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Effect of multipurpose solutions for contact lens care on the in vitro drug-induced spoliation of poly(2-hydroxyethyl methacrylate) in simulated aqueous humour

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Abstract

Drug-induced spoliation of hydrogels as contact lenses or as implants in the anterior eye is a frequent occurrence in clinical practice. This study explores the capacity of three commercial multipurpose solutions for contact lens care to reduce the spoliation of poly(2-hydroxyethyl methacrylate) (PHEMA) specimens exposed to a simulated aqueous humour formulation and to three topical drugs commonly administered after insertion of artificial corneas (Predsol, Optimol and Depo-Ralovera). ReNu MultiPlus® (Bausch & Lomb), Complete® Blink-N-Clean™ Lens Drops (Allergan) and Complete Protein Remover Tablets dissolved in Complete® ComfortPLUS™ (both from Allergan) were evaluated. All multipurpose solutions were able to dislodge passively the deposits formed on hydrogels in the simulated aqueous and in the presence of Predsol and Optimol, but none were effective against the deposits induced by Depo-Ralovera. A reduction of the calcium content in deposits caused by Predsol and Optimol was confirmed after treatment with the protein remover preparation, while the other multipurpose solutions caused the complete removal of the deposits. In experiments designed to evaluate the preventive action of the multipurpose solutions, no such effects were observed regardless of the drug involved. The prospect of using multipurpose solutions as eye drops following implantation of a hydrogel artificial cornea is a valid alternative for reducing device spoliation, however it appears to depend on the nature of the postoperative medication.

Keywords: Hydrogels; Spoliation; Artificial cornea; Multipurpose solutions; Aqueous humour; Topical medication

1. Introduction

Spoliation of synthetic hydrogels is a frequent occurrence when these polymers are used as materials for contact lenses or intraocular implants. Considering the ensuing discomfort to the patient, loss of transparency and associated pathologic complications, tendency for spoliation is a serious drawback of the hydrogels, which otherwise have a proven record of satisfactory performance as biomaterials in many medical applications.

Spoliation of hydrophilic contact lenses has been extensively investigated over the past three decades. Under the influence of a complex array of causative factors, the lens materials (hydrogels) allow deposition of proteins, mucins, lipids and mineral components of the tear film, leading to deposits that may differ greatly in their morphology and composition [1–16]. It is generally agreed that the spoliation of contact lenses must be a result of interaction between polymers and the ocular microenvironment, primarily tears. The deposits on hydrophilic contact lenses can contain precipitated mineral salts, however the previous investigators stopped short of implying a causal relationship between their deposition and the deposition of proteins and/or lipids, mainly because the involvement of the inorganic ions in the initial stages of the deposit formation (basal layers) has never been satisfactory explained. Calcium phosphate, in its thermodynamically stable form hydroxyapatite, occurs

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regularly in certain types of deposits such as white films, lens coatings and surface plaques [14,15], where it forms basal layers, which may be covered by lipids, proteins and mucins in various amounts. Calcium salts are also present in the discrete elevated deposits known as ''white spots''; in this case, they are not localized strictly in the basal layers of these deposits, and sometimes are present in very low amounts, suggesting a deposition mechanism different from that underlying the formation of films and plaques [15]. The relationship between administration of drugs, either systemic or topical, and contact lens wear is complex and results in a multitude of complications including deposition of organic and/or inorganic matter [17].

The deposits detected in some vision-restorative hydrogel implants have been consistently reported to contain calcium phosphate phases of compositions similar to that of hydroxyapatite. Such deposits have been found in a variety of hydrogel intraocular lenses (IOLs), especially in those made from acrylic hydrogels based on 2-hydroxyethyl methacrylate (HEMA), such as the homopolymer (PHEMA) (Alcon's IOGEL™ 1103 [18]), HEMA/methyl methacrylate copolymers (MDR's SC60B-OUV model [19] and Ciba Vision's MemoryLens™ [20]), a HEMA/6-hydroxyhexyl methacrylate copolymer (Bausch & Lomb's Hydroview™ [21–28]) and in an IOL made from a HEMA-based hydrogel of unspecified composition (OII's Aqua-Sense™ [29]).

