The effect of Hyaluronic acid on skin aging

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Abstract

Hyaluronic acid is a natural hydrocarbon and organic chemical compound found in the outer matrix of cells and tissues of the body, including skin, bones, eyes and cartilage. This substance is the basis of the connective tissue of the skin and is the strongest substance that absorbs moisture and nutrients for the skin, which is also effective in healing wounds. The human body contains approximately 15 grams of hyaluronic acid, which is present in all parts of the body, and one-third of it is decomposed and synthesized daily (decomposition of materials to produce new material or materials). More than 70% of the total body hyaluronic acid inthe skin is located because it is needed for the stability and maintenance of the internal matrix and many cell functions.One of the ways to heal skin wounds is to use fillers containing jelly. hyaluronic acid is external because these substances do not have an internal human origin and from animalsor bacteria, in many cases cause skin allergies and They have a short half-life. Efforts to preserve or increase the secretion of hyaluronic acid by human skin fibroblasts in preventing and eliminating the symptoms of skin aging.

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Introduction

Old age is a multifactorial and complex process whose main cause is still unknown and is explained based on a set of theories. Unlike evolutionary theory, which sees aging as the result of reduced natural selection, molecular theory emphasizes the effect of genetic change. Also in systemic theory, aging occurs as a result of neuroendocrine changes and immunological processes. Cellular aging is generally explained by theories such as telomere shortening and damage caused by free radicals. The skin aging process is controlled by internal and external factors. External factors include exposure to ultraviolet radiation, environmental air pollution, and smoking. Exposure to ultraviolet light lead to increases reactive oxygen species (ROS) by disrupting collagen synthesis, inducing collagen production, and enzymes that break down proteins in the extracellular matrix, leading to the destruction of cellular DNA, changes in the structure, and function of proteins. And finally causes skin damage. Internal factors include the formation of large amounts of reactive oxygen species during cellular metabolism and genetic factors, as well as the gradual decline in sex hormone production in the mid-twenties and the decline in menopausal estrogen and progesterone. Skin aging is also associated with a loss of skin moisture. The key molecule involved in moisturizing the skin is Huronic Acid with unique oven properties (Pickart,2008: Fuller-Iglesias etal,2009). The presence of hyaluronic acid improves the moisture of the hair and maintains more moisture on the scalp. On the

other hand, due to the role of this substance in cell health, hair growth is also improved. Because healthier cells lead to better hair follicle growth and thicker and fuller hair. Hyaluronic Acid (HA), or hyaluronan, is a dominant mechanism for skin moisture that must be involved in the aging process.Hyaluronan has a large amount of water absorption. The water that surrounds the hyaluronic acid molecules is not in equilibrium with the rest of the body's water but contains its components.In fact, a 60 kg person has 15 g of hyaluronic acid, half of which is in the skin. Hyaluronic acid conversion with a half-life of 1 to 2 days is also done quickly on the skin .Of course, the biology of skin hyaluronic acid and its associated water as a function of age has not yet been well studied (Podolskiy DI, Gladyshev,2016).

Understanding HA metabolism, its reactions in the skin, and the interaction of hyaluronic acid with other components of the skin facilitates the understanding of skin aging as well as the reduction of skin moisture.In humans, hyaluronic acid is found in abundance in tissues such as synovial fluid, cartilage, and middle membranes of the skin, which clearly play an important structural role depending on the hydrodynamic properties and how it relates to other components of the extracellular matrix.Hyaluronic acid, on the other hand, plays an important role in cell signal transduction during dynamic cellular processes such as morphogenesis, inflammation, wound healing, and cancer, in which the hyaluronan-receptor interaction is activated.And cooperates in guiding the signaling pathways of countless cell division .Also, hyaluronic acid in skin tissue engineering for the production of scaffolding is one of the materials used in addition to collagen, chitosan, gelatin, polycaprolactone, polylactic acid.Hyaluronic acid (HA) is a type of glycosaminoglycan containing one unit of D-glucuronic acid (UDP-GlcNAc), acetylglucosamine-N and UDP-GlcUA.Molecular weight of hyaluronic acid, which consists of more than 50,000 units of repetitive disaccharides; Reaches several million Daltons(Toole,2009).

