

Section: Original Research

Title: Investigating the permeation properties of contact lenses and its influence on tear electrolyte composition

Authors: Aisling Mann¹, Virginia Sáez-Martinez¹, Fiona Lydon¹, Brian Tighe¹.

Short Title: Ion permeation and water structuring in contact lenses.

Footnotes: ¹Biomaterials Research Unit, School of Engineering and Applied Science, Aston University, Birmingham, B4 7ET, UK.

Competing interests: none

Declarations of interest: none

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Corresponding author: Aisling Mann, Biomaterials Research Unit, School of Engineering and Applied Science, Aston University, Birmingham, B4 7ET, UK. Tel. +44 (0121) 204 3407. Email: a.m.[mann@aston.ac.uk](mailto:a.m.mann@aston.ac.uk)

ABSTRACT:

The health of the cornea is paramount, the aim of this study was to assess the permeation of essential tear electrolytes through a range of commercial contact lenses. Donor/receiver conductivity measurements were recorded using a dual-chamber diffusion system which allowed material permeability profiles and coefficients to be calculated. Water structuring properties of the contact lenses were measured by differential scanning calorimetry. Freezing water was subdivided into 'ice-like' water (free, non-bound and has a melting point close to that of pure water) and polymer associated water (free but loosely bound to the polymer matrix). Each material interacts differently with each of the three salts, for example; lotrafilcon B (34% EWC) shows a higher and larger range of receiver concentrations post KCl, NaCl, CaCl₂ permeation (76, 59 and 42 mM respectively) compared with the lower and tighter range exhibited by lotrafilcon A (22% EWC) (36, 22 and 18 mM respectively). Additionally, in terms of the relationship between permeation and water structure, balafilcon A (34% EWC) has a high KCl permeation ($P_{60} 258 \times 10^{-8} \text{ cm}^2/\text{s}$) and ice-like water (14%), but narafilcon A (44% EWC) has a low ion permeation ($P_{60} 3.9 \times 10^{-8} \text{ cm}^2/\text{s}$) and significantly less ice-like water (4%). The permeation trends for the silicone hydrogel materials could not be fully explained by water content and structuring. Composition and, in particular, the microstructure and morphology of these materials must impart a greater influence on permeation capability.

Keywords: Ion permeability; ice-like water; diffusion cell; tear electrolytes; contact lens materials; posterior tear film.

1. Introduction

In contrast to most tissues in the body the cornea is avascular and thus has no blood vessels to nourish or protect it against infection. Consequently, corneal homeostasis depends upon the tear film and the underlying aqueous humour to maintain normal function and the metabolic requirement for oxygen is sourced from the external environment.^{1,2} The importance of oxygen for corneal metabolism and the physiological consequences of oxygen deprivation in contact lens (CL) wear have long been recognised.²⁻⁷ Oxygen availability to the cornea is affected by the presence of a contact lens and its transport through the lens was recognised as the dominant mode of transfer to the cornea, this was found to be the case even with complex lens designs and piggyback systems.^{8,9,10}

Just as optimisation of the cornea-tear-lens system requires an analysis of the modes of oxygen transport the same is true of tear electrolyte mobility. The movement of electrolytes (and water) is critical in enabling the free movement of nutrients, the removal of metabolic waste products, and the distribution of tear film components.¹¹ Similarities in the role of hydration in oxygen and ion transport suggest that considerations affecting oxygen transport in the lens-wearing eye will also govern electrolyte movement.¹²

The lacrimal gland is the major source of tear electrolytes,¹³ although vascular permeability also provides a secondary source of tear components such as albumin.¹⁴ Thus it is logical to assume that electrolytes may also move into the tear film by this route and this expectation is strengthened by the similarities of the normal osmolarity reported range for serum (ca 290 - 310 mOsmol/L) and that reported for normal healthy tears (ca 270 - 300 mOsmol/L).^{15,16} Sodium represents approximately 80% by mass of tear cations. Potassium ion concentration in tears, at ca 15-30 mM, is much higher than those determined in serum (ca 4.5 mM), which

points to an active potassium secretion in tears. Calcium and magnesium concentrations in tears are lower than in serum but are closer to those in the interstitial fluids (tear calcium: ca 0.4-0.8 mM, serum ca 1.09-1.33mM; tear magnesium: ca 0.5-1.1 mM and serum ca 4.36-5.32 mM.¹⁷⁻²¹). This unique tear electrolyte composition is clearly essential for corneal homeostasis maintenance; the anterior ocular surfaces work hard to maintain specific tear electrolyte levels which are distinct from normal systemic concentrations. The effects altered electrolyte profiles have on the ocular surfaces and the consequent chemical potential of the surrounding cells are largely unknown.

