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Abstract

Natural products have attracted wide attention in the cosmetics market due to their safety and high efficiency. As a highly active substance in nature, natural polysaccharides have been reported in recent years to have various cosmetic activities such as moisturizing, whitening, anti-aging and repairing skin, and are becoming a hot research topic in cosmetics industry. At present, the mechanism of polysaccharide exerting cosmetic activity has been widely studied, but the relationship between polysaccharide's chemical structure and cosmetic activity has not been effectively analyzed, which leads to the limitation of polysaccharide development. In this review, the mechanism of polysaccharides exerting cosmetic activities such as moisturizing, whitening, anti-aging and skin repair was introduced. The potential relationship between the structure and activity of polysaccharides was summarized by analyzing the influence of physical and chemical properties of polysaccharides, such as extraction method, molecular weight, monosaccharide composition, functional group and structural modification, etc., which laid a foundation for the analysis of the structure activity relationship of polysaccharides and improved its cosmetic value.

Keywords: Polysaccharide; Cosmetics; Physical and chemical properties; Structure-activity relationship; Biological activity.

1. Introduction

With the pursuit of high efficiency and safety of cosmetics by consumers, cosmetics containing natural ingredients have attracted increasing attention. Natural components can be understood as substances extracted and separated from plants, animals and microorganisms existing in nature through chemical or physical means, rather than synthetic active analogues, which are efficient and sustainable.[1] Compared with many synthetic products, low toxicity, easy access, and high activity are becoming the labels of natural cosmetics.[2] As the market value of natural cosmetics increases year by year, the development of its activity is particularly important.[3] It is necessary to analyze the mechanism of polysaccharide's cosmetic activity, improve the product utilization rate, and solve the market demand.

As a natural product, polysaccharides are widely found in natural plants, animals, bacteria and other organisms.[4] Polysaccharides that have been studied have a variety of biological activities, such as immune regulation, anti-aging, anti-tumor and nerve protection, and have high medicinal values.[5] With the development of the application field of polysaccharides, the cosmetic activities of polysaccharides, such as moisturizing, whitening and anti-aging, have attracted increasing attention.[6] The complex long chain structure of polysaccharides is often the basis for exerting various activities. For example, more polar groups such as hydroxyl and carboxylic groups can trap and lock water molecules through hydrogen bonding and form network structures to exert moisturizing activity.[7] Polysaccharides inhibit tyrosinase, scavenging free radicals and other activities, and show promoting effects on skin whitening and antioxidant.[8,9] Skin creams formulated with polysaccharides showed significant moisturizing and anti-aging activities in the skin tests of volunteers, indicating the effectiveness of polysaccharides in application.[10] In addition, polysaccharides have a repairing effect on damaged skin, which is similar to cosmeceuticals, and may be a potential active ingredient in restorative cosmetics.[11] It can be seen that the development of multiple activities of polysaccharides can be an effective way to produce safer and more efficient cosmetics.

This review summarized the mechanism of polysaccharide's cosmetic activity, including moisturizing activity, whitening activity, anti-aging activity and skin damage repair activity, and summarized together with the physical and chemical properties of polysaccharide. The possible biological signal pathway of polysaccharide activity was speculated, and the method of the strongest aesthetic activity of each polysaccharide was explored by regulating the physical and chemical properties of polysaccharide, such as extraction method, molecular weight, monosaccharide composition, functional group and structural modification, which laid the foundation for the analysis of the structures-activity relationship of polysaccharide.

2. The beauty effect of polysaccharides

As a macromolecular long-chain substance, polysaccharides contain many active functional groups inside, those affect the beauty and related effects of polysaccharides. In the structure-activity relationship of polysaccharides, different structural compositions are often responsible for the appearance of various cosmetic activities of polysaccharides such as moisturizing, whitening, anti-aging and skin repair.[6,12] More polar groups in polysaccharides are conducive to displaying hygroscopic and moisturizing activity.[13] By regulating biological pathways, tyrosinase synthesis is inhibited and melanin production is reduced, which is conducive to skin whitening.[14] In response to external stimuli such as radiation, it can effectively inhibit the generation of collagenase, reduce the generation of wrinkles, and remove free radicals to reduce oxidative damage and delay the aging of the body.[15] For damaged skin, polysaccharides can strengthen skin barrier and promote wound healing, which can improve the protective barrier and improve skin resistance.[16] These activities show broad application prospects of polysaccharides in the field of cosmetics. Through the application and development of various activities of polysaccharides tested at present, polysaccharides may become the effective ingredients of new cosmetics. Compared with traditional cosmetics, the biggest advantage of polysaccharides is that they have strong activity and low toxicity. Most of the polysaccharides existed in nature and are easily obtained.[17] Compared with some traditional cosmetics that are currently used, many polysaccharides also show similar or more effective moisturizing, whitening, anti-aging and other activities. Its lower toxic side effects can also reduce the damage to the skin, and may be applied to the market as a more efficient cosmetic raw material.

2.1. Moisturizing effect of polysaccharides

As an important activity of beauty, the moisture level of skin is always the prerequisite for cosmetics to maintain a beautiful appearance. When the moisture content of the epidermal environment is higher, the skin will be softer and more elastic, with fewer wrinkles,[18] and delay aging. When the epidermis is in a dry environment for a long time, the skin will lose water, dry, fall off, aging and other phenomena will occur. At this time, the protective barrier will be damaged, which may lead to some dry skin diseases, such as specific dermatitis, ichthyosis and other chronic skin diseases,[19-20] and accelerate skin aging.

When the skin is in an abnormal environment such as dry for a long time, water loss will occur, and timely intervention is needed to improve the moisturizing activity of the skin, improve the skin hydration environment, and protect the skin. At present, it is believed that the polar groups of moisturizing factors combine with water molecules to form hydrogen bonds, which is one of the main mechanisms of trapping and locking water molecules to exert moisturizing activity. Under this mechanism, glycerol, propylene glycol, sorbitol and other polyols containing multiple hydroxyl groups are commonly used as moisturizing substances, called traditional moisturizers.[21] Due to its low price and good security,[22] it has been widely used. However, when used for a long time, it is found that the excessive hygroscopicity of such substances is also easy to prone Harm. When the skin is in a dry and hot environment for a long time, the moisturizer is

easy to absorb water internally, and the water is easy to be lost outwardly, which will cause skin damage to a certain extent.[4] Compared with polyols, polysaccharides also exhibit excellent hydrophilic activity because they contain more hydroxyl, carboxyl, acetyl and other polar groups in their chains. Among them, the most famous moisturizing polysaccharide is hyaluronic acid, which was first reported in 1934 and isolated from bovine vitreous body,[23] and was once known as the best moisturizing material, but it was difficult to obtain and expensive to promote.[24] Fortunately, natural polysaccharides are widely found in nature. In recent years, many other polysaccharides have been found to have good moisturizing activity,[25,26] which has gradually become a research hotspot of moisturizing cosmetics and is expected to replace hyaluronic acid.

The moisturizing activity of polysaccharide is mainly manifested in two aspects: water trapping and water locking.[4] Firstly, polysaccharides capture epidermal moisture by hydrogen bonding with water molecules through rich polar groups such as hydroxyl and carboxyl. Secondly, polysaccharides can also act on human epidermal keratinocytes to improve cell activity and accelerate proliferation.[27] Promote the production of skin moisturizing factors such as hydration protein and hyaluronic acid, and improve the skin's moisturizing ability.[28,29] The captured water molecules are usually locked by hydration proteins and transported by transporters to the interior of epidermal cells for locking and absorption,[30] and a variety of moisturizing factors work together to lock water. As for various moisturizing pathways, it has been confirmed that the moisturizing mechanisms that may be regulated by polysaccharides are as follows: First, the interior of polysaccharides is an interwoven network structure of molecular chains,[13] and the tight and complex three-dimensional network space can trap water molecules in the interior. By enzymatically hydrolyzing *Sargassum horneri* polysaccharides with large molecular weight,[31] Chen et al. found that the moisturizing activity increases significantly as the molecular weight of polysaccharides decreases, possibly because the increased polysaccharide chains intermingle to form a tighter grid structure, which is beneficial for water retention.[7] Secondly, polysaccharides promote the synthesis of moisturizing factors such as water transporter protein (AQP), epidermatic-keratin cohesive junction protein (TJ), etc. They have strong self-hydration ability or can promote the transport of water molecules between keratin and inner layer cells.[32] Yang et al. It was determined that Tremella polysaccharide (FTPS-2) significantly promoted Caspase-14 (CASP14) in Human keratinocytes (HaCaT),[33] Filaggrin (FLG) [34] and Aquaporin-3 (AQP3).[35] The synthesis of these three protein moisturizing factors and confirmed that the moisturizing activity of FTPS 2 was superior to glycerol.[30] In addition, moisturizing factors can also interact with each other, and more polar groups are conducive to the formation of complex mesh structures. Yang et al also speculated that a deep moisturizing mechanism may be that hydrophilic proteins can form an elastic network on the skin surface to lock in water,[30] which may also be the reason for the high viscosity and easy film formation of moisturizing agents on the skin surface.[36] The ultimate result is reduced water loss and a moisturized skin environment.