The main components of the skin have been well defined in recent decades. The first studies focused on the cells that make up the skin:

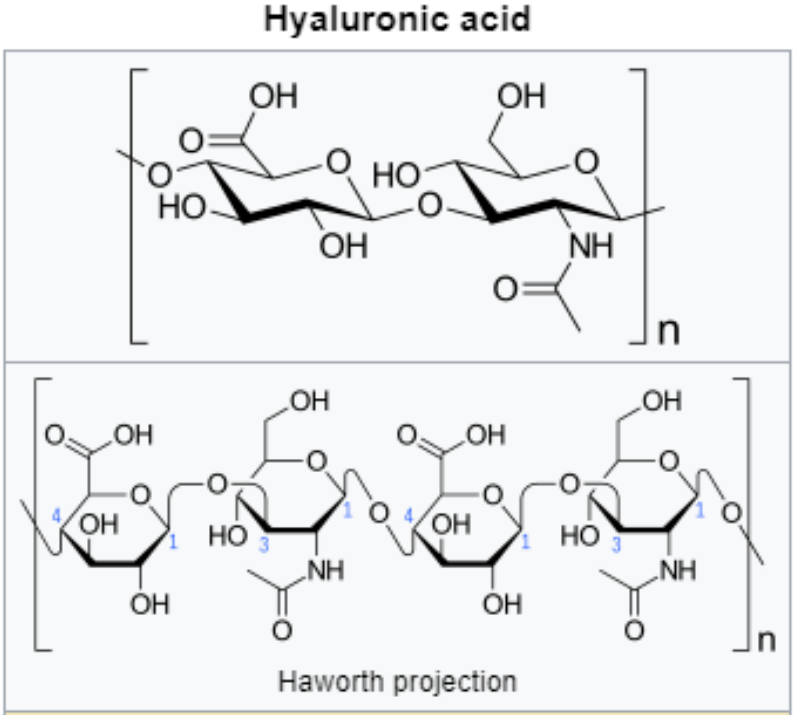
Epidermis, dermis and subcutaneous tissue. It is commendable that the materials between the cells are being considered today.Matrix components play informative roles for cell and tissue activity.Although the Extracellular matrix (ECM) looks irregular under a light microscope, However, the highly organized structure of glycosaminoglycans (GAGs), proteoglycans, glycoproteins, peptide growth factors, and structural proteins (such as collagen and to a lesser extent elastin) is questionable. Most skin hyaluronic acid is in the ECM .In fact, hyaluronic acid is the predominant ECM in the skin.Recent advances in the details of hyaluronic acid metabolism can shed light on a long and valuable observation that shows oxidative damage from free radicals and reactive oxygen species and damage from ultraviolet light causes premature aging. It becomes skin .These processes have a mechanism similar to natural aging in which hyaluronic acid is a common derivative.Efforts to increase the moisture content of skin components, in the most elementary terms, increase the level and duration of hyaluronic acid presence in the skin, maintain the optimal length of the polymer chain, and increase the expression of the best set of proteins bound to hyaluronic acid for It is the decoration of moleculesHyaluronic acid is not a bacterial immunogen; Therefore, bacteria are a good source for the production of hyaluronic acid for medical purposes . Separation of hyaluronic acid from the culture medium of microbial fermentation fluid with high yield is a relatively simple process.An important and additional advantage of microbial hyaluronic acid production is that microbial cells can adapt physiologically or metabolically to produce more hyaluronic acid with a higher molecular weight.Therefore, the production of microbial hyaluronic acid, either using pathogenic streptococci or using safe recombinant hosts that contain essential

hyaluronic acid synthase, is increasingly preferred today.To prevent the risk of exotoxin contamination of streptococcal pathogenic bacteria in hyaluronic acid products, genetically engineered safe organisms by inserting hyaluronic synthase genes from Streptococcus or Mycorrhizal Taeniidae strains .Using this method, hyaluronic acid producing strains including Enterococcus faecalis, coli. E, Bacillus subtilis, Agrobacterium, Lactobacillus lactis are obtained and used to produce hyaluronic acid. (Farage,2009)

The structure of hyaluronan

In humans, hyaluronan is abundant in tissues such as synovial fluid, cartilage, and middle membranes of the skin, which clearly play an important structural role depending on the hydrodynamic properties and how it relates to other components of the extracellular matrix.Hyaluronan also plays an important role in cell signal transduction during cellular dynamic processes such as morphogenesis, inflammation, wound healing, and cancer, in which the hyaluronan-receptor interaction is activated and co-directs the signaling pathways of numerous cell divisions (Qur,2005).Hyaluronan was introduced by Karl Meyer in 1938 as a substance containing hexoronic acid (which causes swelling of the clear substance in the eye).