In terms of CL wear, the in-situ lens can potentially produce an enhanced evaporation of the tear film and an electrolyte imbalance between anterior and posterior tear film. Both can lead to an alteration in normal ocular function; changes in osmolarity and electrolyte concentration are, for example, known to be associated with dry eye syndrome.²² Although the mechanism of electrolyte-related changes is unclear, in the lens-wearing eye the ion permeability of the lens material and the factors that control it are of obvious importance. For example, clinical differences have been observed with balafilcon A and senofilcon A, two silicone hydrogel materials with similar equilibrium water contents (EWC) at 36% and 38% respectively. However, in terms of adverse events, and specifically corneal infiltrative events (CIEs), the rate of incidence with balafilcon A was found to be in the region of ~3% compared with the senofilcon A material at ~6%.²³ The significance of which is very important in terms of wearer satisfaction and comfort and yet the fundamental reason(s) for this (and other) distinctive clinical outcomes have yet to be determined.

The question of a correlation between ion transport and CL movement has been raised, suggesting that a threshold permeability is necessary to maintain adequate lens movement

during blinking.²⁴⁻²⁶ This is highlighted in the CIBA Vision 1996 patent which proposed permeation threshold values for on-eye lens movement.²⁷ Given the unusual balance of individual cation concentrations in tears and the importance of tear electrolyte concentrations to corneal homeostasis, the contribution of lens permeability to individual tear cations is potentially important.

Earlier studies of simple conventional hydrogels have included data for calcium and potassium ion transport^{28,29} however, sodium chloride is almost certainly the most widely studied salt permeant in contact lens studies.^{2, 12, 30} Tears contain a variety of highly regulated ions and it is important to investigate and understand the behaviour and transport of other ions in addition to sodium ions. CL materials are now inherently more complex mainly due to the growing importance of the silicone hydrogels. In consequence we have examined the transport behaviour of three important tear cations with a comprehensive range of currently available conventional and silicone-based contact lens materials. Kinetic profiles and endpoint permeation measurements for each material with the three salt solutions, sodium, potassium and calcium chlorides (NaCl, KCl and CaCl₂) using Franz cell diffusion systems were carried out and correlations between water contents and water structure examined.

2. Methods

2.1. Materials

Seventeen commercial CLs were studied: 12 silicone hydrogels (Table 1) and five conventional hydrogel materials (Table 2). A standard lens power of -3.00 was used. All CLs were pre-soaked in deionised (DI) water for seven days prior to analysis, changing the water daily, to remove carry-over conductive contaminants from the lens packing solution. Lens thickness and equilibrium water content (EWC) were measured post-water soak ($n \geq 3$). All

EWCs referred to hereafter relate to the ‘*measured*’ water soaked EWC as opposed to the manufacturers’ quoted packing solution values. NaCl, KCl, and CaCl₂, were all sourced from Sigma-Aldrich Ltd (Dorset, England). DI water with a purity of 18.2 MΩ·cm (<20 μS/cm) was generated with a Purite purification system (Purite Ltd., Oxon, UK) and used to prepare 300, 400 and 800 mM aqueous standard salt solutions.

2.2. *Permeation cell configuration*

The permeation set-up (Franz Flow Cell, PermeGear Inc., Hellertown, PA, USA) consisted of a donor and receiver cell. 4 ml of 18.2 MΩ·cm water was placed in the lower receiver cell and 2 ml of 300 mM donor salt solution was added to the upper compartment. A Teflon™ stirrer bar was placed into the lower chamber. Individual CLs were sandwiched between the top and bottom chambers, tightly sealed by two silicone washers with an exposed area of 0.64 cm² to allow permeation across the test lenses. A clamp was used to bind both chambers with the lens/washer set-up in between and the set-up was then mounted on a customised magnetic stirrer plate. At least three replicates of each lens-salt combination were carried out at room temperature.

2.3. *Conductivity calibration and measurements*

A microconductivity probe (IsoPod™, Edaq Pty. Ltd., NSW, Australia) equipped with Pod-Vu™ software was used to monitor the receiver solution conductivity as a function of time, which in turn was interfaced to Pod-Vu software (Edaq Pty. Ltd., NSW, Australia), for automatic data collection. Conductivity measurements were automatically recorded every 30 seconds for the duration of each eight hour (480 min) experiment. A concentration versus time profile was obtained for all salt/lens combinations. Calibration curves for each salt were used to convert conductivity (mS) to concentration (mM). Ion chromatography (Dionex -

Thermo Scientific, Sunnyvale, CA) was used in parallel to provide an independent validation of individual salt concentration values and will be used in future studies to investigate the permeation of multi-ions and mixed salt solutions.

2.4. Permeability coefficients

The permeation coefficients (P) were calculated according to the equation:

$$P = \frac{G_t V_r \cdot h}{S \cdot C_d} \quad \text{Equation [1]}$$

- P is the permeation coefficient ($\text{cm}^2 \cdot \text{s}^{-1}$),
- G_t is the number of ions permeating with time (C_t/t),
 - C_t is concentration in the receiver (mM),
 - t is time (s),
- V_r is the receiver volume (cm^3),
- h is the thickness of the lens (in water) (cm),
- S is the available section for permeation (cm^2),
- C_d is the initial concentration of the species in the donor chamber (mM).