With the improvement of the quality requirements of moisturizers, the moisturizing activities of various natural polysaccharides are being developed. Gabriel et al. extracted and purified the refined polysaccharide from *Prosopis juliflora*. Cell experiments showed that the polysaccharide significantly improved the water content of epidermal keratinocytes and repaired the water loss rate of dry epidermal cells within 1 hour. The formula containing the polysaccharide had cosmetic effects such as improving skin softness and reducing wrinkles[17]. Sangthong and others will contain Polysaccharides from *Volvariella volvacea* moisturizing cream (VVP) compared with the

basic formula, found that the experimental group water content of the daub the recipe, skin and hair elasticity and net have a certain degree of increase, It showed a higher moisturizing and anti-wrinkle effect. Secondly, the effects on skin roughness, skin scale and other skin moisture loss symptoms were also tested, and it was found that the roughness and scale of the gel cream containing 0.2%VVP were effectively improved after 8 weeks of use, indicating that the formula had moisturizing and anti-drying damage effects.[37] Claudia et al. developed a new moisturizer containing polysaccharide, a by-product of Sisal, and tested it on the skin surface of volunteers. It was found that the moisturizing effect of polysaccharide moisturizer appeared in the first hour, and the hydration value in the following four hours was significantly higher than that of the basic formula, showing significant moisture absorption and moisturizing activity.[10] Due to its unique multi-polar groups and long chain structure, natural polysaccharides have unique advantages in improving the moisture absorption and moisturizing activity of moisturizers. In addition, the advantages of readily availability in nature, low price and good safety also show great development potential.

2.2 Whitening effect of polysaccharides

In most places, it is natural to think that fair skin will make people more beautiful.[38] Generally, the degree of skin whitening is mediated by melanin, which widely exists in various tissues and organs of the human body and controls the color and normal function of human hair, eyes, mucosa, skin and other tissues and organs,[39] playing an important role in human health. As the first barrier of human self-protection, melanin in the skin is of great significance in resisting external radiation. The generation of melanin can absorb external radiation[40] and protect the skin. However, when the external stimulation is too strong, melanin will often show excessive synthesis, which will cause the affected part to be darker,[41] and even the phenomenon of pigment disorders, such as freckles and melasma.[40] Therefore, it is necessary to develop anti-melanin production cosmetics, control the excessive synthesis of melanin. It is of great significance to realize skin whitening and health.

At present, whitening cosmetics are widely developed, and the whitening ingredients commonly used include arbutin, kojic acid and vitamin C, etc.,[42,43] all of which show good whitening activity in combating pigmentation. However, with the increasing popularity of cosmetics, synthetic whitening agents may have two sides. They have good activity when used in appropriate amounts, but may affect skin photosensitivity when used excessively.[44] In addition, arbutin decomposition products contain benzene metabolites, which are potentially toxic to bone marrow.[45] Kojic acid is unstable under intense light and heating,[46] and long-term use may be carcinogenic.[41] These phenomena indicate that many synthetic whitening ingredients have potential cytotoxicity and adverse reactions when used for a long time.[42] Therefore, it is imperative to find safe and efficient whitening compounds to improve the quality of whitening cosmetics.

The synthesis and deposition of melanin usually occurs in melanocytes, fibroblasts and keratinocytes in the epidermis, and is synthesized by melanocytes and transported to various cells.[47] As the main site of melanin synthesis, melanocytes contain a large number of enzymes related to melanin synthesis, the most critical of which is tyrosinase (TYR),[48] which is the rate-limiting enzyme of melanin synthesis and the necessary mediator for melanin synthesis. At

present, most whitening agents are mainly used to achieve whitening effect by inhibiting the synthesis of tyrosinase or reducing the activity of tyrosinase.[49] A large number of studies have reported that natural polysaccharides extracted from many plants can also inhibit tyrosinase activity and reduce melanin synthesis, and many polysaccharides show better whitening effect,[50] and some natural polysaccharides may be potential effective ingredients in whitening cosmetics.

Many melanin synthesis pathways have been confirmed,[51] and blocking the occurrence of these pathways is the main way that polysaccharides inhibit melanin synthesis.[14] Melanin synthesis pathway is often regulated by multiple protein signals. Such as the production of epidermal cells of alpha-melanocyte-stimulating hormone (α-MSH) and adrenocorticotropic hormone (ACTH) can be used as the conduction factors acting on the melanin cells, Promote the synthesis of microphthalmia associated transcription factor (MITF).[52] The content of MITF directly affects the synthesis of tyrosinase [41]. Tyrosinase oxidizes tyrosine to produce 3,4-dihydroxyphenyl-L-alanine (L-DOPA), and then further oxidizes to produce dopA quinone, which is prone to spontaneous polymerization to form high-molecular weight pigment substances.[53] Melanin is finally synthesized through complex coordination of various protein mediators. Regulating the synthesis of each signal can be an effective way to indirectly control the production of melanin.

At present, it has been reported that the main pathway of polysaccharide regulation of melanin synthesis is to block the occurrence of synthetic pathway, and the two possible routes are as follows: When external ultraviolet rays, hormones, and inflammatory immunity act on epidermal keratinocytes, fibroblasts, and melanocytes, the synthesis and cleavage of intracellular proopiomelanocortin (POMC) will be accelerated,[54] which is a protein produced by all epidermal cells, and POMC cleavage will produce alpha-melanocyte stimulating hormone and adrenocortical hormone. These two hormones act as mediators to stimulate melanocytes in an autocrine or paracrine way[14] by binding to the melanocortin-1 receptor (MC1R) in melanocytes to promote the synthesis of cyclic adenosine monophosphate (cAMP),[55] at which time melanocytes are activated for melanin synthesis. cAMP can activate protein kinase A (PKA), and the activated PKA will further phosphorylate cAMP response element binding (CREB) protein, which can act as the upstream transcription factor to promote the expression of MITF.[14] MITF will bind to the tyrosinase promoter, increase the content of tyrosinase and improve its activity, and promote the generation of melanin. This pathway is a widely reported cAMP/PKA signaling pathway.[14] For cAMP/PKA signaling pathway, many polysaccharides can inhibit the expression of transcription factor MITF by reducing the synthesis of α-MSH in epidermal cells,[56] down-regulating the expression of MC1R protein, controlling CREB phosphorylation, and finally inhibiting tyrosinase activity and reducing the production of melanin.[41] In addition, MAPK signaling pathway has also been reported to be affected by polysaccharides,[41] which accelerates the synthesis and derivation of POMC in epidermal cells when ultraviolet radiation is irradiated on the skin surface.[47] The derivative basic fibroblast growth factor 2 (FGF2) binds to the fibroblast growth factor 2 receptor (FGF2R) in melanocytes by paracrine, activates melanocytes, and induces the phosphorylation of proteins such as fibroblast growth factor receptor substrate 2 (FRS-2), p38, c-Jun N-terminal kinases (JNK), and extracellular signal-regulated kinase (ERK).[47,57] Mitogen-activated protein kinase (MAPK) signaling pathway is activated to promote the expression of MITF transcription factors, and further promote the synthesis and activity of TYR and its related enzymes TYRP1 and TYRP2,[58] and accelerate the production of melanin. For the MAPK signaling pathway, some

polysaccharides successfully down-regulated the expression of IL-6 gene in epidermal cells and inhibited the phosphorylation of STAT3 protein, which inhibited POMC derivation to FGF2,[47] thus reducing the secretion of this conductive factor and inhibiting the MAPK signaling pathway in melanocytes, thereby reducing the synthesis of melanin and achieving whitening effect. **Figure 1** shows the mechanism of polysaccharide regulating melanin synthesis through two pathways.[41,59] Studies show that polysaccharide inhibits the production of α-MSH and FGF2 respectively, thus inhibiting the synthesis of MITF, reducing the content of tyrosinase and inhibits the production of melanin by blocking the synthesis pathway.[14,47]

