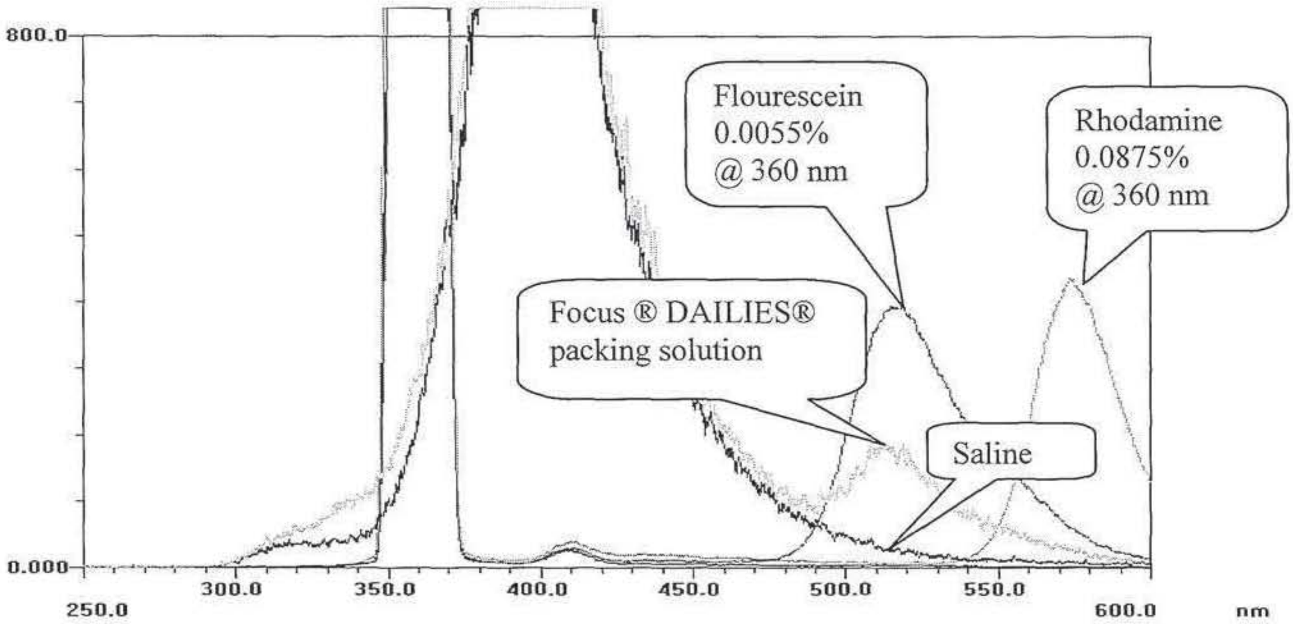


Figure 3.17: 2D fluorescence Scan of the Fluorescent tags, Saline Blank and a Lens

Figure 3.17 shows the differences between the two different fluorescent tags; fluorescein and rhodamine, in where their excitation peaks occurs. It also shows that the packing solution of the fluorescently tagged lens only shows the presence of the fluorescein tag. There is no sign of the rhodamine tag in the lenses packing solution 2D spectra. The rhodamine tag was found to give a weaker signal at the same concentrations as the fluorescein tag, and was attached to the higher molecular weight PVA. Whereas, the fluorescein tag was attached to uncross-linked with the lower molecular weight PVA. Thus, suggesting that the molecular weight of PVA is important in controlling the amount and rate of release.

3.7.1: The Release of PVA from Focus® DAILIES® Analysed by Fluorescence.

An in-eye mimic release model was carried out on the fluorescently tagged Focus® DAILIES® lenses obtained from CIBA Vision. The fluorescence spectrometer, however, requires 400 µl of sample to get accurate fluorescence readings therefore, each 100 µl extract was with diluted with 300 µl of saline. These six 400 µl dilutions then had a 2D fluorescence scan run at 280 nm. Fluorescent intensity was recorded and the value for saline subtracted to give the fluorescence from only the fluorescently tagged soluble PVA.

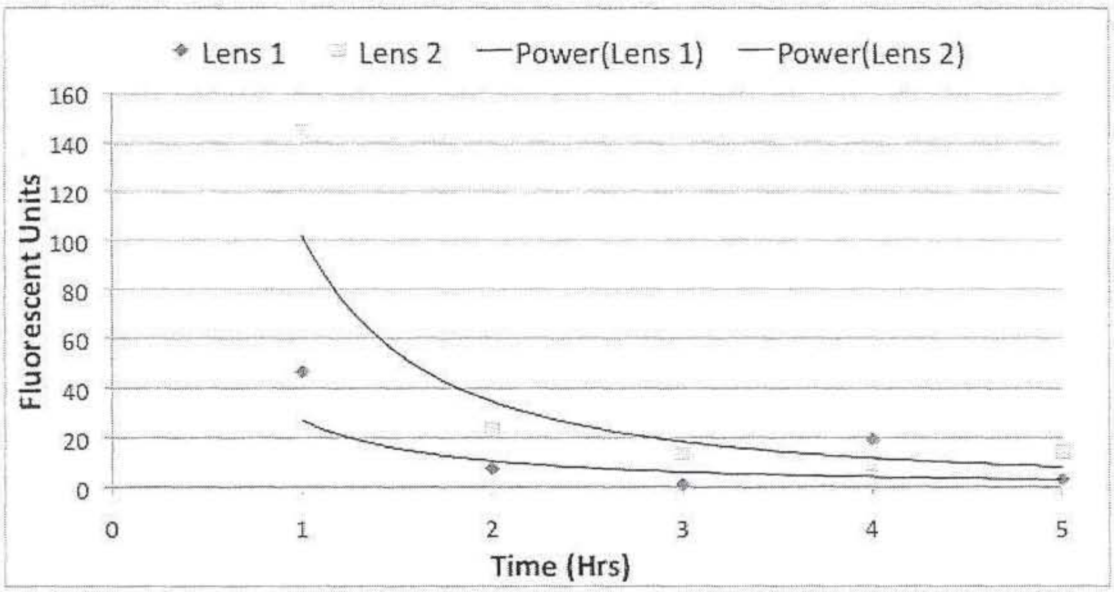


Figure 3.18: Relative Fluorescence of the Released from Focus® DAILIES® Lenses.

Figure 3.18 shows the fluorescence results from the release of the two fluorescently tagged Focus® DAILIES® lenses. Although the results show a similar trend, the dilution may have had an effect of some of the later hour extractions.

As the fluorescence spectrometer needs a minimum 400µl to give accurate readings, the release model was therefore modified so that there were four fluorescently-tagged lenses used in 400µl of saline for each hour. This still gave the same about of medium used per hour per lens, when compared to the previous release model. With the added advantage that there was no need to dilute down the samples.

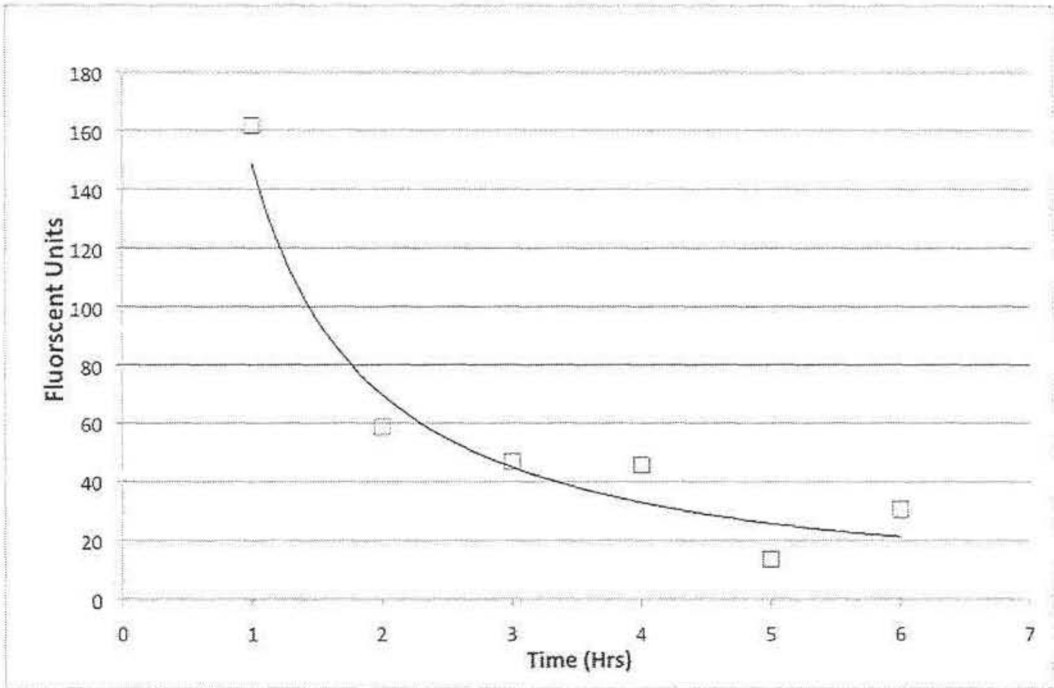


Figure 3.19: Relative Fluorescence of Four Extracted Lenses

Figure 3.19 shows that the majority of the fluorescently tagged soluble PVA is released in the first hour, and then tails off on further hour extracts which suggests that the extra-added PVA is released as a burst effect. Although there is no tail off in overall release according to the RI measurements as shown in figures 3.12. This suggests that the actual matrix of the lens still contributes the majority of the PVA released in these modified Focus® DAILIES® lenses.

3.7.2: Analysis of the Surface Fluorescence of the Fluorescently Tagged Focus® DAILIES® Lenses.

It is possible to study the surface fluorescence of a contact lens (Franklin, V., 1990). Two of the fluorescently tagged Focus® DAILIES® lenses had their surface fluorescence analysed. One lens was taken straight from the packing solution and the other lens had just undergone a 6-hour release. The results are shown below with a bar chart of the amount of fluorescently tagged PVA that had been released during the release process.

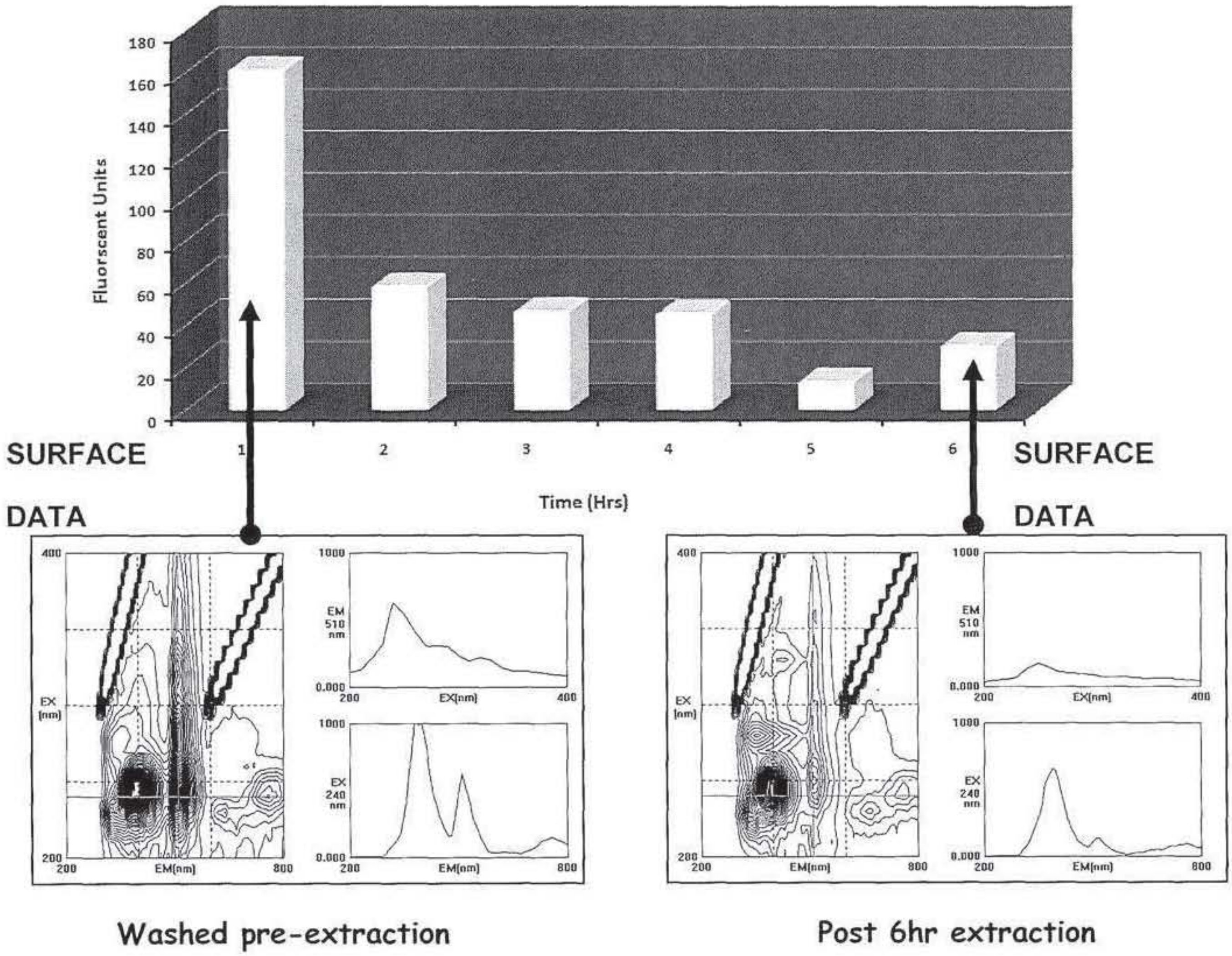


Figure 3.20: Surface Fluorescence of Focus® DAILIES® Lens Before and After Release.

The surface fluorescence shown in the 3D scans clearly show that the majority of the surface fluorescent-tagged PVA has been released from the contact lens. However, if the post extraction lens is left to re-equilibrate in saline for a few days and the surface fluorescence is retaken, the surface fluorescence increases back towards the state of the pre-extracted lens. This happens via passive diffusion, as there is plenty of PVA still in the bulk of the lens that has the potential to be released.

3.8: Discussion

The four main chemical analytical techniques (IR, NMR, UV & Mass Spec) failed to monitor PVA released from the lens matrix effectively. Refractive index can use very small volumes of aqueous solution to measure polymer concentrations. An Index Instruments automatic refractometer GPR 11 – 37X was first accessed for accuracy using saline, this was also the same saline that was later used as the release medium. The refractometer proved to be accurate and very precise, measuring the refractive index (RI) to 5 decimal places with a very low standard deviation.

Now proven to be accurate, the refractometer was used to measure varying concentrations of PVA in solution; the results gave a linear relationship of RI against PVA concentration. Thus, refractive index is a very useful tool in analysing the release media for detecting possible PVA release.

At this point with a detection method available it was possible to investigate the Focus® DAILIES® paradox. That a supposedly fully cross-linked PVA matrix was showing signs that PVA was being released out into the packing solution. Lenses were obtained with different expiry dates and the RI was taken, the resulting graph showed as predicted that older lenses (therefore been stored for longer) had higher refractive indices. Suggesting that they had released more PVA passively from the lens matrix, this also suggested that this was a slow process.

Next step was to increase the amount released to see if the release ended, 2ml of saline was used as the extraction media and the RI was measured at different time points up to 250hrs. Results showed that PVA was still being eluted from the lens after 250 hrs suggesting that the lens had more PVA to be released during wear (i.e. not used up by passive diffusion in packing solution).

The long-term release however, does not adequately reflect that of the lens during wear. Therefore, a new release model was developed that was closer to the conditions found throughout wear: such as the amount of aqueous (tear film) present and the mechanical agitation (eye lid) on the lens. The model used 100µl of release media per hour, which is similar to the amount predicted for the tear flow rate over the same period. Lenses were vortexed for periods of 30 seconds at the start of each hour to provide mechanical agitation. This model was tested and proved to be reproducible. The new release model was then used to compare lenses taken straight from the packing solution against lenses that had been worn for 8 hours the previous day. Lenses that had been worn for 8 hours released less PVA, which suggests that the lenses had been releasing PVA during wear.

Results discussed so far do not suggest the way in which or where the PVA is released. Mechanism of release is important for helping to understand the Focus® DAILIES® paradox, the hypothesis investigated was that the PVA being released was soluble uncross-linked PVA left over from the manufacture process. Gamma ray exposure is known to increase the cross-link density, it was used in this case to cross-link any uncross-linked PVA in the matrix. Sodium periodate is known to cleave the head to head OH groups in PVA, thus decreasing the cross-linked density. If the hypothesis that soluble PVA is the PVA eluting from the lens, then the lenses treated with sodium periodate should release more PVA, and the lens exposed to gamma ray exposure will release less PVA. This is what the results indicated in both cases.
To help increase the amount of PVA that was being released from the lens, lenses were obtained from CIBA Vision that contained 2% extra-added uncross-linked soluble PVA. This PVA was added before the polymerisation process. These lenses had the developed in-vitro release model carried out and compared to a control lens (Original Focus® DAILIES®). These results also helped to prove the hypothesis that the soluble uncross-linked PVA is released, as the lenses with the extra 2% PVA released more PVA than the control lenses.

The Focus® DAILIES® paradox is also that Focus® DAILIES® lenses suffer more from end of day discomfort than other similar lenses. This suggests that the lens is changing during the course of the day. Some lenses were obtained from CIBA vision that contained two different fluoresent tags on the PVA. One tag was added to the 47K molecular weight uncross-linked PVA and the other tagged onto the 61K molecular weight uncross-linked PVA. The results from the release studies carried out on these lenses showed that most of the fluorscein tagged PVA was released in the first hour. Thus, confirming that the uncross-linked PVA is released as a burst effect. The 3D spectra of the surface fluorescence from a lens, pre and post extraction showed that the uncross-linked PVA is coming from the surface of the lens. This may help explain why the lens is suffering from discomfort towards the end of the end. The surface release of PVA is out stripping the ability of the lens matrix to resupply the surface. The lens has plenty of PVA in the matrix available for release as seen in the long-term release and also passive diffusion of PVA into the packing solution of older lenses.

Chapter 4

Development of a Novel Technique for Measuring the Friction Coefficient of Contact Lenses

4.1: Introduction

'Tribology' is derived from the Greek word 'tribos' meaning to rub. Which focuses on friction, wear and lubrication of interacting surfaces in relative motion, is a new field of science defined in 1967 by the committee of Organization for Economic Co-operation and Development. Tribology is therefore a very new field of science, most of the knowledge being gained after the Second World War. In comparison many basic engineering subjects, e.g. thermodynamics, mechanics and plasticity, are relatively old and established. Tribology in a traditional form has been in existence since the beginning of recorded history. There are many well documented examples of how early civilizations developed bearings and low friction surfaces (Dowson., 1979). The scientific study of tribology also has a long history. Leonardo da Vinci was the first to deduce correctly the basic laws of friction in 1519, when he was interested in the music made by the friction of heavenly spheres. Amonton then discussed the basic laws in 1699, which were experimentally verified by Coulomb in 1785. Coulomb stated that the empirical law for the friction force between two sliding solids was as follows:

1. The friction force is independent of the apparent contact area between the sliding surfaces.
2. The friction force is proportional to the load N, i.e., the force perpendicular to the sliding surface, which presses the two solids together. The proportionality factor is called the friction coefficient.
3. The kinetic friction (i.e. the force to keep a body sliding at a constant velocity) does not depend on the sliding velocity. It is less than or equal to the static friction i.e. the force to start sliding. The static coefficient of friction is greater than the kinetic coefficient.

The third law of friction as stated by Coulomb is now usually left out, as there are cases when the law does not hold. The equation below shows the equation used to obtain the coefficient of friction (Moore., 1972)

$$F = \mu W \text{ or } \mu = F/W$$

Where: F = Frictional Force, W = Load, μ = Coefficient of friction

Equation 4.1: Law of Friction by French physicist Guillaume Amonton in 1699

Until the publication of Osborne Reynolds's paper on hydrodynamic lubrication in 1886, there was relatively little understanding of tribology. Reynolds proved that the hydrodynamic pressure of liquid entrained between sliding surfaces was sufficient to prevent contact between surfaces even at very low sliding speeds. His research had immediate practical application and led to the removal of an oil hole from the load line of railways axle bearings. Oil, instead of being drained away by the hole, was now able to generate a hydrodynamic film and much lower friction resulted. The work of Reynolds initiated countless other research efforts aimed at improving the interaction between two contacting surfaces and continues to this day. This has led to there being higher levels of sophistication in bearings. Wear and the fundamentals of friction are a far more complex problem, the experimental investigation of which is dependent on advances in instrumentation such as scanning electron microscopy and atomic force microscopy. Therefore, it has only recently been possible to study these processes on a microscopic scale where a true understanding of their nature can be found.

Wear is the major cause of material wastage and loss of mechanical performance, and any reduction of wear can result in considerable savings. Friction is a principal cause of wear and energy dissipation. Savings can be made by improving friction control, it was estimated that one-third of the world's energy resources in present use is needed to overcome friction in one form or another. (Stachowiak., 2005)

The area of friction that is associated with the body is called Biotribology, which is the study of the lubrication, friction and wear, at biological interfaces. Tribological studies are becoming increasingly important in many areas of research, especially in the body with the design of material surfaces. Most work on the area of biotribology has predictably been in the field of joint replacements, looking into ways of extending the life of the implant by reducing the overall wear of the material.

Frictional studies show that both synthetic hydrogels and natural hydrogels (e.g. the cornea) are normally lubricated by a hydrodynamic (water) boundary layer (Gong., 2002). This dominates the dynamic coefficient of friction to the extent that when a good lubricant forms a layer, which separates the hydrogel and the substrate, it is the lubricant properties rather than those of the material or substrate, which govern the value of sliding friction. The simplest analogy is a car aquaplaning – the ease of the tyre sliding is independent of the rubber used. When the water layer breaks down there is an increase in the resistance to sliding.

The clinical consequences of these facts are relatively simple to state but complex to relate directly to in vitro measurements. Most conventional hydrogels have adequate wettability and frictional behaviour when fully hydrated, no matter what water content. Problems only arise because of progressive dehydration and the dynamic responsiveness of the lens material to air and lipids, which is primarily caused by tear break-up. The processes in turn influence the irreversible deposition of tear components and the onset of symptoms such as end of day dryness and discomfort.

4.2: Development of the Tribological Technique for Measuring Contact lenses

There is a growing interest in biominesis, the design of synthetic materials based on nature's models. The way in which natural surfaces are hydrated and lubricated presents a very useful template for the design of synthetic biomaterials. Recently there has emerged a trend of using hydrophilic macromolecules to help maintain surface hydration.

There have been several complications associated with contact lenses that can be linked to the movement and thus the forces involved in contact lens wear such as: mucin balls, superior epithelial arcuate lesions (SEALS), Contact lens papillary conjunctivitis (CLPC) and general discomfort. The problem faced was trying to develop a technique for measuring the coefficient of friction for contact lenses. The difficulty arises from the very small forces involved and small amount of lubricant present. The tear film compared with other body sites such as the articular joints where tribological testing has been studied for many years. The figure 4.1 shows a schematic of the movements seen in contact lens wear.

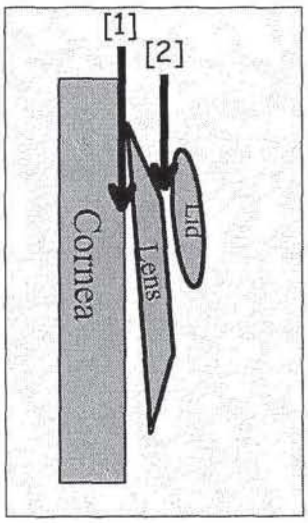


Figure 4.1: A Schematic of the Contact Lens During Wear

Their have been few researchers who have attempted to measure the coefficient of friction for contact lenses (Nairn et al., 1995, Kim et al., 2001, Rennie et al., 2005), however, this is very little when compared to other body sites such as the articulated joints. Their is still no 100% accepted technique and all the techniques have failed in one or more ways. These include the failure to mimic the movement of the eyelid, the fact that the eye carries the tear meniscus over the lens or the fact that the actual tribometer cannot measure accurately and reproducibly down to efficiently low values. Therefore, the first choice in the development of the technique was which type of tribometer would the technique be based upon; pin-on-disc, calo tester, or scratch tester.

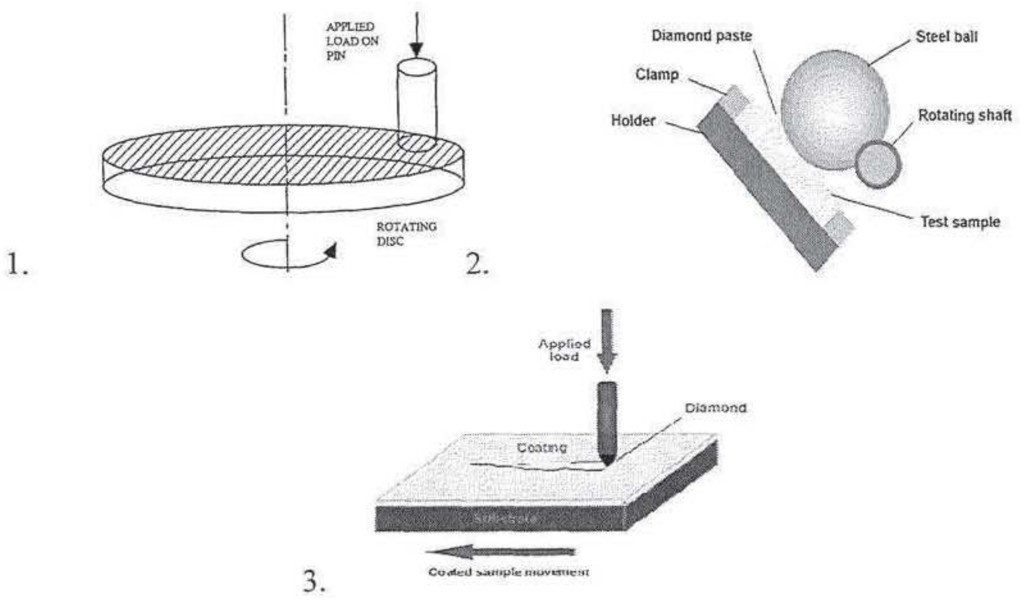


Figure 4.2: The Three Different Types of Tribometer; 1) Pin-on-Disc 2) Calo Tester 3) Scratch Tester

Figure 4.2 shows schematics of the three major types of tribometer systems. Most of the work done on the coefficient of friction previously in the field had been based on the pin-on-disc technique. The technique that was developed in this chapter was based upon the scratch tester technique, as this technique allowed the several key requirements to be fulfilled. These requirements were as follows:

- The measurement of the coefficient of friction below 0.1μ
- The use of small amounts of lubricant (~100 μl)
- The conditions mimic the eye – Load, speed, and distance

The way in which the tribometer measures the coefficient of friction was also important. Mimicking the eye as closely as possible is goal when choosing the ideal tribometer. With this respect the scratch tester was the closest to the human eye; the substrate is moved back and forth at a set speed and load, the same as the human eyelid is moved over the eye (and contact lens) during wear.

The tribometer chosen was made by CSM instruments; it was modified from a nano-scratch tester. Main reasons for this were the degree of sensitivity, the ability to use various substrates, and the load and speed ranges were of suitable values. A modification to the tribometer is to replace the pin of the scratch tester with a polypropylene contact lens mould. A mould is inserted upside down then the contact lens is then placed up on to the lens mould as seen in figure 4.3.

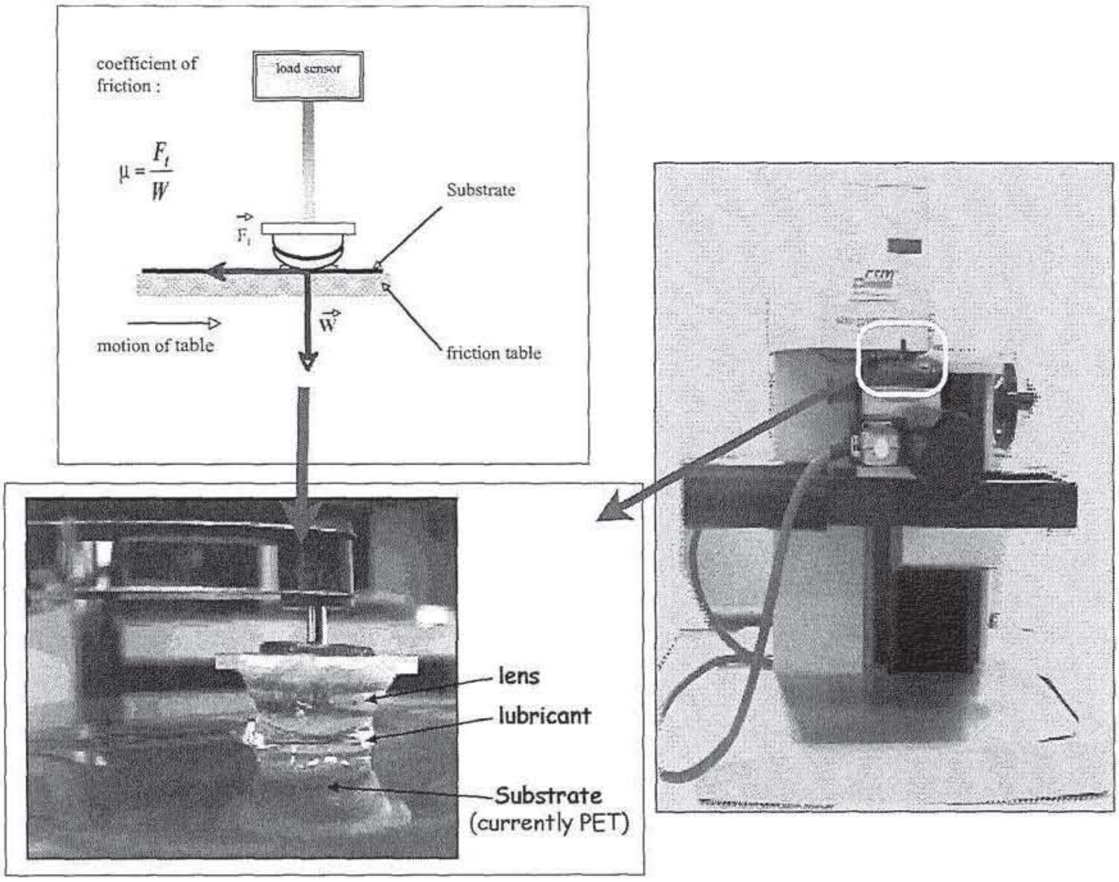


Figure 4.3: The Experimental Setup of the Modified Nano-Scratch Tester

Figure 4.3 shows the experimental setup of the tribometer, the picture in the left corner shows how the lens sits on the contact lens mould, which drags the lubricant across the substrate in an analogous way to which the eyelid carries the tear film over the cornea in the upper meniscus during a blink.

The experimental procedure for the modified nano scratch tester was as follows:

1. The substrate was cut and placed onto the friction table
2. The contact lens was removed from the packing solution and blotted with filter paper to remove any carried over packing solution
3. The lens was placed onto the plastic contact lens mould using the filter paper
4. The appropriate amount of lubricant was placed directly under the contact lens
5. The friction table was then raised until contact was almost made between the contact lens and the substrate
6. The software then took over and automatically made contact between the contact lens and the substrate
7. The set load was applied and then the friction table moved at the set speed for the 20 mm selected distance
8. When the friction table has moved the set distance, the load was removed (contact was still maintained) and the friction table returned to the start point.
9. This was repeated until the set amount of passes had been completed (usually 10)

The above experimental procedure was used for all the friction coefficients measured in this work. This chapter will focus on the variables that affect the coefficient of friction such as: substrate, load, speed, and amount of lubricant. Using commercially available contact lenses and solutions with various properties to help highlight or exaggerate differences.