It took twenty years to prove the chemical structure of hyaluronic acid. It was later discovered that this substance is present in all vertebrate tissues. Hyaluronan is a high molecular weight, highly anionic polysaccharide, and the smooth GAG chain consists of replicating units of glucuronic acid and N-acetylglucosamine, all with βGlcAb (1: 1) b (1: 3) b (1: 1) 4) are interconnected, which may reach 107 Da. Hyaluronan is the simplest and only non-sulfated GAG, a glycosaminoglycan that is not covalently attached to a protein center and is not made by the Golgi apparatus (Lee JY 2000, Toole ,2000)



The subject of link b was not a simple curiosity of carbohydrate chemists, but far beyond their interests. Glycogen is a polymer with α-glucose bonds. Changing the bonds to β converts the polymer bond to cellulose. Chitin, as a high molecular weight chain, is N-acetylglucosamine with β-bonds. However, chitin and cellulose are the most abundant sugar polymers on the surface of the earth. However, such sugary polymers with β-bonds are not abundant in vertebrate tissues, and the enzymes needed to burn them in tissues are limited, which for their

precursor can last for centuries. Stay. Hyaluronan is formed by covalent bonding to proteins such as the intra-alpha trypsin inhibitor, a plasma protein that acts as a stabilizer of hyaluronic acid-rich structures, such as a dense cloud mass. It surrounds the mammalian egg (Podolskiy D,2016).The second molecule of hyaluronic acid contains a large volume of water that is dispersed in the extracellular space. Water delivers to the tissue, and is responsible for maintaining skin moisture in the dermis.It is also a major component of swelling in the inflammatory response.Hyaluronan has the ability to expand the level of its solubility domain, even up to 1000 times its actual volume. Hyaluronic acid has a high density even at low concentrations.Hyaluronic acid is seen as a linear polymer under an electron microscope. It is very polydisperse, but usually has a molecular mass of millions.Hyaluronic acid in solution with physiological pH and salt concentrations is a wide random spiral with a diameter of 500 nm. Existing models suggest that for high molecular weight hyaluronic acid, a molecular superorganism is composed of networks whose molecules move in parallel hundreds of nanometers in length, forming flat layers. And become tubular structures that are then joined together in similar masses.There is strong evidence that a water bridge between the acetamide and carboxyl groups is involved in the secondary structure.In addition, the hydrogen-bonded secondary structure exhibits large sequences of interconnected CH groups that give hydrophobic properties to parts of the polymer that may be transverse in density or Self-bonding and is important for membrane interaction .This hydrophobicity may be involved in the separation of newly formed hyaluronic acid chains from the cytoplasmic surface of the plasma membrane (where HAS is located) through the membrane outside the cell. The third unusual structure of the polymer trait is based on the same hydrophobic interactions (Boeriu,2013).

Report Hyaluronic acid

Despite its simple structure, hyaluronan is surprisingly broad in its functions.At high concentrations, as found in the ECM dermis and epidermis, it regulates water balance and osmotic pressure, acts as an ion-exchange resin, and ions flow Organized by Mickey.Hyaluronan acts as a sieve, releasing a series of specific molecules to develop the extracellular domain of cell surfaces, especially the transparent surface of endothelial cells. It can also act as a lubricant and shock absorber.Hyaluronan can also act as a structural molecule, such as that found in the retina, joint fluid, and Wharton jelly.Hyaluronan enhances cell motility, inhibits cell-cell interaction, regulates cell adhesion to the matrix, enhances growth and proliferation, and reduces differentiation.Participates in basic processes such as development and embryo formation, wound healing, repair and regeneration, and inflammation.Hyaluronan levels increase in response to severe stress, and expand as the tumor progresses and invades.Recent studies have shown that intracellular hyaluronic acid is also present. However, the functions of intracellular hyaluronic acid are currently unknown (Evanko,1999). Although the constant presence of hyaluronic acid also prevents cell differentiation, it instead creates an environment that enhances cell proliferation. Elevated anti-adhesion levels of surface hyaluronic acid, which promote cell separation, also allow embryonic cells to migrate and tumor cells to move and metastasize.Water uptake also provides spaces for creating an environment conducive to such cellular movement.