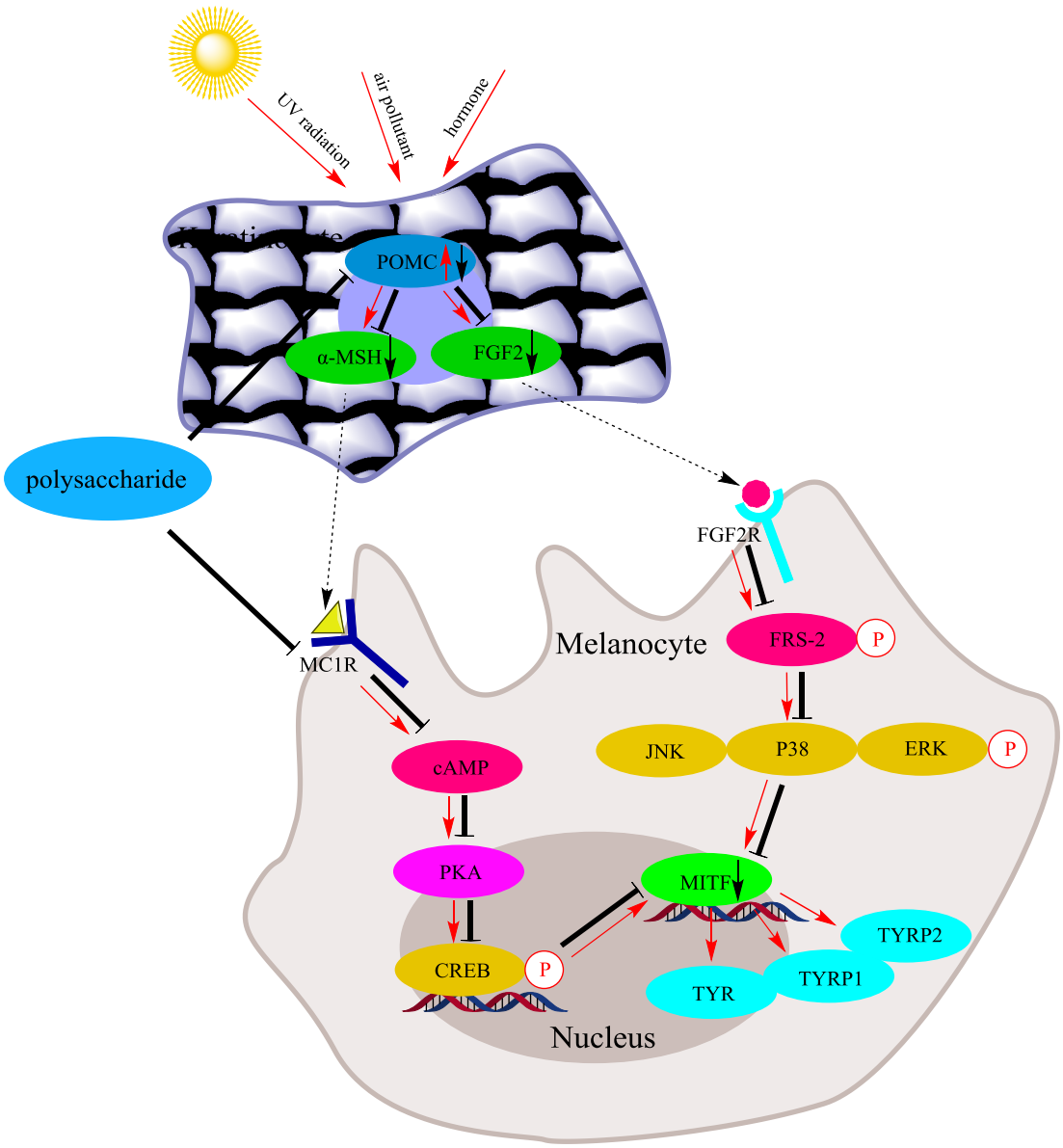

Figure 1 Mechanism diagram of polysaccharide regulating melanin synthesis through two pathways.

POMC, Proopiomelanocortin; α-MSH, alpha-melanocyte-stimulating hormone; MC1R, melanocortin-1 receptor; cAMP, cyclic adenosine monophosphate; PKA, protein kinase A; CREB, cAMP response element binding; MITF, microphthalmia associated transcription factor; TYR, tyrosinase; TYRP1, TYR-related protein 1; TYRP2, TYR-related protein 2; FGF2, fibroblast growth factor 2; FGF2R, fibroblast growth factor 2 receptor; FRS-2, fibroblast growth factor receptor substrate 2; JNK, c-Jun N-terminal kinases; ERK, extracellular signal-regulated

kinase.

Inhibition of tyrosinase activity to reduce melanin synthesis is currently recognized as the main way for polysaccharide to exert whitening activity.[8,60] Sangthong et al. extracted *Volvariella volvacea* polysaccharide (VVP) by three methods of hot water oscillation, microwave assistance and ultrasound assistance respectively, and prepared cosmetic gel cream with 0.2% VVP content. L Dopa was used as the substrate for determining tyrosinase inhibitory and found that hot water oscillation extraction polysaccharides to clear the activity of tyrosinase, best It was also introduced that polysaccharides containing tyrosinase inhibiting activity may be used as whitening agents in cosmetics.[37] Tang et al. extracted crude polysaccharide UEP from Chinese chestnut and purified it to obtain polysaccharide UEP1-1. The inhibitory effect of polysaccharide UEP1-1 on tyrosinase activity was measured. The results showed that the inhibitory rate increased with the increase of polysaccharide concentration, and the IC_{50} value for tyrosinase was 6.62 mg/mL. Compared with positive control arbutin (16.41 mg/mL), it showed good tyrosinase inhibition,[61] and the inhibition mode may be competitive inhibition.[62] Wang et al. extracted HFPS from *Hizikia fusiforme* and determined that the inhibition rates of HFPS on tyrosinase at 25, 50 and 100 μg/mL concentrations were 4.36 %, 11.97 % and 36.66 %, respectively. Compared with the previously extracted *Undaria pinnatifida* polysaccharide (UPEF), it showed better tyrosinase inhibitory activity, possibly because it contained more sulfuric acid groups (63.56 %).[60] A large number of experiments have shown that polysaccharides can restrict the production of melanin in various ways, such as regulating the expression of genes related to melanin synthesis or binding with tyrosinase, which indicates that natural polysaccharides may become a safe and efficient new whitening ingredient.

2.3. Anti-aging effect of polysaccharides

Aging is a problem that all mankind must face. Externally, aging is manifested as sagging skin and loss of vitality; internally, functions of various organs will decline, metabolism will slow down, metabolites will be difficult to clear and other phenomena,[63] which will eventually lead to the decline of the body's immunity and the increase of the risk of age-related diseases.[64] In the search for anti-aging, researchers have found that polysaccharide, as an important active substance, has activities such as delaying, improving immunity and enhancing metabolism.[65,66] Moreover, the advantages of natural polysaccharides, such as non-toxicity and high efficiency, show broad prospects. As for the cause of skin aging, it is currently recognized that it is closely related to the production of reactive oxygen species and matrix metalloproteinases.[15,65] Reactive oxygen species (ROS) are the main source of free radicals in the body. According to the free machine theory, when ROS is difficult to balance in the body, it will accelerate the production of free radicals, promote oxidative damage of cells,[15] and lead to cell senescence and apoptosis.[67] When this oxidation occurs in the epidermis, the elastic fibers of the skin will be damaged,[68] resulting in skin relaxation, roughness and other aging phenomena. In addition, collagenase in matrix metalloproteinase is also one of the main causes of skin aging.[69] When the content of collagenase exceeds the standard, it will accelerate the breakdown of collagen in the skin, damage the epidermal fiber structure, destroy the toughness of the skin,[70] and cause wrinkles. There are various pathways of aging, and the related regulatory mechanisms are more complex.[9,71] According to the different mechanisms of aging, the following three kinds of anti-aging pathways

that can be regulated by polysaccharides were summarized and their mechanisms were introduced in sections.