The advent of an artificial cornea made from PHEMA, developed in our laboratories (initially known as ''Chirila keratoprosthesis'' [30–33]) and currently distributed as AlphaCor™ by CooperVision Surgical Inc., triggered renewed interest in the spoliation of hydrogel implants. To date (end of July, 2004), 165 AlphaCor™ devices have been inserted in human patients, with a maximum follow-up of 69 months (mean 11.6 months). The clinical assessment indicated white intraoptic calcific deposits in 4.2%, and surface spoliation in 3.6% of the cases [34–36]. Our preliminary investigations [37] showed that PHEMA hydrogel has an inherent propensity to induce the spontaneous precipitation of calcium phosphate on the polymer matrix, even in the absence of any biological agent, in nothing else but water, calcium ions and phosphate ions. When treated in a simulated aqueous humour formulation alone, or in the presence of certain drugs commonly used after ocular surgery, deposits were formed on all PHEMA hydrogel samples [38]. The majority of these deposits contained calcium phosphate, but certain drugs induced deposits where calcium could not be detected.

The system currently preferred for contact lens care is the use of multipurpose solutions (MPSs), which are formulated to perform rinsing, disinfection and cleaning of contact lenses, including specifically the removal or reduction of deposits [39–41]. Generally, MPSs contain antimicrobial agents, surfactants, sequestering agents, buffering agents and (occasionally) lubricants. Some commercial brands of MPSs are routinely included in the care regimens for contact lenses. Many existing formulations have been assessed for their performance [39,42–44], biological effects [45–49] and comfort to patients [50–52]. Also available on the market are MPSs that contain additional enzymes able to digest the proteins deposited on the contact lenses [41,53], but they showed little efficacy in removing proteins that penetrated the matrix of the lens' polymer [13,43].

In assessing the efficacy of MPSs so far, only the fate of deposited proteins has been investigated, while the effect on the deposited calcium phases was largely ignored. If present in a deposit, calcium salt particles coexist with, and probably would be embedded into, deposited proteins and other organic matter. When proteins are dislodged and carried away in the MPS, the accompanying mineral particles must be also carried away. The apparent obviousness of this assumption would account for the lack of reports on the fate of calcium deposits following treatment with MPSs, although this aspect was never explicitly discussed in the previous literature.

In the present study, our strategy was to induce deposit formation on polymer specimens and to examine changes in the deposited matter following treatment with MPSs and, in certain cases, to monitor the reduction of deposited calcium. Discs of PHEMA were used as polymer substrates for calcification, and simulated aqueous humour (SAH) as a calcifying medium. SAH was chosen based on the following rationale. Two ocular fluids can function as bathing media for devices placed in the anterior segment: tears (for contact lenses and for the anterior surface of artificial corneas) and aqueous humour (for the posterior surface of artificial corneas). Of these two fluids, the aqueous humour contains significantly more calcium (1.25–1.35 mmol/L) [54,55] than the tears (0.4–0.8 mmol/L) [56] and hence we decided to use the former as the test medium. Three drugs, prednisolone sodium phosphate (as Predsol, Sigma Pharmaceuticals), timolol maleate (as Optimol, Alphapharm) and medroxyprogesterone acetate (as Depo-Ralovera, Kenral-Pharmacia) were included in the experiments. We have previously proved [38] that these drugs were able to induce calcification of PHEMA in SAH. Three commercial MPS formulations were selected for this investigation: ReNu MultiPlus® (Bausch & Lomb), Complete® Blink-N-Clean™ Lens Drops (Allergan) and Complete Protein Remover Tablets dissolved in Complete® ComfortPLUS™ (both from Allergan).

2. Materials and methods

2.1. PHEMA hydrogel specimens

The PHEMA hydrogel used as a substrate for calcium deposition was produced by the polymerization of a solution of 70% HEMA (from Bimax, USA, with 99% purity) in water. In all experiments, high purity, sterile and nonpyrogenic ''water for injections BP'', with zero osmolality (Viaflex®, from Baxter Healthcare, Australia) was used,