The extracellular matrix that surrounds the cells also contains various levels of hyaluronic acidThe extracellular environment is markedly composed of structural proteins such as collagen and elastin, as well as proteoglycans and a number of glycoproteins. The amount of hyaluronic acid is highest in fetal ECM, and in tissues that are changing and repairing. The septum or basement membrane that separates the dermis and epidermis is also an ECM structure. The basement membrane contains

hyaluronic acid, although its exact structure is not yet known. Loss of the lower membrane hyaluronic acid in the skin of diabetic patients is correlated with their skin hardness. A number of growth factors located within the ECM have been concentrated by ECM components to protect against degradation, and such factors have been introduced into cells as a growth control mechanism and performance modulator. . Heparan sulfated proteoglycans bind members of the FGF and EGF families, while hyaluronic acid can bind growth factors such as TGF-β, preventing them from being digested. Protected by proteoglycans. Of course, a complex picture emerges in the mind that two types of GAGS, hyaluronic acid and heparan sulfate, have opposite functions. While heparan sulfate proteoglycans enhance differentiation, while heparan sulfate proteoglycan promotes differentiation, a hyaluronic acid-rich environment maintains an undifferentiated, pluripotent, cellular, and stimulatory state. It is necessary.

However, the concentration of hyaluronic acid in the ECM can be very different. Even when the level of hyaluronic acid is reduced (such as certain areas of fibrosis), it acts as an ECM organizer as a scaffold in which other ECM macromolecules find their direction. The dimensions of the collagen fibers are adjusted by the amount of hyaluronic acid, which means that thinner and finer fibers are more preferred in the high-concentration hyaluronic acid region. In fibroblast cultures, the addition of external hyaluronic acid to the medium reduces the diameter of the accumulated collagen fibers. The ability of hyaluronic acid to stimulate cell proliferation depends in part on the size of the hyaluronic acid molecule, ie, opposite effects are obtained in high and medium sizes. High molecular weight hyaluronic acid is anti-angiogenic, while medium molecular weight hyaluronic acid is highly angiogenic, stimulates the growth of endothelial cells, and absorbs inflammatory cells. It also increases the expression of inflammatory cytokines. Hyaluronic acid may be partially degraded may have the opposite effect, perhaps because it is no longer able to retain and release growth factors such as TGF-β. These observations relate to understanding the pathological aspects of the skin. For example, severe staining for hyaluronic acid in psoriatic lesion 1 may be due to degradation of part of the angiogenic hyaluronic acid, and may be a mechanism for the growth of specific and inflammatory capillaries that these lesions haveSpecifies.Efforts have been made to stimulate the storage of hyaluronic acid in the skin in order to improve water retention in the skin and reverse the effects of aging, which should be done with caution and care should be taken that the stored hyaluronic acid is of high molecular weight. This can be done by preventing the catalyst from breaking the free radical chain and accurately preventing the catabolic reactions of hyaluronidase.One of the most recent developments is the realization that hyaluronic acid and its associated hyaluronic acids are intracellular, and have important effects on cellular fuel metabolism. Much progress has been made in the ability to remove ECMs from cultured cells using streptomyces's hyaluronidase. By permeating the cells and using a focal microscope, locating methods may be used to identify intracellular hyaluronic acid and its associated proteins.Some intracellular hyaluronic acid complexes (in a wide range of cell types) appear to be part of the nucleus matrix and are important in regulating cell cycle and transcription of genes.However, so far no definite function of them has been shown. The ability of hyaluronic acid to bind to itself, to cell surface receptors, to proteins, or to other GAGs indicates the extraordinary versatility of this molecule.The criteria for storing hyaluronic acid with these extensive steps depend on the exact levels of the synthesis and degradation networks. In general, hyaluronan is produced in the intercellular space, in the body's mesenchymal connective tissue, and is mostly the product of fibroblasts. It reaches the blood through the lymph.Most HA changes (approximately 85%) occur in the lymphatic system. The rest (15%) that reaches the