2.3.1. Anti-photoaging

Skin aging caused by external radiation stimulation is called photoaging, and photoaging is the main cause of exogenous aging, which is manifested as skin relaxation. Among all external radiation, ultraviolet radiation is the most important radiation component, and ultraviolet radiation can enter the dermis of human skin at the deepest level.[72] Long-term irradiation will slow down the metabolism of epidermal cells and even destroy the cell structure, resulting in the phenomenon of photoaging.[73] The main mechanism of photoaging is the increase of reactive oxygen species (ROS) and matrix metalloproteinases (MMPs) in epidermal cells.[74] When excessive ROS in the skin environment is difficult to be cleared by the defense system, it is easy to cause oxidative stress of cells and slow down cell proliferation.[74] ROS also oxidizes lipids, nucleic acids and other macromolecules,[75] causing damage to cell membranes and organelles, and accelerating cell damage. MMPs are a group of calcium- and zinc-dependent endopeptidases containing more than 25 that are responsible for extracellular matrix (ECM) degradation.[70] Among them, MMP-1 is collagenase, MMP-2 and MMP-9 are gelatinase, and MMP-3 is stromatolytic enzyme. The increase of these enzymes will accelerate the decomposition of collagen in the epidermal connective tissue,[72] damage the fiber structure of the epidermis, and cause the loss of elasticity of ECM, resulting in photoaging. In addition, the content of polysaccharides and protein components in some skin also indirectly reflects the aging of skin, such as hyaluronic acid (HA), because HA provides a scaffold for many collagen proteins in ECM, and together constitute a glycoprotein network,[76] ensuring the integrity of skin collagen fibers and maintaining skin elasticity.[77] Therefore, the content of hyaluronic acid degrading enzyme can also indirectly represent the degree of aging damage of skin.

The synthesis of MMPs is often thought to be closely related to the expression of transcription factor activating protein 1 (AP-1) and nuclear factor KB (NF-KB).[78,79] When excessive ultraviolet radiation to the surface of the skin, stimulate skin cells improve nicotinamide adenine dinucleotide phosphate oxidase (NOX) activity,[80] accelerate the production of ROS, ROS will produce reactive oxygen radicals such as superoxide anion and singlet oxygen.[81] Excessive ROS will also activate MAPK signaling pathway and activate AP-1, which will act as an upstream signal to accelerate the synthesis of MMPs,[78] which will degrade collagen and damage skin toughness, resulting in photoaging. Secondly, UV irradiation can also activate the NF-kB signaling pathway, directly stimulate the transcription of inflammatory factors such as interleukin (IL-1β) and tumor necrosis factor α (TNF-α),[82] and promote the synthesis and secretion of MMPs. In addition, there will be feedback and mutual promotion between MMPs and ROS,[53] which accelerates the degradation of collagen. Inflammatory factors such as IL-1β and TNF-α can also promote apoptosis[83] and aggravate skin aging. Many researchers have used natural polysaccharides to treat UV-damaged epidermal cells, and found that they can effectively inhibit the occurrence of MAPK signaling pathway and NF-kB signaling pathway, and delay photoaging.[9] In addition, when polysaccharides were used to treat HaCaT cells that were photoaged by ultraviolet irradiation, intracellular ROS, inflammatory factors and MMPs damage factors were effectively controlled.[74,84] Some levels of oxidative damage and cell senescence are even close to

normal levels.[15] The natural polysaccharide has excellent regulation effect on photoaging, which indicates that polysaccharide has effective protection potential against UV light aging.

2.3.2. Antioxidant

Pathological studies have shown that damage caused by oxidative stress in epidermal cells is one of the main causes of skin aging.[85] When the REDOX balance around cells is unbalanced, reactive oxygen species will accumulate excessively, which will accelerate the production of free radicals,[86] promote the destruction of macromolecules by oxidation,[87] damage the cell structure, and cause skin relaxation, roughness and other phenomena.

At present, the main ways to prevent skin oxidative aging are to remove reactive oxygen species[88] or improve the activity of enzymes or non-enzymatic antioxidants in the body.[89] The principle is to improve the antioxidant capacity of cells by blocking the occurrence of oxidative stress chain reaction.[90] Among them, for the ability to remove free radicals, first of all, the clearance level of some antioxidants can be tested directly through in vitro antioxidant experiments. The antioxidant activity of antioxidants is manifested by directly binding with free radicals or metal ions catalyzed by chelating catalytic free radicals.[91] These two pathways are also the main ways of polysaccharide antioxidant. Antioxidant experiments have shown that many polysaccharides have an effective scavenging effect on some of the free radicals such as DPPH, ABTS, OH and O^{2-},[9,92] which may be due to the fact that polysaccharides contain more reducing hydroxyl groups.[93] Secondly, transition metals such as iron, copper and zinc usually catalyze the synthesis of free radicals, and some polysaccharides have been found to effectively chelate metal ions such as ferrous and copper ions *in vitro* experiments.[94] Polysaccharide itself often has good reducibility, and many experiments also take reducing ability and iron ion reducing antioxidant ability (FRAP) as potential criteria to evaluate antioxidant activity.[95,96] Another antioxidant pathway is to block the occurrence of oxidative chain reactions and balance the excess ROS through the normal cell's own defense system, synthase or non-enzymatic antioxidants.[97] Enzymatic antioxidants play an important role in endogenous antioxidants, usually including superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), etc.,[98] which control ROS homeostasis in vivo. The final product of oxidative stress is mainly malondialdehyde (MDA), which is the main product of lipid peroxidation.[99] The increase of MDA content will destroy the structure of mitochondrial cell membrane and induce apoptosis.[100] When the content of free radicals is too high, the content of MDA will increase significantly, resulting in cell damage and senescence. For ROS imbalance caused by abnormal external environment, it is difficult for normal antioxidant enzymes to remove excess ROS, and external intervention is often needed to accelerate the generation of enzymatic antioxidants[101] to reduce cellular oxidative damage. A large number of experiments have shown that polysaccharide can effectively promote the generation of endogenous antioxidant enzymes,[102,103] which is closely related to the expression of erythroid 2-related Factor2 (Nrf2), a key transcription factor in the synthetic pathway.[104] In normal cells, Nrf2 is inhibited by REDOX sensitive protein (Keap1), which controls the maintenance of antioxidant enzymes at normal levels in vivo.[105] However, in the peroxide model constructed due to external damage, the coupling between Nrf2 and Keap1 is removed, which makes Nrf2 transfer from the cytoplasm to the nucleus, bind to the promoter region of the antioxidant response element (ARE) gene,[104] promote the synthesis of antioxidant enzymes, and reduce the oxidative damage of

cells. This mechanism has been demonstrated in cell experiments.[15,105] Polysaccharide can effectively reduce the excessive ROS content in H_2O_2-induced and UVB-induced fibroblasts, and increase the content of SOD, CAT and other antioxidant enzymes. The peroxidation scavenging ability of polysaccharides on the biological level has also been confirmed.[106] Some polysaccharides can effectively reduce the oxidative stress level of D-galactose-induced aging mice, increase the level of antioxidant enzymes, reduce the content of MDA, and reduce the oxidative aging of mice. Polysaccharides show excellent antioxidant and anti-aging ability in response to oxidative stress,[107] indicating that polysaccharides can effectively cope with skin aging caused by oxidation and can be used as an effective anti-aging component.

2.3.3 Inhibit apoptosis

In studying anti-aging researchers have found that fine，there is a significant correlation between cell apoptosis and aging and the aging of biological individuals,[9] many aging traits, and diseases of old age are the end result of apoptosis. When normal cells are damaged by the outside world, there will be metabolic dysfunction, mitochondrial dysfunction, cellular oxidative damage and other aging phenomena.[108,109] These phenomena will activate the apoptosis process through a variety of mechanisms to remove damaged cells. Normal cell apoptosis is conducive to the growth and development of the body, maintaining the stability of the internal environment, delaying aging, and preventing the occurrence of related diseases.[110] However, excessive external stimulation may cause cell apoptosis defects, accelerate the aging of the body, premature aging and other phenomena.[111] Therefore, slowing down the excessive apoptosis of cells may be one of the effective ways to delay aging.

