Significance of hyaluronic acid in cosmetic industry and aesthetic medicine

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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 the 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 cosmetology 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 β-1,4 and β-1,3 glycosidic bonds. (Fig.1.) and has a molecular weight of approximately 400 Da.

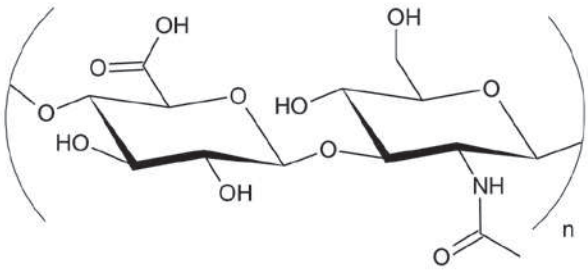

Fig. 1. Chemical structure of hyaluronic acid

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 4×10^6 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 anticellulite 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 Biomatrix (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 water loss (TEWL) and the high-molecular-weight hyaluronic acid moisturises the inner layer of the skin (epidermis). In cosmetic formulations HA functions as humectant which means it draws water to the skin and increases the water content of the epidermis and prevents the cosmetic formulation from becoming dry [4, 9].

In recent years cosmetic companies have been trying to produce innovative products which combine hyaluronic acid with other active ingredients.

Vichy Laboratories produced cosmetic formulation containing both hyaluronic acid and retinol-A. However, L'oreal added pro-xylan to HA, while Eucerin Research Centrum introduced saponin which penetrates deep into the skin to reinvigorate the production of the skin's own hyaluronic acid. Hyaluronic acid is applied in creams produced by L'oreal, Avon, Olay Regenersit, Vichy, Beiersdorf, Bielenda.

Hyaluronic acid in aesthetic medicine

Even better results can be obtained by injecting the hyaluronic acid into the dermis, therefore in aesthetic medicine HA gained in popularity as a filler component [14]. Injectable hyaluronic acid gels are applied to reduce static wrinkles, to model cheeks, correct facial line and lips shape, to improve elasticity and hydration of facial, hand, neckline skin [8, 15]. HA has no species specificity and theoretically does not pose any risk of allergy [5]. However, HA has a very short half-life in skin and it is quickly broken down by enzymes and resorbed. Chemical modification and cross-linking can make HA resistant to being broken down [15, 16]. The most widely used modification method is cross-linking by epoxides, aldehydes or vinyl sulphone that increases the viscosity and improves biocompatibility and longer presence of HA in tissues. The application of hyaluronic acid in aesthetic medicine is safe and effective. The techniques of wrinkle filling together with the injection of botulinum toxin give a significant anti-aging effect of appearance of the face skin without surgical treatment.

The first HA filler approved for use by Food and Drug Administration (FDA) was Restylane® produced by Medicis Aesthetics Inc Scottsdale, AZ. Restylane® fillers are highly effective due to the application of high pure hyaluronic acid, which is stabilized by NASHA™ technology (Non-Animal, Stabilized, Hialuronic Acid) patented by Q-MED. The effectiveness of Restylane® was proven in clinical trials [17]. Other fillers (Hylaform, Hylaform Plus and Captique) were introduced into the market in 2004 [18]. A comparative analysis of these products can be found in Table 1. The effectiveness of hyaluronic acid activity depends on its molecular weight, particle size and character of cross-linking.

Table 1

Product Differences

	Restylane	Hylaform	Hylaform Plus	Captique
Concentration	20 mg/ml	5.5 mg/ml	5.5 mg/ml	5.5 mg/ml
Particle size	300 μm	500 μm	700 μm	500 μm
Polymer	Short chain	Long chain	Long chain	Short chain

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

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Applicants must be available for full time employment
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Applicant must be currently enrolled in an academic degree program and will be returning to school following this assignment.

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