4.2.1: The Reproducibility of the Tribometer

The most important property of any analytical instrument should be the ability to measure results reproducibly. To test the reproducibility of the tribometer a series of 25 mean coefficient of friction measurements were made on the same brand of contact lens. All the other parameters were kept the same; the lens was replaced with a fresh lens from the packing solution for each measurement. The lens chosen was the Focus® DAILIES® branded lens, as this lens gives a low coefficient of friction and therefore, if the tribometer could measure the friction reproducibly for a lens with a low coefficient of friction then lenses with higher coefficients of friction should also give consistent results.

A bar chart of the mean coefficient of friction for each of the twenty-five individual lenses together with the overall mean.

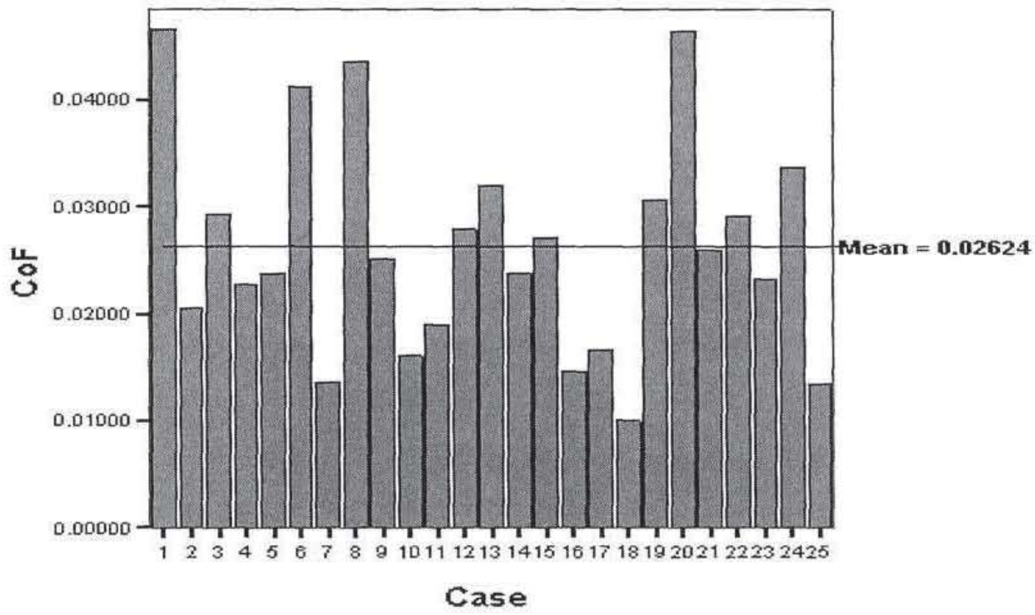


Figure 4.4: Coefficient of friction for 25 Focus® DAILIES® Lenses

Figure 4.4 shows the results from 25 repeat coefficients of friction of Focus® DAILIES® branded Lenses. The speed and load for these results were 30 mm/min and 30 mN respectively. The substrate used was the standard PET sheet and the lubricant used was HypoTears™.

Figure 4.5 shows the statistical break down from the twenty five Focus® DAILIES® coefficients of friction.

			Statistic	Std. Error
CoF	Mean		.0262354	.00204558
	95% Confidence Interval for Mean	Lower Bound	.0220135	
		Upper Bound	.0304573	
	5% Trimmed Mean		.0259688	
	Median		.0251020	
	Variance		.000	
	Std. Deviation		.01022790	
	Minimum		.01002	
	Maximum		.04658	
	Range		.03656	
	Interquartile Range		.01342	
	Skewness		.574	.464
	Kurtosis		-.251	.902

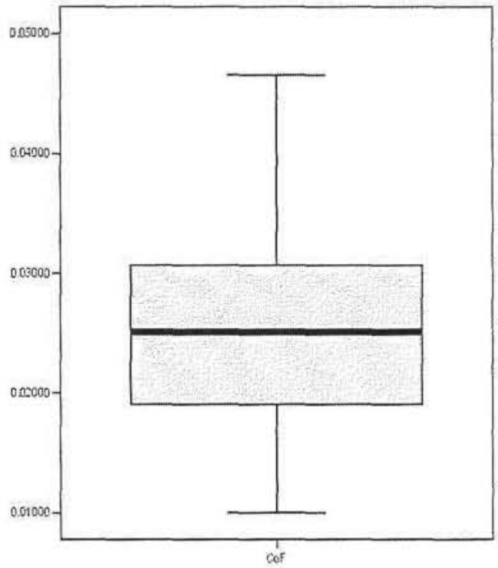


Figure 4.5: Data Analysis of 25 Focus® DAILIES® Lenses Friction Coefficients.

Figure 4.5 shows the data from the twenty-five repeated lenses that were analysed using SPSS statistics program. Mean of the results give a mean coefficient of friction of 0.026 to three decimal places with a standard deviation of 0.010. The range of the results was 0.037 with a minimum of 0.010 and maximum of 0.047.

These results show that the developed tribometer can give reliable and reproducible friction coefficients with contact lenses at genuinely low values of friction.

4.3: The Effect of Altering the Tribometer Conditions

This section will investigate the effects on the coefficient of friction of changing the variables on the tribometer. The variables that will be examined are the applied load, the speed of the moving friction table, the type of substrate used and the quantity of lubricant.

4.3.1: The Effect of Load

Load applied on the contact lens during the friction test can be varied from 5mN to 120 mN. The load applied is a fundamental part of the equation for the coefficient of friction (Equation 4.1).

The equation states that the coefficient of friction is equal to the friction force divided by the load applied. In metal on metal friction it is known that changing the load does not significantly alter the coefficient of friction.

To investigate whether the friction of contact lenses follows the same rules as metal on metal friction, two different lenses were studied using different loads but keeping the rest of the variables the same.

Two lenses chosen were Focus® Night & Day™ (FND) and Focus® DAILIES® (DAILIES) these lenses vary greatly with FND being a silicone hydrogel with a PMMA surface treatment that can be worn continuously for 30 days, and Focus® DAILIES™ being a daily disposable contact lens based on polyvinyl alcohol with soluble PVA leaching out of the lens during wear (see Chapter 3). The moduli of these lenses was also different.

Figure 4.6 shows the mean coefficients of friction for FND at the speed of 30 mm/min, the loads used ranged from 20 to 80 mN in 10 mN steps.

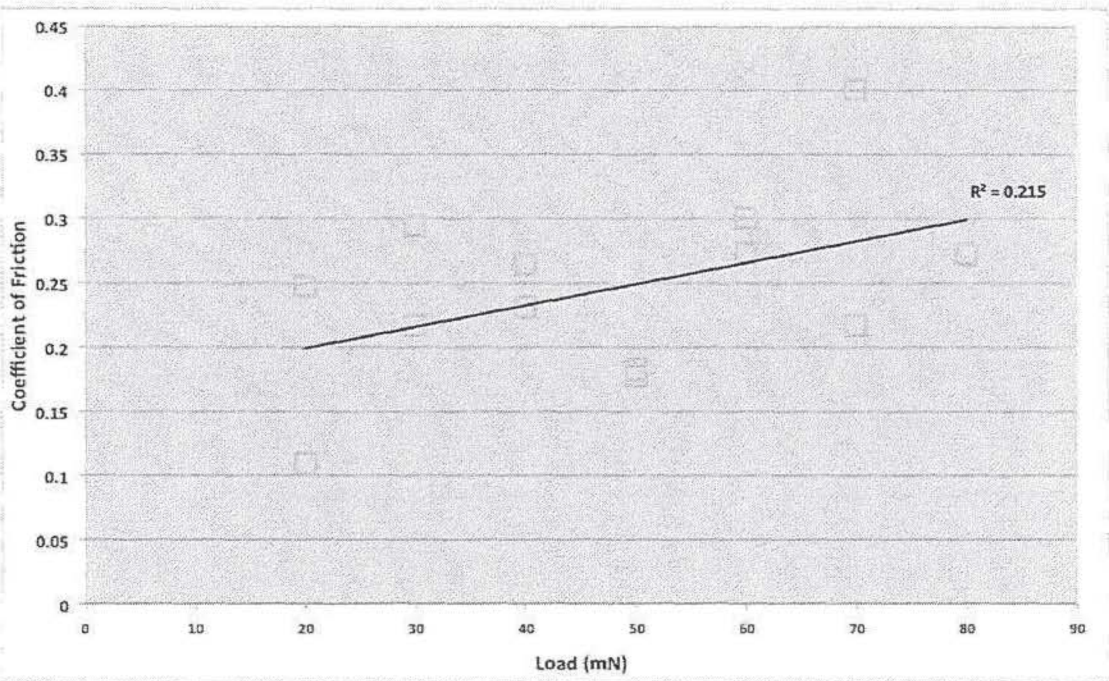


Figure 4.6: X-Y Scatter Graph Showing the Effect of Load on the Mean Coefficient of Friction for Focus® Night & Day™.

Figure 4.6 shows the results from varying the load on a high modulus contact lens - Focus® Night & Day™. The X-Y scatter graph shows there is a slight trend for the coefficient of friction to rise as the load is increased but the R^2 value for this is 0.215, which suggests that this is not an actual trend to predict load versus coefficient of friction.

The results from varying the load with Focus® Night & Day™ showed there was not a trend for a high modulus contact lens. Focus® DAILIES® is a lower modulus lens, the lens was tested with varying loads ranging from 10 to 70 mN with 10 mN increment steps.

Figure 4.7 shows the mean coefficients of friction obtained from the Focus® DAILIES® lenses with varied load. There looks to be a trend that the coefficient of friction decreases as the load increases. This was further investigated by plotting the means in an X – Y scatter graph and adding a trend line.

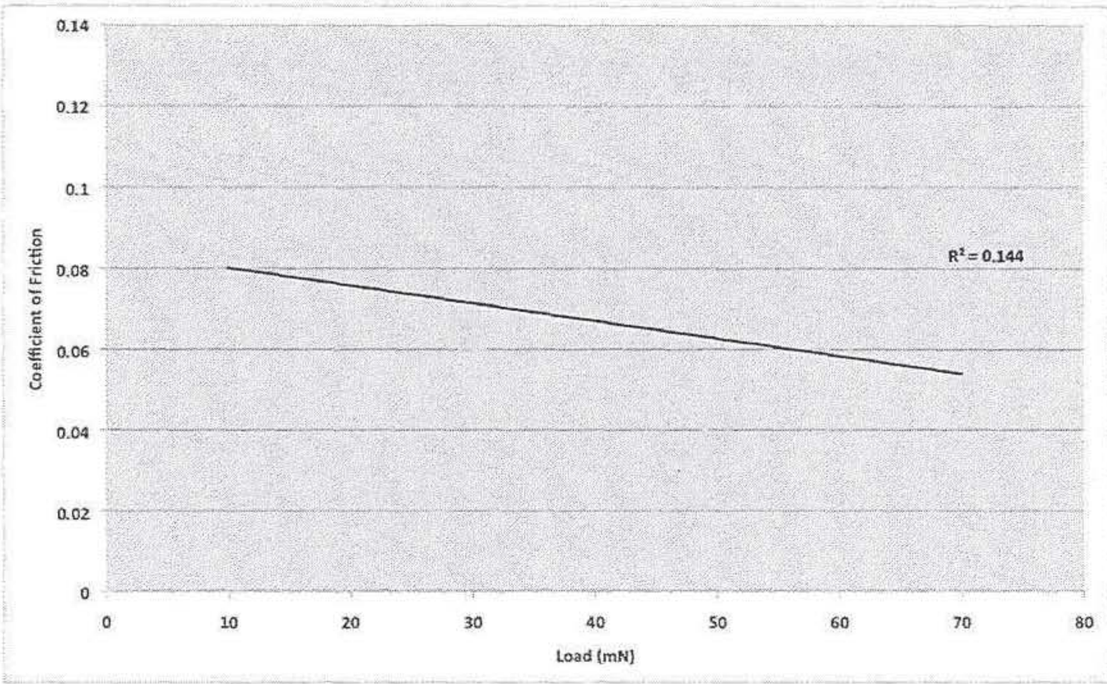


Figure 4.7: X-Y Scatter Graph Showing the Effect of Load on the Mean Coefficient of Friction for Focus® Night & Day™.

Figure 4.7 shows the X – Y scatter graph with varying loads applied to Focus® DAILIES® contact lenses at a constant speed of 30 mm/min on a PET substrate. The trend line shows a slight decrease in coefficient of friction with increasing load. However, the R^2 value is 0.144, which suggests this is not a true trend.

The results of varying load with both Focus® Night & Day™ and Focus® DAILIES® show that there is no trend in the coefficient of friction when varying the load. This agrees with the basic friction equation and work reported with other materials.

4.3.2: The Effect of Speed on the Coefficient of friction

Speed at which the lens is moved across the substrate is one of the main variables that can be easily altered with this technique. The range of speeds that can be used ranges from 5 mm/min to 550 mm/min; the only consideration needed is that the length of the track made by the lens is usually set to 20 mm.

The third law of friction is sometimes stated that friction is independent of the speed of the system. This suggests that the speed at which the substrate is moved pass the lens will have not have an effect on the coefficient of friction obtained.

To study the effect of speed on the coefficient of friction of contact lenses using a nano-scratch tester, a range of different speeds were used. The speeds used were from 5 mm/min to 300 mm/min, the lens used was Focus® Night & Day™ with a load applied of 40 mN on the standard melinex® substrate.

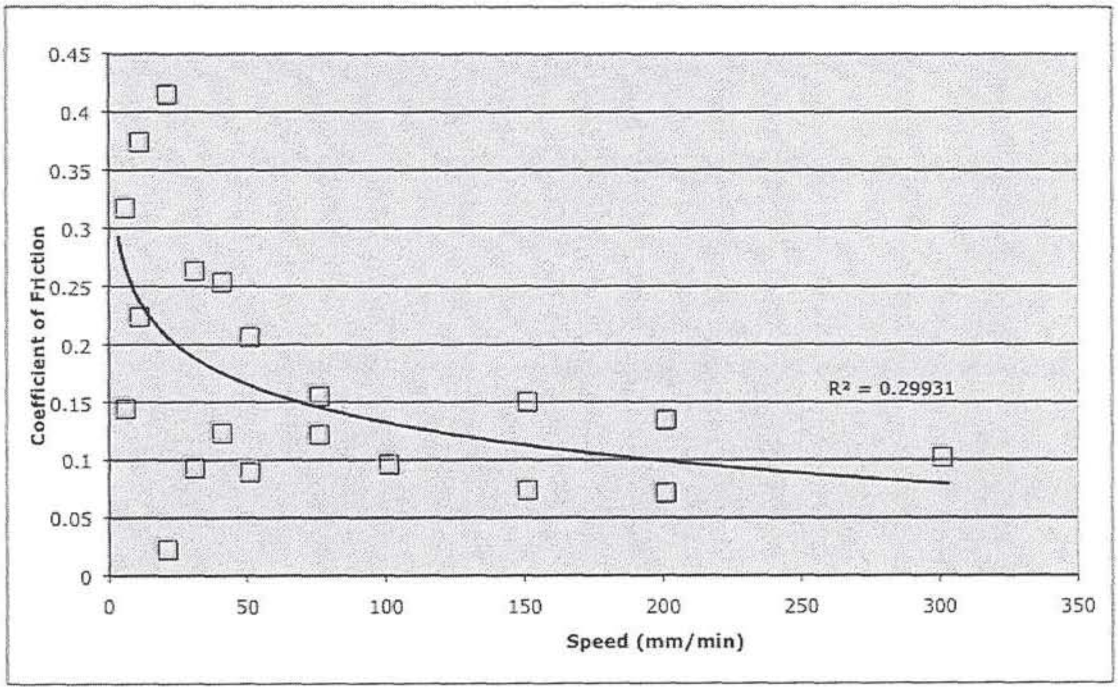


Figure 4.8: X-Y Scatter Graph Showing the Effect of Speed on the Mean Coefficient of Friction for Focus® Night & Day™.

The trend-line in the above figure shows that there is a slight trend for the coefficient of friction to decrease as the speed of the substrate increases. This is the same trend as seen in the study of the kinetic friction of ice by Evans in 1976 (Evans., 1976).

The results in figure 4.9 show the coefficient of friction with differing speeds at three different loads, with Focus® Night & Day™ as the test contact lens.

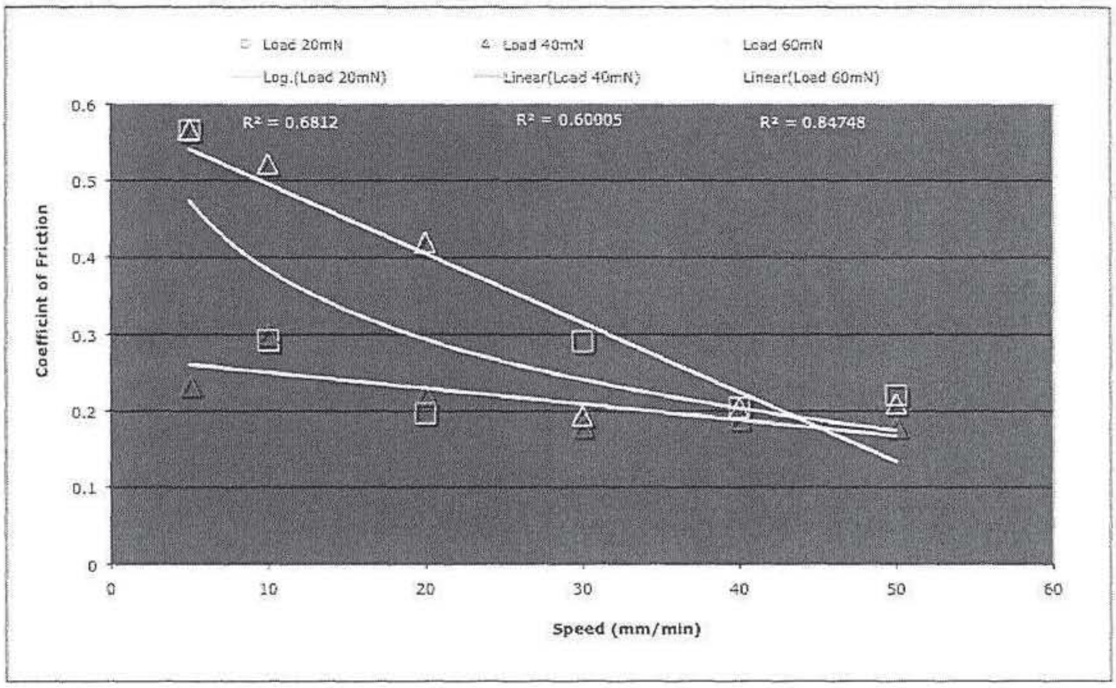


Figure 4.9: X-Y Scatter Graph Showing the Effect of Speed on the Mean Coefficient of Friction For Focus® Night & Day™ at Three Different Loads

Figure 4.9 shows again a general trend of the coefficient of friction decreasing with an increase in the speed the substrate is moved. Results show that all the three loads having similar trends. The coefficients of friction falls as the speed is increased.

4.3.3: The Effect of the Substrate on the Coefficient of Friction

When starting the friction work the first choice made was what substrate to run the samples on. The classic choices are glass or steel, however, the problem with this is they require cleaning after every use. An alterative substrate was looked at in the form of a polymeric sheet. The body does not like high surface energy species, and modifies any that come into contact with biological sites, such as contact lenses that are coated with proteins and lipids. A thin polyethylene terephthalate (PET) sheet was chosen as the standard substrate. The sheet has a medium surface energy, unlike the high surface energy substrates such as glass and metals. The PET sheets were bought in large quantities with the trade name of Melinex®; these polymeric sheets gave good reproducible results as seen earlier in this chapter.

Another polymeric substrate was investigated, to use as an extra tool in the studying of the differences between different contact lenses. The other polymeric substrate used was a polyurethane adhesive sheet; this sheet was layered over the PET sheet. The bar chart below shows the mean coefficient of friction with two different contact lenses (Focus® Night & Day™ and Acuvue® Advance™) on the two different substrates.

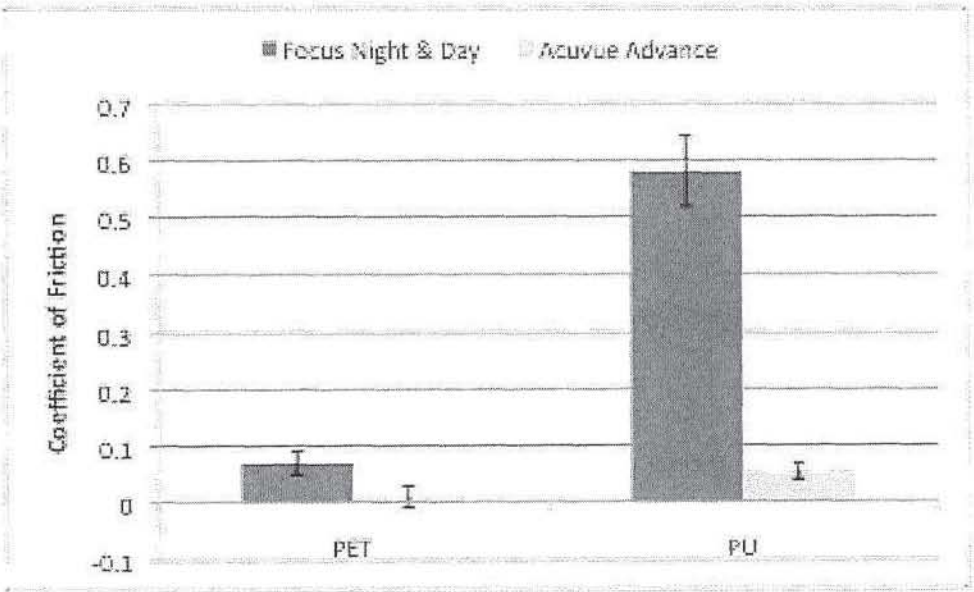


Figure 4.10: Bar Chart Showing the Effect Two Different Substrates on the Mean Coefficient of Friction.

Bar chart in figure 4.10 shows the results from two different contact lenses using two different substrates. The substrate labeled 'PET' is the standard substrate (Melinex®) and the substrate labeled 'PU' is a polyurethane adhesive sheet fixed onto the standard PET sheet. PU substrate gave the same trends as the PET substrate with regards which lens had the higher mean coefficient of friction. However, the mean coefficients of friction with PU as the substrate, are much higher than those obtained with PET. This has the effect of exaggerating any differences between different contact lenses.

4.3.4: The Quantity of Lubricant

The previous results in this chapter have used 100 μl as the standard amount of lubricant for all the friction results obtained. The purpose of the following study was to investigate if smaller volumes of lubricant could be used, but still maintain the lens in the hydrodynamic lubrication regime. The idea of using smaller amount of lubricant would allow for biological fluids to be used such as tears.

The amount of lubricant that can be used for the measurement for the coefficient of friction of a contact lens was measured by running Acuvue® Advance™ with different volumes of lubricant, keeping the other conditions the same (Load, Speed, and Substrate). The following bar chart shows the results obtained.

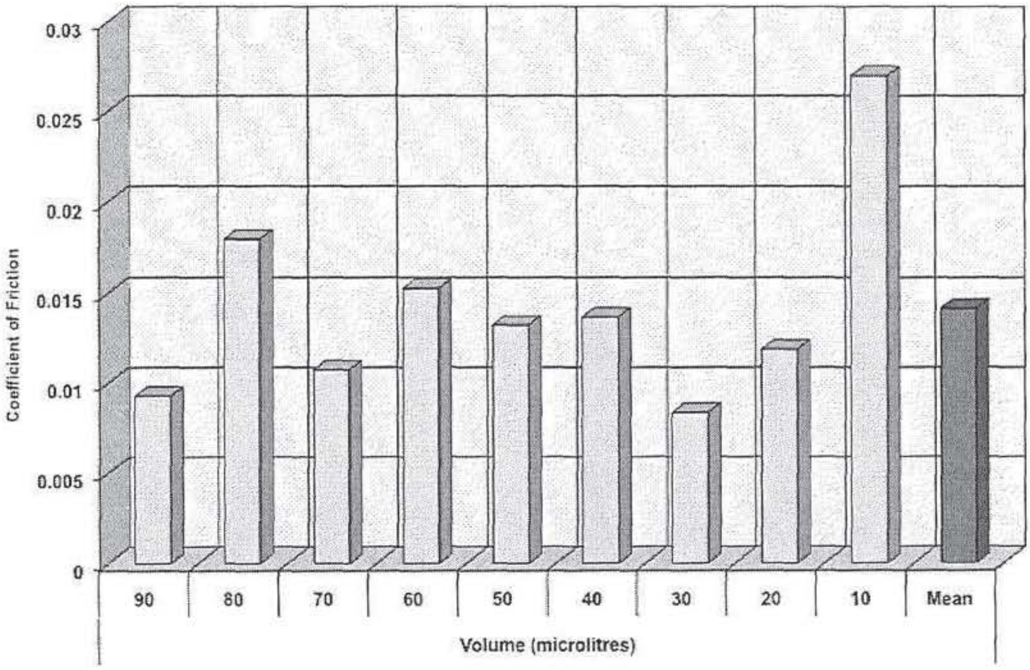


Figure 4.11: Bar Chart Showing the Effect of Different Amounts of Lubricant on the Mean Coefficient of Friction.

From the results in the figure 4.11 the amount of lubricant used with this lens did not have a large effect on the coefficients of friction acquired down to 20 μl. Which will allow future experiments to be undertaken that use tears, taken from the eye as the lubricant.

4.4: Detailed Characteristics of Contact Lenses using the Developed Tribology Technique

It is important to be able to distinguish between contact lenses with very low coefficients of friction. The old friction setup of the biomaterials research unit was unable to distinguish the differences of lenses with coefficients of friction below 0.1μ. The old friction instrument only had a very basic data handling system so obtaining a large number of coefficients of friction in a short space of time was very difficult.

The tribometer developed in this chapter is able to measure the coefficient of friction at 1000 data points across the set distance that the friction table moves. This, coupled with the ability to measure the coefficient of friction accurately and reproducibly at very low values of friction, has enabled the development of more in depth studies of lens / lubricant systems.

The next section will describe three different techniques that aim to probe the surfaces of contact lenses and contact lens systems (packing solution, comfort drops, or MPS). The three techniques are:

- Comparing the mean coefficients of friction
- The friction profile given by the tribometer
- The difference in coefficient of friction in the presence of a 'good' and in a 'poor' lubricant

4.4.1: The Mean Coefficient of Friction

The easiest technique to distinguish the differences in friction between different contact lenses is to measure the mean coefficients of friction. The mean coefficient of friction is calculated, in this case, by ignoring the first two runs of the 10 total passes. The remaining eight runs are averaged to give the mean coefficient of friction. The reason for not including the first two runs is that if there is any inconsistency it comes in the first and second 20 mm passes of the substrate.

Figure 4.12 is an example of the mean coefficient of friction for two different contact lenses run under the same conditions (Load, Speed, Substrate, & Lubricant).

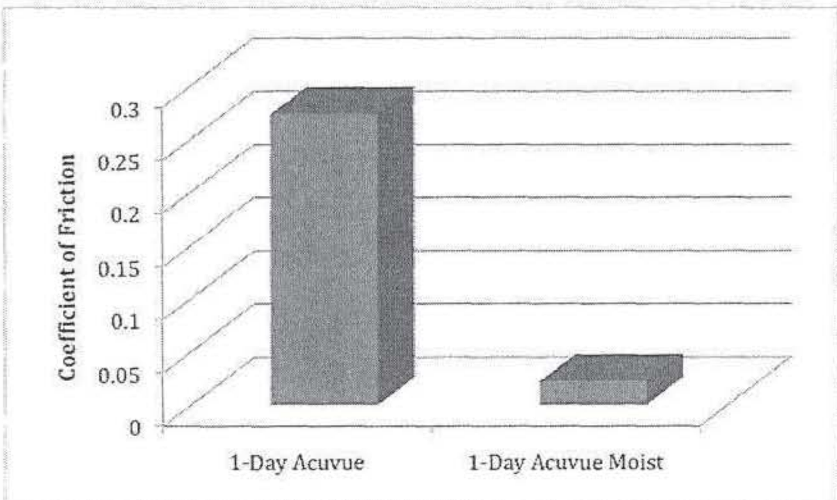


Figure 4.12: An Example Bar Chart Showing the Mean Coefficient of Friction Between the Packing Solutions of the Two Different Lenses

Figure 4.12 shows that by using the mean coefficient of friction differences in the coefficient of friction can be seen. However, the mean coefficient of friction does not give all the information about the lens frictional properties or all differences between lenses.

4.4.2: The Coefficient of Friction Profile

The previous section showed one way of differentiating between contact lenses of different types, this section describes another way. When the lens is run on the tribometer the friction force is measured at 1000 points across the distance (usually 20 mm) that the substrate is moved. In the friction equation (Equation 4.1) the friction force is the main force that the coefficient of friction is derived from. Therefore, it is possible to track changes in the coefficient of friction over the distance the substrate is moved. Figure 4.13 shows the friction profiles of two different contact lenses (Focus® Monthly and Proclear™).

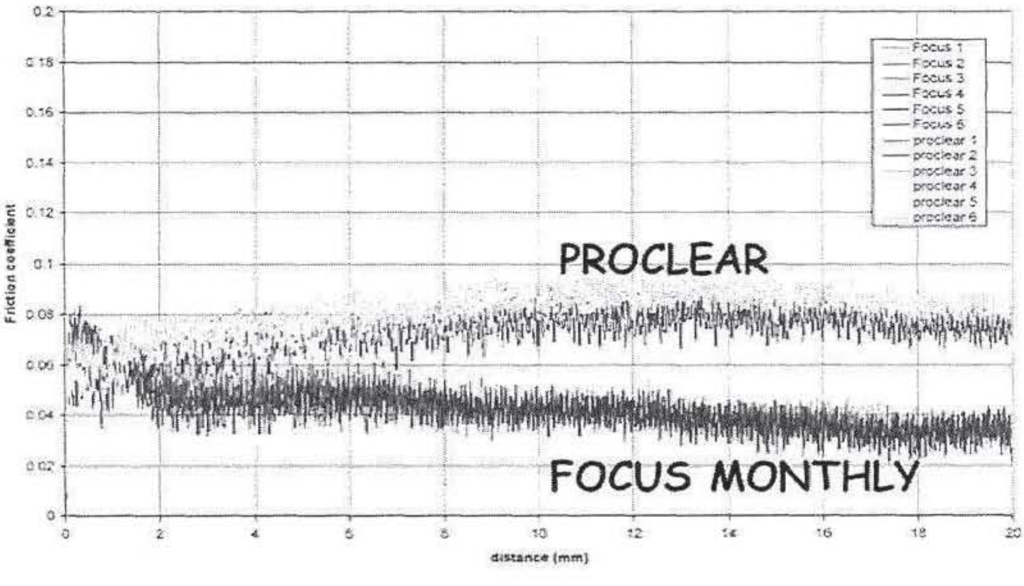


Figure 4.13: A Graph Showing the Differences in the Friction Profiles Between Proclear™ and Focus® Monthly.

