



HEALTH GRADUATE STUDIES / COSMETOLOGY

HYALURONIC ACID

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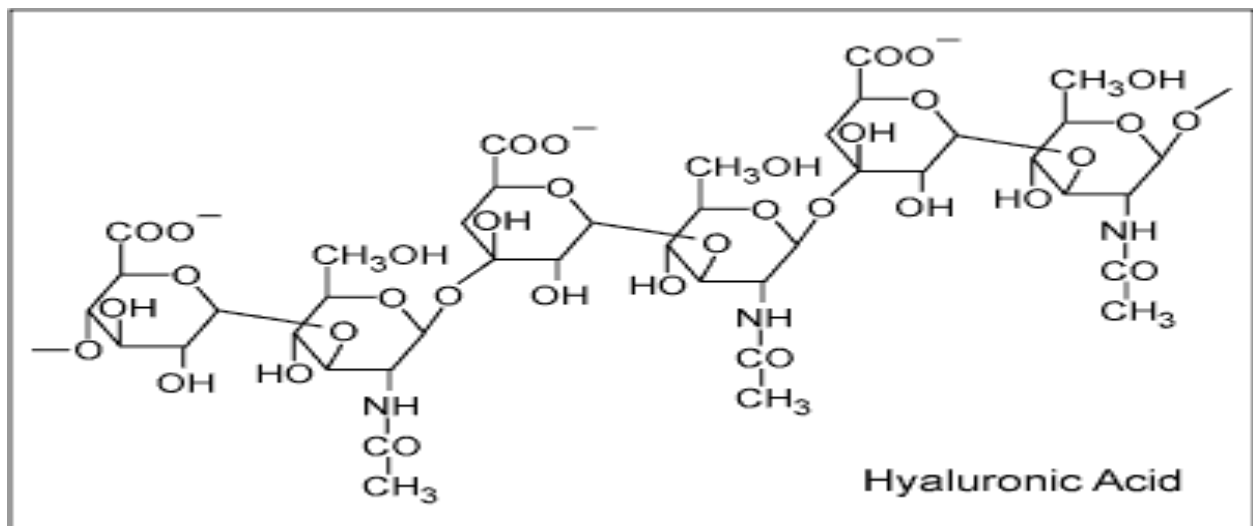
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Structure:

Hyaluronic acid (hyaluronan, HA), a high molecular mass polysaccharide, was discovered by Meyer and Palmer in 1934 in the vitreous humor of cattle eyes^[1]. This polysaccharide is most frequently referred to as “hyaluronan”, because HA exists as a poly anion form and not as the free acid form. However, the name “hyaluronic acid” is often used in the pharmaceutical area. HA is generally of very high molecular mass but can also exist as small fragments or oligosaccharides. HA is a linear, unbranched polymer, which is composed of a simple repeating disaccharide. The disaccharide consists of N-acetyl-D-glucosamine (GlcNAc) and D-glucuronic acid (GlcA) linked through a β 1-4 glycosidic bond. The disaccharides are linked through β 1-3 bonds to form the HA chain. Thus, HA is a quite homogeneous polymer, but the distribution of its molecular size is of wide range. Although HA is widely distributed in the intercellular matrix of mammalian connective tissues, it is obtained from bovine vitreous humor, rooster combs, and umbilical cords, and also produced by some bacteria such as *Streptococcus zooepidemicus*^[2].





History:

Since 1996, hyaluronic acid (HA) has been launched onto the market in Europe. HA is produced by bacterial fermentation from a specific strain of streptococci. Hyaluronic acid (HA) is a mucopolysaccharide consisting of alternating N-acetyl-d-glucosamine and d-glucuronic acid, which has received great interest in the medical and cosmetic markets. In recent years, HA from microbial fermentation, rather than extraction from animal sources, is receiving increased attention for avoidance of cross species viral infection. HA fermentations have been mostly by *Streptococci* spp., where HA is a capsular biopolymer shedding to the medium^[4]. To aid the competence of the fermentation process, the development of an economical process for mass production is necessary.^[3]

Location of HA In Human Body

The total amount of HA in the human body is around 12g. The umbilical cord, synovial fluid (3500mg/l), and the vitreous (200mg/l) contain the highest concentrations. Skin contains the highest quantity of HA (7g). HA is a glycosaminoglycan polysaccharide composed of alternating residues of them on osaccharided-glucuronic acid and N-acetyl-d-glucosamine present in the human body.^[5] The valuable pharmaceutical polymer, hyaluronic acid, is produced industrially using the gram-positive bacterium *Streptococcus zooepidemicus*. Hyaluronic acid (HA) is a naturally occurring, high molecular weight polysaccharide that has applications in ophthalmics, orthopaedics, wound healing, tissue engineering, drug delivery, cosmetics, and as a vaccine aid (Crescenzi, 1995). This polymer is produced commercially by extraction from avian and bovine sources and increasingly by fermentation of the Lancefield group C streptococci, *Streptococcus* and *S. equi* sub species *zooepidemicus*.^[6]



WHERE IS HYALURONIC ACID LOCATED IN THE BODY?



