



Mechanically triggered solute uptake in soft contact lenses



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ABSTRACT

Molecular arrangement plays a role in the diffusion of water and solutes across soft contact lenses. In particular, the uptake of solutes in hydrated contact lenses can occur as long as free water is available for diffusion. In this work, we investigated the effect of mechanical vibrations of low frequency (200 Hz) on the solute uptake. Hyaluronan, a polysaccharide of ophthalmic use, was taken as example of solute of interest. For a specific water-hydrated hydrogel material, differential scanning calorimetry experiments showed that a large fraction of the hydration water accounted for loosely-bound water, both before and after one week of daily-wear of the lenses. The size (of the order of magnitude of few hundreds of nanometers) of hyaluronan in aqueous solution was found to be less than the size of the pores of the lens observed by scanning electron microscopy. However, solute uptake in already-hydrated lenses was negligible by simple immersion, while a significant increase occurred under mechanical vibrations of 200 Hz, thus providing experimental evidence of mechanically triggered enhanced solute uptake, which is attributed to the release of interfacial loosely-bound water. Also other materials were taken into consideration. However, the effectiveness of mechanical vibrations for hyaluronan uptake is restricted to lenses containing interfacial loosely-bound water. Indeed, loosely-bound water is expected to be bound to the polymer with bonding energies of the order of magnitude of 10–100 J/g, which are compatible with the energy input supplied by the vibrations.

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1. Introduction

Soft contact lenses (CLs) are widely used for the correction of refractive errors of the eye. In recent years, the lens absorption of various molecules and macromolecules has been increasingly taken into consideration [1–6]. One reason to study the CL absorption of various molecules is the presence of molecules and macromolecules both in the tear fluid and in the CL maintenance solutions. Another reason is the interest in CLs as reservoir and release systems of drugs and macromolecules for specific applications. Most of the conventional ophthalmic formulations require, indeed, direct application of doses at high concentrations due to the large and rapid draining of the drug through the lachrymal duct, with also possible undesirable effects. Hyaluronan (also called hyaluronic acid, HA) is one of the molecular species of special interest for its ophthalmic advantages. HA is a polysaccharide present in many human tissues (e.g. connective, epithelial, and neural), with applications in medicine, pharmacy, biotechnology, and

ophthalmology [7–14]. The HA uptake in CLs could also improve the comfort performance of the CLs due to its high hydrophilicity; in addition, HA can prevent the adsorption in the polymeric network of detrimental substances, which could possibly give rise to several problems during the wear, such as cytotoxicity and ocular irritation. In this respect, the HA uptake capability of a CL and the possibility to reload the CL in its hydrated state during the wear period are relevant aspects. HA can also be considered a model system to discuss the uptake capability of the CLs and to investigate the uptake mechanisms of ocular drugs, as potential controlled-release delivery platforms [1–6]. A recent work was reported on the HA distribution and penetration depth inside a siloxane-hydrogel CL [15,16]. HA was found to fill the CL pores, which could be seen by electronic and fluorescence microscopic techniques on the surface of the CL (Filcon V). However, the HA was found to reach a penetration depth of the order of 5–10 μm , to be compared with the much larger thickness ($\sim 100 \mu\text{m}$) of the whole CL. This experimental evidence suggested that a better understanding of the uptake of a solute in CLs can be achieved by investigating the compatibility between CL (in terms of morphology and porosity) and solute (in terms of size of the molecules and/or size of possible aggregates of such molecules).

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Another very important aspect for the uptake of solutes in hydrated CLs is related to the properties of the hydration water. For example, a detailed study was reported by Tranoudis and Efron, who examined the state of water in several soft CLs [17]. The authors found that low water-content CLs have approximately the same amount of bound water as those with much higher water-content. The excess of water in the latter ones is represented by loosely-bound water at the water–polymer interface and, eventually, free water in the bulk. Based on the typical classification of the state of water in hydrogels [18], tightly-bound water has a direct hydrogen bonding with the polar groups of the polymer. Free water does not interact with the polymer and has hydrogen-bonding characteristic of pure water. Loosely-bound water is interfacial. It remains in liquid state slightly below the normal freezing temperature (with negative freezing temperature between 0 °C and –10 °C). A typical example of interfacial loosely-bound water is represented by water in swollen polymers [17]. Free water is able to participate to diffusion, so that it is relevant for solute uptake in CLs exposed to solutions. Loosely-bound water could be released, thus becoming free, if some energy is provided of the order of 10–100 J/g. This value is approximately the expected binding energy of loosely-bound water to the polymer [19,20]. This bonding energy is much lower than the typical strength of hydrogen bonds and also much lower than the expected bonding energy of tightly-bound water to the polymer [21]. For this reason, external triggers could possibly be used as energy input for the release of loosely-bound water from CLs, which in turn would promote both diffusion and solute uptake. An example of external trigger is given by the application of mechanical vibrations. In the literature, the effects of mechanical vibrations were discussed as far as the fracture of the HA backbone is concerned under sonication at a relatively very high frequency (2×10^4 Hz) and power (7.5 W) [22].