The graph in figure 4.13 shows the friction profiles of Bausch & Lombs Proclear™ lens against CIBA Visions Focus® Monthly lens. These results clearly show a difference in the coefficient of friction at the end of each pass, there is also a difference in the behaviour of the lenses over the course of the distance traveled. The two lenses have very similar start up friction profiles although the friction profiles are different with Proclear™ moving low to high and Focus® Monthly moving high to low. The lenses also have different trends in the dynamic region of the friction profile with Focus® Monthly showing a decreasing coefficient of friction as the lens moves across the substrate and Proclear™ shows that the coefficient of friction increases for the first half of the distance traveled before leveling off.

Friction profiles can give a lot of information about the lens surface; chapter 5 of this thesis uses some of the information interpreted from the friction profiles to understand the mechanisms of enhancement that is occurring in the daily disposable contact lenses.

4.4.3: The Effect of Different Lubricants

Another useful experimental technique that has been termed "solution hysteresis" was developed for investigating the friction differences in contact lenses. The technique investigates the ability of the lens to maintain a low coefficient of friction under different lubrication conditions. Solution hysteresis in this case is described as the difference in coefficient of friction between a 'good' lubricant and a 'poor' lubricant.

Figure 4.14 shows an example of solution hysteresis using two different contact lenses, a daily disposable contact lens (CIBA Vision's Focus® DAILIES®) and a silicone hydrogel (CIBA Vision's Focus® Night & Day). The two lubricants used were; an ophthalmic solution and HPLC water. The ophthalmic solution was Novartis HypoTears™ and was defined as the 'good' lubricant; the HPLC water was defined as a 'poor' lubricant for this experiment.

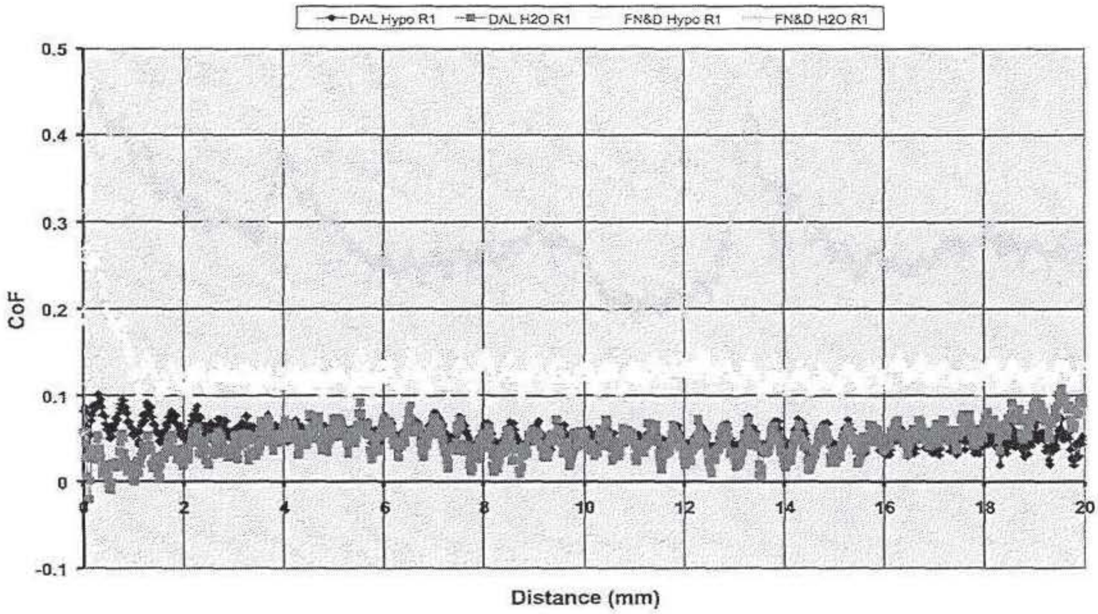


Figure 4.14: Graph Showing the Effect of Different Lubricants on Two Different Contact Lenses: Focus® DAILIES® & Focus® Night & Day™.

The graph in figure 4.14 shows the results for the solution hysteresis, the effect of what was labeled a 'good' and 'poor' lubricant for the focus® DAILIES® lenses had very little impact on the coefficient of friction (although the coefficient of friction does slightly increase). The results for the Focus® Night & Day™ lenses however showed very different behaviour in the two lubricants, having a low consistent coefficient of friction in the good lubricant (HypoTears™) and having a higher more inconsistent coefficient of friction in the poorer lubricant (HPLC Water).

This is a useful investigative tool when the coefficients of friction are the same in a chosen lubricant. A different lubricant can be selected that will 'challenge' the contact lenses to maintain a low coefficient of friction.

4.5: Discussion

This chapter focuses on the testing and development of a novel technique for measuring the coefficient of friction of contact lenses. The first section assessed the accuracy and reproducibility of the nano-scratch tester. This was evaluated by measuring twenty five mean friction coefficients using the same type of contact lens and comparing the results obtained. The contact lens chosen was CIBA Visions Focus® DAILIES®, this gave a mean coefficient of friction of 0.026μ to three decimal places with a standard deviation of 0.010. Range of the results was 0.037μ with a minimum of 0.010μ and maximum of 0.047μ. Therefore, the results obtained confirmed the tribometer was a reliable and accurate analytical tool.

The nano-scratch tester has the ability for numerous test conditions to be varied in order to study in more detail the friction properties of the lens. Conditions that can be easily altered are as follows:

- **The Load** – The load applied vertically down though the contact lenses onto the substrate, a vital component in the equation of the coefficient of friction.

- **The Speed** – The speed at which the friction table (and therefore the substrate) is moved across the contact lens.

- **The Substrate** – The material that the contact lens coefficient of friction is measured against.

- **The Lubricant** – The lubricant used to help reduce the measured coefficient of friction, this can be altered in both type and quantity.

All of the above variables mentioned were studied, the first variable analysed was the load applied to the contact lens. The tribometer has a load range of 5 to 120 mN, the range of loads used when the studying the load was 10 to 80 mN. The decision was made to use two different contact lens types, with varying surface and mechanical properties. Focus® Night & Day™ was the first lens studied which is a silicone hydrogel contact lens, with a plasma coating, which presents a relatively hard surface. The modulus of Focus® Night & Day™ (FN&D) is 1.4 MPa which makes it the stiffest of any commercially available contact lens. Second lens used to study the load was Focus® DAILIES® which is a soft conventional contact lenses used under a daily disposable wear modality. This lens gives a very low coefficient of friction and has lower modulus than FN&D. Results obtained were measured by calculating the mean friction coefficients, while changing the load in 10 mN steps from 10 to 80 mN. Results showed that there were no trends in the coefficient of friction for both of the contact lenses. This would be expected, as the load is part of the equation for the coefficient of friction.

Speed of the friction table is moved across the contact lens was the next variable studied. The third law of friction is sometimes quoted, as friction is independent of the speed used. Speed has been shown to influence the measured coefficient of friction in other tribological systems such as metals sliding on ice (Evans., 1976). Focus® Night & Day™ was the contact lens used to measure of the effect of speed on the friction coefficient of contact lenses, The tribometer can move the table at speeds ranging from 5 to 550 mm/min. For the study of the speed the range used was from 5 to 300 mm/min. Results obtained showed that as the speed of the table increases the measured coefficient of friction decreases, which is inline with the results obtained from metals sliding on ice.

Choice of substrate is key in measuring the coefficient of friction. The decision was taken to use a substrate that did not require any cleaning, and was of good quality with a reproducible surface. The substrate chosen was a high quality thin sheet of polyethylene terephthalate (PET) with the trade name Melinex®. Another polymeric substrate was investigated, to use as an extra tool in the study of differences between contact lenses. Another polymeric substrate used was a polyurethane (PU) adhesive sheet; this sheet was layered over the PET sheet. Results of the mean coefficient of friction obtained by the PU sheet were that the trends in the coefficient of friction were the same i.e. the order of the friction coefficient of different lenses. However, the coefficient of frictions obtained exaggerated any differences in the mean values of friction.

The last variable to be investigated was the quantity of lubricant that could be used to obtain a consistent friction coefficient. This was investigated, as natural biological fluids are small in quantity and difficult to obtain. Therefore, if a small amount of lubricant was could be used to obtain a coefficient of friction, tears could be used as the lubricant. The results attained showed that is was possible to use quantities of lubricant as low as 20 μl and not greatly increase the mean coefficient of friction of the contact lens.

The last section of this chapter investigated the ability to study the detailed frictional properties of the contact lenses, in particular possible ways on exaggerating and searching for differences in the friction behaviour. Three different techniques were studied with the aim of probing the surface of contact lenses and contact lens systems (packing solution, comfort drops, or MPS). The three techniques studied were:

- Comparing the mean coefficients of friction
- The friction profile given by the tribometer
- The difference in coefficient of friction in a 'good' and 'poor' lubricant

Results obtained from each of the three techniques stated above allowed differences in friction behaviour of different contact lenses to be studied and compared. The mean coefficient of friction outlines differences between contact lenses, however, the whole story of the lenses friction is sometimes masked such as the lenses friction may de- or increasing on progressive passes of the substrate, or the lens may have a high static coefficient of friction.

The results from this chapter only show a small percentage of the possible capacity of the nano-scratch tester.

Chapter 5

Application of the Tribology Technique: Daily Disposable Contact Lenses

5.1: Introduction

Since daily disposable soft contact lenses were first launched in the USA in 1994 (Nilsson S., 1997), the simplicity, convenience and clinical benefits of this wear modality have demonstrated great acceptance with patients and practitioners alike. The daily disposable contact lenses market now makes up over one third (40% - 2007 Morgan et al., 2007) of contact lenses sold today in the United Kingdom, which has increased year on year from only a small market share of around 28% of soft lenses fitting in 1998 (Morgan et al., 2006).

The last few years have seen a new direction in the design of daily disposable contact lens materials. Since their launch, the available lenses have remained fairly constant, with very little change in the products being offered by the major contact lens manufactures; Bausch & Lomb, CIBA Vision, and Johnson & Johnson Vision Care.

This new direction was driven by the necessity to overcome the main reason of contact lens discontinuation, the comfort of the lens during wear. The major complaint is the lens feeling dry and uncomfortable towards the end of the day (Nichols et al., 2005, Fonn., 2007).

With the release of the CIBA Visions, 'Focus® DAILIES® AQUA Release' in 2006, CIBA vision started the ball rolling of improving the comfort of the lens whilst maintaining the key element of daily disposable contact lens production; the preservation of low cost. Chapter 3 described the way in which the first of the new breed of daily disposable lenses was improved. This improvement came from the release of a hydrophilic polymer from the lens matrix though the surface of the lens during the day.

In the 18 months after the launch of the CIBA material the other two leading daily disposable lens manufacturers, (Johnson & Johnson Vision Care and Bausch & Lomb) responded by releasing new versions of their daily disposable contact lenses.

In 2006, Johnson & Johnson Vision Care released a new version of their 1-Day Acuvue® lens, the new version has the trade name 1-Day Acuvue® Moist™ which still uses etafilcon A as the base for the matrix but with Lacreon technology.

The Lacreon technology is discussed in greater detail in section 5.3 of this chapter, although a clue is the packing solution of 1-Day Acuvue® Moist™ contains 1% Povidone.

The Bausch & Lomb new daily disposable lens is a slight break from the trend previously seen, as the new version of the lens uses a different bulk lens material. The original Bausch & Lomb (B&L) daily disposable Soflens® One Day had the base material of Hilafilcon A whereas, the new version Soflens® Daily Disposable is comprised from the bulk material Hilafilcon B. Hilafilcon B was the basis of another B&L contact lens; Soflens 59, which is a two weekly replacement lens. The other difference from the previous version of the lens is that the packing solution contains a poloxamine.

The last daily disposable lens discussed here is the second lens to appear from CIBA Vision. Their first modified lens had extra soluble PVA added into the lens matrix, when it was found that the original lenses eluted PVA from the lens and when this effect depleted the lens became less comfortable. CIBA Visions newest lens has not only free PVA, but also polyethylene glycol (PEG) in the lens matrix.

Table 5.1 shows the manufacturer, the brand names, the trade name and the United States adopted name (USAN) for the daily disposable contact lenses discussed in this chapter.

Manufacturer	Brand Name	Lens Trade Names (USAN Names)
Bausch & Lomb	Soflens®	Soflens® One day (Hilafilcon A) Soflens® Daily Disposable (Hilafilcon B)
CIBA Vision	Focus® DAILIES®	Focus® DAILIES® Focus® DAILIES® All Day Comfort* Focus® DAILIES® Aqua Comfort Plus™ (All Nelfilcon A)
Johnson & Johnson Vision Care (Vistakon US)	1-Day Acuvue®	1-Day Acuvue® 1-Day Acuvue® Moist™ (All Etafilcon A)

Table 5.1: Information on the Leading Daily Disposable Contact Lenses.

5.1.1: Aim

This chapter uses the tribology technique described in chapter 4 along with various other techniques to study the mechanisms of lubrication of daily disposable contact lenses. The way in which the lenses have been modified was investigated by analysing the coefficient of friction of lenses, pre and post modification.

5.2: CIBA Visions Focus® DAILIES® Daily Disposable contact lenses

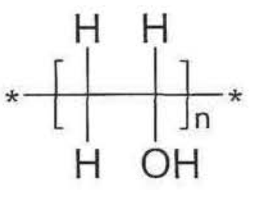
CIBA Visions material Focus® DAILIES® uses Nelfilcon A as the lens polymer which is a modified PVA structure. Newer versions of DAILIES® also use Nelfilcon A as the lens polymer but with extra additives. Additives for the updated versions to the lens matrix are shown in table 5.2.

Lens Trade Name	Polymeric additive
Focus® DAILIES® Basic	None
Focus® DAILIES® All Day Comfort	Soluble PVA
Focus® DAILIES® Aqua Comfort Plus™	Soluble PVA, PEG

Table 5.2: The trade name and polymeric additive of the Focus® DAILIES® Band.

The packing solution for all the Focus® DAILIES® lenses now contains a poloxamer, this will be discussed later on.

Focus® DAILIES® All Day Comfort uses soluble polyvinyl alcohol as the added hydrophilic polymer. Polyvinyl alcohol is a hydrophilic polymer that is used in various ophthalmic applications such as artificial tears and comfort drops. The structure of PVA is show in the figure below.

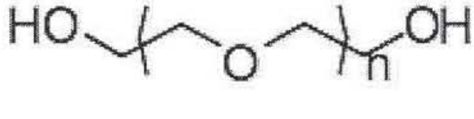


Polyvinyl Alcohol

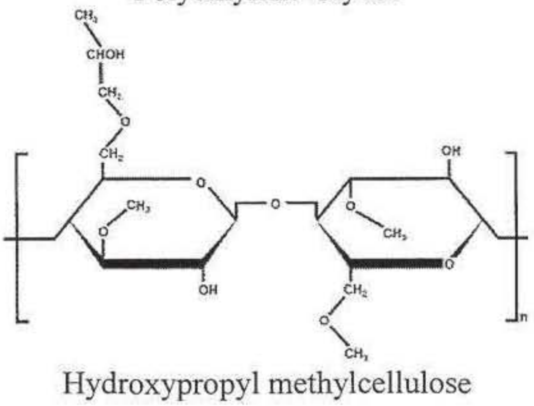
Figure 5.1: The structure of Polyvinyl Alcohol

Focus® DAILIES® Aqua Comfort Plus™ also uses soluble PVA but with an additional soluble linear polymer in the lens matrix, this extra polymer is polyethylene glycol (PEG). PEG is used as a lubricant in artificial tears and comfort drops; in particular HypoTears™, which is a dry eye drop that uses 1% PEG, 1% PVA as the lubricating ingredients, HypoTears™ is produced by Novartis the parent company of CIBA Vision.

The packing solution for Focus® DAILIES® Aqua Comfort Plus™ is different from the other versions of DAILIES. The packing solution contains 0.05% poloxamer instead of only 0.02% and the packing solution also contains PEG. The poloxamer used is hydroxypropyl methylcellulose (HPMC). HPMC has also been used in ophthalmic solutions such as multi purpose solutions from Advance Medical Optic (AMO). Figure 5.2 shows the structures of these polymers.



Polyethylene Glycol



Hydroxypropyl methylcellulose

Figure 5.2: The structures of Polyethylene Glycol and Hydroxypropyl methylcellulose.

5.2.1: Focus® DAILIES® Contact lenses Lens Friction Traces

This section focuses on the friction profiles of the original DAILIES® lenses and the DAILIES® lenses with the added 2% soluble PVA.

A Focus® DAILIES® Basic (original Focus® DAILIES®) had its coefficient of friction tested and compared with a Focus® DAILIES® Aqua Release (name at test date, although now renamed to All Day Comfort). The friction test was run under the following tribometer conditions; Substrate - Melinex®, Load – 30 mN, Speed – 5 mm/min, and the lubricant used was the artificial tear, HypoTears™ (100 μl).

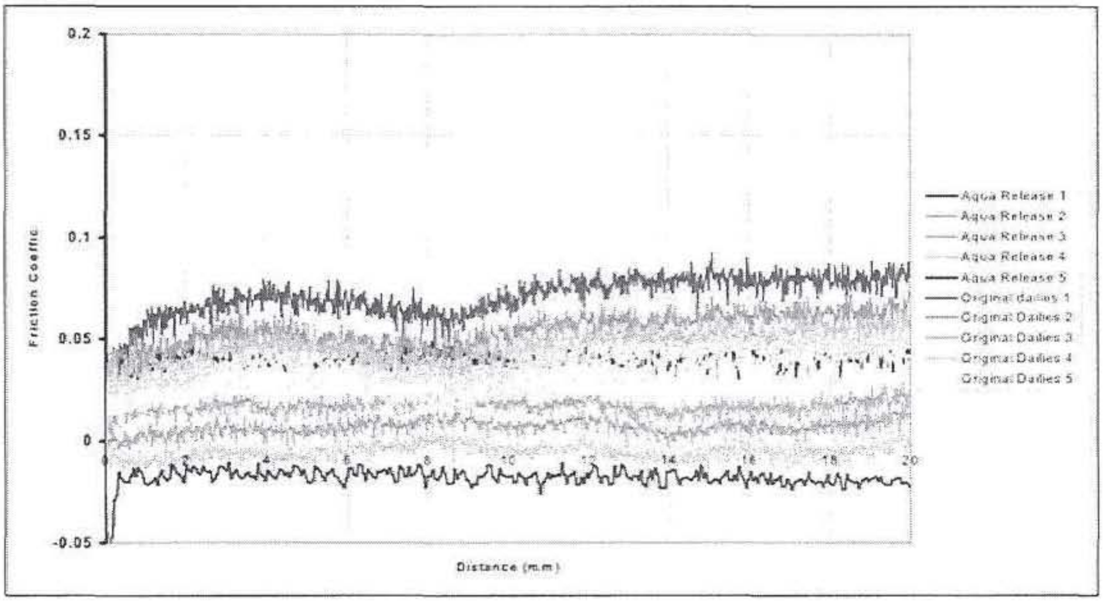


Figure 5.3: Friction Profiles of Focus® DAILIES® Basic and Focus® DAILIES® All Day Comfort.

The figure 5.3 shows that the new lens Focus® DAILIES® All Day Comfort had a lower coefficient of friction than the old Focus® DAILIES® Basic. The friction profiles of the two lenses are very similar; this is because the modification of Focus® DAILIES® All Day Comfort is an addition of the existing effect of PVA being released from the lens matrix. The modified lens has 2% extra uncross-linked PVA that allows the lens to release more PVA, for a longer period of time, this resulted in more soluble PVA being released.

5.2.2: Mean Coefficients of Friction

The previous section compares the coefficient of friction for the first two types of Focus® DAILIES® contact lenses. Original and Focus® DAILIES® All Day Comfort, which is very similar to the original in the constituents, with the difference being Focus® DAILIES® All Day Comfort has more soluble PVA in the lens matrix. There is, however, now a third member of the Focus® DAILIES® brand, named Focus® DAILIES® Aqua Comfort Plus™ which is still the same bulk material Nelfilcon A and also the same water content of 69%, but now contains polyethylene glycol (PEG).

The mean coefficient of friction was measured by taking the average of the last seven passes over the whole 20 mm run distance then the coefficient of friction at every point along the 20 mm distance was averaged to obtain a single value for the coefficient of friction.

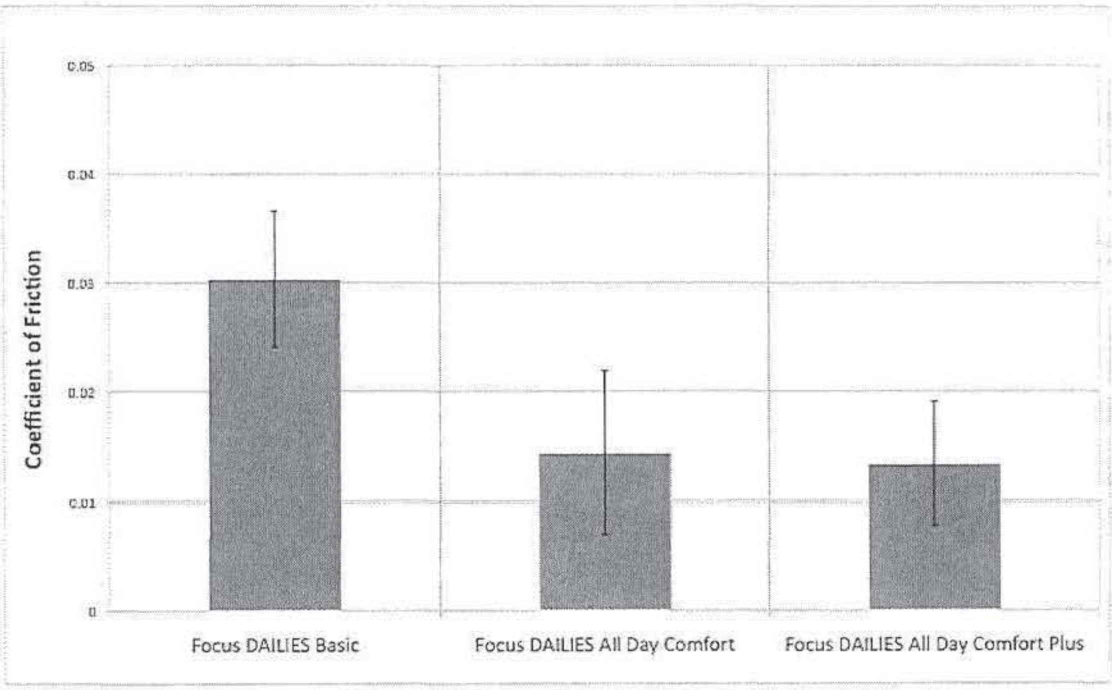


Figure 5.4: Mean Coefficient of Friction for the Focus® DAILIES® Branded Contact Lenses in HypoTears™.

Figure 5.4 shows the average coefficient of friction for the three lenses, Focus® DAILIES® Basic had the highest coefficient of friction of the three lenses with Focus® DAILIES® All Day Comfort and Focus® DAILIES® Aqua Comfort Plus™ having a very similar friction value, although the newer lens Focus® DAILIES® Aqua Comfort Plus™ value is slightly lower.

5.2.3: Packing solution – friction

The solution, in which a contact lens is stored before use, is called the packing solution and is of great importance in providing the contact lens, initial comfort and can also help to provide better initial wettability.

The coefficient of friction of the packing solutions of the Focus® DAILIES® branded contact lenses were measured using 100 µl of the packing solution as the lubricant. A standard lens was used for all three of the different types of DAILES® lenses. The conditions used on the tribometer were speed – 30 mm/min, load – 30 mN, substrate - Melinex®, Lens – AIR OPTIX™.

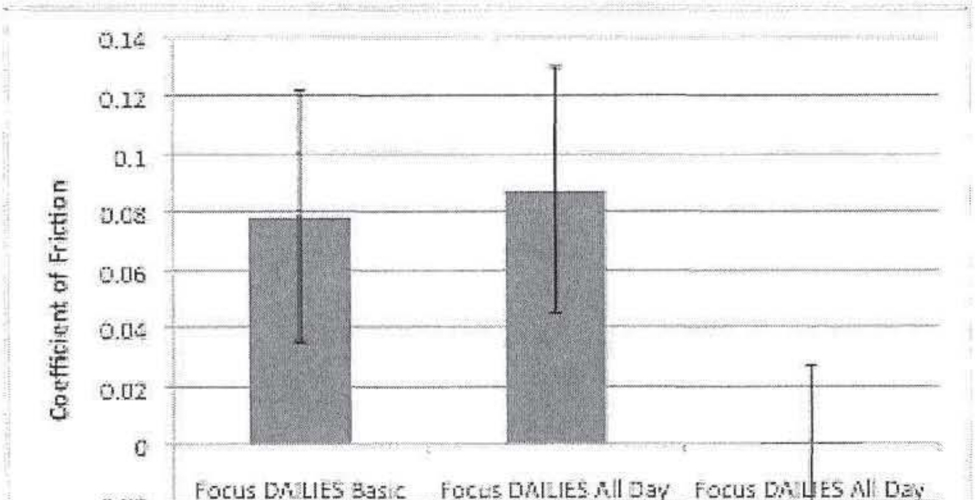


Figure 5.5: Mean Coefficient of Friction for the Packing Solutions for the Focus® DAILIES® Branded Lenses.

The results from figure 5.5 show that the coefficients of friction for the Focus® DAILIES® Basic and Focus® DAILIES® All Day Comfort were very similar. Whereas, Focus® DAILIES® Aqua Comfort Plus™ had a very much lower coefficient of friction. The differences between the Focus® DAILIES® Aqua Comfort Plus™ (FDACP) packing solution and the other two lenses packing solution is that there is more poloxamer present; 0.05% compared to 0.02%. The FDACP lens also contains added polyethylene glycol in the lens matrix. Some of this PEG in the lens matrix will leach out into the packing solution in the same way as PVA leaches out of the lens. Thus, the packing solution for Focus® DAILIES® Aqua Comfort Plus™ contains PVA, PEG and poloaxamer.

5.2.4: The Friction Coefficient of Extracts of Focus® DAILIES®

There is an eye drop for dry eyes called HypoTears® which has 1 % Polyethylene glycol 400 (PEG) and 1 % Polyvinyl Alcohol (PVA) as lubricating ingredients. During our initial friction studies HypoTears™ was defined as our 'good' lubricant for the solution hysteresis studies. Since the newest DAILIES® lens also contains PEG and PVA. The in-eye mimic release model described in chapter 3 section 3.4 was used on a FDACP lens. A 100 µl extract was used as a lubricant with CIBA Visions AIR OPTIX™ contact lens. The friction of this extraction was compared to the extraction media (CIBA Saline) and also HypoTears™.

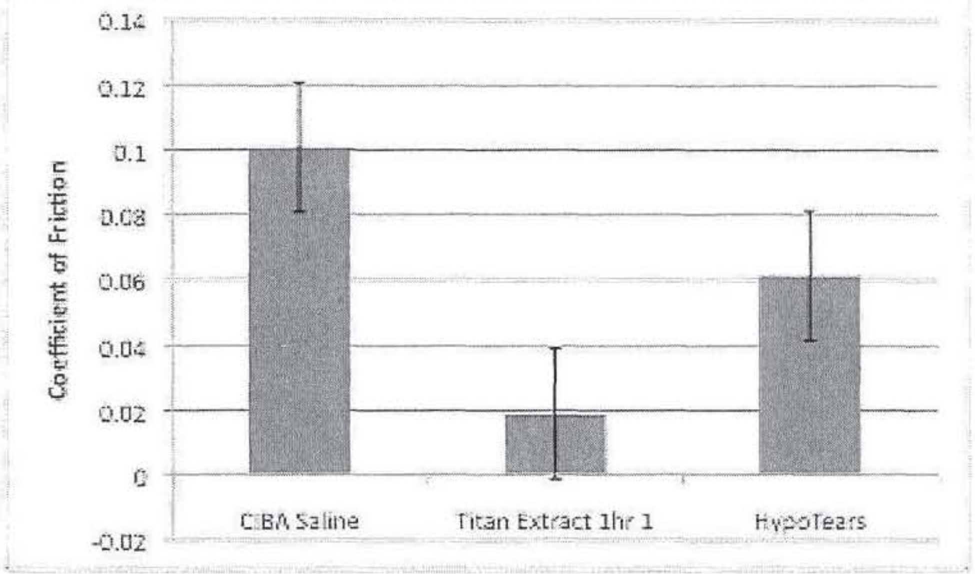


Figure 5.6: Mean Coefficient of Friction for the various lubricants with AIR OPTIX™.

Figure 5.6 shows the mean coefficients of friction calculated using the method described in section 4.3. Results show that the bar labeled Titan (FDACP) Extract 1hr, had the lowest coefficient of friction when compared to CIBA saline and HypoTears™. Since the only difference between the extract and CIBA saline (which is the control) is that the extract has been exposed to a FDACP lens plus vortexing for 30 seconds directly after coming in contact with the lens.

Further examination of the differences between the extract of FDACP and HypoTears™ is interesting and unexpected. The main difference in the components of HypoTears™ that would alter the surface properties is the benzalkonium chloride, which is used as a preservative. Some HypoTears™ was obtained which did not contain benzalkonium chloride or any other preservative; this HypoTears™ was labelled unpreserved HypoTears™ for this experiment. The coefficient of friction was measured using AIR OPTIX™ as the contact lens and using the following tribometer conditions; Substrate – Melinex®, Speed – 30 mm/min Load – 30 mN.

Figure 5.7: Mean Coefficient of Friction for the various mixtures of HypoTears™ as a lubricant with AIR OPTIX™.

Figure 5.7 shows the mean coefficient of friction for HypoTears™ containing various amounts of preservative. The HypoTears™ that did not contain any benzalkonium chloride (BAK) had lower coefficients of friction, when compared to HypoTears™ that did contain BAK.

The fact that BAK increases the coefficient of friction with AIR OPTIX™ helps to explain the results in figure 5.6, with the extract giving a lower coefficient of friction than HypoTears™.

The next uncertainty was to see how long the effect of lowered extract friction lasted. The packing solution friction of both Focus® DAILIES® Basic and Focus® DAILIES® All Day Comfort is greater than the coefficient of friction of Focus® DAILIES® Aqua Comfort Plus™ see figure 5.5.

The release model that was used to obtain the 1-hour extract in figure 5.6 was carried out for five hours in total with 100µl of media used for each hour. The coefficient of friction was measured using the final extract (hour five) as a lubricant for AIR OPTIX™ this was compared to the pre extraction media (CIBA saline) and the extract from the first hour.