From the tangent to the initial stage of the permeation process ($t < 60$ minutes, Fig. 2) the value of C_t/t corresponding to the initial concentration differential across the membrane was obtained. This allowed the permeation coefficient (P_{60}) to be calculated using equation [1].

2.5. Thermal analysis

Thermograms were obtained using a differential scanning calorimeter (DSC7, Perkin Elmer, London, UK) attached to a cooling system. Fully hydrated lenses were used but excess surface water was removed with blotting. A sample of the CL was cut and weighed and then hermetically sealed in an aluminium sample pan. Samples were scanned from -50°C to 25°C

with a heating rate of 5 °C/min. The area under the melting (endotherm) peak and the heat of fusion of pure water (79.72 cal/g = 333.55 J/g) were used to calculate the percentage of free or freezing water. The area under a typical thermogram endotherm peak was used to calculate the total freezing water content within a CL (Fig 1). This can be conveniently subdivided into ice-like water (free, non-bound); which has a melting point close to that of pure water and the polymer-associated water (free but loosely bound) which has a lower melting point. The non-freezing water (bound) content is calculated by the subtraction of the total freezing water from the measured equilibrium water content. All water fractions were expressed as percentages of the total weight of the hydrated lens.

3. Results

3.1. Kinetic permeation profiles

A concentration versus time permeation profile was obtained for all salt and lens combinations. Figure 2 shows the potassium chloride profile as the example. Kinetic profiles for the sodium and calcium salt solutions were also established and are summarised by their permeation coefficients (Tables 4 and 5). The transport rates with the potassium salt varied widely and a distinct concentration profile for each material is clearly evident. Omaficon A and B showed highest permeation rates while narafilcon A exhibited the lowest and slowest rate. Overall, conventional CLs demonstrated higher and faster permeation rates in comparison with silicone hydrogel-based CLs and, in general the higher the water content - the higher the permeation rate. While the rates of each permeation kinetic profile differ from material to material, the different ions produce a profile that fit the same first order kinetic model when the same donor concentration is used.

3.2. Endpoint receiver concentration

The post-permeation endpoint concentration in the receiver side was recorded for all the lens-salt combinations (Fig. 3). The materials have been presented and arranged in order by ascending, but not linear, percentage EWC for both conventional and silicone hydrogel lenses separately. In terms of the lower water content silicone hydrogel lenses a small rise in the endpoint receiver concentration from the 22% through to the 37% EWC materials was observed. However, this dipped dramatically with the two 44-45% EWC (narafilecon A and B) materials before a steady, but not uniform, rise in permeation with increasing EWC. Interestingly, there was little difference between the receiver concentrations of the 34% silicone material (balafilcon A) and the two silicone materials tested with the highest EWCs at 54 and 57% EWC (stenfilcon A and somofilcon A respectively).

A contrasting range of post-NaCl permeation receiver side endpoint molar concentrations for the individual materials was observed. Omafilecon B and nesofilcon A, with post-eight-hour receiver concentrations at 156 ± 12 and 149 ± 5 mM respectively, represent the most permeable materials. At the other end of the spectrum the two least permeable materials studied were found to be lotrafilecon A and narafilecon A, with receiver side endpoint concentrations at 22 ± 2 and 4 ± 0.2 mM respectively. The concentrations vary widely for the 17 materials investigated but the trend for higher permeation rates with the conventional materials in comparison with the silicone hydrogel materials was obvious. Additionally, each material behaved differently with each of the three salts, for example, lotrafilecon B (34% EWC) showed a higher and larger range of receiver concentrations post KCl, NaCl, CaCl₂ permeation (76 ± 1 , 59 ± 19 and 42 ± 10 mM respectively) compared with the lower and tighter range exhibited by lotrafilecon A (22% EWC) (36 ± 2 , 22 ± 2 and 18 ± 3 mM respectively).

As expected the conventional lens materials, with their relatively high water content, demonstrated high permeability and endpoint receiver concentrations, largely in excess of those exhibited by the silicone materials; although no clear pattern of water content associated permeation was apparent. Essentially, there was little difference in permeation values between the lowest water content materials, omafilcon A and B at 61% EWC, and the highest water content material, nesofilcon A at 78% EWC. Both conductivity and ion chromatography measurements were obtained; the two procedures were performed in parallel to validate the results but for simplicity only the conductivity measurements are shown. Concentrations detected with the conductivity probe were approximately two times higher than those values determined by ion chromatography, this is due to the fact that conductivity measures both the contribution of the cation and anion of the salt and ion chromatography simply measures the cation.