The apoptosis process of cells is regulated by many genes, and these apoptosis factors can be divided into two categories: promotion and inhibition. Anti-aging studies have shown that the pathway by which polysaccharides regulate aging is closely related to the expression of anti-apoptotic genes,[9,112] which can slow down the excessive apoptosis of cells by inhibiting the production of apoptotic factors. The signaling pathway of inhibiting apoptosis by polysaccharides is composed of several apoptosis-related protein families. Including Akt family of serine/threonine-directed kinases (Akt), deacetylase family proteins (Sirt1), Forkhead box (Fox) class O (FoxO1) family proteins and B-cell lymphoma 2 (BCL2) family proteins (Bcl-2, Bax), cysteine proteases family proteins (Caspase-3) and tumor suppressor (p16, p21 and p53) such as conditioning Dead gene.[15,113,114] Among them, pro-apoptotic factors included FoxO, p16, p21, p53, Bax and Caspase-3, while anti-apoptotic factors included Akt, Sirt1 and Bcl-2. The model experiment of apoptosis of fibroblasts by polysaccharides showed that when fibroblasts were treated with ultraviolet light or H_2O_2, cell vitality decreased, oxidative stress and apoptosis increased.[15] In the experiment of apoptosis, the function and signal pathway of each apoptosis factor detected may be as follows: UV treatment of fibroblasts can inhibit the phosphorylation of Akt, reduce the level of si-Akt, and inhibit the expression of Sirt1 in the next step.[108] Sirt1 plays an important role in the regulation of cellular homeostasis, which can repair the damage caused by oxidative stress, aging, apoptosis and other phenomena in cells, and inhibit the occurrence of apoptosis.[113] Sirt1 inhibits the acetylation of downstream FoxO1 protein and inhibits its expression.[115] FoxO family proteins can regulate transcriptional activity through acetylation and deacetylation, and acetylation will inhibit their expression and prevent FoxO1 from activating

apoptosis factors.[116] In addition, Sirt1 can also control the transcription and synthesis of p53 and reduce the occurrence of apoptosis.[117] p53 can promote the expression of downstream p21 protein. With the participation of p21, p53 exerts its activity to control the cell growth cycle, prevent proliferating cells from entering the S phase,[118] slow down cell proliferation and promote cell apoptosis at the same time. Bcl-2 and Bax are two key regulatory factors of apoptosis through mitochondria.[90] Under normal circumstances, Bax and Bcl-2 are stable and can form heterodimers to balance each other. However, when Bax expression increases, homologous dimers will be formed within Bax itself, and the increase of their content will activate the apoptosis pathway of cells.[119] The process of Bax increases the permeability of mitochondrial membrane, promotes the release of apoptotic factors from mitochondria, and accelerates apoptosis.[120] Apoptosis factors released from mitochondria contain Cylc, a precursor signal that activates caspase-3 protein, which will intensify the synthesis of caspase-3 protein,[121] and caspase-3, as the final apoptosis signal, will cause irreversible apoptosis of cells.[122] Polysaccharide showed obvious anti-apoptotic effect on apoptosis-inducing cells. Fibroblasts were usually treated with H_2O_2 and ultraviolet light to construct apoptosis models, and the expression of pro-apoptotic factors was significantly increased.[71] The apoptotic cells were treated with polysaccharides, and the survival rate of cells was increased. The expression of apoptotic factors was detected, and it was found that although the expression of apoptotic factors was increased by external interference, the expression level of anti-apoptotic factors was more significant in the cells treated with polysaccharides, and it showed effective binding or inhibiting effect on pro-apoptotic factors,[113] and even the optimized level was close to the normal level. It repaired cell apoptosis caused by external stimulation,[15] indicating that polysaccharide can be used as a potential cosmetic ingredient to delay abnormal senescence and prevent apoptotic senescence.

2.3.4 Antiglycation

Advanced glycation endproducts (AGEs) is also thought is closely related to cell senescence, AGEs refers to the products of non-enzymatic glycosylation reaction between carbonyl group and amino group, usually occur between reducing sugar and protein within the biology, as the reducing sugar binds to amino groups of protein and lipids, it will reduce its activity and destroy its normal function.[123] Studies have shown that AGEs accelerate aging in many ways. First, AGEs cross-link proteins, enzymes and nucleic acids in tissues. When AGEs combine with collagen in the epidermis, they destroy the epidermal fiber framework, while when combined with antioxidant enzymes, they aggravate oxidative aging of cells.[124] Secondly, oxidizing substances such as free radicals and metal ions in the body tend to promote the production of AGEs, and AGEs can also be used as a site to catalyze the production of free radicals and accelerate the oxidation of the body.[125] In addition, receptors for AGEs exist on the surface of many cells, such as epidermal keratinocytes and fibroblasts. AGEs can promote the release of inflammatory factors by acting on the receptors, which will regulate the cell cycle and accelerate cell apoptosis.[123] Therefore, AGEs are often considered to be one of the signs of aging. Under normal circumstances, AGEs exist widely in organisms, are balanced by anti-glycation defense mechanism, and are eliminated with tissue renewal.[126] However, when exogenous intake or endogenous generation of AGEs are difficult to metabolize and eliminate, they accumulate, destroy tissue structure, and accelerate the oxidative aging of the body.[127] Studies have shown that the content of AGEs in the senescent cell

model supplemented with polysaccharides is significantly reduced compared with the control group,[128] which may be attributed to the antioxidant activity of polysaccharides, which inhibits the generation of AGEs by scavenging free radicals and chelating metal ions.[129] Some natural polysaccharides may also inhibit the production of AGEs by cross-linking some precursors in the process of age formation and delay the oxidative aging of the body.[128] At present, many polysaccharides have shown the activity of inhibiting the production of AGEs.[111,128] However, it is still necessary to further study whether polysaccharides can jointly inhibit the production of AGEs through various ways, and timely degrade, metabolize and clear accumulated AGEs, and ultimately slow down the aging of the body.

2.4. Skin repair effect of polysaccharides

The skin acts as the first barrier to protect the body from radiation, pollution and pathogens.[130] The skin is composed of epidermis and dermis, with the outermost layer being the epidermis,[131] which is responsible for maintaining the skin's hydrated environment and controlling the diffusion and transport of molecules between internal cells.[132] Due to long-term exposure to the external environment, excessive stimulation may cause damage, resulting in barrier defects or tissue damage.[133] Timely repair is needed to prevent the skin from dry, sensitive and other damage symptoms, which can lead to many skin diseases such as specific dermatitis, ichthyosis, psoriasis, etc.[134,135] According to different injury mechanisms, the repair process can be divided into barrier repair and wound healing.[136] At present, some synthetic skin care products contain metals, hydroquinone, etc., and investigations have shown that long-term use has cytotoxicity.[137] In recent years, with the development of natural products, many natural polysaccharides have shown high activity in repairing skin damage,[138] which may be used as an effective ingredient in repairing cosmetics.

2.4.1 Strengthen the skin barrier

The outermost layer of the skin is the epidermis, which is responsible for protecting the skin from external damage and maintaining a stable internal environment. Skin plays a protective role through a unique barrier. The epidermal barrier is mainly composed of stratum corneum (SC) and tight junction (TJ).[139,140] Excessive external environmental stimuli such as radiation and environmental pollution may lead to barrier damage[141] and symptoms of skin barrier defects such as specific dermatitis. There are many ways to strengthen the protective barrier to reduce skin damage, among which enhancing the expression of barrier proteins and thus improving the barrier strength is considered to be an effective way.[142] Compared with traditional repair cosmetics, natural polysaccharides also show excellent activity in repairing skin damage caused by defective barrier proteins.[143]

SC barrier is one of the main protective barriers in the epidermis, among which filaggrin (FLG), loricrin (LOR) and involucrin (IVL) are the main protein factors.[144,145] FLG is an important hydrating protein in the epidermis, which participates in the growth and development of epidermal cells and maintains the aqueous environment for epidermal growth and development.[146] IVL and LOR are important protein precursors of the cuticle barrier,[147] and the three barrier proteins together constitute the integrity of the SC barrier. These barrier proteins constitute the

framework of the stratum corneum. Firstly, filaggrin will aggregate with the intermediate filaments of keratin to form keratin fibers and form the scaffold structure.[148] After that, IVL and LOR cross-link and coat keratin fibers to form a barrier framework.[149] At present, monitoring the expression of these three proteins can be used as a means to confirm the integrity of the SC barrier.[150] When the expression of barrier protein is low, that is, SC barrier defects often show dry skin, pruritus and other phenomena.[151] The mechanism of such damage is related to inflammatory response and insufficient skin hydration.[152] With the development of cosmetics, many natural polysaccharides have shown therapeutic effects on injury-induced epidermal fibroblast or AD model mice, and the mechanism may be that polysaccharides promote the expression of barrier proteins such as FLG, LOR and IVL in injury models.[143] After the final treatment, the epidermal water content increased, and the symptoms of dryness and pruritus of mice were effectively alleviated.[153]

