COSMECEUTICALS AND COSMETIC INGREDIENTS

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CHAPTER 24

Humectants

Humectants are water-soluble materials with high water absorption capabilities. They are hygroscopic and therefore able to attract water from the atmosphere (if atmospheric humidity is greater than 80 percent) and from the underlying epidermis. Although humectants may draw water from the environment to help hydrate the skin, in low-humidity conditions they may take water from the deeper epidermis and dermis, resulting in increased skin dryness.[1] For this reason, they work better when combined with occlusives. Humectants are also popular additives to cosmetic moisturizers for many reasons. They prevent product evaporation and thickening, which increases the shelf life of formulations, and some humectants help prevent bacterial growth in products.[2] Humectants can cause an almost immediate improvement in skin texture because they draw water into the skin, causing a slight swelling of the stratum corneum (SC) that gives the perception of smoother skin with fewer wrinkles. Humectants, by inducing swelling, can temporarily give the user the perception of increased skin firmness. Humectants have been shown to enhance the penetration of other ingredients by causing swelling of keratinocytes,[3] and disruption of the skin barrier by loosening the closely packed SC cells.[4] Propylene glycol enhances penetration of minoxidil and steroids,[5] while hyaluronic acid increases drug delivery in prescription medications such as Diclofenac.[4] Examples of commonly used humectants include glycerin, sorbitol, sodium hyaluronate (hyaluronic acid), urea, propylene glycol, α-hydroxy acids, and sugars.

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CHAPTER 26

Hyaluronic Acid

Activities:

Humectant, antiaging

Important Chemical Components:

Hyaluronic acid (HA) is formed by repeating units of the disaccharides D-glucuronic acid and D-N-acetylglucosamine, which are linked to each other by alternating β-1,4 and β-1,3 glycosidic bonds. HA is composed of carbon, hydrogen, nitrogen, and oxygen (molecular formula: $C_{14}H_{21}NO_{11}$). See Figure 26-1.

Origin Classification:

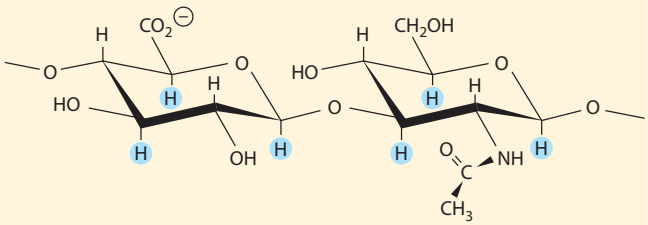
HA is isolated from bacterial or yeast cultures, so it is considered natural but laboratory made. It is not considered organic.

Personal Care Category:

Humectant, moisturizer

Recommended for the following Baumann Skin Types:

DRNT, DRNW, DRPT, DRPW, DSNT, DSNW, DSPT, and DSPW, but only if used in a humid environment or with an occlusive ingredient. ORNW, ORPW, OSNW, and OSPW in any environment.



▲ **FIGURE 26-1** Hyaluronic acid is composed of repeating dimers of glucuronic acid and N-acetyl glucosamine assembled into long chains.

SOURCE

Hyaluronic acid (HA), or hyaluronan, is the most abundant glycosaminoglycan (GAG) found in the human dermis (Table 26-1). GAGs are polysaccharide chains made up of repeating disaccharide units linked to a core protein. Together the GAGs (HA, dermatan sulfate, heparin, heparin sulfate, keratin sulfate, chondroitin-4, and chondroitin-6-sulfate) and attached core proteins form proteoglycans. The only nonsulfated GAG and the only one not synthesized on a core protein, HA is produced by an enzyme complex of the plasma membrane.[1] In addition, HA is a hygroscopic sugar that can bind over 1,000 times its weight in water. It is responsible for giving skin its plumpness and volume. HA is made by fibroblasts and broken down by the enzyme hyaluronidase.

The HA used in skin care products and injectables was originally harvested from rooster combs but now most HA in skin care products is derived from a bacterial origin and produced in the laboratory setting. The molecular weight of the HA varies according to its source and chain length. The HA isolation process can be adjusted to determine its corresponding molecular weight, altering its physiochemical properties.

Uncrosslinked chains of HA in the skin are broken down by hyaluronidase and free radicals in approximately 24 to 36 hours. Chemical modifications, such as crosslinking HA chains with 1,4-butanediol diglycidyl ether (BDDE), can increase the amount of time that HA resides in the skin. Dermal fillers such as Restylane are crosslinked with BDDE so that the HA lasts in the skin for six or more months; however, these crosslinked HA chains are too large to penetrate into the skin and must be injected.[2] Topical forms of HA must have a small enough molecular weight to pass into the skin, thus obviating the use of crosslinked HA.

TABLE 26-1
Pros and Cons of Hyaluronic Acid

Pros	Cons
Strong humectant	Penetration into skin depends on size
Nonimmunogenic	Does not penetrate into the dermis
Forms reservoirs in the epidermis	High consumer recognition
May effect cytokines	Dehydrates skin in a dry environment
Enhances drug delivery	
Various biological/medical applications	

HISTORY

HA was discovered in bovine vitreous humor by Meyer and Palmer in 1934.[3] It was named based on its glassy appearance (the Greek word for glass is *hyalos*) and the presence of a sugar known as uronic acid. HA, which appears freely in the dermis and is more concentrated in areas where cells are less densely packed, is an important dermal component responsible for attracting water and giving the dermis its volume. The popularity of HA fillers for injection into the dermis to correct wrinkles emerged in the 1990s and available products now include the Juvéderm line, Belotero, Restylane, Perlane, and Voluma. HA is also a popular ingredient in cosmetic products because of its humectant activity. However, traditionally, the HA found in many moisturizers, because of its large size, could not penetrate the epidermis and enter the dermis when topically applied, despite the claims of manufacturers.[4] Conflicting reports claim that smaller sizes of HA may penetrate into the epidermis when used in the proper formulations. In the author's knowledge, there are no published studies demonstrating the penetration of topical HA into the dermis.