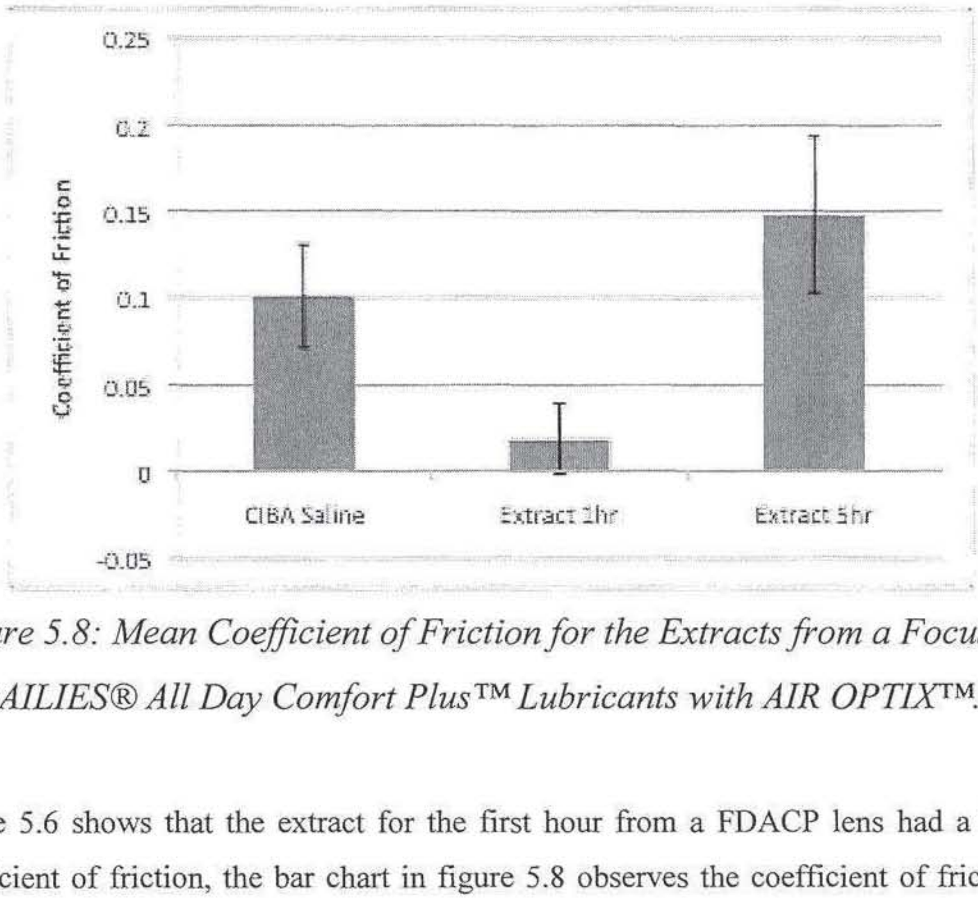


Figure 5.8: Mean Coefficient of Friction for the Extracts from a Focus® DAILIES® All Day Comfort Plus™ Lubricants with AIR OPTIX™.

Figure 5.6 shows that the extract for the first hour from a FDACP lens had a low coefficient of friction, the bar chart in figure 5.8 observes the coefficient of friction from the fifth hour extract. The fifth hour extract has a higher coefficient than the first hour extract. This suggests that the effect that is lowering the coefficient of friction in the first extract is no longer present.

5.3: Johnson and Johnson's Vision Cares 1-Day Acuvue® Daily Disposable Contact Lenses

The original 1-Day Acuvue® daily disposable was released in 1995, this lens has remained a popular choice of lens for millions of contact lenses wearers and is still many people's preferred lens even today 14 years after its launch. For more than 10 years 1-Day Acuvue® was the only daily disposable contact lenses manufactured by J & J Vision Care, however, this changed in 2006 with the launch of 1-Day Acuvue® Moist™. Patent and supporting literature at the time of release mentioned Lacreon technology as the method of modification. Since the only clue to the enhancement at the time of launch was that the packing solution of 1-Day Acuvue® Moist™ contains Povidone.

Povidone is another name for a hydrophilic polymer called poly (vinyl pyrrolidone) (PVP), which has been used in various ophthalmic applications. The structure of PVP is shown below.

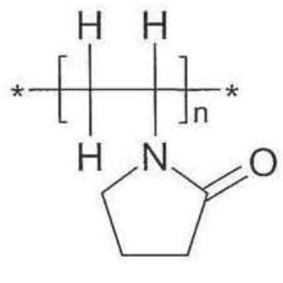


Figure 5.9: The structure of Polyvinyl Pyrrolidone

Results that follow in this section aim to investigate the way the PVP has been used in the enhancement of the lens. Since the friction of both the lenses and the packing solutions of both the original 1-Day Acuvue® and 1-Day Acuvue® Moist™ lens are measured and compared.

5.3.1: 1-Day Acuvue® Contact lenses Lens Friction Traces

The results that follow show the friction profiles of the 1-Day Acuvue® Brand lenses, the 1-Day Acuvue® lenses had their coefficient of friction profiles measured under the following tribometer conditions; Substrate - Melinex®, Load – 30 mN, Speed – 5 mm/min, Lubricant -HypoTears™.

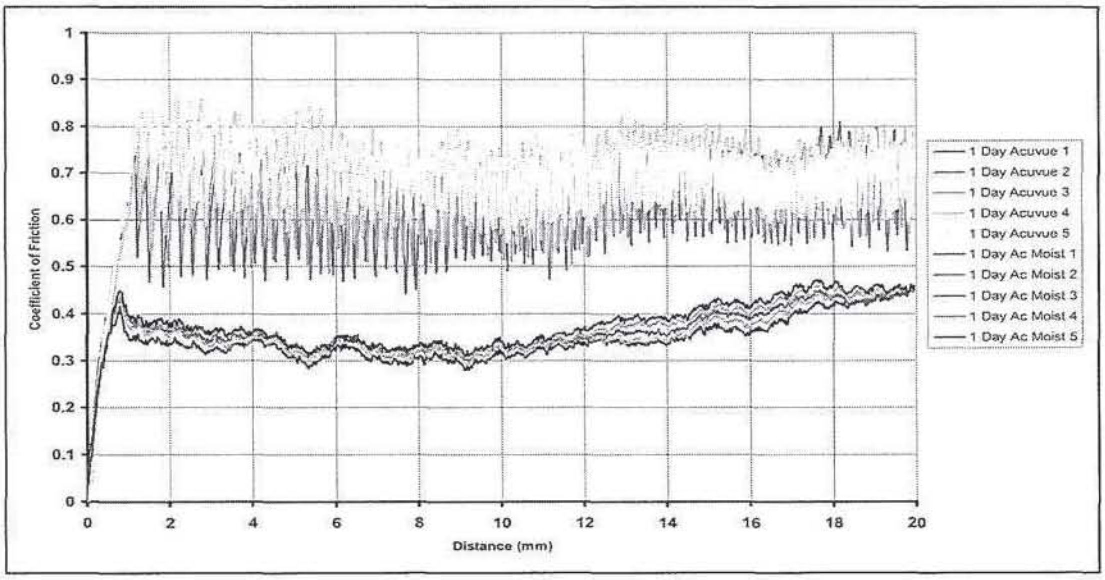


Figure 5.10: Friction Profiles of 1-Day Acuvue® and 1-Day Acuvue® Moist™.

Figure 5.10 shows the friction traces for 1-Day Acuvue® (reds and yellows) and 1-day Acuvue® Moist™ (blues and greens). 1-Day Acuvue® Moist™ (1DAM) has a lower coefficient of friction than 1-Day Acuvue® (1DA), also the nature of the friction for 1DAM is different. Since the 1DAM profile shows much less stick-slip behaviour than that of 1DA. The only difference between 1-Day Acuvue® and 1-Day Acuvue® Moist™ from what is written on the packaging or from the FDA website is that the packing solution now contains Povidone, or its more generally used name poly (vinyl pyrrolidone) (PVP).

5.3.2: Packing solution friction of 1-Day Acuvue®

The coefficient for friction of the packing solutions of the 1-Day Acuvue® branded contact lenses was measured using 100 µl of the packing solution as the lubricant with a standard lens for the two different types of 1-Day Acuvue® packing solutions. The conditions used on the tribometer were; Speed – 30 mm/min, Load – 30 mN, Substrate - Melinex®, Lens – AIR OPTIX™.

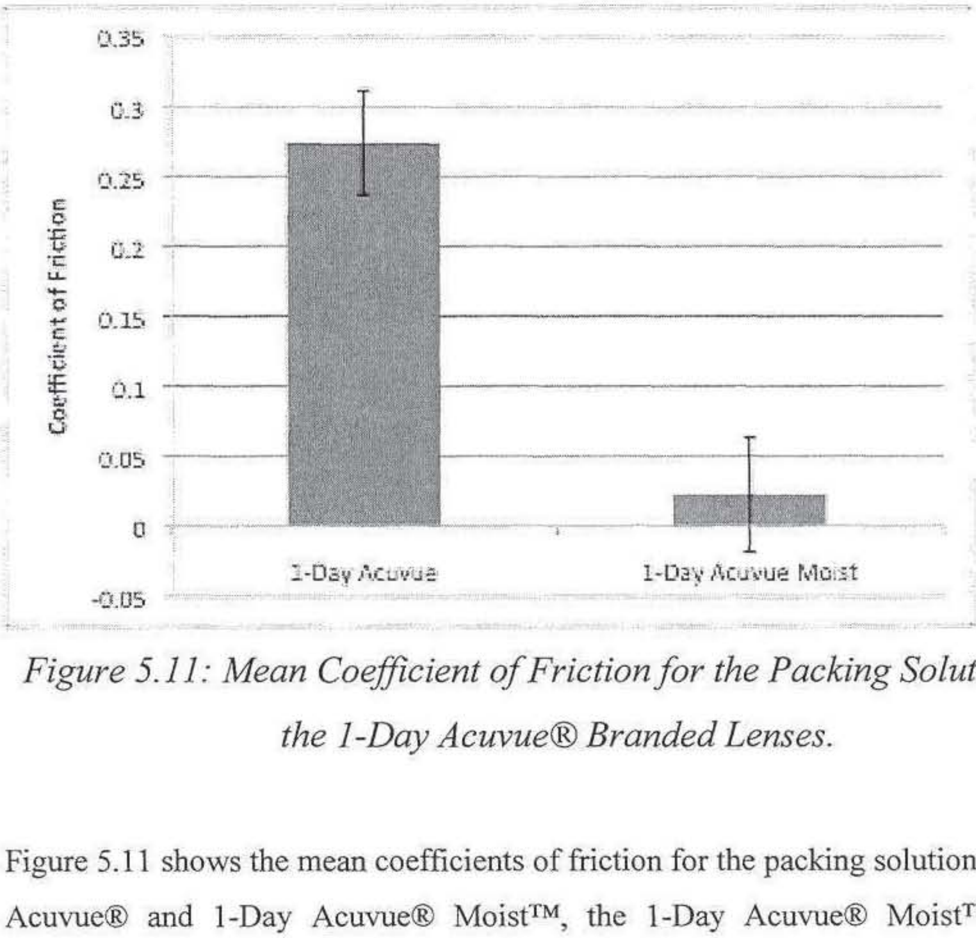


Figure 5.11: Mean Coefficient of Friction for the Packing Solutions for the 1-Day Acuvue® Branded Lenses.

Figure 5.11 shows the mean coefficients of friction for the packing solutions of 1-Day Acuvue® and 1-Day Acuvue® Moist™, the 1-Day Acuvue® Moist™ packing solution has a lower coefficient of friction than 1-Day Acuvue®. The only difference between the two packing solutions from the information on the box is that Moist™ has Povidone (PVP) although there is no mention of the percentage of Povidone added.

5.3.3: The Investigation of the 1-Day Acuvue® Moist™ Packing Solution

There is a colorimetric assay using a potassium iodide (KI) / iodine (I) solution that changes colour when coming into contact with polyvinyl pyrrolidone. This technique dates back to work done by H. Campbell and G. Hunter in the 1950's (Campbell., 1953), the technique is very sensitive and can detect very low concentrations of PVP.

Figure 5.12 shows the colour difference between the KI / Iodine solution and a mixture of the KI / Iodine solution and a 0.06% poly (vinyl pyrrolidone) solution in a 50:50 ratio.

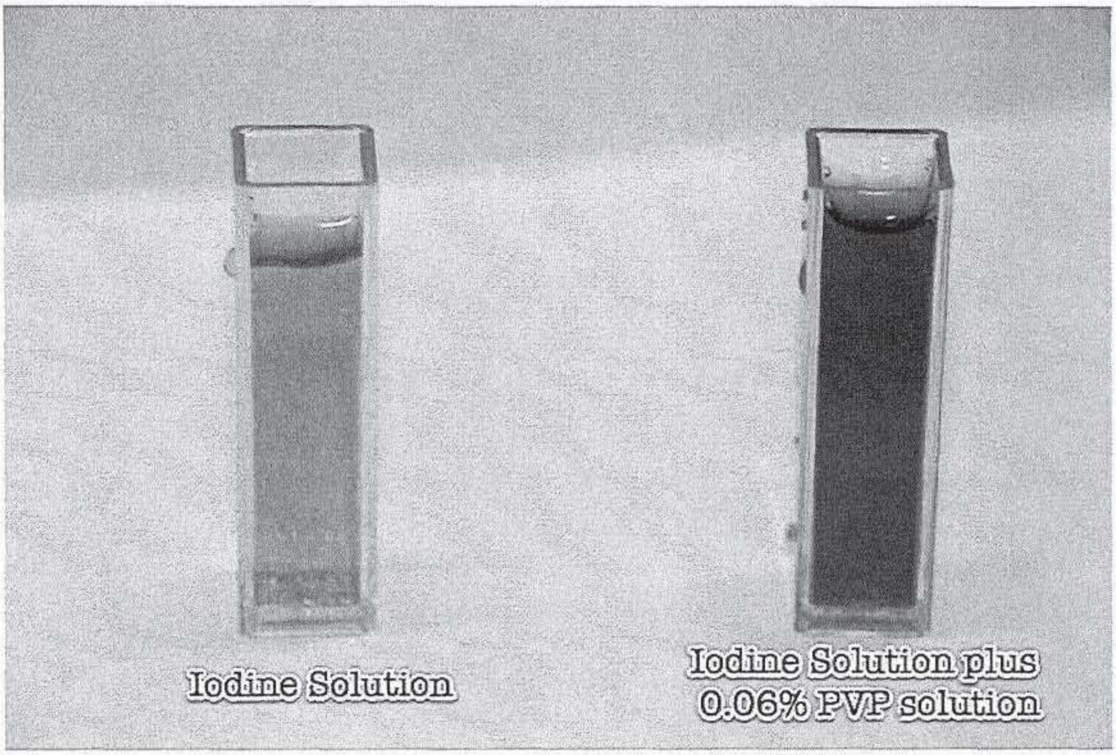


Figure 5.12: Colour Differences between the KI/I Solution and a KI/I Solution with Polyvinyl Pyrrolidone.

Figure 5.12 shows the colour difference when the KI / iodine solution is into contact with PVP. This technique clearly identifies if there is any PVP present in a solution.

Figure 5.13 shows the results from adding 1 ml of the KI / Iodine solution to the entire packing solution from the blister pack (2 ml) of a 1-Day Acuvue® and 1-Day Acuvue® Moist™ lenses.

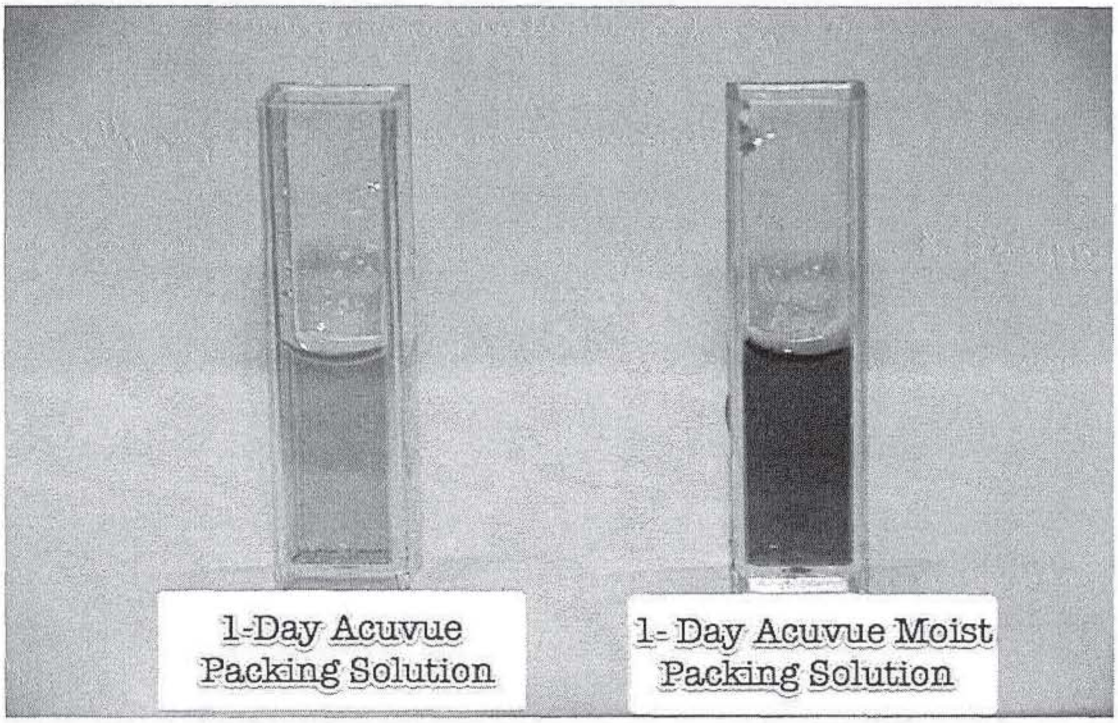


Figure 5.13: Colour Differences between the Packing Solutions of the 1-Day branded Daily Disposables.

Figure 5.13 clearly illustrates that the packing solution of 1-Day Acuvue® Moist™ reacts with the KI / Iodine solution changing the colour from yellow to brown. Thus indicating that PVP is present in the 1-Day Acuvue® Moist™ packing solution but not present in the packing solution of 1-Day Acuvue®.

5.3.4: Colorimetric Analysis of 1-Day Acuvue® Lenses

Previous results have shown that the packing solution for 1-Day Acuvue® Moist™ contains PVP, this has helped to improve various properties; such as the packing solution having an improved lubricant behaviour. The 1-Day Acuvue® Moist™ lens itself also has improved surface properties, which show a lower mean coefficient of friction and also a friction profile that is different to 1-Day Acuvue®. This suggests that the surface of 1-Day Acuvue® Moist™ different to that of 1-Day Acuvue®.

The two Acuvue® branded lenses were analysed using the KI / Iodine solution to determine if the PVP was present in the contact lens. Contact lenses were taken from their packing solution; the surface packing solution was removed by blotting on filter paper. The lens was then soaked in the KI / Iodine solution for one minute, on removal from the KI / Iodine solution the lens was then left for another minute for the colour to fully develop before pictures were taken to capture the differences.

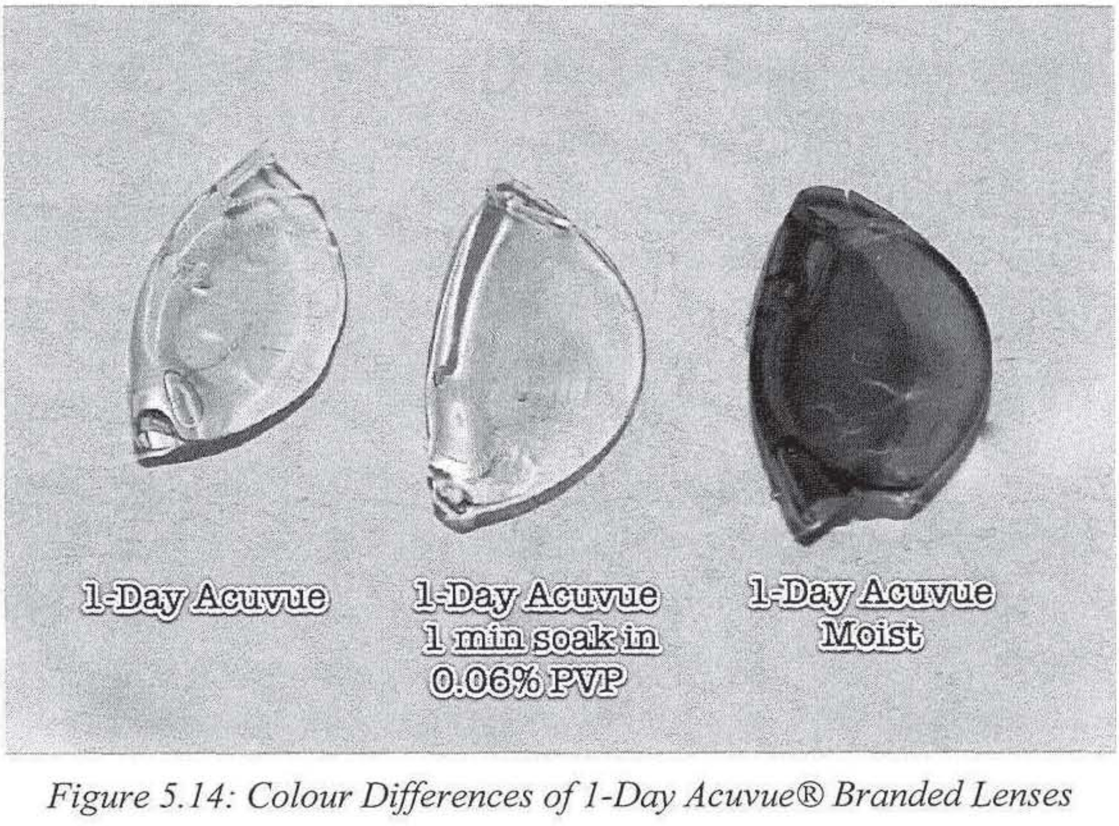


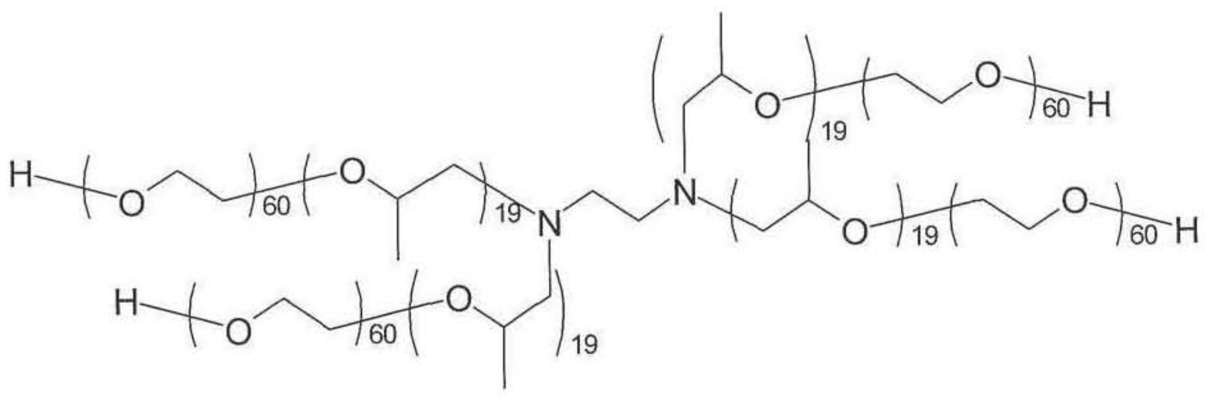
Figure 5.14: Colour Differences of 1-Day Acuvue® Branded Lenses Soaked in a KI / Iodine Solution.

Figure 5.14 shows the results from the one minute soak in the KI / Iodine solution. The picture clearly shows that the 1-Day Acuvue® Moist™ lens has a detectable amount of PVP on the surface of the contact lens. Whereas, the 1-Day Acuvue® lenses colour remains the same as the KI / Iodine solution. A 1-Day Acuvue® lens was soaked in a 0.063% PVP solution for one minute, which was then blotted with filter paper to removed any carried over PVP solution, this lens was then exposed to the KI / Iodine solution for one minute. This lens shows a slight colour difference from a 1-Day Acuvue® lens straight from the packing solution, but the colour intensity is far from that of the 1-Day Acuvue® Moist™ contact lens. This suggests that the lens surface of 1-Day Acuvue® Moist™ has been successfully modified from that of 1-Day Acuvue®.

5.4: Bausch & Lombs Soflens® Daily Disposable Contact Lenses

The third and final daily disposable brand that was studied was the Soflens® Daily Disposable, the old lens is now no longer available for sale (Basuch.com). Old Soflens® One Day had Hilafilcon A as the lens material, this lens has now been completely replaced by a newer version with Hilafilcon B as the base material with the trade name Soflens® Daily Disposable. Hilafilcon B was sold before as Soflens® 59 which was a 2 week replacement lens with a water content of 41%, the new Soflens® Daily Disposable has the same material name, Hilafilcon B, but has a water content of 59%. The other change to the Soflens® Daily Disposable lens is that the packing solution contains Poloxamine (Cairns., 2007).

Bausch and Lomb use Poloxamine in other ophthalmic products such as their multi purpose solution ReNu MultiPlus®. The poloxamine that is used in the multi purpose solution is Tetronic® 1107. As B & L already use Tetronic® 1107 in their multipurpose solutions it is logical that this is the poloxamine present in the packing solution of the new Soflens® Daily Disposable. Tetronic 1107 is a hydrophilic surface-active polymer based on chains of polyethylene oxide (PEO) and polypropylene oxide (PPO) block copolymer, as shown in figure 5.15.



Poloxamine - Tetronic 1107

Figure 5.15: The General Structure of a Poloxamine.

5.3.1: Soflens® Daily Disposable Contact lenses Lens Friction Traces

Figure 5.16 compares the friction profiles of Hilafilcon B (Soflens® 59) with the new lens, Soflens® Daily Disposable, labeled here as Medalist Plus the Japanese trade name. In Japan, both Medalist (Soflens® One Day) and Medalist Plus (Soflens® Daily Disposable) are sold. The conditions used were the same as used in comparing of the other daily disposable brands, (Substrate - Melinex®, Load – 30 mN, Speed – 5 mm/min, Lubricant - HypoTears™).

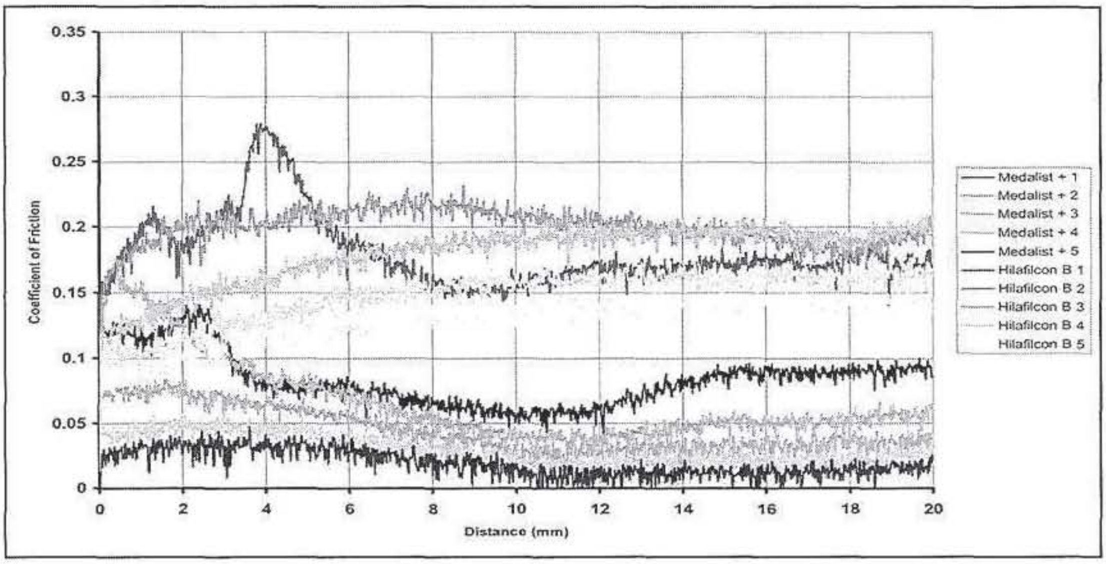


Figure 5.16: Friction traces of Hilafilcon B and Medalist Plus

Results from figure 5.16 show that Soflens® Daily Disposable has a lower coefficient than that of Hilafilcon B (Soflens® 59). The trend of the friction profiles of the two lenses are also different, in that they both start at very similar coefficients of friction but the overall gradients are different with Hilafilcon B rising slightly and Soflens® Daily Disposable falling slightly, before they both level off at the respective values.

5.4.2: Packing solution friction of Soflens® Daily Disposable

The mean coefficient of friction of the packing solutions of the Bausch & Lomb branded contact lenses was measured using 100 µl of packing solution as the lubricant with a standard lens for the two different types of Bausch & Lomb daily disposable contact lens packing solutions. The conditions used on the tribometer were; Speed – 30 mm/min, Load – 30 mN, Substrate - Melinex®, Lens – AIR OPTIX™.

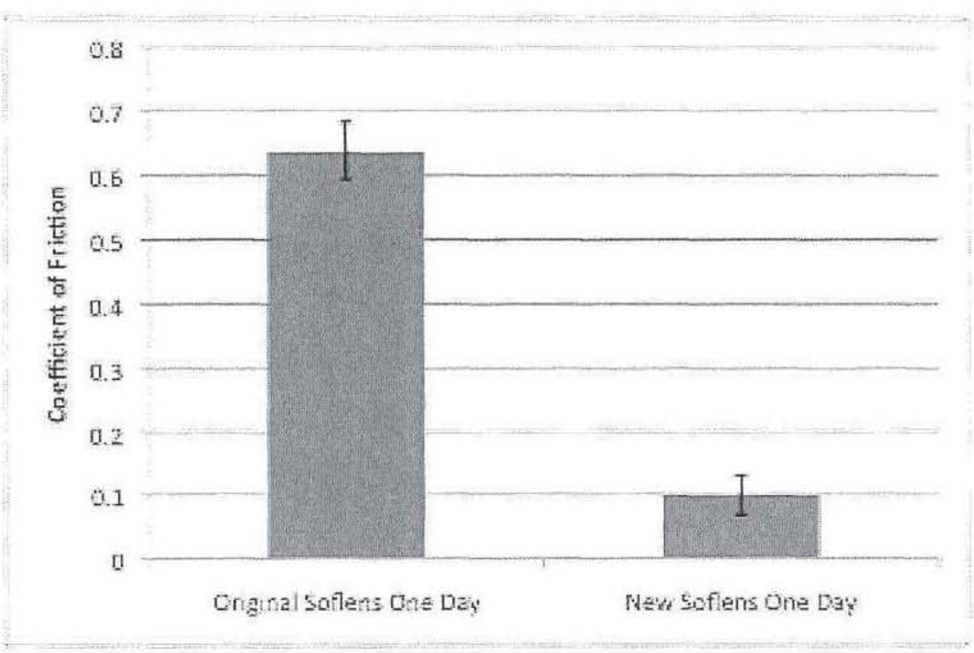


Figure 5.17: Mean Coefficient of Friction for the Packing Solutions for the Bausch & Lomb Branded Daily Disposable Contact Lenses.

Figure 5.17 shows the coefficients of friction for Soflens® One Day (Hilafilcon A – 70% EWC) and Soflens® Daily Disposable (Hilafilcon B – 59% EWC). The packing solution Soflens® Daily Disposable contains a Poloxamine (Tetronic® 1107) which would explain why the packing solution behaved as a better lubricant with AIR OPTIX™ as the control lens.

5.4.3: The Effect of Soaking in MPS on Coefficient of Friction of Soflens® Daily Disposable

The results from the packing solution friction show that the packing solution has been altered from the previous version of the lens with a poloaxmine that possesses surface activity.

To study the coefficient of friction without the effect of the packing solution a series of contact lenses had their coefficients of friction measured straight from the packing solution, at the same time a lens from the same type and from the same row in the blister pack was placed into Opti-free Express multipurpose solution and left for one week. After the one-week period had ended the coefficient of friction was measured using the same condition as the lenses that had the coefficient of friction measured one week earlier. The results are shown in figure 5.18.