3.3. Effect of donor concentration

Three donor concentrations at 300, 400 and 800 mM were investigated using NaCl. The data suggests that donor concentration does not greatly influence the permeability coefficient values obtained (Table 3). The average P_{60} value over the range of concentrations for the nesofilcon A lens was $659 \times 10^{-8} \text{ cm}^2/\text{s}$ with only a ~10% deviation ($\pm 7.8 \times 10^{-8}$). Three structurally different materials were investigated, two conventional and one silicone, and even this diverse set of lenses demonstrated a well-behaved transport mechanism independent of donor concentration. Consequently, a single donor concentration, at 300 mM, was chosen thereafter.

3.4. Permeation coefficients

The kinetic profile of the permeation through each of the materials was not linear (Fig. 2). For that reason, to compare the permeability of the different salts for each specific material, these permeation profiles were converted into permeation coefficients (P) as explained previously in *Section 2.4*. The differences in the transport properties of each material with the different ions were apparent when comparing the permeability coefficients (P (cm²/s)) of the ions for each lens (Tables 4 and 5). These data confirm the general trend that the permeation rates are lower for the silicone materials compared with those of the conventional hydrogels. In terms of silicone hydrogels a 100-fold difference in permeation coefficient, from the highest to the lowest was also observed. The permeation rates for potassium and sodium salts were generally higher than those observed for calcium permeation.

3.5. The effect of water structuring properties on ion permeability

The DSC water structuring profiles for all the materials have been broken down into sub-categories (Fig. 4). All the water fractions for each material were expressed as percentages of the total weight of the hydrated lens. The effect of water structuring on ion permeation is evident and clearly different for conventional and silicone hydrogels, which show much more complex behaviour. In general, high ice-like water and low polymer-associated water resulted in higher permeation, but with some exceptions. Essentially, the silicone hydrogel materials showed appreciable proportions of polymer associated water (up to 26%) and lower levels of ice-like water (4-14%), whereas the high (>60%) water content conventional hydrogels showed the highest levels of ice-like water in the region of 20 to 47%. Nelfilcon A is an exception with a very distinctive water structure. It is a relatively high water content material (70% EWC) but unexpectedly most of the free water is polymer-associated water (~50%) with only ~3% ice-like water. The non-freezing water content was very similar for all the

materials - in the region of 17%. Significantly, the silicone hydrogel with the highest water content, somofilcon A (57%), showed low ion permeability behaviour compared with the lower water content comfilcon A (48%) and balafilcon A (34%) materials. The most obvious explanation for this apparent anomaly lies in the fact that the mobile ice-like water of somofilcon A is appreciably lower than that of the other two materials. In terms of pre- and post-permeation water structuring no significant difference was observed for any of the ion-lens combinations investigated.

4. Discussion

Tables 4 and 5 list the KCl, NaCl and CaCl₂ permeabilities (P) for 17 materials investigated. The data are in relative agreement with those reported in the literature where silicone hydrogel permeability coefficients were lower than those observed with conventional lens materials. For example, the more commonly investigated NaCl P coefficients (at P₆₀) determined here for lotrafilcon A and omafilcon A were 27 and 405 x10⁻⁸ cm²/s respectively compared with 12 and 470 x10⁻⁸ cm²/s reported by Guan et al.,¹² and 13 and 377 x10⁻⁸ cm²/s quoted by Gavara and Compañ,³⁰ respectively.

It is clear that with conventional hydrogels there is a strong general relationship between the total water content and both oxygen and salt permeability.¹² Results presented here concur with that observation. In several earlier studies the nature of water in conventional hydrogel lenses was not observed to have any significant effect on oxygen permeabilities; total water content was repeatedly shown to have the dominant influence.^{31,32} However, in terms of ion permeation - where both the size and extent of hydration of the permeating species can vary considerably, water structuring effects of the hydrogel matrix had not been extensively studied. Successive studies have shown that water binding behaviour, characterised by

freezing and non-freezing water contents, provides greater insight into the effects of hydration behaviour.^{28,33} In the present paper we have shown that a more detailed analysis in terms of water structure - in particular the roles of polymer associated, and ice-like water subdivisions of the freezing water fraction - provides a more useful explanation of discrepancies in the water content – salt permeation correlation.

An interesting way of visualising the complex structure of water in these materials is by using a triangular graph plot (Fig. 5). The plot presents the respective proportions of ice-like, polymer-associated and non-freezing water contents of each material. In order to compare these ratios for different lenses water contents are normalized to a value of 100%. The lenses are seen to group predominantly within three areas – representing different ratios of the three water types. One group (dark grey shaded box) is characteristic of high ice-like water containing materials and is seen to contain most of the non-silicone hydrogels but, interestingly, includes balafilcon A. The inclusion of balafilcon A in this grouping suggests that an additional structural factor, such as morphology of its polymer chains, may also have an effect on its permeation profile. This may, in part, be explained by the the fact that balafilcon A has an average pore diameter larger than the average porosity of standard hydrogel lenses,³⁴ and thus suggests that pore structure may have a marked effect on material permeability. Previous studies of salt rejection properties of hydrated membranes have illustrated the fact that polymer structure variations represent a useful way of manipulating the ratio between water and salt flux.^{33,35} The proposition that polymer structure might be used to over-ride a simple hydration-based model of permeation and salt rejection goes back almost fifty years³⁶ and as the results of contact lens permeation studies presented here and in recent papers^{12,30} show, this is illustrated in silicone hydrogels. The detailed water structuring

analysis presented in the present paper emphasised the need to understand these deviations from the simple expectation that salt permeation will parallel total water content.