This paper is aimed at investigating the effects of mechanical vibrations of about 150 mW and 200 Hz on the uptake of HA in soft CLs in their hydrated state, both before and after one week of wear. A preliminary combined characterization was first performed. On one hand, some CLs were characterized by scanning electron microscopy (to gather information on their structure and porosity) and by differential scanning calorimetry (to gather information on the state of the hydration water), both before and after wear. On the other hand, aqueous solutions of HA were characterized by dynamic light scattering to deduce the size distribution of hydrated HA molecules/aggregates. Then, the quantity of absorbed solute per lens in solution was determined both without and under mechanical vibrations. Results are discussed on the basis of the properties of both the CLs and the hydration water and on the basis of the energy provided by the vibrations, which was found to be sufficient for the possible release of interfacial loosely-bound water, i.e. for restoring water diffusion mechanisms.

2. Materials and methods

Three types of commercial CLs were taken into consideration: (i) Methafilcon 1B (Safilens, IV FDA group) [13], a hydroxyl-ethyl-methacrylate (HEMA) copolymer and methacrylic acid (MA), (ii) Filcon V (Safilens, I FDA group) [15,16] containing dimethyl-acrylamide, tris-trimethylsilyl, poly-(dimethyl-siloxane)-dimethacrylate, ethyleneglycol-dimethacrylate, and phthalocyanine copper, and (iii) Senofilcon A (Johnson&Johnson, I FDA group) containing polydimethyl-siloxane (PDMS), N,N-dimethylacrylamide (DMA), polyvinyl-pyrrolidone, and HEMA. As far as the experiments on unworn CLs are concerned, only in one case the CLs were rinsed in saline aqueous solution (0.9% NaCl) purchased from Alcon Italia, to compare their hydration volume in either saline solution or deionized water. In all other

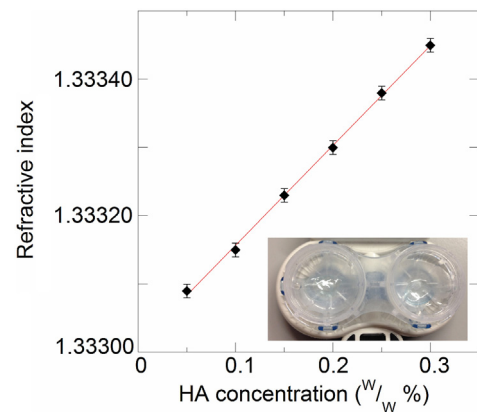


Fig. 1. Calibration line: measured refractive index of HA aqueous solutions with different concentrations and line obtained by linear fitting of the experimental data. Error bars indicate the std dev obtained by repeating the measurements at least 6 times for each concentration. Inset: image of the plastic vessel for CLs anchored to the generator of mechanical vibrations.

cases, the CLs were rinsed and hydrated in deionized water. As far as the experiments on worn CLs are concerned, Methafilcon 1B CLs were used for (8 ± 1) h every day for one week. Overnight, the CLs were maintained in a multi-purpose solution (ReNu MultiPlus).

Scanning electron microscopy (SEM) micrographs of the CL surfaces were obtained with the goal of acquiring information on the structure and porosity of the CLs. The CLs were examined using a LEO 1430 (Carl Zeiss, Oberkochen, Germany) operating at 20 kV and 3×10^{-3} Torr. Before analysis, samples were freeze-dried (–55 °C, 0.63 mbar \times 24 h) using an ALPHA 1-2 LDplus freeze dryer (Martin Christ, Osterode am Harz, Germany) and then sputter-coated with gold to a thickness of approximately 10 nm using a Sempreg 2 sputter coater (Nanotech Ltd., Prestwick, UK) at 10 mA.

Melting endotherms of water in water-hydrated CLs were determined by differential scanning calorimetry (DSC) by a Mettler Toledo DSC 1 Stare System. Samples of (7 ± 1) mg were characterized with the following method: (i) 3 min isotherm –40 °C, (ii) –40 °C to +30 °C @ 5 °C/min. All segments were driven under 80 mL/min N_2 flux. Before analyses, CLs were lightly blotted with tissue to remove excess surface water and then mechanically sealed in 40 μ L aluminum pan. The blotted samples were prepared following the procedure of Tranoudis and Efron [17]. By avoiding water evaporation before scanning, reproducibility of results was achieved also for materials prone to fast dehydration. By measuring temperature and heat flow associated with specimen transition, quantitative data were obtained on endothermic (heat absorption) processes.

Bacillus subtilis derived HA (MW 800 kDa) was purchased from Novozyme. HA solutions in deionized water were prepared with different concentrations and their refractive index was measured using a refractometer Atago RX5000- α (resolution 10^{-5}) at (20.00 ± 0.01) °C. The measured refractive index of reference HA solutions with concentrations ranging from 0.05 to 0.3% (w/w) is reported in Fig. 1. The experimental data are well described by a linear dependence of the refractive index on the HA concentration ($R > 0.999$). The result of the linear regression is also indicated in Fig. 1 by a line, which represents the calibration curve for the following analyses.

The HA solutions were also characterized by dynamic light scattering (DLS) at 25 °C by a Malvern Instruments Nano Series Zetasizer optical unit (Continuous Wave 4 mW He–Ne class 1 internal laser operating at 632.8 nm, measurement angles at 13° and 175° with Avalanche photodiode detector with Q.E. > 50% at 633 nm).

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