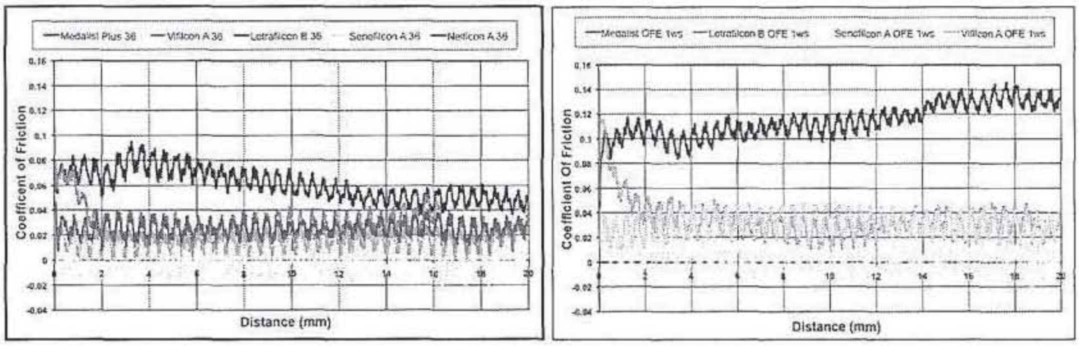


Figure 5.18: Coefficient of Friction for Various Contact Lenses Before and after one week Soaking in Opti-Free Express.

Figure 5.18 show that the differences in the coefficient of friction before and after soaking contact lenses in Opti-Free Express for one week. The one week soak didn't affect the majority of the contact lenses measured, there was however, one lens, coefficient of friction that did change significantly and that lens was Soflens® Daily Disposable.

The coefficient of friction of this lens was investigated further using the same soaking period of one week and still in the multipurpose solution Opti-Free Express, but using a slower sliding speed for the tribometer. The speed of 5 mm/min was used instead of 30 mm/min, which was used in previous experiment (figure 5.18).

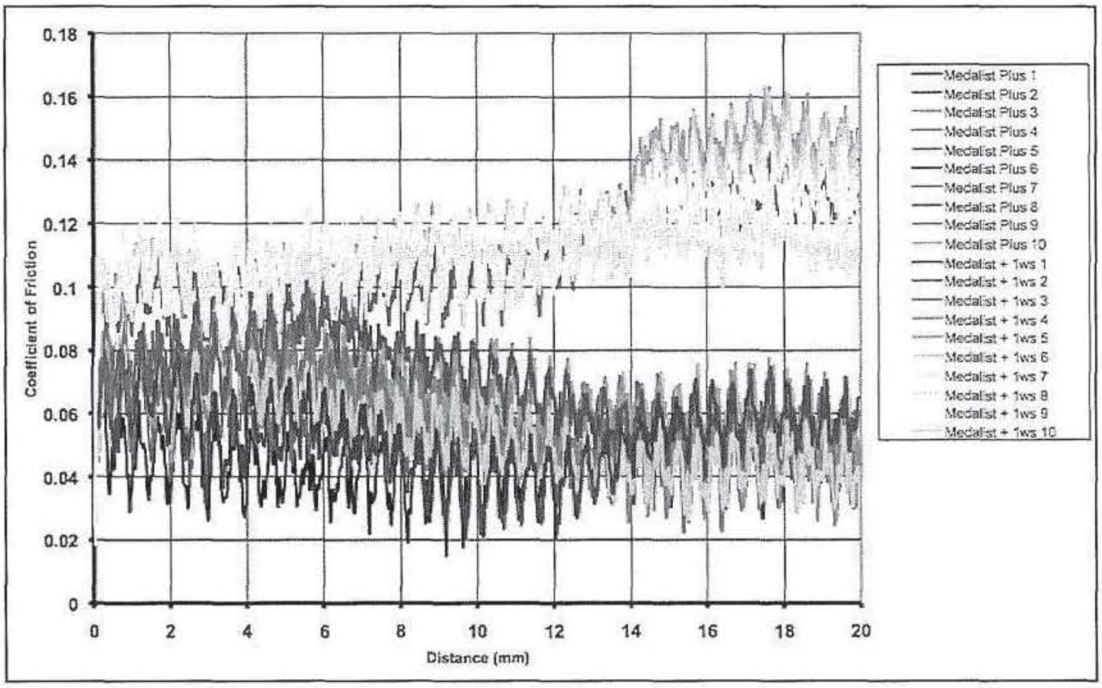


Figure 5.19: Coefficient of Friction for Bausch & Lomb Branded Daily Disposable Contact Lenses.

Figure 5.19 shows in more detail the effect of removing Soflens® Daily Disposable from its packing solution. The static coefficient of friction (the first 2-3mm in distance) remains very similar however the dynamic coefficient of friction has altered. Instead of showing a decreasing trend, the lens that was soaked in MPS shows a increasing trend very similar to that of Soflens® 59 (Hilafilcon B) which does not include any surfactant in the packing solution and therefore none absorbed onto the lens surface.

5.5: Discussion

5.5.1: Focus® DAILIES®

The first test performed was to compare the friction of Focus® DAILIES® Basic (FAB) and Focus® DAILIES® AQUA Release (FDAR). Results showed that there was a difference in the mean coefficient of friction, although the friction profiles of the lenses had similar shaped traces. This was expected, as the enhancement was an extension of an already existing effect, which was described in more detail in chapter 3 of this thesis.

The mean coefficient of friction values of FDB and FDAR were also compared to the mean coefficient of friction of Focus® DAILIES® Aqua Comfort Plus™ (FDACP) which was released a year after FDAR as the third daily disposable contact lens from CIBA Vision. Since the Focus® DAILIES® Aqua Comfort Plus™ lens possesses a more complex enhancement than FDAR. Enhancement of the FDACP lens uses a multi polymeric system with both PVA and PEG used in the bulk material. The packing solution is also altered with PEG added along with extra poloxamer. The packing solution friction shows the benefits of this multi polymeric system in terms of lubricity, with FDACP giving a far lower coefficient of friction that the other DAILIES branded lenses.

In chapter 3 a release model was developed that attempted to mimic the agitation and tear flow rate that a lens undergoes during wear. This model was used to carry out an extraction on the FDACP lenses.

There is a dry eye drop named HypoTears™ manufactured by Novartis, the parent company of CIBA Vision, which uses PEG and PVA as its main lubricating agents. As shown in chapter 3, PVA is eluted from Focus® DAILIES® lenses into the packing solution, therefore, Focus® DAILIES® Aqua Comfort Plus™ has both PVA and PEG present in the packing solution. The mean coefficient of friction was measured using the 100 μl from the extract compared to the extraction media. The first hour extract from the FDACP lens was also compared to HypoTears™, with the friction being measured using AIR OPTIX™ as the lens for all of these lubricants. The results showed that the extract gave the lowest mean coefficient of friction with HypoTears™ the next lowest, this was not expected as HypoTears™ contained more PVA and PEG than the estimated amount present in the extract. HypoTear™ also contains another component that has surface activity, the preservative, benzalkonium chloride. The friction of preserved, unpreserved and unpreserved with benzalkonium chloride was measured again using AIR OPTIX™ as the control lens. The results showed that the test lubricants that did not contain any benzalkonium chloride had a lower coefficient of friction than those that did contain the preservative. Thus, giving the reason for the FDACP lenses first hour extract having a lower mean coefficient of friction than HypoTears™.

The added PEG is low molecular weight that is not chemically attached to the lens matrix. This suggests that the release from the lens will be rapid; workers at CIBA Vision have shown that the entire PEG is released *in vitro* in 2 hours (Pruitt et al., 2009). The release model was carried out on a FDACP lens for 5 hours and the friction of the first and fifth extract compared to each other. This was to see how long the effect of the low mean friction coefficient for the extract remained. The results show that the fifth extract has a higher coefficient of friction, when compared to the first extract. This was because the PEG had already been released from the lenses in the first period of the extract process and also any poloxamer carried over from the packing solution has long been removed. The work presented in this chapter and also in chapter 3 has lead to the following enhancement mechanism being proposed.

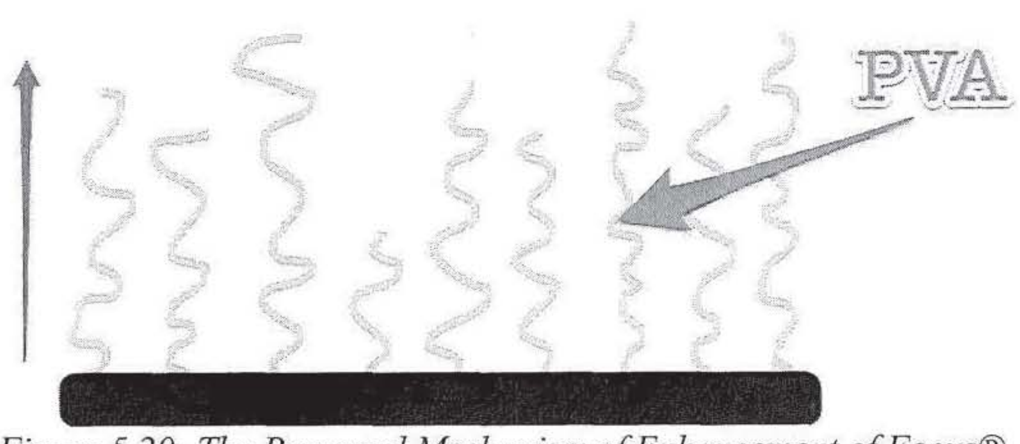


Figure 5.20: The Proposed Mechanism of Enhancement of Focus® DAILIES® Lenses.

Figure 5.20 shows the mechanism proposed for the enhancement of Focus® DAILIES® lenses by PVA. PVA is released by reptation from the surface of the lens during the day, helped by the natural mechanical agitation of the eyelid. The release of PEG from the FDACP lens also follows the same mechanism but at a faster rate. This is mainly due to the smaller molecular weight of PEG and that PEG has less affiliation for the nelfilcon A matrix.

5.5.2: 1-Day Acuvue®

As with the investigation of the Focus® DAILIES® brand, the friction profiles of 1-Day Acuvue® (1DA) and 1-Day Acuvue® Moist™ (1DAM) were analysed first. However, unlike the DAILIES brand, both the values and the frictional profiles of 1DA and 1DAM were different. Mean coefficient of friction of 1DAM has been reduced by more than 50% when compared to 1DA under the same conditions. Friction profiles were also different with 1DAM showing much less stick-slip behaviour than 1DA.

Packing solutions of the lenses were examined using the friction as an initial probe. The packing solution of 1DA and 1DAM are different with the packing solution of 1DAM containing an unknown amount of polyvinyl pyrrolidone (PVP). Mean coefficients of friction for both of the packing solutions were measured using AIR OPTIX™ as the control lens. The packing solution of 1DAM had a much lower mean coefficient of friction than 1DA.

There is a colorimetric technique for detecting the presence of PVP that dates back to the 1950's. This technique is based on a complex that is formed between iodine, iodide ions and poly (vinyl pyrrolidone). This colorimetric assay was first tested with a low concentration PVP solution, upon addition of the KI / Iodine solution with the PVP solution. The mixture changes colour from yellow to a brown solution (figure 5.12). Next step was to mix both of the 1-Day Acuvue® lenses packing solutions with the KI / Iodine solution. Results showed the 1DAM packing solution was the only one to turn the brown colour, which was expected from the information on the packaging. The colorimetric assay can also be on the actual contact lens; figure 5.13 shows the results from soaking lenses in the KI / Iodine solution for one minute. Figure 5.14 shows that the 1-Day Acuvue® Moist™ lens was dyed the same brown colour as the iodine / iodide, and PVP solution. Whereas, the 1-Day Acuvue® lens was a yellow colour, the same as the iodine / iodide solution on its own. The colour intensity gives evidence that PVP is strongly attached to the surface of the 1DAM lens. This result also helps to explain the lens friction results, as the surfaces of the two lenses 1-Day Acuvue® and 1-Day Acuvue® Moist™ are very different. Hence the different mean coefficient of friction values and also the different frictional behaviour shown, especially the different stick-slip properties exhibited by the lenses. The work presented in this chapter and from literature about 1DAM allows the following mechanism of the enhancement to be predicted.

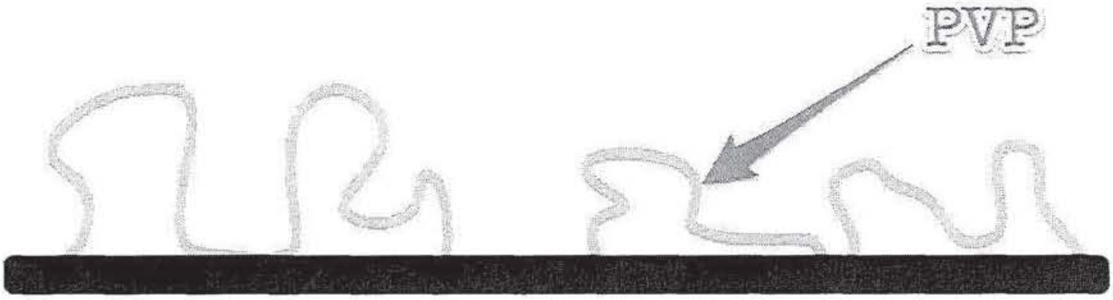


Figure 5.21: The Proposed Mechanism of Enhancement of 1-Day Acuvue® Moist™

Figure 5.21 shows the suggested enhancement mechanism of the 1-Day Acuvue® Moist™ lens, the mechanism shows the PVP anchored at various points along the lens matrix. The PVP presents sections of loops and coils of the polymer along the surface of the lens.

5.5.3: Soflens® Daily Disposable

The Soflens® Daily Disposable brand has undergone the most substantial changes. It is the only daily disposable lens discussed here to have a change in bulk material and water content. The graph in figure 5.16 shows the friction profiles of the new lenses, Soflens® Daily Disposable and Soflens® 59, which use the same base material, Hilafilcon B. There equilibrium water contents (EWC) are different 41% to 59%, with Soflens® Daily Disposable having the higher EWC. The Soflens® Daily Disposable has the lower mean coefficient of friction straight from the packing solution. However, the friction profiles are not the same, even though the bulk material is. The Soflens® 59 material's coefficient of friction rises as the lens is moved across the substrate. Soflens® Daily Disposable starts were a very similar static coefficient of friction but unlike the Soflens® 59 material the friction decreases during movement across the substrate. Mean coefficient of friction of the packing solution was compared between Soflens® One Day and Soflens® Daily Disposable. Since the new lens Soflens® Daily Disposable had a much lower coefficient of friction that its predecessor, which is not surprising as Soflens® Daily Disposable has packing solution contains poloxamine in the packing solution.

The poloxamine added to the packing solution has both hydrophobic and hydrophilic sections of the polymer. Therefore, the poloxamine is able to adsorb onto surfaces. To test if this was the reason the friction profiles were different a Soflens® Daily Disposable lens was soaked in an MPS for a week. This lens was then run on the tribometer and had its coefficient of friction profile compared to that of Soflens® Daily Disposable taken straight from the packing solution. Figure 5.19 shows the results from this experiment, the graph shows that the friction profiles are different with the soaked lenses friction profile very similar to that of Soflens® 59. Thus, it is logical that the poloxamine is loosely adsorbed onto the surface of Soflens® Daily Disposable lens, and is removed during the soaking of the lens. This would also occur during the wear of the lens. Figure 5.22 shows a schematic of the how the polymer would adsorb to the surface of the lens, the hydrophobic sections of the poloxamine being loosely bound to the hydrophobic sections of the bulk material.

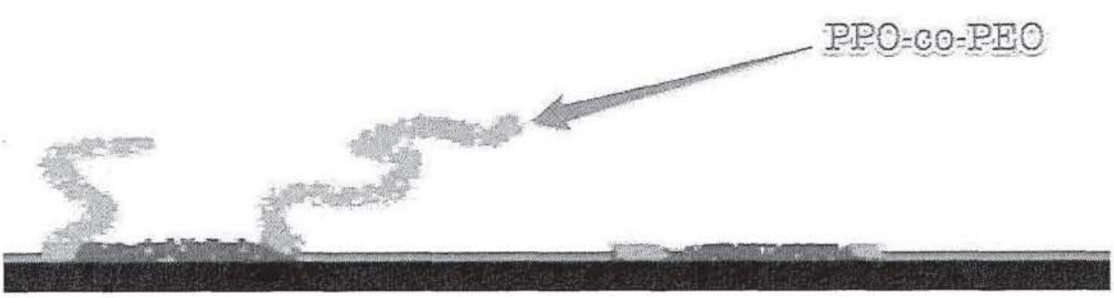


Figure 5.22: The Proposed Mechanism of Enhancement of Soflens® Daily Disposable.

5.5.4: Overview

The bulk properties of the three major daily disposable contact lenses – typified by the EWC and mechanical properties have remained substantially unchanged for a decade, suggesting that they are believed to provide a near-optimal balance between handling and comfort.

Surface properties (particularly the coefficient of friction) of each brands of lenses has undergone significant changes. Lens packing solutions have also been modified. The outcome of both of these changes is improved lubricity and greater wearer comfort.

The enhancements made to the daily disposable contact lens surfaces have happened by harnessing linear soluble hydrophilic macromolecules. Each lens uses a different way to incorporate these hydrophilic species at the lens surface. Soflens® has been modified by simple physical adsorption of a poloxamine, 1-Day Acuvue® has been modified by the locking of polyvinyl pyrrolidone at the lens surface and Focus® DAILIES® has been modified be incorporating soluble polyvinyl alcohol (and now, additionally, PEG) into the matrix, allowing emergence from the surface during wear.

The lubricity of the lens packing solutions has been improved in two ways. Soluble macromolecules are weakly bound to the lens structure and leach into the packing solution, but more particularly additional polymers, such as modified cellulosics, are added separately. Different manufacturers use different combinations of approaches but the end goal is improved comfort on insertion, which can be seen in the figures showing the mean coefficient of friction of the lens packing solutions.

Chapter 6

Application of the Tribology Technique: Silicone Hydrogel Contact Lenses

6.1: Introduction

The last decade has been very significant for the development of contact lens materials. This period's most important feature has been the commercial appearance of the so-called silicone hydrogels, which differ from conventional hydrogels in their enhanced oxygen permeabilities. This is a direct consequence of the inclusion of a significant proportion of siloxy groups. In this way silicon has re-emerged as a vitally important element in ophthalmic biomaterials.

It has depended upon the uniquely high oxygen permeability of long molecular chains (polymers) based on the siloxy group, which in its most commonly encountered form is known as silicone rubber. Oxygen is so vital to the human body and because the oxygen permeability of silicone rubber and related compounds is much higher than that of any natural material, there have been many attempts over the last forty years to harness the softness and oxygen permeability of silicone rubber in the contact lens field. It was not until the commercial appearance of silicone hydrogel lenses, in 1998, that any significant success was achieved.

Because of their enhanced oxygen permeability they were developed primarily with extended wear in mind, but they have proved attractive to practitioners for both overnight and daily wear modalities. Oxygen permeability is the ability to allow oxygen to pass through the lens to the cornea.

The oxygen permeability in silicone hydrogels is different to that of conventional hydrogel contact lenses. Conventional hygrogels obtain their oxygen permeability from the water present in the lens, so as the water content increases the oxygen permeability increases. Whereas silicone hydrogel contact lenses lose their oxygen permeability as water content increases. Figure 6.1 shows oxygen permeabilities of numerous silicone and conventional hydrogels with the commercial silicone hydrogels also plotted.

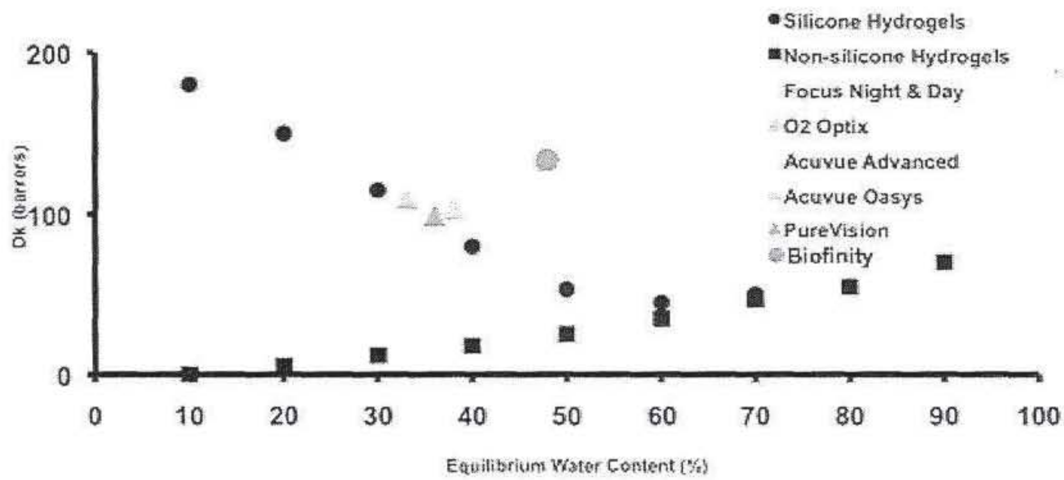


Figure 6.1: The oxygen permeabilities of commercial silicone hydrogel contact lenses (Adapted from Tighe., 2004).

The dual modality has provided a platform for improvements in all three critical contact lens material properties – permeability behaviour, surface properties and mechanical properties (e.g. modulus) – rather than oxygen permeability alone. At the time of writing there are six commercial materials and more known to be in the pipeline. Between them they cover water contents from 24% to 48%, oxygen permeabilities (Dk) from 60 Barrers to 140 Barrers, initial moduli (stiffness) from 0.4 to 1.4 MPa and surface treatments ranging from plasma oxidation and coating, through entrapped polyvinyl pyrrolidone (PVP) to none at all. Table 6.1 summarises the relevant information.

Proprietary Name	Focus Night & Day	AIR Optix	PureVision	Acuvue Oasys	Acuvue Advance	Biofinity
Untied States Adopted Name	Lotrafilcon A	Lotrafilicon B	Balafilcon A	Senofilcon A	Galyfilcon A	Comfilcon A
Manufacturer	CIBA Vision	CIBA Vision	Bausch & Lomb	J & J Vision Care	J & J Vision Care	Coopervision
Water Content	24%	33%	36%	38%	47%	48%
Oxygen Permeability ($X 10^{-11}$)	140	110	99	103	60	128
Modulus (Mpa)	1.5	1.0	1.1	0.72	0.43	0.8
Initial Advancing Contact Angle (^{o})	80	78	95	68	65	N/A
Relative Initial Dehydration Rate	1	1.5	1.9	1.8	2.4	N/A
Surface Treatment	25nm plasma coating with high refractive index	25nm plasma coating with high refractive index	Plasma oxidation, producing glassy islands	No surface treatment. Internal wetting agent (PVP)	No surface treatment. Internal wetting agent (PVP)	No surface treatment.

Table 6.1: General properties of the five commercially available silicone hydrogel contact lenses

Measured at Aston and collected from various sources

The fact that silicone rubber has such high oxygen permeability is the single feature that has driven the development of commercial silicone hydrogels – as did the earlier development of rigid gas permeable lenses (RGPs). Despite attempts to harness the outstanding oxygen permeability and resilience of silicone rubber, it was not until the development of the silicon-containing "Tris" monomer (figure 6.2), and its use to convert PMMA into gas permeable rigid lenses, that silicon made any real commercial impact in ophthalmic polymers.

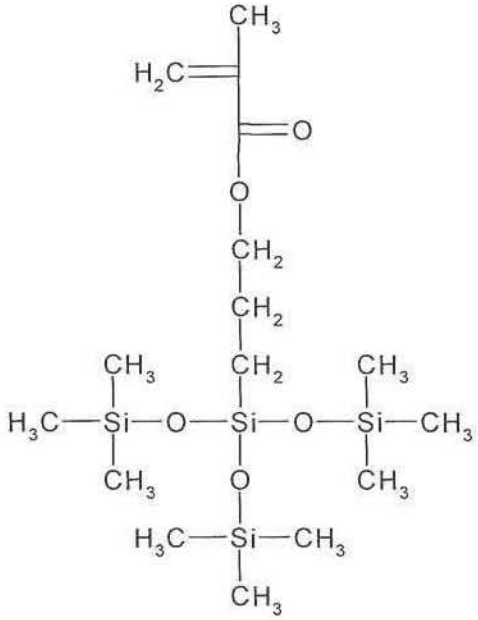


Figure 6.2: The structure of Tris (trimethyl-siloxy-γ-methacryloxy-propylsilane)

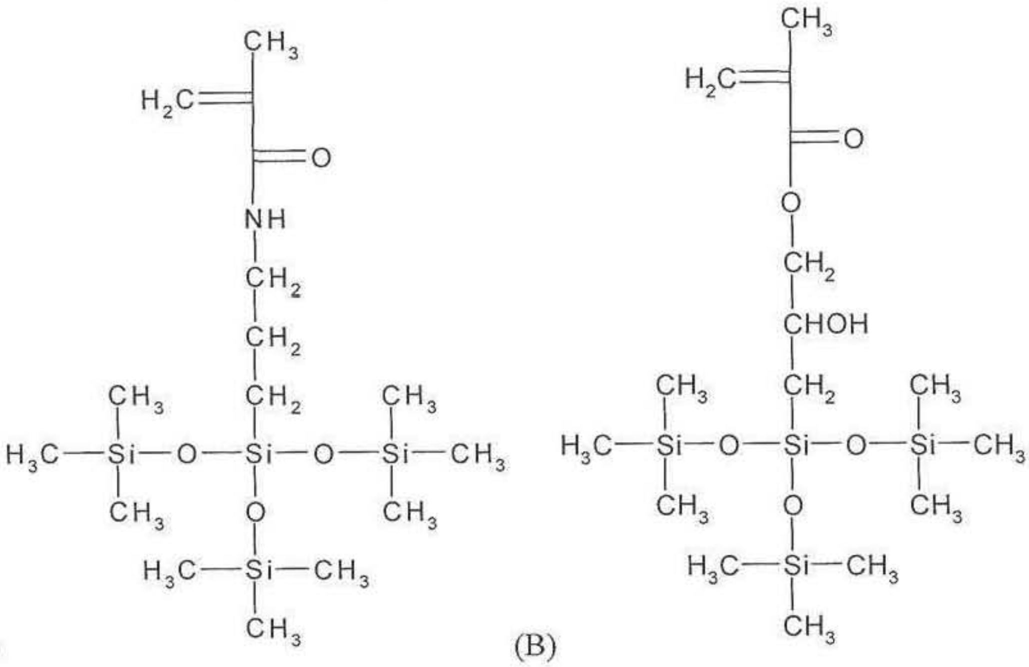
The fact that twenty years elapsed between the publication of the first patent (Tanaka) that contained an indication of how the structure of Tris monomer could be modified to make it compatible with hydrogels and the widespread launch of silicone-hydrogel contact lenses illustrates the point that the problems are more complex than might have been initially assumed.

The same fundamental difficulty exists in trying to combine oil and water to form an optically clear product. Phase separation occurs and the optical clarity of the product is impaired. Phase separation is only a visual problem if the size of the discrete phases is of the order of the wavelength of light or greater. Some degree of segregation probably occurs in all silicone hydrogels and has been used as a positive benefit in products such as CIBA Visions Focus® Night & Day™.

The advantage of incorporation of siloxy groups on the oxygen permeability is illustrated schematically in figure 6.1.

Figure 6.1 shows the oxygen permeability of a range of commercial products: There are two important factors relating to achievable values of Dk. Firstly, that the Dk of water itself is only around 100 Barrers, and secondly, that the oxygen permeability of a polymer entirely composed of Tris (Dk around 175 Barrers) is only about one third of that achievable with silicone rubber. The consequence is that higher oxygen permeabilities are achievable with silicone hydrogels prepared from macromers such as; Biofinity™, than those based on modified Tris structures.

The first two silicone hydrogel products to be launched commercially were Focus® Night&Day™ and PureVision®, which were launched within months of each other. Examination of the patents that led up to and underpin these products reveal that Bausch & Lomb have concentrated on the "modified Tris" approach outlined above, and developed a range of novel monomers, typified by the monomer that forms the basis of PureVision® (Figure 6.3).



(A) (B)

Figure 6.3: Modified TRIS Structures

The CIBA Vision approach, on the other hand, has been more focused on macromers containing silicone rubber sequences (e.g. Figure 6.4) and polymerisation methodologies to combine these with unmodified Tris.

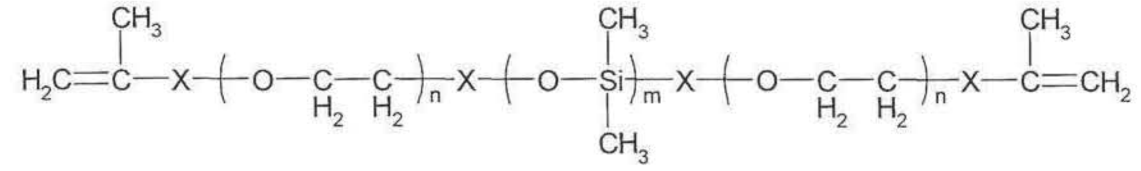


Figure 6.4: Example of Silicone Macromer

One final feature that must be highlighted is the fact that the first two commercial silicone hydrogels, PureVision® and Focus® Night & Day™, are modified by surface treatment processes carried out after the lens has been fabricated. Both are treated using gas plasma techniques. Bausch & Lomb have opted for plasma oxidation and CIBA Vision applied a plasma coating. In the former case (PureVision®), oxidation of TRIS produces hydrophilic glassy silicate islands on the surface, whereas the surface of Focus® Night & Day™ is coated with a 25 nm thick, dense, high refractive index coating.

Much of the commercial realisation of this silicone hydrogel technology and especially the timing of product launches have been governed by patent ownership and litigation. Although Tanaka's monomer (Figure 6.3 (B)) was the first monomer of this type to be exemplified in the patent literature it was not converted into a commercial silicone hydrogel in the lifetime of the patent. It actually formed the basis of the third commercial silicone hydrogel lens. Tanaka's initial intent seems to have been to use it in rigid gas permeable materials, primarily in an attempt to improve surface properties, although there is no evidence that it was successful in that role. Its use in silicone hydrogels did not come until the original 1979 patent had expired twenty-five years later. Workers at Vistakon developed a much-improved synthesis for the Tanaka monomer and were thus able to use it as a key component of Acuvue® Advance™ (galyfilcon-A) which was launched in 2004 upon the expiry of the original patent, followed by a higher Dk material (Acuvue® Oasys™, senofilcon-A). Both materials utilise the Tanaka monomer in conjunction with a siloxy macromer and hydrophilic monomers such as HEMA and *N, N*- dimethyl acrylamide (DMA). Acuvue® Oasys™ has a water content of 38% and a Dk of 103 Barrers. Whilst Acuvue® Advance™ has the highest water content of the group (47%) and the lowest Dk (60 Barrers) and, as a consequence is only approved for daily wear.

The emergence of Acuvue Advance and Oasys was significant in relation to both surface and mechanical properties. They were the first commercial materials that did not employ a surface treatment as a separate step after fabrication of the lens. This has the advantage of avoiding possible patent infringement and reducing manufacturing costs. Both Acuvue® Advance™ and Acuvue® Oasys™ use an internal wetting agent (Hydraclear™), which is high molecular weight poly (vinyl pyrrolidone).