TJ barrier is composed of tight connections between tissues in the epidermis[154] and is responsible for controlling the degree of free diffusion between tissues and cells.[155] Among them, the transmembrane protein claudin (CLDN) and the blocking protein zonula occludens (ZO) are the main functional proteins of the epidermal TJ barrier.[156] Two proteins are thought to be responsible for the permeability of the paracellular barrier and act as molecular channels.[157] CLDN1 is one of the main proteins in the claudin family that play the function of skin barrier, and the defective expression of CLDN1 will directly lead to many skin barrier diseases.[158] The measurement of transendothelial/epithelial electrical resistance (TEER) can be used as a way to detect the expression degree of TJ protein.[16] TEER is produced by ion penetration in keratinocytes, and the larger the measured value, the lower the ion permeability and the higher the membrane protein content.[159] Therefore, the higher the TEER value, the more difficult the free diffusion inside and outside the cell, and the stronger the anti-damage ability of the epidermal barrier. At present, increasing the expression of CLDN1 is considered to be an effective way to regulate the TJ barrier, and specific regulatory pathways can be affected by ERK, PKC and other signals.[16] ERK, PKC and other signals are important biological regulatory pathways, controlling physiological processes such as cell proliferation, differentiation and metabolism,[160] but overexpression will inhibit the synthesis of CLDN1. Resulting in skin barrier defects. Studies have shown that inhibiting the phosphorylation of ERK and controlling its overexpression is an effective way for polysaccharides to enhance the TJ barrier strength, which can improve the synthesis of CLDN1 protein and enhance the TJ barrier strength.[16] In addition, ZO protein in TJ barrier is also thought to control the paraposmotic function of epithelial cells.[156] Among them, ZO-1 and ZO-2 may control the formation of TJ barrier as precursor proteins, and the mechanism may be that ZO protein may control the synthesis of other tightly linked proteins, such as CLDN protein, and together form the TJ barrier.[161] Decreased expression of ZO protein as a marker protein has been detected in many TJ injury models.[162] At present, the mechanism of the therapeutic effect of polysaccharide on keratinocyte models induced by TJ injury may be closely related to the promotion of ZO protein expression by polysaccharide, and further promotion of CLDN1 barrier protein expression and restoration of TJ barrier.[143] The activity of polysaccharides in improving the expression of barrier proteins and ensuring the integrity of the epidermal barrier suggests that polysaccharides can be used as potential cosmetic ingredients to enhance the strength of the epidermal barrier and improve the anti-damage activity.

2.4.2 Repair a wound

Polysaccharide has excellent anti-injury activity in promoting wound healing. Wound healing is a series of complex physiological processes, which can be divided into four stages: hemostasis, inflammation, proliferation and remodeling.[163] The hemostasis occurs at the first time of skin injury, during which the platelets in the blood will adhere to the damaged part of the blood vessels and coagitate with specific fibrin to form thrombus for hemostasis.[164] During this process, a mild and moist epidermal environment is thought to be more conducive to the hemostatic process.[165] Many polysaccharide dressings have shown faster wound healing, and the skin was found to be more hydrated at the time of the study.[166] Hemostasis is accompanied by damage repair. Damaged cells will trigger the apoptosis process and release apoptosis factors to activate immune cells， for example, acting on phagocytes will release inflammatory factors to accelerate apoptosis or phagocytize damaged cells.[167]At this stage of inflammation, polysaccharides have been proven to increase the expression of inflammatory factors such as NO and TNF-α by regulating signaling pathways such as NF-KB, AKT and MAPK,[168,169] thus accelerating apoptosis of damaged cells.[170] This stage requires timely regulation. If long-term inflammatory infiltration occurs, the repair process will be an inflammatory stage for a long time, resulting in slow wound healing and chronic healing diseases.[171] Many polysaccharides show excellent anti-inflammatory activity, slow down inflammation, accelerate the repair process to the next stage, and accelerate wound healing.[172] In the later stage of inflammation, fibroblasts and keratinocytes in the epidermis proliferate rapidly, and mitosis occurs under the influence of pathways such as Wnt signal and EGF signal, and proliferation and differentiation enter the cell cycle.[173] At this stage, cells will increase the expression of cell proliferation factor Ki-67, which is often used as a marker of proliferation,[174] which will accelerate mitosis into the S phase and induce proliferation. For induced skin injury models, polysaccharides also significantly increased the expression of this factor. In addition, Wnt/β-catenin pathway signals can regulate cell proliferation, and polysaccharides can control the proliferation and differentiation of skin-related cells by regulating β-catenin in this pathway.[175] In the proliferation stage, polysaccharide can promote β-catenin and show repair activity of damaged tissues.[173] In the stage of cell proliferation, cell proliferation and differentiation are also accompanied by increased blood vessel content, which is used to build skin structure and provide oxygen, energy and waste for cell proliferation.[176] Vascular endothelial growth factor (VEGF) is significantly increased as a signal of angiogenesis.[177] In the process of accelerating tissue regeneration, polysaccharides can accelerate the repair process of damaged tissues by promoting various signal factors. In the later stage of wound healing, cell proliferation tends to normalize along with slowing down, so as to ensure the normal shape of the wound and prevent excessive multiplication to reduce the generation of scars.[178] At this stage, experiments have also shown that polysaccharide can restore normal proliferation level and complete the skin plasticity process by reducing the expression of β-catenin and VEGF value-added factors.[173] In the later stage of wound healing, some polysaccharides can tighten the skin by accelerating collagen production and effectively prevent scars.[179] **Figure. 2** shows the promoting effect of polysaccharide in various stages of skin repair process.[180]

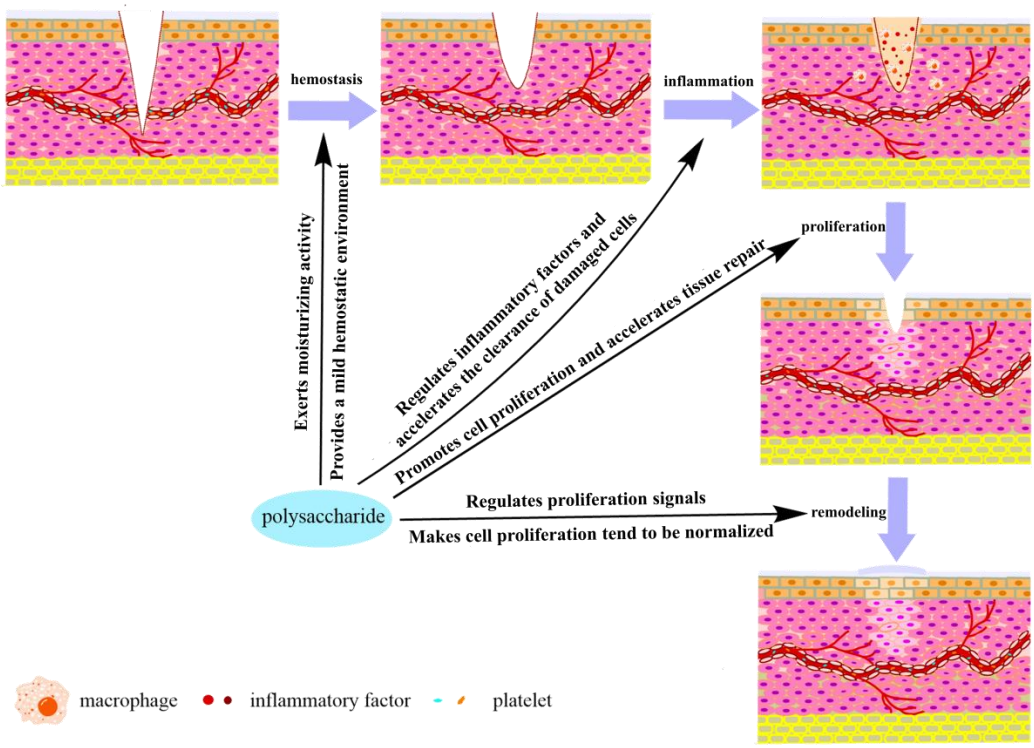

Figure 2 Promoting effect of polysaccharide on wound repair process.

3. Relationship between physicochemical properties and activity of polysaccharides

After understanding the biological mechanism of polysaccharide activity, it is also necessary to analyze the corresponding structural composition of polysaccharide activity and complete the analysis of structure-activity relationship. Studies have shown that different extraction methods and chemical modification can regulate the biological activity by changing the structure of polysaccharides,[181,182] and the structural characteristics of polysaccharides, such as molecular weight, monosaccharide composition and functional groups, will be significantly different due to modification.[183] The regulation of the physical and chemical properties of polysaccharides, combined with the detection of activity changes, is helpful to search for the most active structural composition of polysaccharides.[184] In this chapter, the effects of various physicochemical properties such as extraction methods, molecular weight, monosaccharide composition, functional groups and chemical modification on the activity of polysaccharides were analyzed, and the mechanism of their activity was summarized in order to better improve the cosmetic activity of polysaccharides.

3.1 Influence of extraction method on structure and activity

As the first step of polysaccharide extraction, selecting the appropriate extraction process

may be an effective way to improve the biological activity of polysaccharide. The study of the relationship between extraction methods and bioactivity will be conducive to more comprehensive development of the bioactivity of polysaccharides, reduce resource waste.

