Hyaluronan: Its Properties and Ophthalmic Uses

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Introduction
The body is a complex collection of systems that have evolved to perform essential functions. The eye, as a self-maintaining, self-contained organ, is a perfect example of this. In order to maintain itself, it relies on a host of self-produced elements. For instance, its tear film contains over 450 proteins, some of which are antibacterial enzymes that help disinfect the ocular environment.1 Hyaluronan (HA) is another element that the eye produces, and its main function is to keep the eye lubricated. Some contact lens and contact lens care solution manufacturers have seen the benefits of HA and have incorporated it into their products as a treatment for dry eye and for making contact lenses more comfortable.

What is Hyaluronan?
HA is a glycosaminoglycan that is found naturally throughout the body in the connective tissue of the skin, the umbilical cord, and in the synovial fluid in joints. It can also be found in several places in the eye, including normal human tears,2 lacrimal tissue,3 and corneal epithelium.4 In addition to its lubricating effect, HA may have a protective effect against oxidative damage caused by free radicals.5 It may also have an impact on wound healing, as well as possess anti-inflammatory properties.6 HA is currently utilized during several surgical procedures, including corneal surgery (as a vitreous replacement), cataract surgery (as a protective element for the corneal endothelium, and corneal transplant surgery (to provide better graft transparency).7,8

Hyaluronan’s Lubricating Properties
HA has unique water-retention properties and viscoelasticity thanks to its random coil structure, which allows each HA molecule to hold up to 1000 times its weight in water.9 However, changes in temperature, pH, and shear rate can have a detrimental effect on this ability.10,11 HA has two distinct roles, one when the eye is open, and one when a blink occurs. When the eye is open, it is more viscous and coats the surface of the eye without draining, resulting in an improvement in tear break-up time.12,13 During a blink, its viscosity is reduced resulting in the spread of HA across the eye as the eye lid retreat to their original positions.9

Efficacy of Hyaluronan in Artificial Tear Studies
The ability of HA to bind with water makes it an ideal element for artificial tears, as it is in fact already included in some commercially available tear drops (e.g., AqueaLyte, Lasting Comfort Drops [CibaVision, Duluth GA], Blink Contacts® Lubricating Eye Drops [Abbott Medical Optics, Santa Ana CA]). Table 1 lists several studies of artificial tears containing HA and their effects on dry eye and associated symptoms. These studies include patients with mild to severe dry eye, and who may have been experiencing corneal disorders (e.g., epithelial corneal dyskeraesis, contact lens-induced irritation, ocular pemphigoid, filamentary keratitis, neurotrophic keratitis).12,14 Most of the primary outcomes of these studies focused on the results from subjective questionnaires and objective measurements of tear break-up time, but other dry eye test results (e.g., phenol red thread test, tear meniscus height, non-invasive tear break-up time, bulbar hyperemia) have also been studied.12,15

Table 1: Summary of studies on the effects of HA on dry eye

| Study 1 | 0.1% sodium hyaluronate: | Results: Patients reported relief of dry eye symptoms. There was objective improvement in corneal staining. |
| Study 2 | 0.1% sodium hyaluronate vs 0.1% sodium hyaluronate vs placebo: | Results: No significant difference in Shimer testing, tear break-up time, and rose Bengal staining for 0.1% HA vs placebo. Significant difference in objective testing for 0.2% HA vs placebo. Most patients preferred HA treatment. |
| Study 3 | 0.05% sodium hyaluronate vs 0.2% sodium hyaluronate vs 3% sodium hyaluronate vs vehicle: | Results: No significant effect on tear break-up time noted for vehicle or 0.05% HA. Break-up time significantly delayed at all measurement times up to 3 hours for 0.1% and 0.3% HA. |
| Study 4 | 0.1% sodium hyaluronate vs 0.3% sodium hyaluronate vs 0.9% saline: | Results: Significant improvement in break-up time up to 6 hours for 0.1% and 0.3% HA. Greatest effect on improvement of symptoms across the entire 6 hour time period of the study for 0.3% HA. |
| Study 5 | 0.18% sodium hyaluronate vs 0.3% hydroxypropylmethylcellulose vs 0.1% dextran: | Results: Significantly greater improvement in break-up time at 30 and 60 minutes for 0.18% HA. |

Table 1 shows the results of these studies, but comparisons should not be made as these trials were not conducted head to head.

Efficacy of Hyaluronan in Contact Lens Studies
There is little data in the literature regarding the effect of HA on contact lenses. However, one study of note, by Itoi and colleagues,16 evaluated the effect of HA on 3 and 9 o’clock staining in patients who were currently rigid gas permeable contact lens wearers.17 In this study, patients were randomized to HA or artificial tears, and although no significant differences in subjective symptoms were noted, significantly less objective signs (corneal staining and conjunctival hyperemia) were noted in the group using HA drops.

Other notable studies exist that examined the effect on protein adsorption of HA when incorporated as a wetting agent in hydrogel and silicone hydrogel lens materials.18 In hydrogel lenses, the incorporation of HA significantly decreased the adsorption of lysozyme, albumin, and the larger protein IgG,19 and in silicone hydrogel lenses, resulted in a reduced uptake of lysozyme.20

Conclusions
HA is produced by the body and can be an inspiration for developing artificial tears, contact lens rewetting agents, and as a wetting agent incorporated into contact lens care products or contact lens materials—all of which can help to combat ocular dryness and discomfort. As advancements continue to be made in contact lens care and design, eye care professionals will be able to offer their contact lens patients improved comfort, which will hopefully lead to a reduction in the number of patients who discontinue wearing contact lenses and an increase in the wearing time of their lenses.

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References
15. Scott JE. Development of a model silicone hydrogel lens material that will hopefully lead to a reduction in the number of patients who discontinue wearing contact lenses and an increase in the wearing time of their lenses. Contact Lens Spectrum. 2009;17:27-32.