The first indication in published literature that morphology of silicone hydrogels is capable of manipulating ion permeation independent of the degree of hydration is contained in the so-called Nicholson patent.^{4, 24, 27} In terms of the triangular graph analysis (Fig. 5) the three Alcon materials - developed by CibaVision from the Nicholson patent²⁷ - are grouped together (white box) and significantly they are the only materials that are based on the “co-continuous morphology” approach described and claimed in that patent. They have a unique combination of high non-freezing and low ice-like water contents. For this reason these materials – and especially the 22% water content lotrafilcon A – have a particular requirement for this morphological feature to reach a minimal level of ion permeation. The post-2000 trend for higher equilibrium water content obviates this requirement. The remaining group (light grey shaded box) contains what might be called “mainstream” silicone hydrogels that have been designed to combine reasonably high oxygen permeabilities with hydrogel-like moduli. This is often – but not exclusively – achieved with materials at 45% - 55% EWC. They are essentially those materials with lower permeability values, with the obvious exception of nelfilcon A which is a high water content material but only ~3% ice-like water. One logical explanation for this is the unique polarisation of the PVA carbon backbone. Although the backbone is atactic the chains form a crystalline network.³⁷ The volume occupied by the hydroxyl groups is so small that they fit neatly into a crystalline lattice without steric disruption, and the polymer can crystallise even with the stereochemically irregular distribution of the OH groups in the backbone. Furthermore, the hydrogen and hydroxyl substituents induces an unusual polarity (alternating partial positive

and negative charges) along the carbon backbone of the polymer.³⁸ This in turn appears to be the feature that induces such its high proportion of polymer-associated water.

Potassium and sodium salt permeation was greater and faster than calcium permeation, in general. This behaviour agrees with the Stokes' (or hydrodynamic) radii which shows an increase in the order $K^+ < Na^+ < Ca^{2+}$. Calcium is a "water hungry" ion, which means that it binds with a higher coordination number, results in more bound water molecules and has a larger effective size that limits its movement. It is important to recognise the potential effects of relative size and hydration of clinically significant cations on permeation behaviour. This is illustrated in Figure 6, which clearly shows that the crystal radius of an ion in its solid state (x-axis) is not a simple predictor of the radius of the hydrated ion. Although potassium has a larger crystal radius than sodium, the hydrated sodium ion is slightly larger than the hydrated potassium ion. Similarly calcium and sodium have very similar radii in the crystalline state but calcium has a significantly larger hydrated radius. This is reflected in the results where calcium chloride, in general, exhibits lower permeation rates compared with the potassium and sodium permeants.

Hydrogels are often thought to behave as dynamically fluctuating water-filled porous materials, with the pore size reducing as the water content decreases. Sodium ion transport diminishes with water content more markedly than the transport of water itself and is substantially impeded at water contents below 20%. As mentioned aqueous solution sodium carries a shell of fluctuating water molecules and is thus impeded from diffusing through low water content materials where both pore size and readiness to exchange with surrounding water molecules is reduced. The chloride anion is frequently chosen for ion transport studies of this type because its modest size does not influence permeation rates of the co-cation.¹⁹ A

comparison of the hydrated radii (Fig. 6) and the permeation data contained in Tables 4 and 5 illustrate that both the water in the gel and the water around the cation influence permeation rates. Although that broad statement is true, more detailed examination shows that water content, water structuring, size of the hydrated ion and also additional structural or morphological effects exert competitive influences in different molecular environments.

5. Conclusions

Two key families of data have emerged from this study: the differential permeation of individual materials to key cations and the material-to-material differences in permeation coefficients for individual cations. Permeability was found to be influenced to some degree by the water content, and to a greater extent, ice-like water, and by and large, a lower water content material creates a more tortuous and complex route for ion transport which results in a lower overall permeability coefficient.

A key contextual aspect of the foregoing points is the fact that homeostasis of the ocular environment is dependent on the specific electrolyte composition of tears and the role of the lacrimal gland in maintaining their normal levels. As such, the contact lens should not interfere with corneal haemostasis, the clinical implications – as yet uncorrelated – could well be significant. The magnitudes and lens-to-lens differences observed in our permeability data provide an explanation for the observed differences in pre- and post-lens electrolyte compositions, clearly an important area for future clinical-based studies. The proposition that a non-homeostatic cornea is a potentially sick cornea, coupled with the concept of corneal athleticism might provide a basis for the apparently random occurrence of CIEs. This study provides a sound and informed basis to monitor the influence of the effects of all these lens materials on the post lens electrolyte composition.