The second significant feature of Advance and Oasys was their mechanical properties. The first two commercial silicone hydrogel lenses were much stiffer than their conventional hydrogel counterparts. This is apparent from inspection of table 6.1.
The stiffness of the first two silicone hydrogel materials, Focus® Night & Day™ and PureVision®, is found to be several times greater than low rigidity conventional materials, such as etafilcon A. The silicone hydrogel material with the highest water content and lowest Dk, Acuvue® Advance™, has a modulus that is much closer to conventional materials, being only around 1.5 times more rigid than etafilcon A. The introduction of O_2 OPTIX™ (now AIR OPTIX™) which has a lower modulus, higher water content version of Focus® Night & Day™ and a newer version of PureVision® was a response to the move towards lower modulus materials. These comparisons illustrate how important water content is in determining properties such as stiffness and oxygen permeability for materials of similar structure. This point is readily illustrated by reference to table 6.1 in which materials have been arranged in order of decreasing water content. We can extend this analysis to the points that have already been made about the intrinsic difference in Dk between silicone rubber and polyTris and the effect that this has on the balance between water content and Dk.

The comfilcon A material (Biofinity™) is solely macromer-based with no Tris derivatives. This is the final entry in the Table and is represented in figure 6.1. It is clear that the Dk value lies well above the notional line that passes through the circles and thus has a superior Dk/water content relationship to all the materials that contain Tris structures.

Biofinity™ is an interesting material for two reasons. First is the fact that the oxygen permeability is, on the basis of existing materials, unexpectedly high for its water content. The second is the absence of either surface treatment or an internal wetting agent.

In Biofinity™ the conventional "Tris" monomer and its derivatives are not used. Instead the patent claims that two siloxy macromers of different sizes, one of which is only monofunctionalised (contains only one polymerisable double bond), when used together produce advantageously high oxygen permeabilities. The patent contains other subtleties, some relating to particular hydrophilic monomers, which, taken together, appear to have enhanced the compatibility of the silicone moieties with the hydrophilic domains. This explains the absence of need for internal wetting agents or surface treatment and produces a very useful addition to the silicone hydrogel product portfolio.

Although higher water contents bring advantage in terms of mechanical properties there are drawbacks. A major problem with contact lenses continues to be their reduction in perceived comfort over the wearing period, particularly as the lens surface dehydrates.

Surface properties are an obvious area for development, perhaps using the techniques of macromolecular entrapment and release currently being exploited in daily disposable lenses, and indeed, to a degree in Acuvue® Advance™ and Acuvue® Oasys™. The aim of such developments is logically enhanced comfort and tear film stability together with reduced lipid deposition and enhanced in-eye biocompatibility. There is considerable scope for parallel developments in care solutions, specifically for silicone hydrogels used in daily wear modality.

Although the conventionally reviewed properties in table 6.1 are important they do not address the most difficult area the manufacture's face, which is how to harness the hydrophobic siloxy materials within the lens matrix and still provide adequate surface properties.

Although the siloxy group functions advantageously with regards to oxygen permeability it detrimentally presents hydrophobic segments that interact with lipids and potentially lends to a deterioration of the surface properties.

The ability to predict effectively longer-term wear is important but simple contact angle measurements of a worn lens does not adequately do this, therefore, the technique of reproducibly measuring the coefficient of friction of contact lenses has been identified as a useful of obtaining adequately detailed characterisation of the lens surface (Tighe., 2006).

Chapter four describes in detail the technique that was used to measure the coefficient of friction for contact lenses, the results obtained for the coefficient of friction in this chapter were acquired using the aforementioned technique.

Results in this chapter will follow the timeline of development and release into the market place of the commercially available silicone hydrogel contact lenses. The driving forces that promoted the evolution of silicone hydrogels will also be discussed.

The major benefit of silicone hydrogels in the first place was oxygen permeability, the problems, however, lie in masking the hydrophobic siloxy groups at the lens surface.

6.2: The Coefficient of Friction of The First Generation Silicone Hydrogels

The first two silicone hydrogels to be launched commercially were CIBA Visions Focus® Night & Day™ and Bausch and Lombs PureVision®, which were launched within months of each other. These two lenses have been labeled the first generation of silicone hydrogel contact lenses, the driving force and requirement for these contact lenses, was to have a Dk that was as high as possible. The reasoning was that the commercial market wanted extended and continuously worn contact lenses, and in order to achieve this the contact lens manufacture's needed to reach a certain value of Dk (87 barrers) (Holden et al., 1984) to prevent hypoxia of the eye during the hours spent asleep.

To obtain the high Dk using a TRIS based monomer the lenses are preordained to have a low water content and high modulus, compared to the contact lenses already in the market place (Table 6.1). The market at the time of launch was dominated by HEMA based materials, which generally have high water contents (FDA defines high water content as greater than 50%) and low modulus.

The following results show the coefficient of friction for CIBA Visions Focus® Night & Day™ and Basuch and Lombs PureVision®. Results are shown in bar chart form and also the friction profiles to show the lenses different friction 'fingerprints'.

6.2.1: The Mean Coefficient of Friction for the First Generation Silicone Hydrogels

The mean coefficient of friction of Focus® Night & Day™ was measured in three different lubricants, using the following tribometer conditions: Load – 30 mN, Speed – 30 mm/min, Substrate – Melinex® (PET).

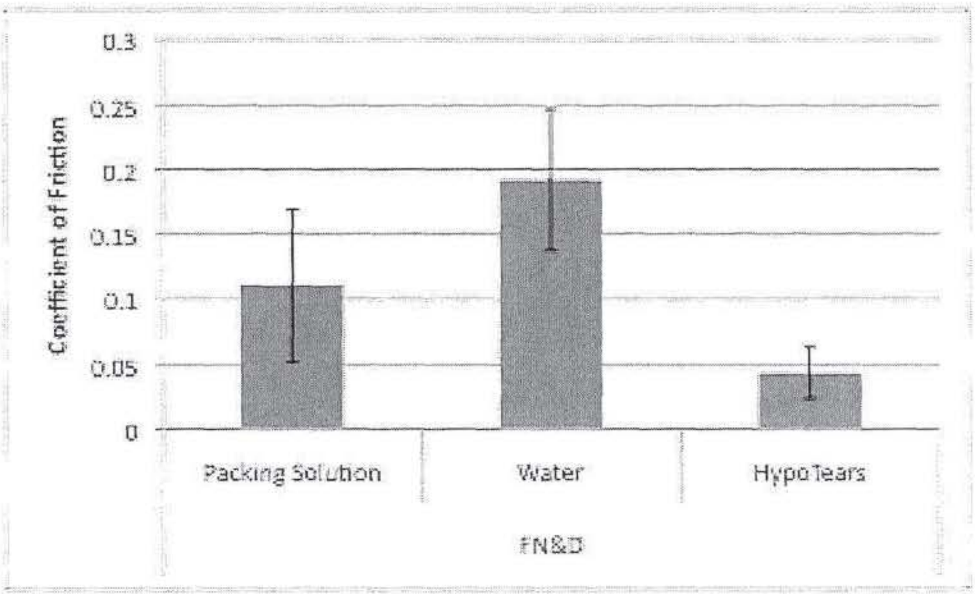


Figure 6.5: The Coefficient of Friction For Focus® Night & Day™ Using Three Different Lubricants.

Figure 6.5 shows the coefficient of friction for Focus® Night & Day™ in the following lubricants; the lens' own packing solution, distilled water, and an artificial tear called HypoTears™, which was defined as a good lubricant in section 4.3.

Results show that the friction coefficient varies in all the lubricants tested, which is to be expected. The lens has the lowest coefficient of friction in HypoTears™ and the highest in distilled water.

Figure 6.6 shows the mean coefficient of friction of PureVision® using the same three lubricants. The following tribometer conditions were used: Load – 30 mN, Speed – 30 mm/min, Substrate - Melinex® (PET)

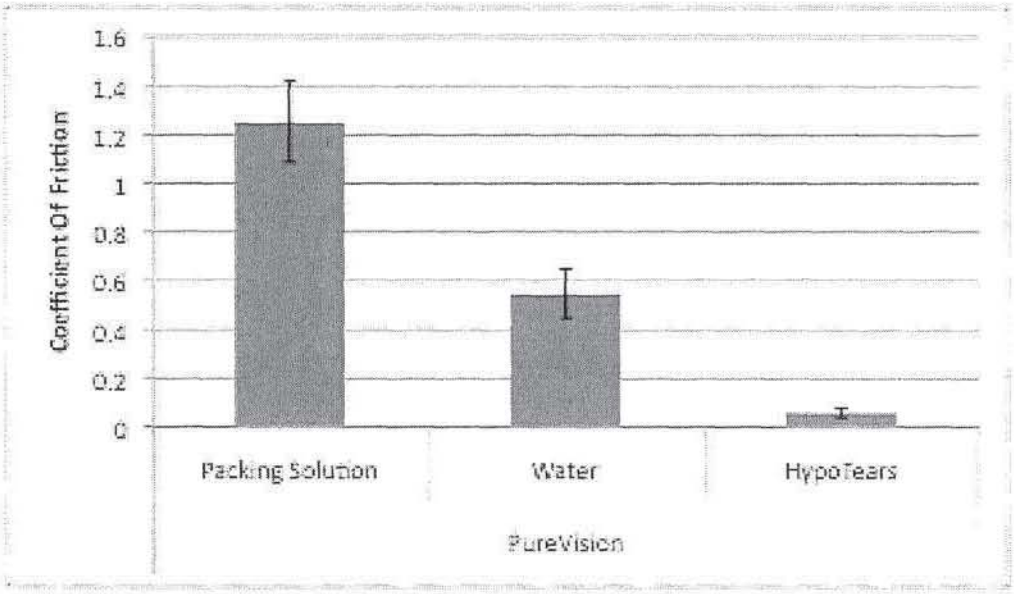


Figure 6.6: The Coefficient of Friction For PureVision® Using Three Different Lubricants.

Figure 6.6 shows the coefficient of friction of PureVision® using the three following lubricants; packing solution, distilled water, and HypoTears™. The PureVision® lens has the lowest coefficient of friction in Hypotears™ with water the next lowest and the lens' packing solution having the highest coefficient of friction of the three lubricants.

Figure 6.7 shows the results from the first generation contact lenses compared against each other. If predicting the coefficient of friction from the bulk properties of each lens then you expect the material with the lower modulus and higher water content to give better friction results. However, friction is dominated by the surface properties of the lens.

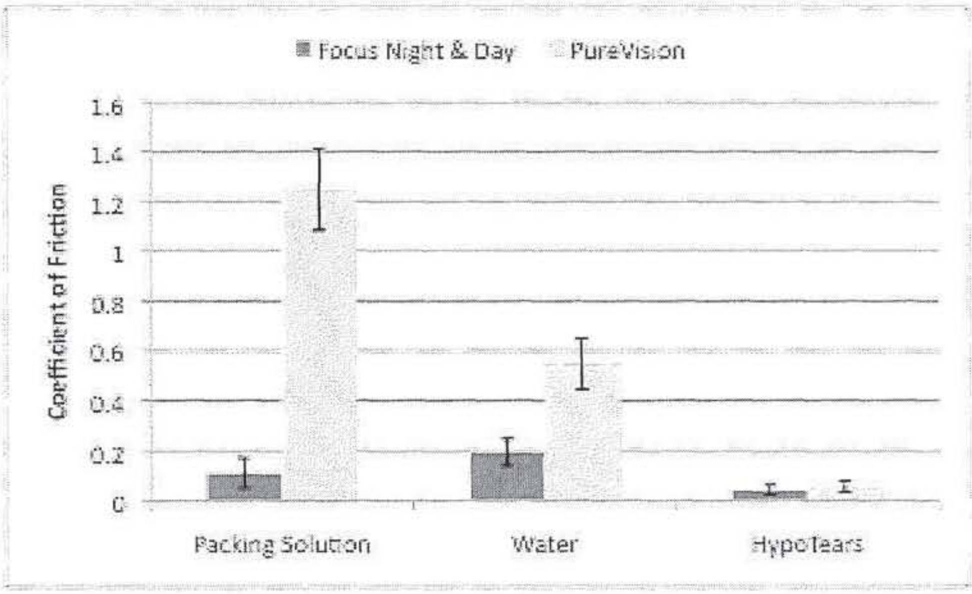


Figure 6.7: A Bar Chart Comparing the Coefficient of Friction For PureVision® and Focus® Night & Day™ Using Three Different Lubricants.

Figure 6.7 compares the results from figures 6.5 and 6.6. The coefficient of friction values show that for HypoTears™ the friction values are very similar, however, when the results for distilled water are compared, there is a large difference with Focus® Night & Day™ having a friction value in water of 0.19μ and Purevision® have a value of 0.55μ.

Interestingly, the coefficient of friction of the lenses measured in their own packing solutions vary even more than HypoTears™ and water.

6.2.2: The Friction Profiles of the First Generation of Silicone Hydrogels

The results so far in this section have focused on a single value giving the mean coefficient of friction; however this does not always tell the whole story and does not give the full details of the frictional behaviour.

Figure 6.8 shows the mean friction traces for the last eight passes of the friction runs for Focus® Night & Day™ and PureVision®. The left hand graph uses HypoTears™ as the lubricant with the right hand graph using distilled water.

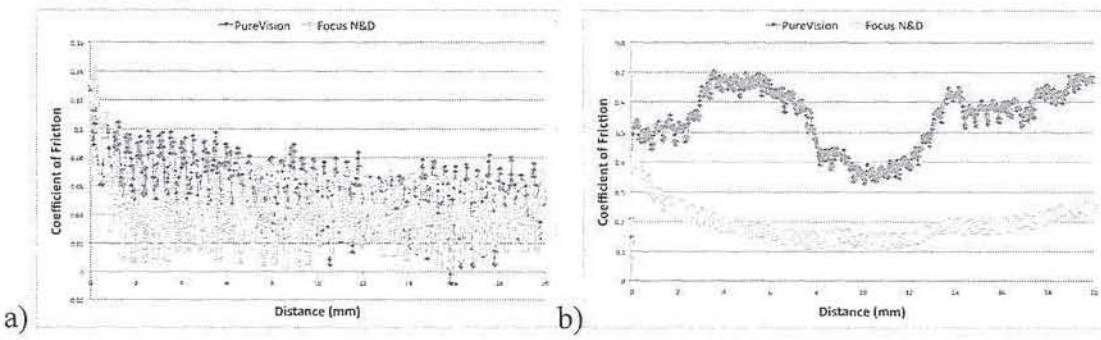


Figure 6.8: Friction Behaviour For PureVision® and Focus® Night & Day™ in a) HypoTears™ and b) Water.

Figure 6.8a shows that when HypoTears™ is used as the lubricant both of the first generation lenses perform very similarly. However, when water is used as the lubricant the lens surfaces behave very differently from each other. The Focus® Night & Day™ lens still shows similar friction behaviour in water to that of HypoTears™, whereas, PureVision® shows a large difference and gives a much higher coefficient of friction.

PureVision® does not have an all over surface coating like the coating found on the Focus® Night & Day™ lens. The PureVision® surface has been described as "like a chess board" with silicate islands or patches. Consequently this could allow the hydrophobic silicone containing groups to reach the surface of the contact lens and cause the higher coefficient of friction shown in figure 6.8.

6.2.3: The Coefficient of Friction of the First Generation of Silicone Hydrogels in Multi Purpose Solutions

Unlike daily disposable contact lenses, the first generation of silicone hydrogel contact lenses were designed for a one month wear period. The wear modality of these lenses can be one of a mixture of daily wear, extended wear (occasional overnight wear) or continuous overnight wear. After the lenses are worn, in either the daily or extended wear modality, they are cleaned and then stored over night, usually in a multi purpose solution. These solutions are complex multi-component solutions, which have more than one function. The solutions are no longer intended simply to clean the lens by removing the protein and lipid, they also have surface active ingredients to try help improve lens comfort on insertion.

Figure 6.9 shows the mean coefficient of friction for PureVison® and Focus® Night & Day™ in four of the most common multi purpose solutions at the time of testing. N.B. Complete MoisturePlus has now been withdrawn from the market after being linked with an increased risk of Acanthamoeba keratitis in the US (Anger., 2008)

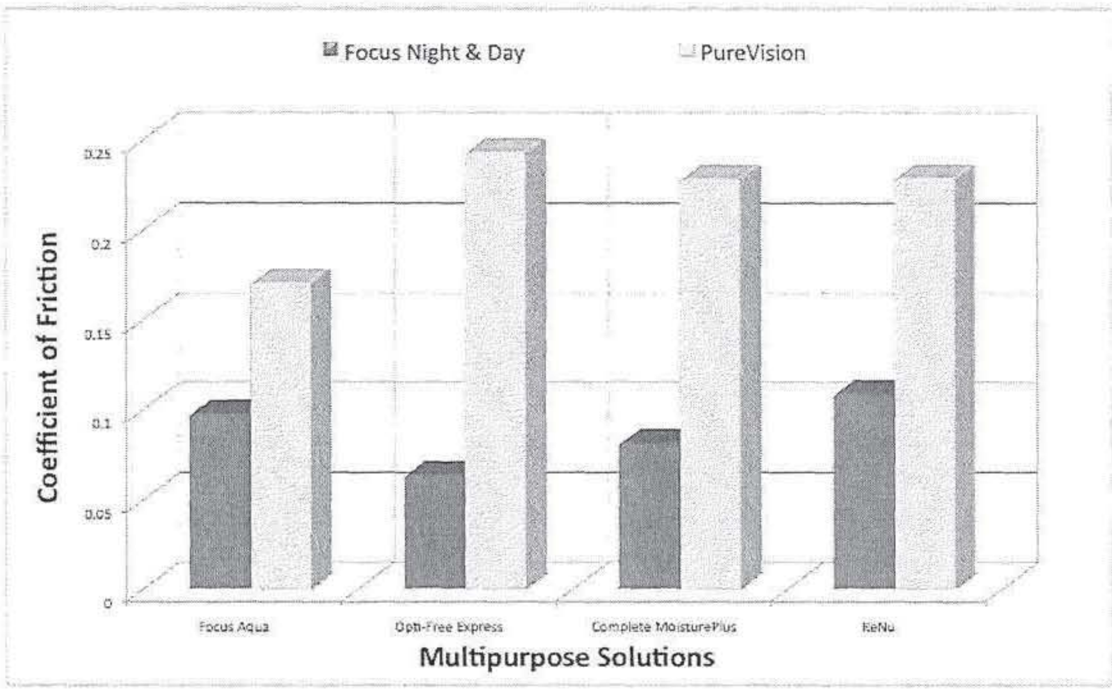


Figure 6.9: Friction Behaviour For PureVision® and Focus® Night & Day™ in Multi Purpose solutions.

Figure 6.9 shows the coefficient of friction for the first generation of silicone hydrogels with four different multi purpose solutions (MPS). It is clear that Focus® Night & Day™ has a lower coefficient of friction with all the MPS used. Interestingly, the lenses have their lowest friction coefficient value with different MPS suggesting different surface interactions with the multi-component solutions.

6.3: The Second Generation of Silicone Hydrogel Contact Lenses

The second-generation, as described here, are the silicone hydrogel contact lenses released during the years 2003 – 2005. In total there were three major silicone hydrogel contact lenses released between these two years. For the first time Johnson & Johnson (J & J) entered the silicone hydrogel market, firstly with Acuvue® Advance™ and then with Acuvue® Oasys™, which received FDA approval in October 2003 and October 2004 respectively. The driving force for the second generation of silicone hydrogel contact lenses was to have improved comfort when compared to the first generation lenses.

The third silicone hydrogel contact lens released during this time was O2 OPTIX™ (now called AIR OPTIX™), which received FDA approval in March 2004. This was in effect a higher water content version of Focus® Night & Day™., (with the water content increasing from 24% to 33%), thus lowering the modulus of the lens. The lens retained the same surface coating treatment as previously used on Focus® Night & Day™.

The reason for introducing new lenses was presumably related to the effect of modulus on perceived comfort. Comfort-related issues were still the biggest cause of contact lens drop out. Thus, to achieve comfort enhancement, certain bulk lens properties, such as, the water content and the modulus had to be altered. Table 6.1 shows various complied properties of silicone hydrogel lenses. The table shows that the second-generation of silicone hydrogels have in all cases a lower modulus than the first generation and also the water contents show an increasing trend, particularly for the J & J materials.

These changes (to help improve comfort) had the general effect of decreasing the Dk of the lenses, which was the driving force for the introduction of silicone hydrogels. The justification for lowering the Dk was that contact lenses wearers wanted more comfortable lenses, and the desire to sleep in contact lenses had become of less importance than comfort.

The J & J contact lenses were designed mainly for daily wear modality, on a two weekly replacement basis, although Acuvue® Oasys™ could be worn overnight for up to a period of one week.

The most interesting element of these new J & J lenses was that they had no surface treatment; instead an internal wetting agent was used called Hydraclear™. Hydraclear™ is simply polyvinyl pyrrolidone, which is incorporated into the contact lens at the manufacturing stage, to help prevent the hydrophobic siloxy groups presenting at the surface of the lens.

6.3.1: The Mean Coefficient of friction of the Second Generation Silicone Hydrogels

This section shows the mean coefficient of friction of the three, second-generation silicone hydrogel contact lenses. These silicone hydrogel contact lenses were designed to out-perform the previous silicone hydrogel lenses in terms of comfort. Figure 6.10 shows the mean coefficients of friction for both the first and second generations of silicone hydrogel contact lenses. The lubricant needed to challenge the contact lenses so that any differences could be studied. Therefore, distilled water was selected as the lubricant. The other tribometer conditions remained constant so the lens was the only variable that was altered.

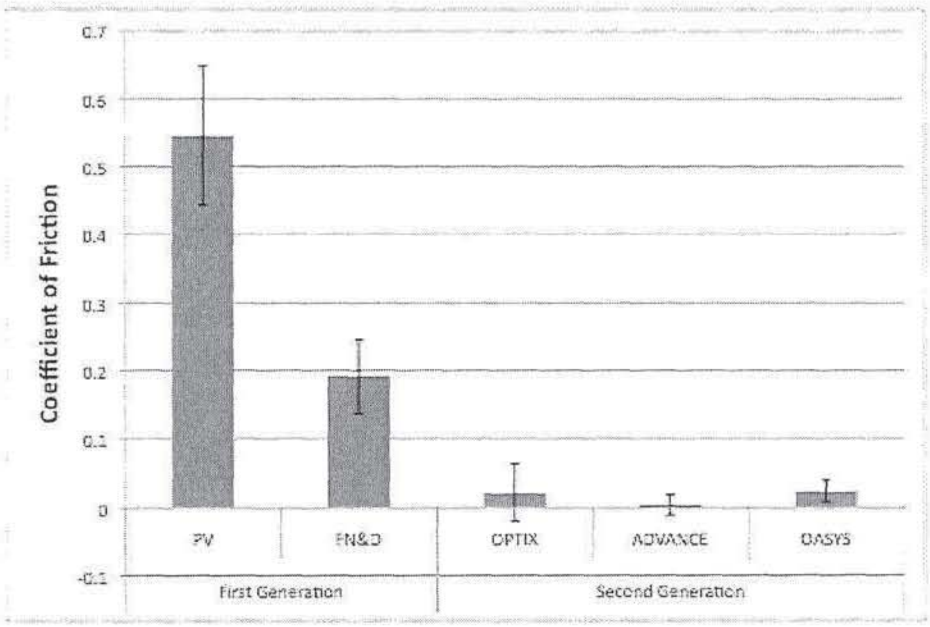


Figure 6.10: Friction Behaviour For First and Second Generation of Silicone Hydrogels in Distilled Water.

Figure 6.10 clearly shows the difference in the mean coefficient of friction between the first (PV and FN&D) and second generation of silicone hydrogels (OPTIX, ADVANCE and OASYS)

The three second-generation silicone hydrogels are not statistically significantly different from each other in the mean coefficient of friction, however, they are statistically significantly different from both of the first generation silicone hydrogels.

6.3.2: Individual Mean Coefficient of Friction of the Second Generation of Silicone Hydrogels

Mean coefficient of friction of the three second-generation silicone hydrogel contact lenses, was measured using three different lubricants. Lubricants used were; the lens' own packing solution, distilled water and HypoTears™.

The friction runs were carried out under the following tribometer conditions: Load – 30 mN, Speed – 30 mm/min, Substrate - Melinex® (PET).

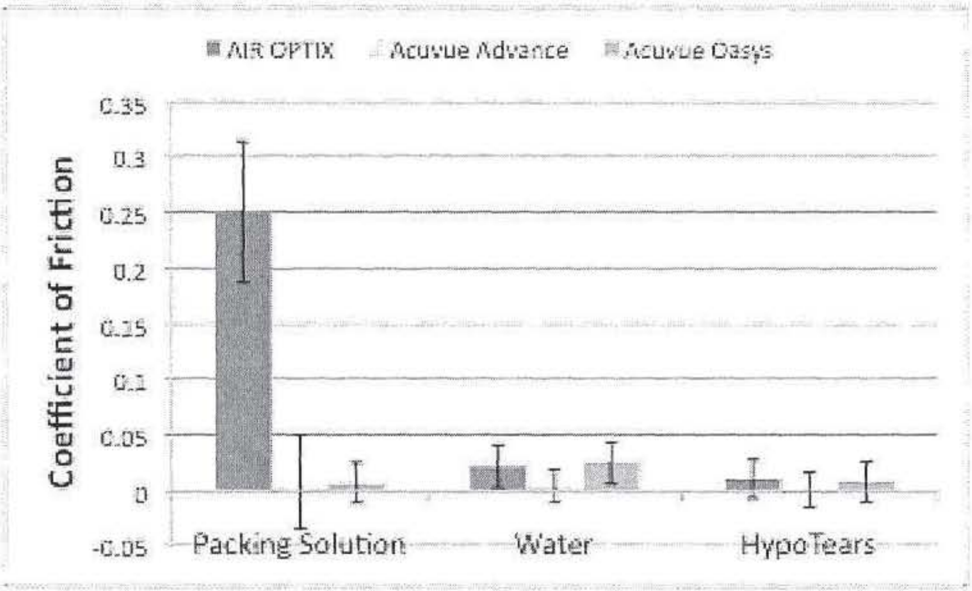


Figure 6.11: Friction Behaviour For the Second Generation of Silicone Hydrogels in Three Different Lubricants.

Figure 6.11 shows that all the second-generation silicone hydrogels have low coefficients of friction in HypoTears™ and distilled water (although slightly higher than that obtained with HypoTears™).

There is a point of interest, however, in the results when the packing solutions are used as the lubricant. The packing solution results for the two J & J silicone hydrogels have very low coefficients of friction when compared with the CIBA Vision material.

The packaging of the J & J materials gives a clue why the friction is lowered. The packing solutions of both Acuvue® Advance™ and Acuvue® Oasys™ contain 0.005% of methyl ether cellulose.

Information about methyl ether cellulose (methylcellulose)

Methylcellulose is a methyl ether of cellulose, produced by substituting the hydrogen atoms of some of the cellulose hydroxyl groups (–OH) with methyl groups (–CH_3), forming methoxy (-OCH_3) groups. Methyl ether cellulose is sold under a variety of trade names and is used as a thickener and emulsifier in various food and cosmetic products. Methyl ether cellulose is not digestible, non toxic, and non allergenic.

Methyl ether cellulose has an extremely wide range of uses, some of which are discussed below.

Thickener and emulsifier

Methylcellulose is often added to hair shampoos, toothpastes and liquid soaps to generate their characteristic thick consistency. Methylcellulose is also added to some foods, for example ice cream or croquette. Methylcellulose is also an important emulsifier, preventing the separation of two mixed liquids.

Lubricant

Methylcellulose is used as a variable viscosity personal lubricant; it is the main ingredient in K-Y Jelly.

Artificial tears and saliva

Solutions containing methylcellulose or similar cellulose derivatives (see below) are used as substitute for tears or saliva if the natural production of these fluids has been disturbed.

Derivatives of methylcellulose, which improve upon the performance characteristics, include methyl hydroxypropyl cellulose (MHPC), hydroxypropyl methyl cellulose (HPMC), methyl hydroxyethyl cellulose (MHEC) and hydroxyethyl methyl cellulose (HEMC). These derivatives typically improve the characteristics such as water retention, vertical surface slip-resistance, open time, etc. (Young., 1986)

6.3.3: The Friction Profiles of the Second Generation of Silicone Hydrogels

The results presented in section 6.3.2 focused on a single value for the coefficient of friction which does not always tell the whole story and does not give the full detail of the lenses frictional behaviour.

Figure 6.12 show the mean friction traces for the last eight passes of the friction runs for all of the second-generation silicone hydrogel contact lenses. The graphs in figure 6.12 show what the friction traces look like with HypoTears™ and distilled water as the lubricants.

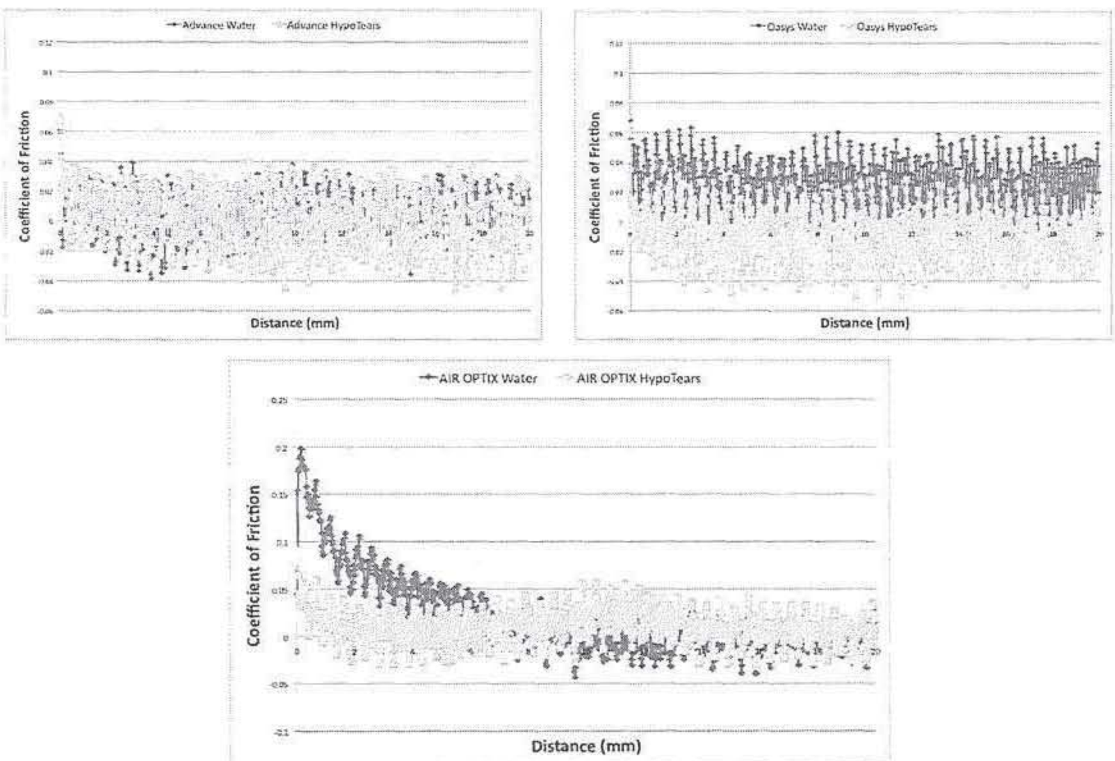


Figure 6.12: Friction Behaviour For Acuvue® Advance™, Acuvue® Oasys™ and AIR OPTIX™ in HypoTears™ and Distilled Water.

The friction 'fingerprints' for Acuvue® Advance™ and Acuvue® Oasys™ are very similar to each other, and also very similar for both HypoTears™ and distilled water.