[7]

Hyaluronic acid (HA) forms a smaller part of the extracellular matrix (ECM) but has the significant advantage of structural conservation regardless of the source and is therefore non allergenic. It is also relatively rare with in the field of tissue engineering as its degradation products may be able to modulate wound healing. This has led to a wealth of research allowing the use of HA in clinical applications as diverse as dermal scaffolds, cartilage defects, glial cell culture and regeneration and even for spermatic motility assessment.^[8]



Usage:

Hyaluronic acid gel has been used extensively in Europe and Canada for facial soft tissue augmentation and volume correction. Since its approval by the Food and Drug Administration in 2003, Restylane (Restylane, Q-Medical, Uppsala, Sweden), a non animal, stabilized hyaluronic acid gel (NASHA), has become the filler of choice in the United States because of its lower immunogenicity and longer duration of correction than collagen. It is indicated for mid to deep dermal implantation to correct moderate to severe facial wrinkles and folds and is frequently used off-label for lip augmentation.^[4]

HA has no species specificity and theoretically has no risk of allergy. No skin testing is necessary before injecting because HA is a biodegradable agent. To be utilized as a filler agent for improving wrinkles, scars, or increasing volumes, HA, as collagen, is one of the components of the skin; it plays an important role in hydration of extracellular space and constitutes a matrix for supporting the normal functions of the cells.^[5]

Nonsurgical procedures have become very popular for the rejuvenation of the aging face. Trends now favor less invasive procedures as well as for more preventative intervention to slow the damage from ultraviolet light and environmental factors, as well as from intrinsic aging. The goal of these procedures is to eliminate or delay the need for corrective surgery. The regular use of sunscreens; retinoids and improved cosmeceuticals; injectable neuro-toxins; soft tissue augmentation products; and minimally invasive laser, light, and radio frequency treatments are decreasing and delaying need for invasive procedures. Injectable fillers entered main stream cosmetic medicine with the development of bovine collagen injections in the 1980s. The availability of improved fillers that are less allergenic and longer lasting has resulted in a renaissance in filler techniques. No single filler has proven to be more popular than the category of hyaluronic acids (HA).^[9]

Science of Hyaluronic Hyaluronic acid (HA) is one of the most prevalent glycosamino glycans in the dermis, so its utility as a dermal filler is obvious. Because HA is not species specific, there is theoretically no need for skin testing for allergenicity. HA is a polysaccharide composed of repeating units of D-glucuronic acid and N-acetylglucosamine. It is found in all tissues of vertebrates and is very prevalent in human skin. It has been demonstrated to be decreased in intrinsically aged skin and to be altered in photo aged skin. HA is highly hydrophilic, binding much more than its weight in water. To be practical as a filler, however, cross linking of the polysaccharide chains is necessary to slow degradation.



Hyaluronic acid fillers are mainly used in the nasolabial fold, which was the site of original testing for FDA approval. They are also commonly used “off label” in many other areas, including the lips and marionette folds . Facial reshaping can be achieved by injecting HA into the cheek prominence and lateral brow. Advanced injectors place HA in the glabella crease, mental crease as well as the ocular sulcus and tear trough region.^[9]

Before

After





Side effects and Complications:

Pain, bruising, and transient redness/edema are common and nonspecific side effects. HA has no species specificity and theoretically there is no risk of allergy. Infact, the raw products may contain as mall quantity of exogenous proteins (either from animal or from bacteria) and the stabilization process modifies the chemical structure of HA. For these reasons, there are very rare hypersensitivity reactions as inflammatory lesions. The prevalence of these reactions is so low that skin testing is not necessary. Nonallergic reactions have also been reported: herpes reactivation, bacterial infections, aseptic abscess, and necrosis and livedoid aspect after intravascular injection. HA is a biodegradable product, and, in case of complications, they will disappear when HA is degraded.

Conclusion:

In cosmetic dermatology, any medical device that used must be as safe as possible. Longevity of the implant is of great importance, and the newest HAs, which are more and more long lasting, are more and more suitable for cosmetic treatments. No one filler agent is for now ideal, but HA has a lot of good characteristics for such an agent.^[5]



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