The structural morphology of silicone hydrogels highlighted in the Nicholson patent²⁷ arises from the hydrophobic nature of the silicone monomers and macromers together with the range of compatibilising diluents and polymerisation conditions used in the fabrication of these materials. As would be expected, this produces differences in self-assembly of the hydrophobic moieties and consequent differences in polymer morphology. Investigation of this phenomenon in commercial silicone hydrogels requires the use of probe techniques such as environmental scanning electron microscopy and small angle X-ray and is clearly beyond the scope and length constraints of this paper, but will be addressed separately.

Data Availability: The datasets generated and analysed for the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Weissman BA, Fatt I, Rasson J. Diffusion of oxygen in human corneas in vivo. *Invest Ophthalmol Vis Sci* 1981;20:123-125.
2. Peng C, Chauhan A. Ion transport in silicone hydrogel contact lenses. *J Membr Sci* 2012;399-400:95-105.
3. Fonn D, Sweeney D, Holden BA, Cavanagh D. Corneal oxygen deficiency. *Eye Cont Lens* 2005;31:23-27.
4. Tighe BJ, Silicone hydrogel materials – how do they work? In: S. David (ed), *Silicone Hydrogels: The Rebirth of Continuous Wear Contact Lenses* Betterworth. Heinemann, Oxford, 2000;1–21.

5. Harvitt DM, Bonanno JA. Re-evaluation of the oxygen diffusion model for predicting minimum contact lens Dk/t values needed to avoid corneal anoxia. *Optom Vis Sci* 1999;76:712–719.
6. Garr-Peters JM, Ho CS. Oxygen transfer in the corneal-contact lens system. *Crit Rev Biomed Eng* 1987;14:289-372.
7. Holden BA and Mertz G. Critical oxygen levels to avoid corneal edema for daily and extended wear contact lenses. *Invest Ophthalmol Vis Sci* 1984;25:1161-1167.
8. Weissman BA, Ye P. Calculated tear oxygen tension under contact lenses offering resistance in series: piggyback and scleral lenses. *Cont Lens Ant Eye* 2006;29:231-237.
9. Forister JF, Chao J, Khy K, Forister E, Weissman BA. Predicted tear layer oxygen tensions under two designs of silicone hydrogel toric lenses. *Cont Lens Ant Eye* 2008;31:228-241.
10. Takatori SC, Radke CJ. A quasi-2-dimensional model for respiration of the cornea with soft contact lens wear. *Cornea* 2012;31:405-417.
11. Domschke A, Lohmann D, Winterton L. On-eye mobility of croft oxygen permeable contact lenses. In: *Proceedings of ACS Spring National Meeting PMSE, San Francisco, 1987.*
12. Guan L, Gonzalez Jimenez ME, Walowski C, Boushehri A, Prausnitz JM, Radke CJ. Permeability and partition coefficient of aqueous sodium chloride in soft contact lenses. *J Appl Polym Sci* 2011;122:1457-1471.
13. Dartt DA. Neural regulation of lacrimal gland secretory processes: relevance in dry eye diseases. *Prog Retin Eye Res* 2009;28:155-177.
14. Franklin RM. The ocular secretory immune system: a review. *Curr Eye Res* 1989;8:599-696.

15. Edman C, Marchelletta RR, Hamm-Alvarez SF. Lacrimal gland overview. In: Dartt, DA, Bex P, D'amore P, Dana R, Mcloon LK, Niederkorn JY, (Eds.) *Ocular Periphery and Disorders* Cambridge MA, USA: Academic Press; 2011;68-73.
16. Stahl U, Willcox M, Stapleton F. Osmolality and tear film dynamics. *Clin Exp Optom* 2012;95:3–11.
17. Avisar R, Savir H, Sidi Y, Pinkhas J. Tear calcium and magnesium levels of normal subjects and patients with hypocalcemia or hypercalcemia. *Invest Ophthalmol Vis Sci* 1977;16:1150-1151.
18. Bright AM, Tighe BJ. The composition and interfacial properties of tears, tear substitutes and tear models. *J Br Cont Lens Assoc* 1993;16:57-66.
19. Miller RB. Tear concentrations of sodium and potassium during adaptation to contact lenses. II. Potassium observations. *Am J Optom Arch Am Acad Optom* 1970;47:773-779.
20. Thaysen JH, Thorn NA. Excretion of urea, sodium, potassium and chloride in human tears. *Am J Physiol* 1954;178:160-164.
21. Uotila MH, Soble RE, Savory J. Measurement of tear calcium levels. *Invest Ophthalmol Vis Sci* 1972;11:258-259.
22. Lemp MA. Report of the National Eye Institute/Industry workshop on clinical trials in dry eyes. *CLAO J* 1995;21:221-232.
23. Szczotka-Flynn L, Diaz M. Risk of corneal inflammatory events with silicone hydrogel and low Dk Hydrogel extended contact lens wear: A Meta-Analysis. *Optom Vis Sci* 2007;84:247-256.
24. Nicolson PC, Vogt J. Soft contact lens polymers: an evolution. *Biomaterials* 2001;22:3273-3283.