The extraction methods of polysaccharides have been extensively studied in recent years, from the initial hydrothermal extraction to ultrasonic, microwave and enzyme-assisted extraction to new alkaline extraction, cold solution and freezing pressure, pulsed electric field assisted extraction, etc.[185-187] It is gradually realized that suitable extraction methods can be selected according to the requirements of chemical structure of polysaccharide such as molecular weight, monosaccharide composition and functional group. Different chemical structures of polysaccharides are often responsible for the mechanism of their expression of different biological activities. For example, many studies have shown that low-molecular weight polysaccharides often have better antioxidant activities. The mechanism may be that the reduction of molecular weight exposes more active hydroxyl groups, provides more H to free radicals, reduces the occurrence of oxidative damage chain reaction.[188] The study between extraction method and antioxidant activity showed that ultrasonic and microwave assisted extraction would destroy the structure of polysaccharide and reduce its molecular weight, which was conducive to improving the antioxidant activity of polysaccharide.[189] Secondly, different extraction methods also have significant effects on the content of functional groups. For example, when polysaccharides are extracted by enzymatic method or cold solution and freeze-pressing method, higher content of uronic acid is detected, which may be due to the protection of the complete structure of polysaccharides by these extraction methods,[186] while polysaccharides with high content of uronic acid often show better ability of scavenging free radicals.[190] In addition, many studies on the struct-activity relationship of polysaccharides have shown that there may be a more direct relationship between monosaccharide composition and biological activity. For example, polysaccharides with higher galactose content are often associated with better antioxidant activity.[188] Therefore, appropriate extraction methods can be selected to regulate the chemical composition of polysaccharides extracted to improve biological activity as much as possible. In summary, choosing the appropriate extraction method, by properly adjusting the molecular weight, functional groups, monosaccharide composition and other chemical structures of polysaccharides, it is possible to improve the biological activity of polysaccharides eventually.

It has been shown that the influence of extraction methods on improving the bioactivity of polysaccharides may not be absolute. Yin et al, respectively, by hot water extraction, ultrasonic assisted extraction, enzyme extraction and acid assisted extraction auxiliary polysaccharide extracted from *Laminaria japonica* polysaccharides and detect the DPPH and ABTS radical scavenging ability and iron reduction force experiment, The results showed that polysaccharide obtained by ultrasonic-assisted extraction had the highest antioxidant activity.[191] Wu et al. also adopt water extraction method, ultrasonic assisted extraction method, enzyme assisted extraction method and ultrasonic enzyme assisted extraction method to extract *Silphium perfoliatum* L. respectively. The experiment was conducted to extract polysaccharides from the plant and test their DPPH, ABTS free radical scavenging ability and iron reducing power. The results showed that polysaccharides obtained by enzyme-assisted extraction of the plant could better express their antioxidant activity.[192] The above research shows that for the same biological activity, different sources of polysaccharides, the same extraction process may not produce the same effective results. According to the different polysaccharides, it is necessary to choose the appropriate

extraction process, so as to maximize the biological activity of polysaccharides.

3.2. Effect of molecular weight on activity

There are many kinds of polysaccharides present in the same plant, and we may extract 2-4 or even more purified polysaccharides in the same extraction. Homologous polysaccharides often have similar structures, such as monosaccharide composition.[193,194] Different extraction conditions will lead to many significant differences in the structure of different polysaccharides, such as the molecular weight and monosaccharide composition of polysaccharides. In the study of structure-activity relationship, it has been found that the molecular weight of polysaccharides has a significant influence on many activities.[195]

Studies have shown that regulating the molecular weight of polysaccharides may be an effective way to improve different activities and show the optimal cosmetic activity of polysaccharides.[196] First of all, for the moisturizing activity of polysaccharide, it is generally believed that polysaccharide shows excellent moisture absorption and moisturizing activity due to its abundant hydrophilic groups. In addition, studies have found that large-molecular weight polysaccharides often have better moisturizing activity, and the mechanism may be that macromolecular polysaccharides can be connected and wound through hydrogen bonds to form complex aggregates,[197] which increases the viscosity of skin care products, facilitates the formation of film structure, better adhesion to the skin surface, and reduces water loss.[30] For small molecular weight polysaccharides, the molecules are connected by hydrogen bonds, and it is difficult to form large complex structures. However, low molecular weight polysaccharides often expose more polar groups, and microstructure characterization shows that the interaction between small molecules can increase the smoothness of the aggregate surface, while high polarity is conducive to excellent emulsification.[198] In addition, small molecule polysaccharides expose more active groups, such as the reducing end, which can improve the antioxidant activity of polysaccharide molecules and show anti-aging activity.[198] As for the methods to change the molecular weight of polysaccharides, at present, acid, enzyme or H_2O_2 treatment can be used as an effective way to degrade polysaccharides,[8,199] which may improve the antioxidant activity of polysaccharides such as free radical scavenging ability or metal ion chelating ability to a certain extent.[200] This can improve the tight structure of macromolecular polysaccharides, the inclusion of active groups, and the low utilization rate.[199] Polysaccharide degradation can be used as an effective way to improve the activity. On the one hand, the degradation of polysaccharide is beneficial to the increase of active groups; on the other hand, biological studies have shown that small molecules of polysaccharide can quickly cross the cell membrane directly through membrane proteins or ion channels, but when the molecular weight of polysaccharide is too large, it can only act on the recipient cell through transmembrane transport such as endocytosis and exocytosis. Influence the activity of polysaccharide.[200] The degradation of macromolecular polysaccharides will also increase their bioavailability to a certain extent.[201] However, in the process of polysaccharide degradation, it is necessary to detect the degree of degradation in time to avoid the destruction of the main functional structure of the polysaccharide, such as the spiral structure.[202] It has been reported that for polysaccharides of high, medium and low molecular weight before and after degradation, the medium molecular weight polysaccharide has the best activity. It is speculated that the medium molecular weight polysaccharide may not destroy the

main structure and expose more active groups. On the other hand, small polysaccharides destroy the main structure.[203]

For the weak activity of large molecular weight polysaccharide, appropriate degradation methods to increase the content of active fragments, combined with structural analysis, can better analyze the structure-activity relationship of polysaccharide. In studies on the correlation between molecular weight and bioactivity of polysaccharides, some researchers have found that molecular weight has a more significant effect on certain bioactivities. Liang et al studied Black garlic polysaccharide degraded by acid treatment and found that in vitro antioxidant experiments, although the lower molecular weight and the content of glucuronic acid both increased the antioxidant activity of the polysaccharide. However, the decrease of molecular weight is more significant for the improvement of activity, and in the tyrosine inhibition experiment, the increase of glucuronic acid content shows a more significant inhibitory effect on tyrosinase.[204] Chen, et al. studied the whitening activity of low-molecular weight Fucoidan and found that if the molecular weight of polysaccharide is controlled within a certain range through degradation, its whitening activity can be comparable to arbutin, which may be used as a potential whitening cosmetics.[8] For polysaccharides with good activity, their molecular weight can be changed through appropriate degradation, the removal of inactive polysaccharide chains will be more conducive to the analysis of macromolecular polysaccharides and improve the application value of polysaccharides in cosmetics and other industries.

3.3 Effect of monosaccharide composition on activity

As the most basic structural unit of polysaccharides, monosaccharides constitute the skeleton structure of polysaccharides. Studies have found that the types, contents and connection modes of monosaccharides may directly affect the biological activity of polysaccharides, and the composition of monosaccharides is closely related to the mechanism of polysaccharide activity.[4, 205] At present, many studies on the structure-activity relationship of polysaccharides have taken the composition of monosaccharides as an important reference for analyzing the activity of polysaccharides. The following is an induction and analysis of the composition of monosaccharides that exist when polysaccharides exert their activities such as moisturizing, antioxidant and anti-inflammatory. The possible mechanism is as follows.

The higher content of uronic acid in the moisturizing polysaccharides is often accompanied by higher water-retaining activity,[206] and there are often more glucose and mannose components in the monosaccharide composition, which may potentially improve the moisturizing activity to some extent.[4] Glucose, galactose and arabinose have the highest proportion in antioxidant activity. Studies have speculated that these monosaccharide residues may serve as the attachment sites of free radicals and express antioxidant activity by increasing the polarity of the polysaccharides chain.[207] In addition, the presence of uronic acid can significantly improve the scavenging activity of free radicals. The mechanism may be that electron-philic groups such as ketones and aldehydes show good hydrogen supply capacity,[208] including glucuronic acid and galacturonic acid, etc. among which galacturonic acid content is high in some polysaccharides, which may come from the cell wall structure.[209] Secondly, polysaccharide coupling of some polar groups may also be the reason for the enhancement of cosmetic activity, such as the increase of antioxidant activity by coupling phenolic or protein groups through ester linking.[210] Studies on polysaccharide

modification found that with the increase of hydroxyl group replacement, the content of some monosaccharides such as galactose in the modified polysaccharide increased in proportion to the antioxidant activity,[211] which indirectly indicated that galactose in the polysaccharide may be the key monosaccharides to exert antioxidant activity. It has been reported that more types of monosaccharides may exhibit higher immune-stimulating activity,[212] and mannose may be one of the key monosaccharides. Polysaccharides with higher mannose content exhibit higher immune-regulating activity, which may be caused by the presence of mannose receptors on the surface of immune cells. By binding mannose to macrophage receptors, it regulates the release of inflammatory factors and enhances the phagocytosis activity of macrophages,[213] thus enhancing the body's immunity. Current studies have shown that different monosaccharides in polysaccharides may co-regulate receptor cells through a variety of complex pathways, and ultimately achieve a variety of cosmetic activities such as moisturizing, antioxidant, and anti-aging.