bloodstream is severely altered with a half-life of 3 to 5 minutes, meaning that it is immediately absorbed by receptors in the liver, and all This is eliminated by an unknown mechanism in the kidney.When the hepatic arteries or kidneys close, the level of circulating hyaluronic acid (in the blood) rises immediately.Such humans make and destroy several grams of hyaluronic acid daily. A rapid increase in circulating hyaluronic acid occurs in people with severe stress (such as when shocked, infection of the blood by purulent organisms or severe damage) and in burn victims.Such an acid may act as a volume enhancer in the form of a mechanism to maintain survival and prevent a sudden drop in blood pressure (myocardial infarction). Some of these rapid increases in hyaluronic acid represent hyaluronic acid utilized from intercellular stores and tissues and from lymph and not fully reflect an increase in construction or a decrease in its degradation.However, under acute stress conditions, its half-life is 20 to 45 minutes, and high plasma levels of hyaluronic acid are closed with reduced rate of conversion. Mean serum and plasma hyaluronic acid levels in healthy young subjects are 20 to 40 mg / L
This number increases with age and probably reflects a slower clearance (clearance) and a decrease in the degradation capacity of hyaluronic acid, although this has not yet been carefully studied.Circulating hyaluronic acid in liver patients (especially in cirrhosis of the liver, and in liver failure) also reflects improper destruction, in rheumatoid arthritis and continuously in some malignant tumors due to increased tumor tissue formationHyaluronic acid receptors contain different proteins that bind HA together, called hyaladherins, which are widely used in ECM, cell surface, cytoplasm and nucleus. Those that bind HA to the cell form the surface of HA receptors. The most prominent of these receptors is the membrane differentiation cluster glycoprotein (CD44), which occurs in many isoforms (Podolskiy,2016).

1. **CD44**

CD44 is a widely distributed cell surface glycoprotein found on hematopoietic cells, fibroblasts, and a large number of tumor cells. It was first identified as gp85 (14) and then shown to be a HA receptor in placental cells when their adherence to immobilized HA was inhibited by anti-CD44 monoclonal antibodies, soluble HA and HYAL (Aruffo,1990, Stamenkovic,1991, Peach,1993). However, the presence of the CD44 HA-binding amino-terminal region does not guarantee that CD44 HA-expressing cells bind. In fact, most CD44-expressing cells derived from normal animals, as well as from CD44 + cell lines, do not bind to HA. The binding of CD44 to HA is cell-specific and depends on the activation state of CD44(Lesley,1997). CD44 has seven extracellular domains, a membrane domain, and a cytoplasmic domain (Idzerda RL,1989). The extracellular structure consists of two regions (amino and amino acids (Idzerda RL,1989) that contain a cluster of essential residues that play the role of BX7B in HA binding. These motifs, found in other HA-binding proteins, including RHAMM, exist as a single copy in the first region, and as an overlapping pair in the second region.Intermolecular disulfide bond pairs are also important for HA binding activity. The HA binding domain located in the amino-terminal region is present in all isoforms (Liao HX,1995). The proximal region of the membrane is less protected and includes the insertion of different slopes of the exon. Membrane and C-terminal cytoplasmic domains are highly protected CD44 is encoded by a single gene. Due to the alternative bonding, several forms of CD44v are produced that are modified by N and O-associated glycosylation. The smallest standard isoform of CD44 (CD44s) lacks variable exons, has an N-terminal signal sequence (exon 1), is a link module to HA (exons 2 and 3), a stem region (exons 4, 5, 16 and 17), A single-pass membrane domain (exon 18), and a cytoplasmic domain (exon 20). In all forms of CD44 cDNAs, exon 19 is interconnected so that the membrane domain encoded by exon 18 is followed by the cytoplasmic domain encoded by exon 20 and the cytoplasmic domain

produces 73 amino acids. CD44s are found in most cells (Misra S,2011), while isoforms that have different numbers of exon insertions (v1 – v10) in the outer region of the proximal plasma membrane, predominantly on cells during inflammation and on cells Tumors are expressed (Turley EA,2002, Naor D,2008, Misra S,2009)

Most importantly, CD44 types, especially CD44v6, increase tumor progression and metastatic potential in lung, breast, and colon cancer (Ponta H,2003, Hofmann M,1991)

Subsequently, several tumors, including colorectal cancer, Hodgkin's lymphoma, gastric cancer, and melanoma, have been screened for CD44 isoforms, indicating some types CD44 play an important role in tumor progression. HA and CD44 are present in the membranes of most vertebrate cells (Koopman,1993) (Heider KH,1993) (Birch M,1991).