25. Cerretani C, Cheng-Chun P, Chauhan A, Radke CJ. Aqueous salt transport through soft contact lenses: An osmotic-withdrawal mechanism for prevention of adherence. *Cont Lens Ant Eye* 2012;35:260-265.
26. Nicolson P, Baron R, Charbrecek P, Court J, Domschkem A, Griesser H, Ho A, Hopken J, Laycock BG, Liu Q, Lohmann D, Meijs GF, Papaspiliotopoulos E, Riffle JS, Schindhelm K, Sweeney D, Terry Jr, WL, Vogt J, Winterton LC. Extended wear ophthalmic lens. 1999 US Patent 5,965,631.
27. Nicholson P, Baron R, Chabrecek P, Court J, Domschkem A, Griesser H, Ho A, Hopken J, Laycock BG, Liu Q, Lohmann D, Meijs GF, Papaspiliotopoulos E, Riffle JS, Schindhelm K, Sweeney D, Terry Jr, WL, Vogt J, Winterton LC. 1996. Continuous wear ophthalmic lens. CIBA Vision. Patent WO 96/31792.
28. Hamilton CJ, Murphy SM, Atherton ND, Tighe BJ. Synthetic hydrogels:4. The permeability of poly(2-hydroxyethyl methacrylate) to cations-an overview of solute-water interactions and transport processes. *Polymer* 1988;29:1879-1886.
29. Murphy SM, Hamilton CJ, Tighe BJ. Synthetic hydrogels: 5. Transport processes in 2-hydroxyethyl methacrylate copolymers. *Polymer* 1988;29:1887-1893.
30. Gavara R, Compañ V. Oxygen, water, and sodium chloride transport in soft contact lenses materials. *J Biomed Mater Res Part B* 2017;105B:2218–2231.
31. Efron N, Morgan PB, Cameron I, Brennan NA, Goodwin M. Oxygen permeability and water content of silicone hydrogel contact lens materials. *Optometry Vis Sci* 2007;84:328-337.
32. Ng CO, Tighe BJ. Polymers in contact lens applications VI. The ‘dissolved’ oxygen permeability of hydrogels and the design of materials for use in continuous-wear lenses. *Polym International* 1976;8:118-123.
33. Pedley DG, Tighe BJ. Water binding properties of hydrogel polymers for reverse osmosis and related applications. *Br Polym J* 1979;11:130-136.

34. López-Alemany A, Compañ V, Refojo MF. Porous structure of Purevision versus Focus Night&Day and conventional hydrogel contact lenses. *J Biomed Mater Res Part B* 2002;63:319-325.
35. Geise GM, Park HB, Sagle AC, Freeman BD, McGrath JE. Water permeability and water/salt selectivity trade off in polymers for desalination. *J Membrane Sci* 2011;369:130–138.
36. Yasuda H, Lamaze CE. Salt rejection by polymer membranes in reverse osmosis. I. Nonionic polymers. *J Poly Sci Part A-2 Polymer Physics* 1971;9:1537-1551.
37. Lee JS, Choi KH, Ghim HD, Kim SS, Chun DH, Kim HY, Lyoo WS. Role of molecular weight of atactic poly(vinyl alcohol) (PVA) in the structure and properties of PVA nanofabric prepared by electrospinning. *J App Polym Sci* 2004;93:1638-1646.
38. Leffler, JE, Gunwald E. In: *Rates and equilibria of organic reactions*. John Wiley and Sons, Inc (New York), 1963.

Figure 1. A typical DSC thermograph showing the water structuring profile for the balafilcon A material in DI water.

Figure 2. Comparative potassium ion permeation profile for all materials ($n \geq 3$). A donor concentration of 300 mM KCl was used in each case. Permeation was monitored with a conductivity probe in the receiver side of the chamber for the duration (480 mins) of the experiment. The legend is arranged in permeability order of the materials from highest to lowest.

Figure 3. End-point post-permeation receiver concentrations ($n \geq 3$) of NaCl (●), KCl (■) and CaCl₂ (▲) after eight hours permeation with a 300 mM donor starting concentration in each case. The conventional and silicone lens materials are shown separately, and the materials are presented in order from the lowest to the highest EWC. Error bars = 1 S.D.

Figure 4. Total water content sub-divided into values for: the individual ice-like water, polymer-associated water and non-freezing water structure for each of the lens materials ($n \geq 3$).

Figure 5. Individual proportions of non-freezing water, ice-like water and polymer-associated water of the study materials, expressed relative to a total water content value of 100%.

Figure 6. Schematic representation of relative hydration shell radii for the Na⁺, K⁺, Ca²⁺ and Cl⁻ ions illustrating the significant difference between the hydrated radius and the ionic crystal radius.

Table 1. Commercial silicone hydrogel contact lenses: oxygen permeation (Dk), equilibrium water contents (EWC) (quoted and measured) and thickness.