CHEMISTRY

HA is a linear, naturally occurring polyanionic polysaccharide that consists of repeating disaccharide units of N-acetyl-D-glucosamine and β-glucuronic acid (D-glucuronate).[5,6]

Present in most biologic fluids and tissues (notably, most vertebrate connective tissue), it is most abundant, and an important component, in the extracellular matrix of soft connective tissues, particularly skin, where it plays a protective, shock-absorbing role.[5,6] Although it can be derived from humans, animals, or bacterial cultures, the structure of HA is identical among all of these species. HA exhibits key functions in cell growth and signaling, membrane receptor function, and adhesion, as well as wound repair and regeneration, morphogenesis, matrix organization, and pathobiology.[6] In young skin, HA is present at the periphery of collagen and elastin fibers and where these fibers interface. Such connections with HA are absent in aged skin.[7] In addition, HA appears to play a role in keratinocyte differentiation and lamellar body formation through its interaction with CD44,[8] a cell surface glycoprotein receptor with HA binding sites.[9–11] It is also thought to foster neutrophil migration, fibroblast proliferation, and neoangiogenesis.[12] In 2000, Sakai et al. used high performance liquid chromatography to show that HA is delivered by keratinocytes and is present in the normal stratum corneum (SC) of mice. Further, they speculated that HA contributes to moisturizing the SC and/or regulating its mechanical properties.[13]

ORAL USES

HA is available in oral supplement form, but the stomach breaks it down rendering it worthless to the skin when taken in an oral form. Glucosamine supplements, however, may help skin increase its production of HA.

TOPICAL USES

HA is the main ingredient in the barrier repair products Bionect and Hylatopic to impart water retention. Bionect contains 0.2 percent HA sodium salt, which acts as a humectant, with other humectant ingredients (e.g., glycerin) and a 70 percent sorbitol solution. Hylatopic combines HA sodium salt with the humectant glycerin in a foam preparation along with occlusive ingredients such as dimethicone and petrolatum.[14] Notably, the Food and Drug Administration (FDA) has approved the barrier repair products Atopiclair and Hylatopic, in which HA is the main ingredient.[14] Topical medications such as 3 percent Diclofenac have HA as an additive in the formulation.[5]

The humectant properties of HA allow it to bind 1,000 times its weight in water. Topical use of HA has been shown to improve skin hydration.[15] It functions as a skin-hydrating agent best when used in a humid environment. In a dry environment, it can draw water from the skin into the HA, thus dehydrating the skin. For this reason, HA should be used in combination with an occlusive ingredient in a dry environment. Individuals with oily skin types have sufficient sebum to impart occlusive properties. Therefore, those with oily skin types can use HA in any environment but people with dry skin should not use it in a dry environment unless the HA is combined with an occlusive agent. Applying HA to the skin in a humid environment attracts water to the skin and can result in immediate improvement of wrinkles. The effect is lessened in a low-humidity environment because there is less water in the atmosphere to draw to the skin. In one study, subjects saw improvement within minutes after using a face product with HA.[16]

SAFETY ISSUES

Studies that considered HA for drug delivery have shown that it can facilitate drug penetration into the epidermis and prevent it from entering the dermis as well as the blood stream.[5]

ENVIRONMENTAL IMPACT

No significant environmental impact is likely due to the production of topical HA products.

FORMULATION CONSIDERATIONS

Although HA is a very important skin component, its topical utility is thwarted by its large size and inability to pass into the dermis. However, if the proper size of HA is used, it can penetrate into the epidermis causing a rapid, if short-lived, improvement of fine lines through its effects on skin hydration. It is important to realize that the process of isolating and chemically processing HA greatly impacts its biological activity so that "not all HA is created equal."

USAGE CONSIDERATIONS

HA can enhance drug penetration, an important consideration when designing a skin care regimen and designating the order in which products will be applied. For example, applying a retinol after using a product with HA could theoretically increase absorption of retinol.[17]

SIGNIFICANT BACKGROUND

HA, in large part due to its viscoelastic nature, biocompatibility, and nonimmunogenicity, is included in multiple clinical applications, including as an oral supplement and injectable to increase HA in synovial fluid in arthritic patients, an eye aid after cataract surgery, a wound-healing agent, a filling agent in cosmetic and soft tissue surgery, a device in various surgical procedures, and in tissue engineering.[5,6] Topically it has become a popular additive in skin care products with claims ranging from decreasing eye puffiness to smoothing wrinkles and firming skin.

Wound Healing

In a small prospective study of 27 patients delivering by cesarean section and 20 patients delivering vaginally with episiotomy, researchers assessed the effects of an HA sodium salt (Bionect) in 15 subjects from the cesarean group and 10 from the episiotomy group (with standard wound care applied to the remaining patients) and found that daily application of the HA treatment yielded a lower incidence of edema, infiltration, and wound exudates compared to standard treatment. One case of wound dehiscence in each standard treatment group occurred, but none in the HA groups.[12]

In a recent 60-day, double-blind, randomized, controlled superiority trial intended to examine the efficacy and safety of a gauze pad containing HA in local treatment of venous leg ulcers in 89 patients, Humbert et al. found that ulcer surface was diminished significantly in the HA group compared to the neutral control group at day 45. In addition, at days 45 and 60, the number of healed ulcers was significantly higher in the HA treatment group. Notably, pain intensity was significantly lower in the HA group at day 30.[18]

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