CD44 is a multifunctional receptor that plays different roles in cellular-cellular and cellular-cellular interactions, cellular circulation, lymph nodes, protimocytes, lymphocyte activation, cell aggregation, release of chemokines and growth factors and their delivery to cells. Traveler CD44 can be a proteoglycan by substituting chondroitin sulfate (CS) or dermatan sulfate (DS). The insertion of exon v3 also includes the potential for heparan sulfate (HS) sulfate replacement, which can be achieved by ligand binding and cellular behavior by allowing CD44 to co-receptor liver growth factor (HGF) with c-Met (van der Voort R,1999). CD44 affinity. For these replacements, GAG depends on post-translational changes, such as oligosaccharides and the addition of GAG and their subsequent functions depend on cell type and growth conditions. These changes can be altered by physiological stimuli, resulting in HA induction. In the immune system, HA binding can be induced in T cells by detecting antigens and when monocytes are activated by inflammatory stimuli Unlike HAS2-deficient mice (19), CD44-null mice grow naturally, indicating that CD44 is not usable for development.

2. **RHAMM**

Another major known receptor for HA is the RHAMM receptor to facilitate HA-mediated movement (RHAMM). This receptor is involved in cell movement, alteration of focal adhesion, and contact inhibition, which are also expressed as different isoforms. The interactions between hyaluronic acid and RHAMM regulate cell movement by a complex network of signal conduction and interaction with the cytoskeleton. Of course, it is also an important regulator of cell growth.

Tumor growth factor beta (TGF-β) stimulates cell proliferation using RHAMM, and TGF-β is a potent stimulus for movement in many different cell types. In fibroblasts, TGF-β promotes transcription, fabrication, membrane expression not only of RHAMM but also of the synthesis and expression of hyaluronic acid and all that occurs at the onset of motion.In summary, CD44 and RHAMM may intervene among the most complex biological molecules, moving in broad cell components, and with a range of activities in signal conduction, movement, and cellular transformation. The apparent instability between the observations of various laboratories in relation to CD44 and RHAMM receptors reflects the subtle ways in which hyaluronic acid exerts a wide range of biological effects and countless mechanisms for controlling the expression levels and storage of helical acid. It is obvious. Especially in the experimental conditions of laboratories, slight changes in culture conditions, differences in cell passage number, culture duration, differences in growth factor conditions in each lot of serum, or differences in foam filling stage. The culture dish has important effects on the expression of HA, its receptors, and the components that adorn the hyaluronic acid molecule, causing age-related changes in cultured skin cells.One of the most important challenges is to identify the specific hyaluronic acid shape of the dermis and epidermis, to describe these proteins and to understand their function in relation to age. In a skin function test for age function, hyaluronic acid levels did not decrease as expected, but instead the binding of hyaluronic acid to stronger tissue proteins and the

extraction of hyaluronic acid increased. It became more difficult 15. Another challenge is to understand how hyaluronic acid, as a precursor to hyaluronidase degradation, is affected by the associated hydroneurins. Of course, it makes sense that the secondary structure of the hyaluronic acid polymer has been modified to some extent by the hyaluronic acid attached to it (Cheung WF,1999)

One mouse with CD44 deficiency (which has been shown to have a fairly reasonable phenotype) suggested that other hyaluronic acid receptors may have replaced CD44. In fact, it is certain that when CD44 deficiency is present, RHAMM is highly regulated. Today, with the database search approach, other receptors have been identified, including lyline, the LYVE-1 endothelium receptor, and several others.