Brand name	Manufacturer	USAN^a	Dk^b	EWC (%) quoted	EWC (%) measured^c	Thickness (μm)^d
AirOptix Night&Day	Alcon	Lotrafilcon A	140	24	22	125 \pm 5
Dailies Total 1	Alcon	Delefilcon A	140	33 ^e	30 ^e	145 \pm 5
AirOptix	Alcon	Lotrafilcon B	110	33	34	130 \pm 10
PureVision	Bausch&Lomb	Balafilcon A	91	36	34	165 \pm 5
Acuvue Oasys	Johnson&Johnson	Senofilcon A	103	38	37	140 \pm 10
Acuvue Trueye	Johnson&Johnson	Narafilcon A	100	46	44	145 \pm 5
Acuvue Advance	Johnson&Johnson	Galyfilcon A	60	47	48	135 \pm 15
Biofinity	CooperVision	Comfilcon A	128	48	48	120 \pm 10
Pega Air	PegaVision	Formofilcon B	101	48	49	150 \pm 20
Acuvue Trueye	Johnson&Johnson	Narafilcon B	55	48	45	125 \pm 20
MyDay	CooperVision	Stenfilcon A	80	54	54	135 \pm 15
Clariti-1 Day	CooperVision	Somofilcon A	60	56	57	140 \pm 10

^a United States Adopted Name

^b $Dk \times 10^{-11} (\text{cm}^2/\text{sec})(\text{mlO}_2/\text{ml X mmHg})$ @ 34-35°C measured in packing solution

^c EWC measured after a 7 day pre-soak in deionised water

^d measured after a 7 day pre-soak in deionised water using a micrometer (Model IDC-1012EB, from Mitutoyo Corp., Japan) taking the 10 mm central portion of the lens. Note: lens-to-lens design differs from centre to periphery and thus makes absolute numbers difficult to achieve to some extent

^e 80% coating

Table 2. Conventional hydrogel contact lenses: oxygen permeation (Dk), equilibrium water contents (EWC) (quoted and measured) and thickness.

Brand name	Manufacturer	USAN^a	Dk^b	EWC (%) quoted	EWC (%) measured^c	Thickness (μm)^d
Focus Monthly	Alcon	Vifilcon A	15	55	66	140 \pm 10
Proclear	CooperVision	Omafilcon A	27	62	61	145 \pm 5
Proclear	CooperVision	Omafilcon B	27	62	61	135 \pm 15
Focus Dailies	Alcon	Nelfilcon A	27	69	70	145 \pm 5
Biotrue	Bausch&Lomb	Nesofilcon A	42	78	78	170 \pm 10

^a United States Adopted Name

^b $Dk \times 10^{-11} (\text{cm}^2/\text{sec})(\text{mlO}_2/\text{ml X mmHg})$ @ 34-35°C measured in packing solution

^c EWC measured after a 7 day pre-soak in deionised water

^d measured after a 7 day pre-soak in deionised water using a micrometer (Model IDC-1012EB, from Mitutoyo Corp., Japan) taking the 10 mm central portion of the lens. Note: lens-to-lens design differs from centre to periphery and thus makes absolute numbers difficult to achieve to some extent

Table 3. Permeation values ($P_{60} \times 10^8 \text{ cm}^2/\text{s}$) as a function of initial NaCl donor concentration.

Material	Donor concentration (mM)		
	300	400	800
Nesofilcon A	668	657	653
Vifilcon A	238	200	183
Stenfilcon A	130	191	184

Table 4. Silicone hydrogel materials permeation coefficients at the initial rate designated the P_{60} . *Measured* equilibrium water content (EWC) values, in water, are also provided. Materials are listed in order of increasing P with the KCl salt.

USAN	% EWC	$P_{(60)} \times 10^8$ (cm ² /s)		
		KCl	CaCl ₂	NaCl
Narafilcon A	44	3.9	0.5	3.7
Lotrafilcon A	22	48	25	27
Senofilcon A	37	44	30	36
Narafilcon B	45	99	68	74
Delefilcon A	30	130	82	102
Lotrafilcon B	34	136	70	89
Formofilcon B	49	155	123	136
Somofilcon A	57	171	128	167
Stenfilcon A	54	214	164	130
Galyfilcon A	48	216	182	145
Comfilcon A	48	228	166	186
Balafilcon A	34	258	175	225

Table 5. Conventional hydrogel materials permeation coefficients at the initial rate designated the P_{60} . *Measured* equilibrium water content (EWC) values, in water, are also provided. Materials are listed in order of increasing P with the KCl salt.

USAN	% EWC	$P_{(60)} \times 10^8$ (cm ² /s)		
		KCl	CaCl ₂	NaCl
Vifilcon A	66	316	172	238
Omafilcon B	61	389	292	447
Omafilcon A	61	493	266	405
Nefilcon A	70	470	366	481
Nesofilcon A	78	573	539	668