Significance of hyaluronic acid in cosmetic industry and aesthetic medicine

Introduction
Skin moisturizing is one of the key aims of the commercially available skin care products. In order to keep the skin in good condition cosmetic formulations should contain active compounds which are able to bind water and hence are responsible for water retention. One of the most widely applied active ingredient showing such properties is hyaluronic acid. Its physicochemical and biological properties are responsible for proper tissue hydration and transport of ions and nutrients.

HA was first isolated from bovine vitreous in 1934 by Karl Meyer and John Palmer [1, 2]. The name of this compound derives from the Greek hyalos (glassy, vitreous) that is related to its physical properties. Since the 1980s, hyaluronic acid (HA) has been launched onto the market and has been incorporated in moisturizing creams to retain moisture, shape face oval and effect skin hydration [3-5].

Hyaluronic acid is also critical to maintain structural integrity of the dermal collagen matrix. The properties of this compound strongly depend on its molecular weight. If the molecular mass of HA is higher than 100 kDa, the ability to penetrate epidermis is limited. The use of this active compound brings also other beneficial effects. Hyaluronic acid gives immediate smoothness to rough surfaces and forms a protective layer which provides a barrier preventing transdermal water loss (TEWL).

HA has become increasingly popular both in cosmology and aesthetic medicine therefore it is essential to become familiar with its structure, physicochemical properties and its functions in human body.

Hyaluronic acid occurrence
HA is a natural, dense and transparent component, highly abundant in all living organisms, the human body included. The average 70 kg adult human body contains approximately 15 g of hyaluronic acid and one-third of which is turned over (degraded and synthesized de novo) every day. High concentration of HA was found during embryonic development, wound healing process as well as in the vitreous of the eye, tear fluid, blood vessels walls, umbilical cord and synovial fluid. However, the highest concentration of HA (over 50%) is located in extracellular matrix of the skin. In physiological conditions, HA is generally present as sodium hyaluronate. According to Tammi et al. [6] the highest concentration of sodium hyaluronate can be found in stratum spinosum and the lowest in stratum basale. However, in stratum spinosum and stratum granulosum HA is not present.

In dermis hyaluronic acid occurs in stratum papillare, collagen microfibrils and between elastic and collagen fibres. The body’s hyaluronic acid levels decrease with age and around 80 years of age it completely disappears [6, 7].

Chemical structure and properties of hyaluronic acid
Hyaluronic acid can be defined as a glucosaminoglycan (GAG) with unbranched polysaccharide chain consisting of repeated disaccharide units linked by glycosidic bonds. However, there are some special properties which enable distinction of HA from other GAG. Unlike in other standard GAG (dermatan sulphate, heparan sulphate and chondroitin sulphate), sulphuric groups are not found in the structure of HA, therefore it is not able to covalently connect with protein core and therefore proteoglycans are not formed [2]. Hyaluronic acid is a polymer of disaccharides, composed of D-glucuronic acid and D-N-acetylglucosamine, linked via alternating \( \beta \)-1,4 and \( \beta \)-1,3 glycosidic bonds. (Fig. 1.) and has a molecular weight of approximately 400 Da.

A single glucosaminoglycan chain is built of 20 to 200 repeated disaccharides sequences. However, the number of repeating disaccharides in hyaluronic acid can reach 10,000 or even more, resulting in molecular weights of \( 4 \times 10^8 \) Da. HA is a highly hygroscopic biopolymer. Each glucuronic acid unit contains a carboxyl group, giving rise to polyanionic character at physiological pH. Therefore, in the presence of water, hyaluronic acid molecules can expand in volume (1000 times) and can form a network stabilized by hydrogen bonds. One HA molecule can bind to approximately 250 water molecules (1 g of HA retains 6 l of water). Hyaluronic acid is nontoxic, non-irritating and non-sensitizing because it occurs naturally in skin [6-8].

Its ability to combine water contributes to its viscoelastic properties, however the actual mechanism has not been fully explained yet.

A characteristic property of hyaluronic acid water solutions is pseudoplasticity related to a decrease in viscosity. The fluidity of HA depends on its concentration and molecular weight.

Application of hyaluronic acid
Products containing hyaluronic acid can be found in various pharmaceutical formulations and are registered as medicines or cosmetics.

Hyaluronic acid in cosmetics formulations
Hyaluronic acid and its sodium and potassium salts are the active ingredients of many moisturizing, protective and anti-age products. HA is formulated in various cosmetics preparations for facial, neck, eye skin care (masks, creams, tonics) and also for body care in antcellulite and antistripe products [9]. Hyaluronic acid and its derivatives act in cosmetics as skin conditioning agents at concentrations up to 2% [10]. Este´e Lauder was the first one in 1982 to apply animal HA in cosmetics [11]. Nowadays HA is produced using biotechnological
methods involving a *Streptococcus zooepidemicus*. HA is marketed by Biomatris (U.S.A.), Bio-Technology General (Israel), Diagnostic Inc. (U.S.A.), Fermentech (U.K.), Genzyme (U.S.A.), Kibun Food Chemifar Co. (U.S.A.), Med. Chem. Products (U.S.A.), Pharmacia (Sweden), and Shiseido Co. (Japan) [12].

The results published in the Journal of Drugs in Dermatology indicated that all 0.1% hyaluronic acid (HA) formulations led to significant improvement in skin hydration and elasticity [13]. The objective of the experiments was to compare and contrast the efficacy of topical application of hyaluronic acid formulations of different molecular weights (50, 130, 300, 800 and 2000 kDa, respectively). Seventy-six females between 30 and 60 years of age were asked to apply one of the formulations twice daily to the periocular wrinkles area.

A significant improvement in wrinkle reduction was observed as a result of application of low molecular weight HA (50 and 130 kDa), which may be due to its better abilities to penetrate the skin in comparison to those of high molecular weight HA. However, the application of hyaluronic acid with high molecular weight could also be beneficial. HA is able to form film on the surface of the skin, which protects stratum corneum. The film hinders the transepidermal weight, particle size and character of cross-linking.

Seventy-six Aesthetics Inc Scottsdale, AZ. Restylane (Hyaluronic Acid) patented by Q-MED. The effectiveness of Restylane both hyaluronic acid and retinol-A. However, L'oreal added pro-


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Dermatological preparations containing hyaluronic acid correct acne scars. In addition HA is responsible for the stabilization of tissue structure and wound healing. Recently, hyaluronic acid biological dressings (HABD) also have been used for the temporary coverage of partial- to full-thickness posttraumatic or postsurgical wounds [19].

Translation into English by the Author

**Literature**


**Table 1**

<table>
<thead>
<tr>
<th>Product Differences</th>
<th>Restylane</th>
<th>Hylaf orm</th>
<th>Hylaf orm Plus</th>
<th>Captique</th>
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<tr>
<td>Concentration</td>
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<td>5.5 mg/ml</td>
<td>5.5 mg/ml</td>
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<td>Particle size</td>
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<td>500 µm</td>
<td>700 µm</td>
<td>500 µm</td>
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<tr>
<td>Polymer</td>
<td>Short chain</td>
<td>Long chain</td>
<td>Long chain</td>
<td>Short chain</td>
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Applicant must be currently enrolled in an academic degree program and will be returning to school following this assignment.

Preferred
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Candidates with organic chemistry laboratory skills are preferred.

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