General observations of hyaluronan and skin

Indeed, hyaluronan is present in all vertebrate tissues and fluids, but the skin is the largest source of hyaluronic acid, accounting for more than 50% of the total. Formalin is an aqueous stabilizer, and most of the tissue-soluble hyaluronic acid is removed by this method. The length of time tissue stays in formalin is a variable that may produce incompatible results that often-come face to face. Acidification and addition of alcohol to the stabilizer further stabilizes the hyaluronic acid, so that subsequent aqueous steps cannot wash out the hyaluronic acid and remove it from the tissue17. Comparisons have been made to determine the location of hyaluronic acid in skin fragments stabilized with conventional formalin / ethanol and formalin. Most hyaluronic acid, especially in the epidermis, is excreted with formalin during stabilization. This phenomenon, compared to the hyaluronic acid in the dermis, indicates that hyaluronic acid in the epidermis is much more tightly attached to cells and tissue structure. 24 hours more incubation in aqueous buffer increases the difference between formalin / alcohol and conventional tissue stabilization methods. When the tissue is exposed to formalin / alcohol, the tissue-dependent hyaluronic acid is firmly stabilized, with a slight decrease in the apparent hyaluronic acid observed in the additional incubation, while the tissues are stabilized. With formalin they show an increasing decrease in the continuous loss of hyaluronic acid.

Hyaluronic acid changes with age

Hyaluronic acid levels are high during pregnancy and decrease shortly after birth. After decades of reaching a steady state, hyaluronic acid levels rise again with age. Elevated levels of hyaluronic acid are found in premature aging syndromes, progeria, and Werner syndrome

This increase in hyaluronic acid is not directly perceived with age and is still not perceived. Increasing the level of hyaluronic acid in the bloodstream reduces immunity. Various methods have been requested at insistence.A layer of hyaluronic acid around the circulating lymphocytes may prevent the ligands from reaching the surface receptors on the lymphocytes. Elevated hyaluronic acid may indicate a mechanism of immunosuppression in the fetus. Recurrence of high hyaluronic acid in old age is also possible.One of the ways to reduce the immune system in the elderly. Elevated hyaluronic acid levels with age may be a reflection of the decline of hydrolytic reactions, including hyaluronidase, which maintains a constant level of hyaluronic acid.This seems to be more of a trend rather than necessarily an increase in HA manufacturing activity. Although dermal hyaluronic acid is responsible for most of the skin's hyaluronic acid, epidermal cells also have the ability to make hyaluronic acid.The marked decrease in hyaluronic acid in the epidermis is the most interesting histological chemical change observed in aging skin. Hyaluronic acid is still present in the dermis of older skin, while the hyaluronic acid in the epidermis is completely gone.The contribution of hyaluronic acid to the epidermis of the total GAG production is greater than that of the dermis, but the reason for its rapid decline with age is unclear. The production of epidermal hyaluronic acid is affected by both the basal

dermis and the surface treatment, such as the use of retinoic acids, which indicates that the epidermal hyaluronic acid is under separate controls from the dermal hyaluronic acid. Contrary to previous observations in vivo and in vitro, recent studies have confirmed that the total amount of hyaluronic acid in the skin remains constant with age. The most fundamental age-related change is an increase in hyaluronic acid cravings for tissue structures with a loss of hyaluronic acid extraction capability. Such added hyaluronic acid may reduce its ability to absorb hydration. This reduction in the hydration volume of hyaluronic acid certainly causes the skin to lose moisture. The exact definition of hyaluronic acid, the proteins attached to hyaluronic acid that make up hyaluronic acid in aging skin, and a comparison of this index with the index of young skin in the dermis and epidermis is research that should be done. It will be addressed in the future. An increasing decrease in the size of the hyaluronic acid polymer in the skin has also been reported as an age function. Increased hyaluronic acid binding to tissue as a function of age can be extracted with age along with progressive collagen cross-linking and uniform loss of collagen. Each of these phenomena leads to the obvious loss of water, dryness, and reduced elasticity that are characteristic of older skin.

Hyaluronic acid and skin aging

The most dramatic histochemical change observed in senescent skin is the marked disappearance of epidermal HA, while HA is still present in the dermis.92 The reasons for this change in HA homeostasis with aging is unknown. As mentioned above, the synthesis of epidermal HA is influenced by the underlying dermis and is under separate controls from the synthesis of dermal HA.16,98 Progressive reduction of the size of the HA polymers in skin as a result of aging has also been reported.109 Thus, the epidermis loses the principle molecule responsible for binding and retaining water molecules, resulting in loss of skin moisture. In the dermis, the major age-related change is the increasing avidity of HA with tissue structures with the concomitant loss of HA extractability. This parallels the progressive cross-linking of collagen and the steady loss of collagen extractability with age.16 All of the above age related phenomena contribute to the apparent dehydration, atrophy and loss of elasticity that characterizes aged skin.