The friction 'fingerprint' for AIR OPTIX™ is different to that of the J & J materials which is not surprising, the AIR OPTIX™ lens has a very distinctive start up peak which levels off to the dynamic part of the friction trace.
This 'fingerprint' is very similar to that of Focus® Night & Day™ although the start up peak is not as large as the Focus® Night & Day™ start up value.

Unlike the J & J material, there is a slight difference between the water and HypoTear™ traces, although most of this most of this difference lies within the first 4 mm of the trace i.e. the start up region of friction, the dynamic friction are very similar.

6.3.4: The Coefficient of Friction of the Second Generation of Silicone Hydrogels in Multi Purpose Solutions

In figure 6.9, the mean coefficient of friction was measured for the first generation of silicone hydrogels in four MPS. Two of the second-generation materials had their coefficient of friction measured in the same four MPS. The two materials chosen were Acuvue® Advance™ and AIR OPTIX™, the figure 6.13 shows the differences in mean coefficient of friction between the two lenses in the MPS.

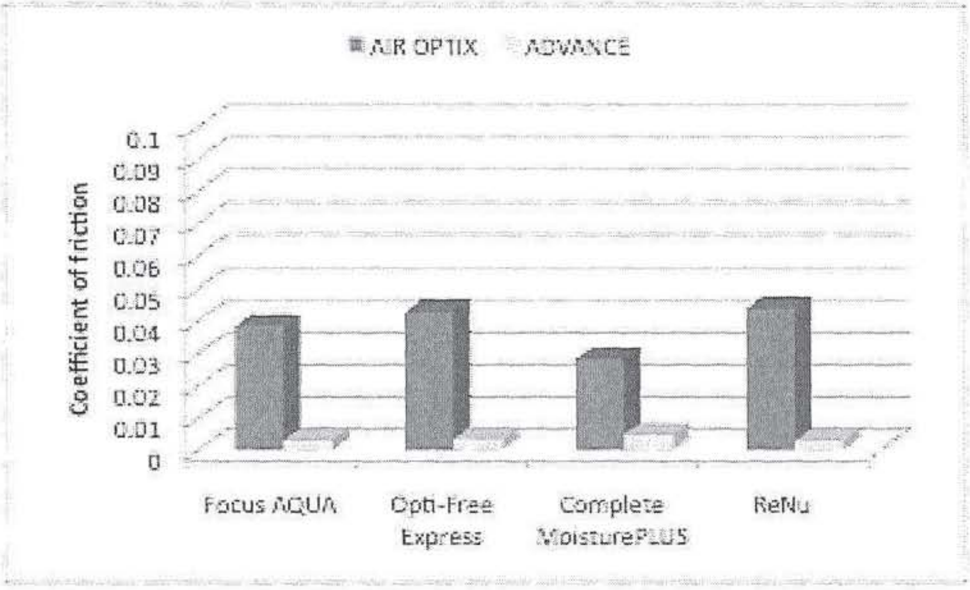


Figure 6.13: Friction Behaviour For Acuvue® Advance™ and AIR OPTIX™ in Multi Purpose Solutions.

Figure 6.13 shows the mean coefficient of friction for Acuvue® Advance™ and AIR OPTIX™ in MPS, both of these lenses perform well in terms of friction in MPS, but with Acuvue® Advance™ performing significantly better in all of the chosen MPS.

Figure 6.14 compares the results obtained from figures 6.9 and 6.13.

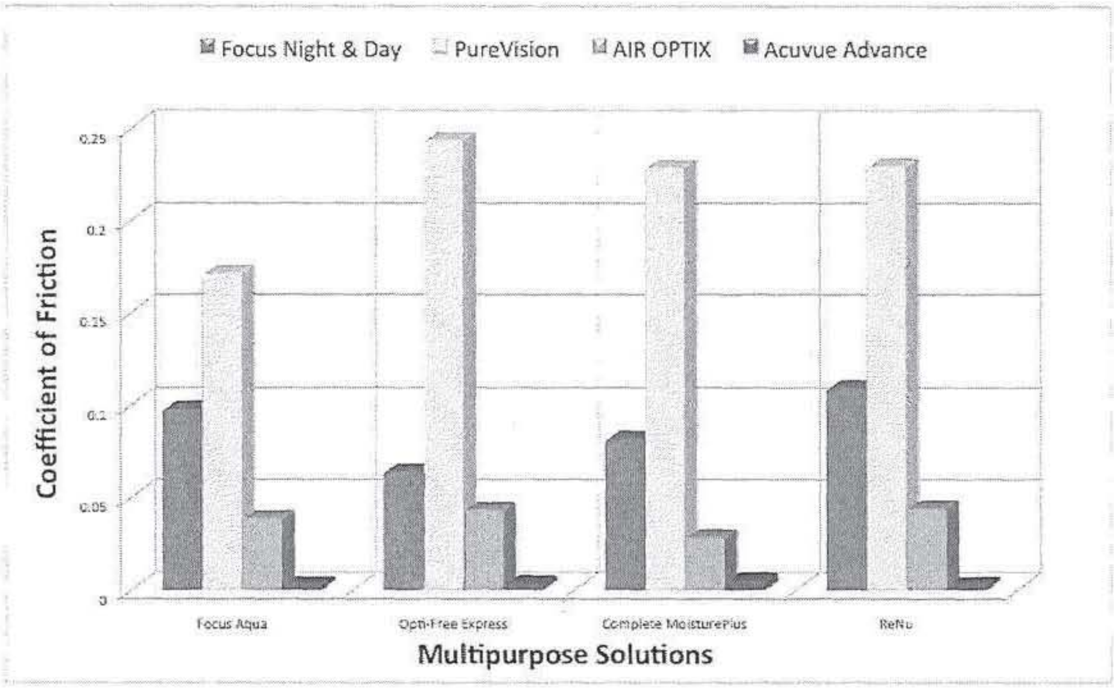


Figure 6.14: Friction Behaviour For PureVision®, Focus® Night & Day™, Acuvue® Advance™ and AIR OPTIX™ in Multi Purpose Solutions.

Figure 6.14 clearly shows that the second generation of silicone hydrogels surpass the first generation of silicone hydrogels in term of lubricity in multi purpose solutions, especially when comparing PureVision® against Acuvue® Advance™.

Another point of interest is the coefficient of AIR OPTIX™, the values obtained for AIR OPTIX™ are lower than that of Focus® Night & Day™. These two lenses have the same surface treatment; therefore, the reason for the differences in coefficient of friction must come from the differences in modulus and water content.

6.4: Silicone Hydrogel Contact Lenses in the Present Day

6.4.1: Introduction

This next section focuses on the major silicone hydrogel contact lenses released since the second generation came on the market (2006-onwards). The silicone hydrogel contact lens market is now moving towards that of the daily disposable contact lens market. This is because the market is driven by three factors: Convenience, Cost and Comfort. Consumers want the most comfortable lens at a reasonable price, which is also convenient to use. Major lenses released since 2006 will be shown below with a brief summary of the lens.

6.4.1.1: Biofinity™

In December 2005, CooperVision became the fourth manufacturer to obtain FDA approval for a silicone hydrogel contact lens. Biofinity™ was again distinctly different from the other silicone hydrogels that had already been released into the market, as this material didn't use a TRIS based structure. The CooperVision material uses, preformed macromers containing silicone rubber units, together with hydrophilic monomers to form the matrix. This enables the lens to have high water content, but still maintain a high Dk value, figure 6.1 shows that the Dk of Biofinity™ is approaching that of Focus® Night & Day™, whereas the water content is slightly higher than that of Acuvue® Advance™ (48% to 47% respectively).

6.4.1.2: New PureVision®

A new version of Bausch and Lombs PureVision® contact lens has been launched, new PureVision®; this new lens has a 28% lower modulus which has moved the lens more in-line with the majority of the other silicone hydrogel lenses.

6.4.1.3: AIR OPTIX™ CUSTOM

There are some prescriptions that the current silicone hydrogels cannot provide, such as; high positive powers. Patients that require high positive power (or other difficult prescriptions) vision correction and want to wear contact lenses have to wear a lathe cut contact lens. In November 2006 CIBA Vision were granted FDA approval for a new silicone hydrogel lens material Sifilcon A. Which when released had the trade name of AIR OPTIX™ CUSTOM, this was the first major lathe cut silicone hydrogel contact lens, which would allow existing lathe cut contact lens wearers the chance to benefit from silicone hydrogel contact lenses. This section will NOT show any friction results for AIR OPTIX™ CUSTOM.

6.4.1.4: AIR OPTIX™ AQUA

Chapters 3 and 5 of this thesis focused on the recent trend in daily disposable contact lens development. This trend is the incorporation of hydrophilic polymer either into or onto the surface of the contact lens by different techniques. CIBA Vision have used one of these techniques to place copolymer 845 on the surface of AIR OPTIX™, the name for this new material is AIR OPTIX™ AQUA.

The technique is to place 1% of copolymer 845 in the packing solution of AIR OPTIX™ AQUA before the sterilisation process, this is a simple, cost-effective way of improving the surface properties of the contact lens, thus, improving comfort.

6.4.1.5: 1-Day Acuvue® TruEye™

The latest silicone hydrogel released is a first for the market place, a daily disposable silicone hydrogel contact lens. The lens materials USAN name is narafilcon A and had received FDA approval in March 2008. The lens will be released with the trade name 1-Day Acuvue® TruEye™ and released first in the UK, during the autumn of 2008. The properties of the lens are show in table 6.2.

??

Proprietary Name	1-Day Acuvue® TruEye™
United States Adopted Name	Narafilcon A
Manufacturer	J & J Vision Care
Water Content	46%
Oxygen Permeability ($x10^{-11}$)	100
Modulus (MPa)	0.66
Surface Treatment	No Surface Treatment. Internal wetting agent (PVP)

Table 6.2: Properties of 1-Day Acuvue® TruEye™.

6.4.2: The Coefficient of Friction of CooperVision's Biofinity™

When Biofinity™ was released in 2006; it became the fifth silicone hydrogel to reach the market place. In many ways Biofinty™ was a first in terms of design; it was the first silicone hydrogel to move away from the TRIS-based structures, shown earlier in this chapter. The lens was also the first to not have any surface treatment or internal wetting agent; instead it relies on the bulk matrix to protect the hydrophobic silicone sections of the material.

Figures 6.15 & 6.16 show the coefficient of friction of Biofinity™ compared to two other silicone hydrogels lenses, Acuvue® Advance™ and AIR OPTIX™. These lenses had their coefficient of friction measured under the following tribometer conditions: Speed – 30 mm/min, Load – 60 mN, Substrate - Melinex®. There were two lubricants used, the first was HypoTears™ and the second, a buffered saline solution similar to a basic packing solution. Two lubricants were used to investigate how the lenses behave in different lubricants, an effect we have defined as 'solution hysteresis'.

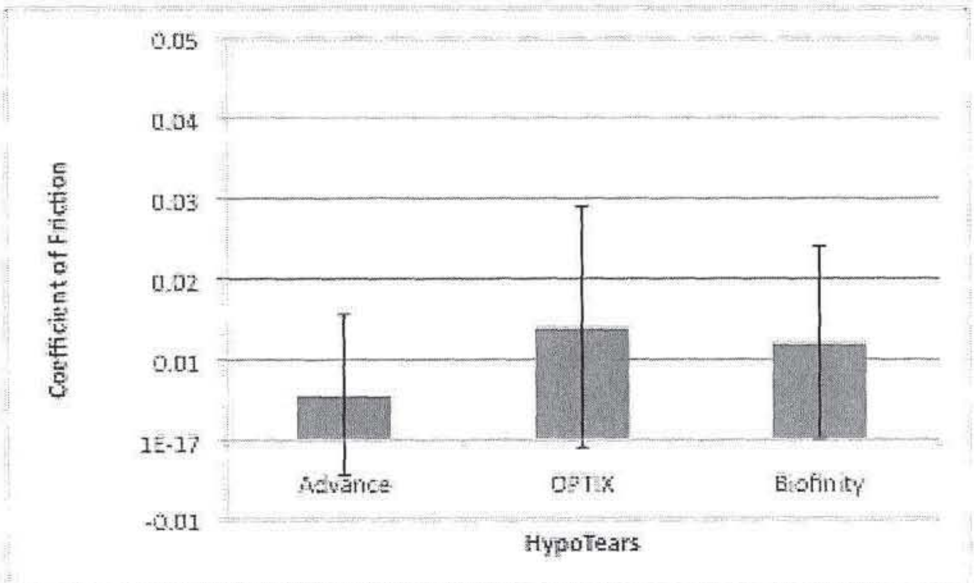


Figure 6.15: The Friction Biofinity™ in HypoTears™ Compared to Acuvue® Advance™ and AIR OPTIX™.

Figure 6.15 shows that when HypoTears™ is used as the lubricant, the silicone hydrogels tested have a similar coefficient of friction. Figure shows the mean coeffcient of friction and also the friction traces of the three silicone hydrogels in a buffered saline solution.

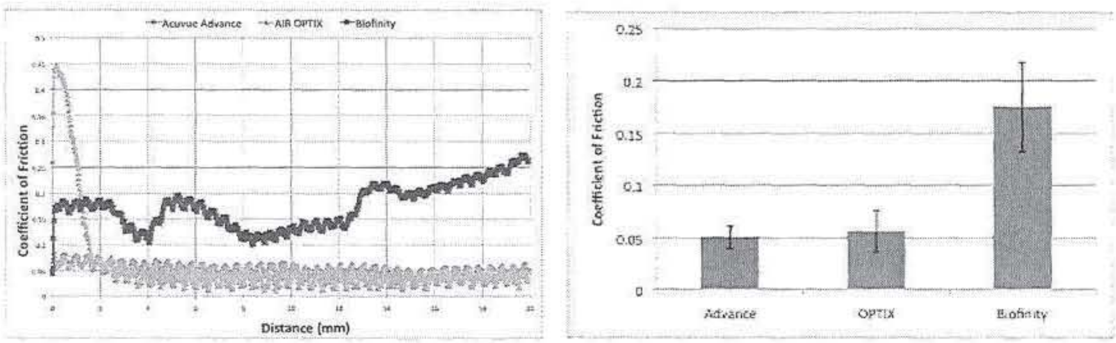


Figure 6.16: The Friction of Biofinity™ in a Saline Solution Compared to Acuvue® Advance™ and AIR OPTIX™.

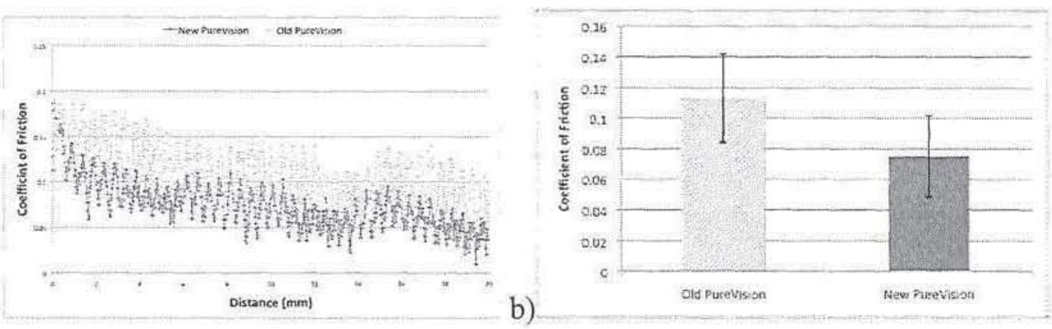
Figure 6.16 show the coefficient of friction for Biofinity™ compared against Acuvue® Advance™ and AIR OPTIX™. The results show that the coefficient of friction of Biofinity™ in saline differs from that of HypoTears™.

The mean coefficient of friction for Biofinity™ in saline is more than 100% greater than that of either of the two, second-generation silicone hydrogels used here. The figure 6.16 shows the friction fingerprint of the lenses. The fingerprints for AIR OPTIX™ and Acuvue® Advance™ remain very similar to that of their traces when in HypoTears™, however, Biofinity™ does not retain the same profile. If comparing the friction fingerprint of Biofinity™ to that of another silicone hydrogel lens, Basuch and Lomb, PureVision® lens shows similar behaviour in a 'poor' lubricant, although it must be noted that the value of coefficient of friction is much lower for Biofinity™. However, this does imply that the surface treatments (or lack of in the case of Biofinity™) are not able to completely prevent the hydrophobic silicone groups reaching the surface of lens, when ideal lubrication is not present, such is the case of saline in this experimental setup.

6.4.3: The Coefficient of Friction of New PureVision®

The new version of Basuch and Lomb's PureVision® silicone hydrogel contact lens is quoted as having 28% lower modulus than the version of PureVision® which proceeded it (www.walmartod.com).

Figure 6.17 shows the coefficient of friction of the new version of PureVision® compared to the original PureVision®. The tribometer conditions for both of the lenses were as follows: Speed – 30 mm/min, Load – 30 mN, Substrate - Melinex®, Lubricant - HypoTears™.



a) b)

Figure 6.17: The Friction of New PureVision® versus Old PureVision®.

Figure 6.17b shows the mean coefficient of friction in HypoTears™ for new and old PureVision®. The results show that the new version of PureVision® has a lower mean coefficient of friction which can also been seen in the friction profile of the lenses.

Although the friction traces (figure 6.17a) shows that the value is lower the shape of the friction fingerprint of the two lenses is virtually identical which suggests that the major surface properties of the lens have remained similar.

6.4.4: The Coefficient of Friction of AIR OPTIX™ AQUA

The results that follow show the mean coefficient of friction and friction traces for AIR OPTIX™ AQUA. The lens was tested in the lens packing solution, distilled water and HypoTears™. The tribometer conditions used for the test were: Speed – 30 mm/min, Load – 30 mN and Substrate - Melinex®.

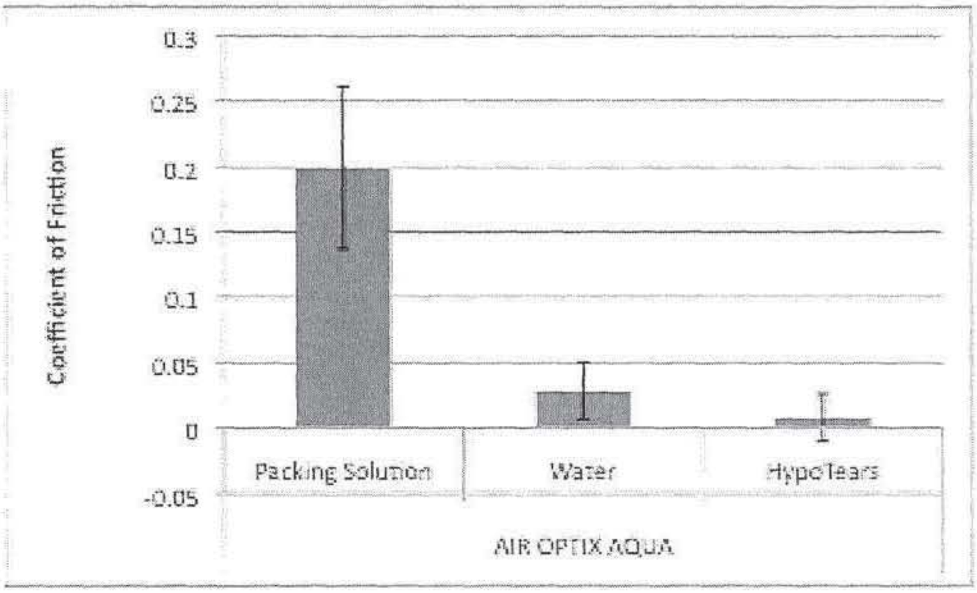


Figure 6.18: The Mean Coefficient of Friction of AIR OPTIX™ AQUA.

Figure 6.18 shows the results obtained for AIR OPTIX™ AQUA, using the three following lubricants; packing solution, distilled water, and HypoTears™. The AIR OPTIX™ AQUA lens has the lowest coefficient of friction in Hypotears™ with water the next lowest and the lenses packing solution having the highest coefficient of friction of the three lubricants.

Figure 6.19 shows the mean coefficient of frictions for the three different lubricants for AIR OPTIX™ and AIR OPTIX™ AQUA compared to each other.

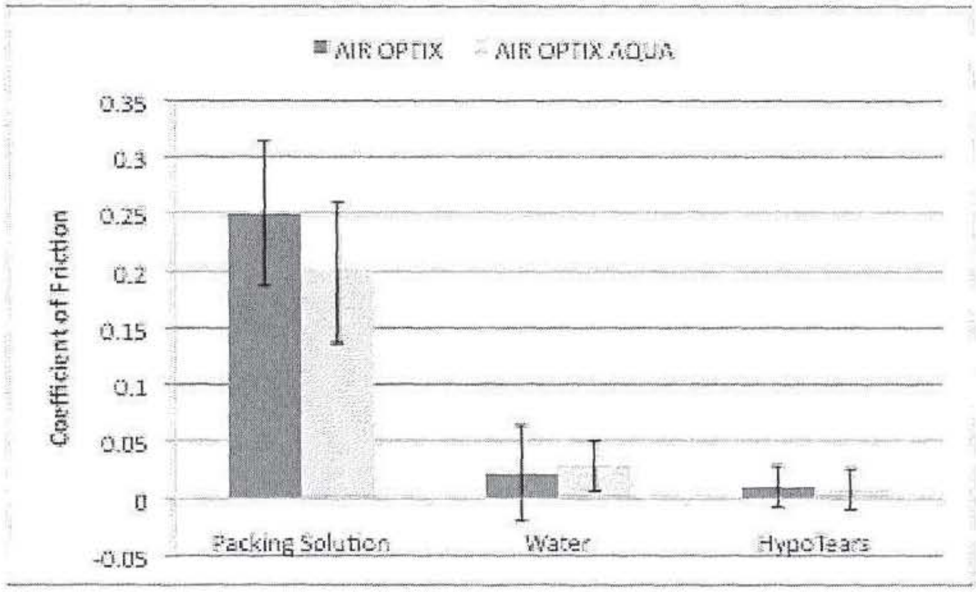


Figure 6.19: A Bar Chart Comparing the Mean Coefficient of Friction of AIR OPTIX™ Versus AIR OPTIX™ AQUA.

Figure 6.19 shows the mean coefficients of friction for AIR OPTIX™ and AIR OPTIX™ AQUA there are some differences in the mean coefficient of friction with selected lubricants. AQUA has a slightly lower coefficient of friction value in HypoTears™ although slightly higher in distilled water. The biggest and most obvious difference is in the mean coefficient obtained when the lenses own packing solution is used as the lubricant. However, this is not a direct like-for-like comparison as the AIR OPTIX™ AQUA packing solution contains 1% of copolymer 845.

The following section investigates AIR OPTIX™ AQUA in terms of looking at the structure of copolymer 845, detection in the packing solution and studying the persistence at the surface of the lens.

6.4.5: Further Investigation of AIR OPTIX™ AQUA

The structure of copolymer 845 as shown in figure 6.20 has sections of vinyl pyrrolidone in the backbone of polymer. Copolymer 845 is used in the hair care industry in styling gels and mousses and is quoted as have the following benefits:

- Provides cushion gel feel during hair application.
- Delivers smooth feel and easy comb-through.
- Provides body to mousse foam.
- Forms clear, smooth-feeling, non-tacky films.
- Two levels of hold and styling with improved shine over PVP alone.
- Substant pseudo-cationic properties for improved compatibility with anionic thickener.

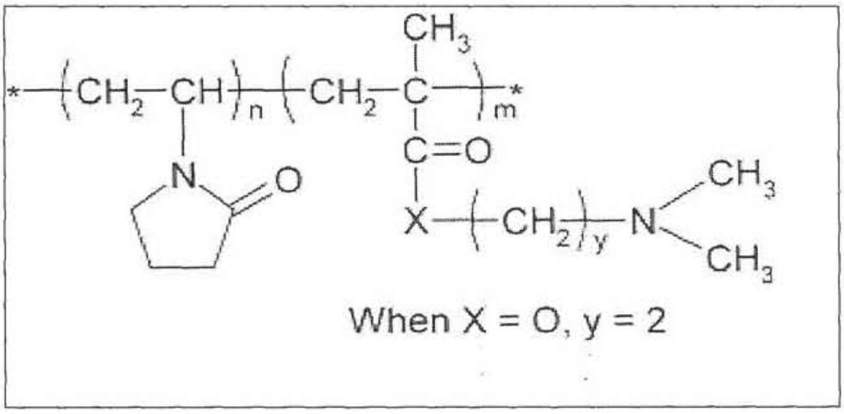


Figure 6.20: The Structure of Copolymer 845.

In chapter 4, the polyvinyl pyrrolidone (PVP) in the packing solution of 1-Day Acuvue® Moist™ was detected by using an iodine / iodide colorimetric assay. The iodine-based solution forms a colour change when complexed with small quantities of PVP.

The figure 6.21 shows the KI / Iodine solution added to; AIR OPTIX™ packing solution, a 2% wt/v PVP solution and AIR OPTIX™ AQUA packing solution.

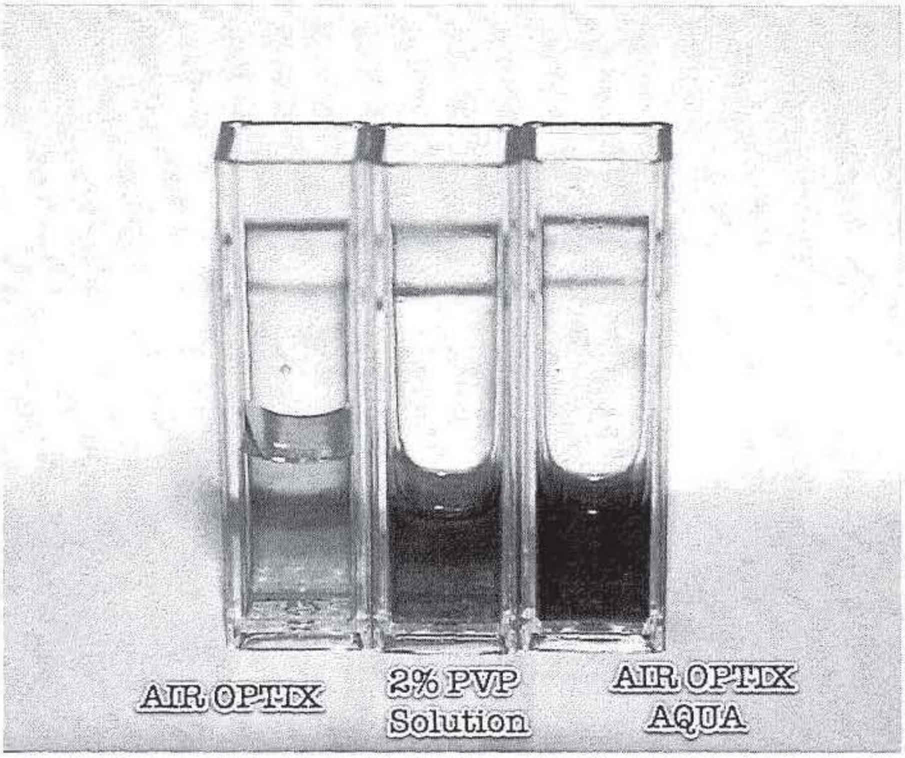


Figure 6.21: Colour changes of AIR OPTIX™ and AIR OPTIX™ AQUA Packing Solutions with an Iodine / Iodide Solution.

Figure 6.21 shows the different colours produced when the KI / Iodine solution is added in a 50:50 ratio with each of the three test samples. It is clear when comparing the colours produced from the packing solutions of AIR OPTIX™ and AIR OPTIX™ AQUA, that the latter packing solution contains quantities of PVP, although the colour is different to that of a 2% PVP solution, thus, suggesting somewhat similar in structure i.e. co-polymer containing PVP. Therefore, this must be the 1% copolymer 845 added to the packing solution of AIR OPTIX™ AQUA.

The KI / Iodine solution can also be used on contact lenses, figure 6.22 shows the effect of soaking AIR OPTIX™ and AIR OPTIX™ AQUA lenses in a 0.1M potassium iodide solution for 1 minute.

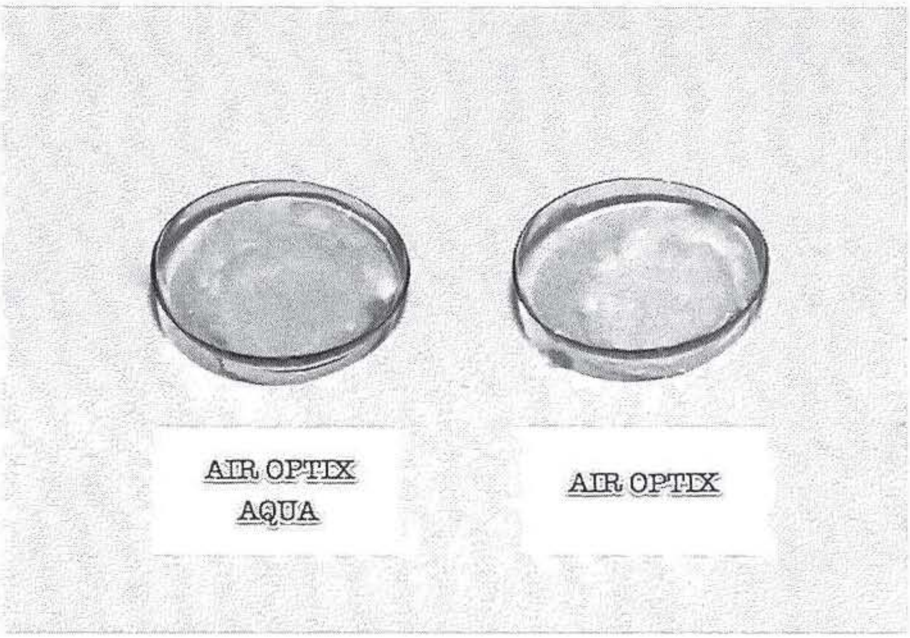


Figure 6.22: Colour Differences Between AIR OPTIX™ and AIR OPTIX™ AQUA.

Figure 6.22 shows the effect of soaking AIR OPTIX™ and AIR OPTIX™ AQUA lenses in the iodine-based solution. From the picture it is apparent that there is a colour difference between the two contact lenses. The AIR OPTIX™ AQUA has a browner colour, than the AIR OPTIX™ lens, (which is a more yellow shade). Thus, there are some PVP groups on the lens surface on the AIR OPTIX™ AQUA lens. However, at present it is unclear if this effect lasts throughout the whole day.

6.4.6: The Coefficient of Friction of 1-Day Acuvue TruEye

The latest silicone hydrogel to be released is a first for the market, a daily disposable silicone hydrogel contact lens. The lens has a water content of 46% and a Dk of 100 barrers. Figure 6.23 shows the mean coefficients of friction for 1-Day Acuvue® TruEye™ in three different lubricants; the lens packing solution, distilled water and HypoTears™.