Premature aging of skin is the result of repeated and extended exposure to UV radiation.110,111 Approximately 80% of facial skin aging is attributed to UV-exposure.112 UV radiation damage causes initially a mild form of wound healing and is associated at first with an increase of dermal HA. As little as 5 min of UV exposure in nude mice caused enhanced deposition of HA, indicating that UV radiation induced skin damage is an extremely rapid event.16 The initial redness of the skin following exposure to UV radiation may be due to a mild edematous reaction induced by the enhanced HA deposition and histamine release. Repeated and extensive exposures to UV ultimately simulate a typical wound healing response with deposition of scarlike type I collagen, rather than the usual types I and III collagen mixture that gives skin resilience and pliability.16

In the skin, photoaging results in abnormal GAG content and distribution compared with that found in scars, or in the wound healing response, with diminished HA and increased levels of chondroitin sulfate proteoglycans.111 In dermal fibroblasts this reduction in HA synthesis was attributed to collagen fragments, which activate αvβ3-integrins and in turn inhibit Rho kinase signaling and nuclear translocation of phosphoERK, resulting in reduced HAS-2 expression.113 We have recently unraveled some of the biochemical changes that may distinguish photoaging and natural aging. Using photoexposed and photoprotected human skin tissue specimens, obtained from the same patient, we have shown a significant increase in the expression of HA of lower molecular mass in photoexposed skin, as compared with photoprotected skin. This increase of degraded

HA was associated with a significant decrease in the expression of HAS-1 and an increased expression of HYAL-1, -2 and -3. Furthermore, the expression of HA receptors CD44 and RHAMM was significantly downregulated in photoexposed, as compared with photoprotected skin. These findings indicate that photoexposed skin, and therefore extrinsic skin aging, is characterized by distinct homeostasis of HA.29 We have also assessed photoprotected skin tissue specimens from adults and juvenile patients and observed that intrinsic skin aging was associated with a significant reduction in the content of HA and downregulation of HAS-1, HAS -2, CD44 and RHAMM.28 Similar results for photoprotected skin have also been reported for both genders for HA, HAS-2 and CD44

Conclusion

Although aging is a gradual and spontaneous change in the structure and function of living organisms due to the passage of time, which is associated with increased irregularity and entropy and eventually death.This reduces the firmness and elasticity and leads to sagging skin. Hyaluronic acid is a natural hydrocarbon and an organic chemical compound found in the outer matrix of cells and tissues of the body, including skin, bones, eyes and cartilage. This substance is the basis of the connective tissue of the skin and is the strongest substance that absorbs moisture and nutrients for the skin, which is also effective in healing wounds.The science of biotechnology, which is itself composed of several disciplines, in addition to combating various diseases that reduce life expectancy, has been able to improve and delay the aging process in individuals. Many dermatologists use hyaluronic acid to highlight certain areas of the face.

Hyaluronic acid is used as a filler in highlighting the lips, cheeks, breasts and buttocks. Absorption of this substance after 8 to 10 months also helps to hydrate the skin of the areas around the injection and open its wrinkles.

Hyaluronic acid is effective in maintaining moisture, tissue repair and skin elasticity; in addition, it is a barrier against microorganisms and helps the growth and repair of collagen and elastin. This substance is a good alternative to reduce the volume of some areas of the body that have wrinkles and dents.

Hyaluronic acid is effective in hydrating and keeping the skin moisturized and plays an essential role in reducing the depth of wrinkles, rejuvenation, firmness and elasticity of the skin (Meyer LJ,1994).

The available data suggest that HA homeostasis exhibits a distinct profile in intrinsic skin aging, which is totally different of that in extrinsic skin aging. Additional insight needs to be gained in understanding the metabolism of HA in skin layers and the interactions of HA with other skin components. Such information will facilitate the ability to modulate skin moisture in a rational manner and may contribute to the refinement of current drugs and the development of novel treatments for skin aging.

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