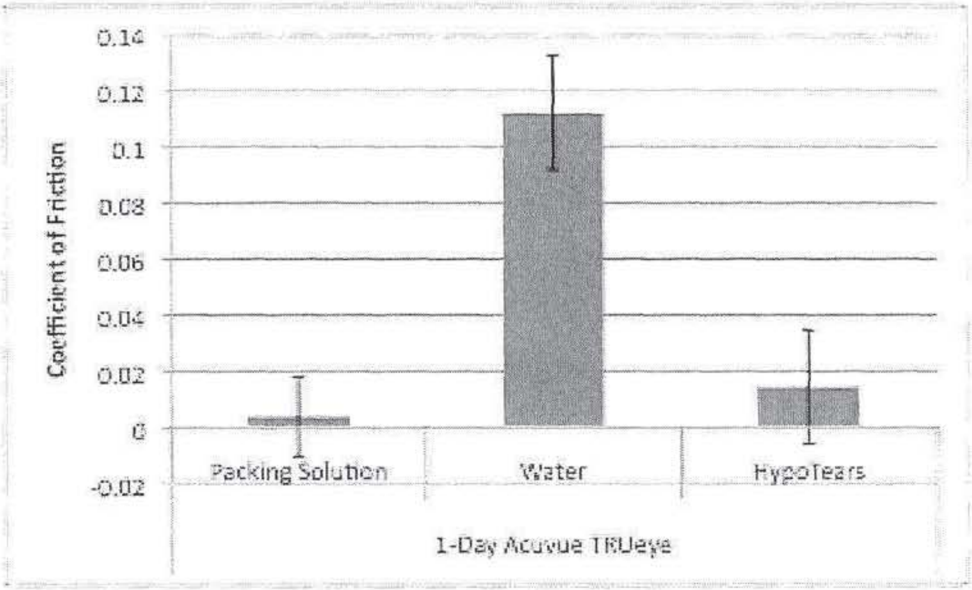


Figure 6.23: Mean Coefficients of Friction for 1-Day Acuvue® TruEye™ in Three Selected Lubricants

Figure 6.23 shows the mean coefficients of friction obtained with 1-Day Acuvue® TruEye™, showing the same trend of friction coefficients at the Acuvue® Oasy™ silicone hydrogel lens (Figure 6.10). However, the values for 1-Day Acuvue® TruEye™ are higher, especially the coefficient of friction in distilled water.

6.5: Discussion

To understand the properties of the silicone hydrogel contact lenses, there is a need to understand the driving force for their development. The driving forces are determined by what patients and practitioners would like to use.

First generation of silicone hydrogel contact lenses; Focus® Night & Day™ and PureVision® were released in 1999 with the main aim for overnight and continuous wear. This required the lenses to have high oxygen permeability, thus, the lenses were low water content and high modulus, as the amount of silicone monomer present in the lenses was high. In order for the lenses to maintain adequate surface properties, a surface treatment was required in the first generation silicone hydrogel contact lenses.

Results in section 6.2 show the coefficients of friction obtained for the first generation of silicone hydrogel contact lenses in various lubricants. These lubricants ranged from the lenses own packing solution to multipurpose solutions. The results show that when both of the lenses' are in a good lubricant, such as HypoTears™, there is not much difference in the coefficient of friction. However, when the lubricant is changed and the lens is challenged, hydrophobic sections of the matrix emerge at the lens surface. When the lenses are challenged Focus® Night & Day™ is able to maintain a lower coefficient of friction than PureVision®. This may also be the reason that PureVision® has had more problems with lipid deposits that Focus® Night & Day™. (Ross et al., 2007)

The next silicone hydrogel contact lenses released were by Johnson & Johnson Vision Care (J & J) with their first silicone hydrogel lens, Acuvue® Advance™ in 2003. In the following two years, CIBA Vision released an updated version of Focus® Night & Day™ named AIR OPTIX™ and J & J released their second silicone hydrogel lens Acuvue® Oasys®. These new silicone hydrogels released from J & J were different from the first generation silicone hydrogels and also AIR OPTIX™ in that they did not have any surface treatment. The lenses instead used an internal wetting agent; the internal wetting agent used was polyvinyl pyrrolidone, which was discussed in more detail in chapter 5.

Friction results for the second generation of silicone hydrogel contact lenses reflects the way in which these lenses were designed; the driving force of the market was no longer solely oxygen permeability but the need to improve on the comfort that the first generation silicone hydrogel lenses achieved. The way in which this was done was to increase the water content and lower the modulus more towards that of conventional hydrogels lenses. The coefficient of friction of the lenses was also improved greatly as shown in the results revealed in section 6.3.

The development in silicone hydrogel contact lenses has continued in the direction of the second generation of silicone hydrogels. Thus, more lenses have been released with lower moduli and higher water contents; with the comfort the patient experiences the number one goal. In 2006 CooperVision released their first silicone hydrogel contact lens Biofinity™. This was the first silicone hydrogel to move completely away from the TRIS based structures that were being used in the rest of the silicone hydrogel contact lenses. The CooperVision lens is based on a silicone macromer. This lens has no surface treatment or internal wetting agent, and instead relies on the matrix to prevent the hydrophobic silicone groups reaching the surface of the lens. Results for this lens show that in a good lubricant the friction is very low, however, when a less lubricious lubricant is used the lens' coefficient of friction increases more than that of lenses which possess surface treatment or an internal wetting agent. Further evidence of this is in the lipid deposition of Biofinity™, which shows high level on the contact lens surface. (Ross et al., 2007)

There have been several modifications in recent years (2007-2008) to lenses already in the market place. The PureVision® lenses have followed the trend of reducing the modulus of the lens. Bausch and Lomb have reported a 28% reduction in modulus plus improved optic design. This reduction in the modulus has also resulted in the coefficient of friction being reduced. Another lens to undergo modification with the sole aim of improving surface properties was AIR OPTIX™. The new version of this lens, AIR OPTIX™ AQUA, has 1% copolymer 845 in the packing solution. This has had the effect of improving the mean coefficient of friction of the lens when run in the packing solution of the lens. The results of the colorimetric analysis with an iodine solution show that the actual lens has some copolymer 845 present at the lens surface.

However, it is unknown at this time if the modification is permanent or removed during wear.

The latest silicone hydrogel contact lens is a first for the silicone hydrogel market, a daily disposable contact lens. In the UK daily disposable contact lenses now make up 40% of the total contact lens sales with the market share in Japan being 60%. The major advantage for daily disposable contact lenses is their convenience of use; there is no need for cleaning or storage. New contact lenses are simply inserted at the start of each day. The mean coefficient of friction results for 1-Day Acuvue® TruEye™ shows a similar trend to that of the other Johnson & Johnson Vision Care silicone hydrogel lenses, although the lens' mean coefficient of friction is higher in water than the other J & J silicone hydrogel lenses. However, the results still show a low coefficient of friction ($\sim 0.1\mu$).

Chapter 7

Summary, Conclusions and Further Work

7.1: Conclusions

There are notable achievements that have been presented in this thesis; the detection and subsequent understanding of macromolecular entrapment and release being the most important. The other noteworthy achievement has been the development and consequent applications of a novel tribometer that has allowed the coefficient of friction of contact lenses to be measured and distinguished at genuinely low values (<<0.1).

Macromolcular release

The exploitation of macromolecular release of PVA in Focus® DAILIES® was a large step in the recent evolution of daily disposable contact lens technology – as reflected in the current market. This step arose by accident, rather than intent. The scientists at CIBA Vision believed that the lens was a fully cross-linked network. Investigations at Aston however, revealed that the packing solution had a surface tension that was lower than predicted. It was reasoned that if nothing was added to the packing solution to alter the surface tension, then the lens itself must be altering the packing solution surface tension. At the time of this work the CIBA Vision lens Focus® DAILIES® had been FDA-approved for 8 years and had been commercially available since 1997. The existence of, or reason for, the lowered packing solution surface tension (the release of PVA) was not detected by CIBA Vision, principally because "outdated" lenses were not retained and studied in detail. They had, therefore, missed the fact that the packing solution of their lenses accumulates increasing quantities of PVA with time.

When CIBA Vision learned of the presence of small quantities of PVA in the packing solution, a clinical trial was set up to study the effect on wear. In a prospective, blind contralateral human trial, 20 subjects were introduced to normal Focus® DAILIES® and Focus® DAILIES® that had been extracted then repackaged. The results from this study showed that the extracted lenses gave reduced comfort, more lens awareness and a reduction in wear time (Winterton et al., 2006). This thesis portrays the part played by the author in this process and indicates the work done in identification and quantification of the role of PVA.

In order to understand and also to possibly improve the in-eye performance of Focus® DAILIES® the elution of PVA was studied in more detail.

After several other analytical techniques were considered a highly sensitive refractometer was identified as the most effective method to measure varying concentrations of PVA in solution. The linear relationship of refractive index to concentration for very low levels made this a very useful tool in analysing the release of PVA (e.g. From Focus® DAILIES® lenses). Lenses were obtained with different expiry dates and the RI was measured. The resulting graph showed that the packing solution of the older lenses (therefore having been stored for longer) had higher refractive indices. This implied that older lenses had released more PVA passively from the lens matrix than newer lenses. This simple yet previously unknown finding provided the key to a whole series of subsequent work on macromolecular entrapment and release as a method of comfort enhancement.

It was important to develop a release model that used individual lenses and closely mimicked the conditions during lens wear. The model used 100 μl of release medium per hour, which is approximately the same amount as predicted for tear flow rate over the same period. To imitate the mechanical agitation experienced by the lens during wear, vortexing was used and, after experimentation a period of 30 seconds at the start of each hour was used. The model was tested and proved to be reproducible. Lenses straight from the packing solution were compared against lenses that had been worn for 8 hours the previous day using the new release model. The worn lens released less PVA than the new lens from the packing solution. This suggests that the worn lens had released PVA during the previous day.

Results discussed so far do not suggest the way in which or where the PVA is released. The hypothesis proposed was that the PVA being released was soluble uncross-linked PVA possibly left over from the manufacturing process. The Focus® DAILIES® lens is produced using a unique method, LightStream technology™. The production method involves UV polymerisation of the nelfilcon A macromer in quartz moulds. However, it is possible that there is left-over uncross-linked PVA from incomplete curing and due to the fact that not all of the nelfilcon A macromer is functionalised.

If unfunctionalised nelfilcon A (therefore uncross-linked PVA) is associated with PVA release then altering the cross-link density will affect the quantity of PVA released. Gamma ray exposure is known to increase the cross-link density of polymers. It was used to cross-link any unincorporated PVA in the lens matrix. Conversely, sodium periodate is known to cleave the head to head OH groups in PVA. This provides a ready method of reducing the perfection of the network effectively decreasing the cross-linked density. Treatment of Focus® DAILIES® lenses with sodium periodate increased the amount of PVA released and lenses exposed to gamma rays released less PVA. The results above are in agreement with the hypothesis that soluble uncross-linked PVA is eluted from the lens matrix.

To help support the hypothesis that the soluble uncross-linked PVA is released from the lens matrix, lenses were obtained from CIBA Vision that contained 2% extra-added uncross-linked soluble PVA, thus potentially aiding the release of PVA from the lens. The lenses with the extra 2% PVA released more PVA than the control lenses. Therefore, enforcing the hypothesis. The lens with added extra 2% PVA became the basis of Focus® DAILIES® All Day Comfort with Aqua Comfort™, where Aqua Comfort™ refers to the perceived effect of incorporation of the extra uncross-linked PVA.

The original Focus® DAILIES® lens suffered more from end of day discomfort than other daily disposable contact lenses, which suggests that not only was PVA released but that the lens changed during the course of the day. Experiments were undertaken to determine whether the soluble PVA at the surface of the lens could be assessed or measured. Lenses were obtained from CIBA vision, which contained fluorescently-tagged linear PVA. There were two fluorescent tags used for the linear uncross-linked PVA at different molecular weights. Fluorescent tags used were fluorescein (tagged to lower molecular weight PVA) and rhodamine (tagged to the higher molecular weight PVA). Results from the release studies carried out on these lenses showed that most of the fluorescein tagged PVA was released in the first hour. Thus, showing that the uncross-linked PVA is released as a burst effect. The 3D spectra from the surface fluorescence of the lens pre and post extraction show that the surface linear PVA has been diminished. This may help explain why the lens is suffering from discomfort towards the end of the day. The surface released PVA is out-stripping the ability of the lens to resupply the surface with PVA by passive diffusion. There is plenty of PVA in the lens matrix for release as the results of the release of PVA by passive diffusion into the packing solution show.

Evolution of the Focus® DAILIES® brand has not stopped with Focus® DAILIES® All Day Comfort. The most recent daily disposable released from CIBA Vision now uses what is termed a 'triple action moisturising agent' containing hydroxypropyl methyl cellulose (HPMC), PVA and poly (ethylene glycol) (PEG). This effect is called Aqua Comfort Plus™, this lens will be discussed later in the context of tribological studies.

Tribometer development

At the start of this summary chapter mentioned the other noteworthy achievement as the development and consequent applications of a novel tribometer, which has allowed the coefficient of friction of contact lenses to be measured and distinguished at genuinely low values. A modified nano-srcatch tester produced by CSM Instruments was the basis of the new tribometer. The first step to this achievement was the evaluation of the tribometer in terms of accuracy and reproducibility. This was accomplished by measuring twenty-five mean coefficients of friction using the same type of contact lens and comparing the results obtained.

The old tribometer set-up was unable to measure coefficients of friction accurately below 0.1 μ. Whereas, the new tribometer can measure coefficients of friction as low as 0.005 μ. In terms of lubricity, the best contact lenses all have coefficients of friction below 0.1 μ. The old tribometer also produced the coefficient of friction manually. The new tribometer software measures the friction force 1000 times per pass, thus, allowing for a more detailed analysis of the frictional properties of the lens.

Various aspects of the test conditions to be altered on the nano-scratch tester; the conditions that can be easily altered are as follows:

- The Load – The load applied vertically down though the contact lenses onto the substrate, a vital component in the equation of the coefficient of friction.
- The Speed – The speed at which the friction table (and therefore the substrate) is moved past the contact lens.
- The Substrate – The material that the coefficient of friction of the lens is measured against.
- The Lubricant – The lubricant is used to represent the lubrication *in-vivo*. However, the lubricant can be altered in both type and quantity.

All of the variables mentioned were studied to establish their effect on the measured coefficient of friction. First variable analysed was the load applied to the contact lens. The decision was made to use two different types of contact lens, with different surface and mechanical properties. Results showed that there was no trend in coefficient of friction with varying load. This would be expected, as the load is part of the equation for the coefficient of friction. For a skin adhesive hydrogel (pressure sensitive adhesive) you would expect friction to rise with pressure at some point. It is the fact that load doesn't change the interface that allows the Amonton equation to be applied.

Speed at which the friction table moves across the contact lens was the next variable studied. The third law of friction is sometimes quoted, as friction is independent of the speed used. Speed has been shown to influence the measured coefficient of friction in other tribological systems, such as metals sliding on ice. Effect of speed on the measured coefficient friction of contact lenses was investigated using Focus® Night & Day. The tribometer can move the table at speeds ranging from 5 to 550mm/min. Results obtained showed that as the speed of the tribometer table increased the measured coefficient of friction decreased, which is comparable with the results obtained from metals sliding on ice. Metal sliding on ice is a type of hydrodynamic lubrication, the same type of lubrication as seen in the eye.

Choice of substrate is key in the measurement of coefficient of friction. A decision was made to use a substrate that was of medium surface energy, did not require any cleaning, and was of good quality with a reproducible surface. The substrate chosen was a high quality thin sheet of poly (ethylene terephthalate) (PET) with the trade name Melinex®. Another polymeric substrate was investigated, to use as an extra tool in the study of differences between contact lenses. Another polymeric substrate used was a polyurethane (PU) with an adhesive coating that allowed the PU to be adhered onto the PET sheet effectively forming a new substrate. Results of the mean coefficient of friction obtained by the PU substrate was that the trends in the coefficient of friction were the same i.e. the order of the friction coefficient of different lenses. However, the coefficient of friction obtained was exaggerated with any differences in the mean friction being greater.

Quantity of lubricant was the last variable investigated . The aim was to establish the minimum volume that could used to obtain a consistent friction coefficient. This was investigated, because natural biological fluids are small in quantity and difficult to obtain. The results obtained showed that it was possible to use quantities of lubricant as low as 10 μl and not greatly increase the mean coefficient of friction of the contact lens. Thus, *ex-vivo* tears could be used as the lubricant. It was this capability that enabled HypoTears™ to be identified as a surrogate for tear fluid in comparison parameter studies of the behaviour of contact lenses.

The ability to study in detail the friction of the contact lenses, in particular ways of searching for, and exaggerating differences in, the friction behaviour is important. Three different methodologies were studied with the aim of probing the surface of contact lenses and contact lens systems (either packing solution, comfort drops, or multi purpose solutions). The three methods studied were:

- Comparing the mean coefficients of friction over the whole pass distance.
- The friction profile given by the tribometer as the lens is passed over the substrate.
- The difference in coefficient of friction in a 'good' and in a 'poor' lubricant.

Results obtained from each of the three methods stated above allow differences in friction behaviour of different contact lenses to be studied and compared. The mean coefficient of friction shows differences between contact lenses. However, the whole story of the lens' friction behaviour is sometimes masked.

The tribometer technique development discussed here has many useful applications in the field of contact lenses and contact lens systems - comfort drops and multi purpose solutions interactions. This thesis main focus is on the application of measuring the coefficient of friction of contact lenses. Frictional properties of contact lenses were considered under two headings: daily disposable contact lenses and silicone hydrogel contact lenses. Information obtained by use of friction properties was focused in different ways for each type of lens. Understanding of how the recent improvements had altered the lenses frictional properties was the focal point of the daily disposable contact lenses. Friction was used as a tool for understanding the macromolecular enhancement mechanism. The focus for the silicone hydrogel contact lenses was, on the other hand, the way that the lenses had developed since their commercial launch.

Frictional studies of daily disposable lens development

Surface enhancement of contact lenses by macromolecular release was discussed earlier in this summary, also a technique was developed that enables small changes in surface properties to be measured. Macromolecular release of PVA from the Focus® DAILIES® brand lenses was the first but not the last daily disposable contact lens to utilise macromolecules in the enhancement mechanism. Surface enhancement of two other brands of daily disposable contact lenses soon followed plus a more complicated polymeric release from DAILIES®. The developed novel biotribological technique was a useful tool in allowing the friction characteristics of these enhanced lenses to be measured and also used in order to understand how each lens exploited the use of hydrophilic macromolecules.

Initial investigation performed was to compare the friction of Focus® DAILIES® Basic and Focus® DAILIES® All Day Comfort with Aqua Comfort™. Results showed that there is a difference in the mean coefficient of friction, although the friction profiles of the lenses remained virtually identical. This was expected, as the enhancement was an extension of an already existing effect.

Mean coefficients of friction of these two lenses were also compared to the mean coefficient of friction of Focus® DAILIES® Aqua Comfort Plus™ (FDACP) which was released a year later as the third daily disposable contact lens from CIBA Vision. Focus® DAILIES® Aqua Comfort Plus™ contact lens is a more intricate enhancement than Focus® DAILIES® All Day Comfort. Enhancement of the FDACP lenses uses a multi polymeric system with both PVA and PEG. The packing solution is also altered with PEG, along with extra poloxamer. Packing solution friction shows the benefits of this multi polymeric system in terms of lubricity, with FDACP giving far lower coefficient of friction that the other DAILIES branded lenses. However, the lens itself only shows a small reduction in the mean coefficient of friction.

In chapter 3 a release model was developed this was used to study the polymers released from the FDACP lenses. PVA was shown to elute from the matrix of Focus® DAILIES® into the packing solution. Therefore, in Focus® DAILIES® Aqua Comfort Plus™ there is both PVA and PEG present in the packing solution. Mean coefficient of friction was measured using 100 μl of the extract provided by the release model. Mean coefficient of friction of the extract was compared to the extraction media and also to that of HypoTears™. HypoTears™ is a dry eye drop manufactured by Novartis, the parent company of CIBA Vision, which uses PEG and PVA in combination as lubricating ingredients. The results showed that the first hour extract gave the lowest mean coefficient of friction with HypoTears™ the next lowest. This was unexpected as HypoTears™ contains more PVA and PEG than the estimated amount present in the lenses first hour extract. HypoTears™ also contains another component that has surface activity, the preservative, benzalkonium chloride. The coefficient of friction of solutions of preserved HypoTears™, unpreserved HypoTears™, and unpreserved HypoTears™ with added benzalkonium chloride was measured using AIR OPTIX™ as the control lens. Results showed that the test lubricants that did not contain any benzalkonium chloride had a lower coefficient of friction than those that did contain the preservative. This suggests that the reason for the first hour extract of FDACP having a lower coefficient of friction than HypoTears™ was due to of the presence of benzalkonium chloride.

As mentioned previously PEG is present in the multi-polymeric enhancement of FDACP. The PEG used is a low molecular weight which is not chemically attached to the lens matrix, therefore, it is safe to assume that the release will be rapid. Workers at CIBA Vision have shown that PEG is released from the lens, using the Aston *in vitro* release model, in 2 hours. FDACP lenses that had undergone the release model for 5 hours, the friction of the first and the fifth hour extract were investigated to see if the effect of the low coefficient of friction seen in the first hour remained. The results show that the fifth extract has a higher coefficient of friction when compared to the first extract. This is because the PEG has already been released from the lens in the first period of the extract process and any poloxamer carried over from the packing solution has long been removed. Additionally, the release profile of PVA from the lens is not linear; being dominated by the burst effect in the first hour.

The proposed mechanism for the release of PVA is by reptation though the surface of the lens during the day's wear, helped by the natural mechanical agitation of the eyelid. The release of PEG from the FDACP lens also occurs by the same mechanism but at a much faster rate because the molecule weight is smaller and PEG has no affinity for the lens matrix.

There is another daily disposable contact lens that has undergone macromolecular enhancement, although the mechanism involved is different to that of Focus® DAILIES®. This lens is manufactured by Johnson & Johnson, under the name 1-Day Acuvue® Moist™, which is an enhanced version of 1-Day Acuvue®. The lenses 1-Day Acuvue® (1DA) and 1-Day Acuvue® Moist™ (1DAM) were investigated to try and understand how 1DAM varies from 1DA. Friction results for 1DA and 1DAM showed differences in both the mean coefficient of friction and also the friction profiles of the two lenses. The mean friction coefficient of 1DAM has been reduced by more than 50% when compared to that of 1DA under the same conditions. Friction profiles of the lenses are also different with 1DAM showing much less stick-slip behaviour than 1DA.

Using friction as the initial probe was the packing solutions of the lenses were examined. The packing solutions of 1DA and 1DAM are different with the packing solution of 1DAM containing an unknown quantity of PVP. Packing solution of 1DAM had a much lower mean coefficient of friction than 1DA.

A well-established colorimetric technique dating back to the 1950's was used to detect the presence of PVP. This technique is based on a complex that is formed between iodine, iodide ions and polyvinyl pyrrolidone. Soaking lenses in the iodine / iodide solution for one minute produces a colour change in the lens which readily identifies the presence of PVP. The 1-Day Acuvue® Moist™ lens is dyed brown corresponding to the formulation of the iodine / PVP complex, whereas, the 1-Day Acuvue® lens shows the yellow colour of the uncomplexed iodine / iodide solution. Colour intensity gives evidence that PVP is attached to the surface of the 1DAM lens. This result explains differences in the coefficient of friction and stick-slip behaviour of 1DA and 1DAM.

The proposed mechanism of enhancement of 1DAM is that the PVP is anchored at various points along the lens matrix. PVP is bound to the lens matrix and penetrates the lens matrix in the autoclave process as the lens is expanded due to the temperature of the sterilisation procedure. PVP presents sections of loops and coils of the polymer along the surface of the lens.

The third and final daily disposable contact lens investigated was Soflens® Daily Disposable manufactured by Bausch & Lomb. Soflens® Daily Disposable lens has undergone the most substantial changes. It is the only daily disposable discussed here to have a change in bulk material and water content; but again there is an enhancement by hydrophilic macromolecules. Macromolecular enhancement in this case uses a completely different technique to that of DAILIES® and 1-Day Acuvue®. Results show the differences between the new lens Soflens® Daily Disposable and Soflens® 59 which uses the same polymeric material, Hilafilcon B. The equilibrium water contents (EWC) of the lenses are different 41% to 59% respectively, with Soflens® Daily Disposable having the higher EWC. Soflens® Daily Disposable lens has the lower coefficient of friction when taken straight from the packing solution. However, the friction profiles of the lenses are not the same, even though the bulk material is; the Soflens® 59 materials friction rises as the lens is moved across the substrate. Conversely, Soflens® Daily Disposable starts with a very similar static coefficient of friction but, unlike the Soflens® 59 material the friction decreases as the lens is moved across the substrate. Mean coefficient of friction of the packing solution was compared between Soflens® One Day and Soflens® Daily Disposable. New lens Soflens® Daily Disposable packing solution had a much lower coefficient of friction that its predecessor, which is not surprising as Soflens® Daily Disposable packing solution contains a poloxamine.

As poloxamine is added to the packing solution and poloxamines have both hydrophobic and hydrophilic sections, it is likely that the poloxamine is able to absorb onto the lens surface. A Soflens® Daily Disposable lens was soaked in a MPS for a week, run on the tribometer and had its coefficient of friction profile compared to that of Soflens® Daily Disposable taken straight from the packing solution. The results showed that the friction profiles were different with the soaked lens friction profile being very similar to that of Soflens® 59. Thus, it is proposed that the enhancement mechanism is that the poloxamine is loosely adsorbed onto the surface of Soflens® Daily Disposable lens, and is removed during the soaking of the lens, and also during wear reducing lens comfort.

Surface properties for each of the lenses (in particular the coefficient of friction) have undergone significant change. The lens packing solutions have also been modified. The outcome of both these changes is the improved lubricity and greater wearer comfort.

The enhancement to the lens surfaces has been brought about by the harnessing of linear soluble hydrophilic macromolecules at the lens surface, but with each lens using a different method to incorporate these hydrophilic species. Soflens® has been modified by simple physical adsorption of a poloxamine, 1-Day Acuvue® has been modified by the locking of polyvinyl pyrrolidone at the lens surface and Focus® DAILIES® has been modified be incorporating soluble polyvinyl alcohol (and now, additionally, PEG) into the matrix, allowing emergence from the surface during wear.

Lubricity of the lens packing solutions has been improved in two ways. Soluble macromolecules weakly bound to the lens structure leach into the packing solution, but more particularly additional polymers such as modified cellulosic's are added separately. Different manufacturers use different combinations of approaches but the end goal is improved comfort on insertion, which can be seen in the figures showing the mean coefficient of friction of the lens packing solutions (Chapter 5)

Frictional studies of silicone hydrogel lenses

To understand the properties of the silicone hydrogel lenses, there is a need to understand the driving force for their development. What patients and practitioners would like to use is the driving force in development. The tribometer was used as an exploratory analytical tool in the study of the silicone hydrogel contact lenses. Results presented in chapter 6 follow the timeline of the development of silicone hydrogels contact lenses into the commercial market.

The first generation of silicone hydrogel contact lenses, Focus® Night & Day™ and PureVision®, were released in 1999 for overnight and continuous wear. This required, more than any other single factor, the lenses to have high oxygen permeability. Thus, the lenses were shown to have low water content and high modulus, as the amount of silicone monomer present in the lenses was high. In order for the lenses to maintain adequate surface properties, a surface treatment was required in both of the first generation silicone hydrogel contact lenses.

The results showed that when both of the lenses are in a good lubricant, such as HypoTears™, there is no significant difference in their mean coefficient of friction. However, when the lubricant is changed and the lens surface is challenged, in a way that exposed hydrophobic sections of the matrix present at the lens surface, the lenses showed different behaviour. Focus® Night & Day™ was able to maintain a lower coefficient of friction than PureVision®. This fact maybe the reason that PureVision® wearers experience more problems with lipid deposition than with Focus® Night & Day™.

At this point the driving force of the market changed from being centered on oxygen permeability. There was a recognised need to improve the comfort of the lenses and also to reduce the associated complication with the first generation silicone hydrogels. The way in which this was done was to increase water content and lower the modulus of the contact lenses, moving more towards in the characteristics of conventional hydrogel contact lenses.

At this point Johnson & Johnson Vision Care (J & J) entered the market, with their first silicone hydrogel lens, Acuvue® Advance™, which was released in 2003. In the next two years, CIBA Vision released a higher water content version of Focus® Night & Day™, (named AIR OPTIX™) and J & J released their second silicone hydrogel lens, Acuvue® Oasys®. Oasys and Advance do not employ any surface treatment; instead the lenses use an internal wetting agent - polyvinyl pyrrolidone. Second generation of silicone hydrogel contact lenses all possessed higher water contents, lower moduli and therefore, lower Dk than the first generation of silicone hydrogel contact lenses. Their characteristics are associated with reduced coefficients of friction, which are much lower than the first generation of silicone hydrogel lenses.

The recent developments of silicone hydrogel contact lenses have continued in the same direction. Thus, more lenses have been released with lower moduli and higher water contents, with the comfort the patient experiences the number one goal. In 2006 CooperVision released their first silicone hydrogel contact lens Biofinity™, which was the first silicone hydrogel to move completely away from the TRIS-based structures that were being used in the rest of the silicone hydrogel lenses. CooperVision's lens is based on a silicone macromer, which has no surface treatment or internal wetting agent, but the lens instead relies on the matrix to prevent the hydrophobic silicone groups reaching the surface of the lens. Results for Biofinity™ show that in a good lubricant the friction is very low. However, when a less lubricious lubricant is used, the coefficient of friction of these lenses increases more than that of the second-generation silicone hydrogels that possess surface treatment or an internal wetting agent. This is consistent with the observed lipid deposition found on the surface of the lens. (Ross., 2007)

Other modifications have been noted in chapter 6, mainly based on pre-exsisting lens platforms. Similarly J & J modified their platform technology to produce the first silicone hydrogel daily disposable lens. The major advantage for daily disposable contact lenses is their convenience of use, there is no need for cleaning or storage, a new contact lens is simply inserted each day. Mean coefficient of friction results for this lens (1-Day Acuvue® TruEeye™) are similar to those of the other Johnson &

Johnson Vision Care silicone hydrogel lenses, although the mean coefficient of friction of the lens is higher in water (<0.1μ) than the other J & J lenses.

Use of the tribometer as both a comparative and investigative tool has provided useful information about both daily disposable and silicone hydrogel contact lenses. Results from the tribometer can be compared to the in-eye performance of lenses from clinical trials. When the same type of contact lenses has seen a reduction in the coefficient of friction, this has also been seen with an improvement in the comfort scores obtained. Although the value of the coefficient of friction alone does not predict comfort scores, as in the case of 1-Day Acuvue® compared to Focus® DAILIES®. Therefore, the current hypothesis is that the comfort of the lens is a combination of a function of the friction but also a function of the lenses other bulk properties as well as optic design.

7.2: Further Work

The work described in this thesis is concerned with mechanisms of contact lens lubrication. There are three major driving forces in contact lens design and development, cost, convenience, and comfort. The three major methods of surface modification used are; release of soluble macromolecules (such as PVA) from the lens matrix; irreversible surface binding of a macromolecule (such as PVP) by charge transfer and the simple polymer adsorption (e.g. pluoronic) at the lens surface.

Interactions between multi purpose solutions and contact lenses, is a very important factor in successful wear. Multi purpose solutions now contain surfactants with the aim of improving lens initial comfort after the lenses have been soaked in the solution overnight. There is at present no standard instrumental technique for studying these interactions. The work described in this thesis highlights a possible way of studying the interactions using an *in vitro* technique that will enable any incompatibility to be shown and avoided in practice.

The work described in this thesis also allows contact lenses that have not come to the market place to be studied and provided an *in vitro* method of predicting wearer comfort.

The potential for the tribometer is almost limitless, some examples follow:

- The effect of substrate hydrophilicity & mechanical properties.
- The use of a biological substrate – to be more 'eyelid like'.
- The development of a method to 'mimic' the progressive dehydration and other changes that occur during a day's contact lens wear.
- The monitoring of worn lenses.

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All websites were correct at date of submission unless stated.