3.4 Effect of functional groups on activity

Functional groups are important structures of polysaccharides, which are closely related to their biological activities. Polysaccharides often contain complex functional groups because of their long chain macromolecular structure. In the study of the mechanism of polysaccharide cosmetic activity, researchers found that functional groups have significant effects on the moisturizing and antioxidant activities of polysaccharides.[4,206] Many functional groups are the key to the improvement of activity, and adjusting the composition of functional groups will help to analyze the structure-activity relationship of polysaccharides. For example, the presence of most functional groups improves the solubility of polysaccharides, the presence of polar groups improves the electronegativity of polysaccharides, etc. High solubility and reducibility are the basis for the expression of biological activity of polysaccharides. Secondly, different functional groups have their own unique mechanisms for regulating aesthetic activity.[214,215]

For some functional groups widely present in polysaccharides, acid groups such as sulfate groups and uronic acids often show higher electronegativity and high antioxidant activity,[216] while sulfuric acid groups can activate hydrogen atoms on telomere carbon, and have better hydrogen supply capacity, which can be used to remove free radicals.[93] In addition, highly electronegative polar groups can be combined with other functional groups or water molecules through hydrogen bonding, so that different molecules can aggregate, and by giving charge, the glycoside bonds can be cross-linked to form a network structure, which changes the rheological properties of polysaccharide solution and improves the moisturizing activity.[4] High electronegativity is also beneficial to improve water solubility, which is conducive to the expression of cosmetic activity. Sulfate is also an important functional group in the anticoagulant effect, and the mechanism is that sulfate is easy to bind to antithrombin,[217] and the anticoagulant effect is gradually enhanced with sulfate content. At present, sulfation modification is considered to be an effective way to improve the anticoagulant effect.[218] In studies of functional groups and activities, it has been found that groups such as sulfate or phosphate may promote the binding of polysaccharides to recipient cells.[219] For example, the presence of acetyl group has been proved to be beneficial to the hydrophobic activity of polysaccharide, and acetyl group can reduce the surface tension of solution, which may be a potential component of emulsifier.[220] Some studies have shown that

crude polysaccharides exhibit higher antioxidant activity to some extent, possibly due to the coupling of more protein or phenolic groups,[213] which can improve the electronegativity of polysaccharides, facilitate the chelation of metal ions through electrostatic action, or adsorption of free radicals to reduce oxidative damage.[221] The above mechanism research shows that functional groups may express cosmetic activity by improving cell environment or directly acting on cells, and the action pathway is complicated. Therefore, it is expected that the variety and content of functional groups can be adjusted to maximize the aesthetic activity of polysaccharide and improve the resource value.

3.5 Effect of polysaccharide modification on activity

When analyzing the structural-activity relationship of polysaccharides, researchers found that many groups could effectively change the activity of polysaccharides when their content changed, and tried to explore effective ways to change functional groups.[216] A series of methods have been introduced to modify polysaccharides to achieve regulation of functional group composition, and many active groups can be added or removed through modification.[222] Modification methods such as sulfation, phosphorylation, acetylation and carboxymethylation are commonly used to improve the cosmetic activities of polysaccharides, such as moisturizing and antioxidant.[223,224] Many modified polysaccharides have been proved to have the potential to improve the cosmetic activities of polysaccharides, and their mechanisms are analyzed as follows.

The modification of polysaccharides often takes place on hydroxyl, ketone and other groups in the sugar chain, and is carried out by acid treatment.[225] The modification process is often accompanied by degradation. On the one hand, polysaccharides will be exposed to more active sites, form new hydrogen bonds, and the polysaccharide chain will easily form a grid structure, regulate rheological properties, and increase moisturizing activity.[4] On the other hand, the introduction of carboxyl, acetyl and other power supply groups through modification can increase the electronegativity of polysaccharides and improve the antioxidant capacity of the body. Inhibition of lipid peroxidation.[226] Sulfuric acid modification can also increase the electronegativity of polysaccharide, and can activate hydrogen atoms on telomere carbon, improve hydrogen supply capacity, make it easier to complex with free radicals, and enhance antioxidant activity.[227] The increase of sulfuric acid groups is also conducive to improving anticoagulant effect.[217] Most modifications, such as sulfation, phosphorylation, carboxymethylation and acetylation, are conducive to the improvement of water solubility of polysaccharides,[4] which will be more conducive to the play of activity. In the studies on the removal of functional groups, there are studies that improve the water solubility and biological activity of polysaccharides through deacetylation.[225] In other modification studies, the modification with phenols is beneficial to hydrophobic and anti-oxidation, and is conducive to chelating metal ions.[228] The introduction of essential human elements into polysaccharides by modification may be an effective way to promote the absorption of the body. For example, selenium is an important regulatory factor of some selenium proteins, such as antioxidant enzymes such as glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD), and selenium modified polysaccharide is conducive to improving the antioxidant capacity of the body.[226] In addition, selenium-modified polysaccharides showed anti-tumor activity, which is speculated to be the mechanism of regulating the release of apoptosis factors in mitochondria and promoting apoptosis of tumor cells.[229] Studies have shown

that appropriate modification will be more conducive to the analysis of the structural-activity relationship of polysaccharides. Some sulfated polysaccharides have better anti-hemagglutination potential than heparin,[217] acetyl-modified polysaccharides can improve emulsification performance,[222] and polysaccharides selenide can inhibit tumor and cell proliferation and have neuroprotective functions.[230,231] The activities exerted by different functional groups and the corresponding mechanisms have been sorted out in **Table 1**. It is expected that a certain degree of substitution will make the polysaccharide have the highest activity or show new activity.[225] At present, the modification of polysaccharides has been studied extensively, which can be considered as one of the effective ways to analyze the structure-activity relationship of polysaccharides, and it needs to be developed to improve the utilization value of polysaccharides in the beauty industry.

Table 1. Biological activities of different functional groups

Functional group	Biological activity	Active mechanism	Reference
Sulfuric acid group	Moisturizing, antioxidation, anti-coagulation, etc.	Sulfuric acid group is a highly electronegative group, which can form a lattice structure through intermolecular hydrogen bonding and play a moisturizing role; Exposing more active sites, improving hydrogen supply capacity and scavenging free radicals; Sulfate is easy to combine with anticoagulant enzyme to improve anticoagulant ability.	4,93,217
Phosphate group	Moisturizing, antioxidant, etc.	Phosphoric acid groups can improve electronegativity and form a grid structure through hydrogen bonds, which plays a moisturizing role; It can improve the hydrogen supply ability of polysaccharide and scavenge free radicals.	4,219
Ethanoyl	Moisturizing, antioxidant, etc.	The existence of acetyl group will reduce the surface tension of polysaccharide solution and increase the emulsifying and moisturizing activities; It can improve the electronegativity of polysaccharide and increase its antioxidant activity.	220,223
Phenols	Antioxidant, etc.	Phenolic groups can improve the electronegativity of polysaccharides, chelate metal ions or scavenge free radicals through electrostatic action, and exert antioxidant activity.	221
Selenium group	Antioxidant, anti-tumor, etc.	Increase the absorption of selenium, promote the synthesis of selenium antioxidant protease, and improve the antioxidant capacity; It can regulate the release of apoptosis factors in mitochondria of tumor cells and inhibit the proliferation of tumor cells.	224,227

4. Conclusions

With the increasing application of natural ingredients in the cosmetics industry, the beauty activity of natural polysaccharides has been effectively developed. The moisturizing activity of some polysaccharides is better than that of hyaluronic acid, and the whitening activity of some polysaccharides is equivalent to arbutin. The application and development of some polysaccharides are expected to replace some artificial and expensive traditional cosmetics.

In this review, the biological mechanism of polysaccharide's cosmetic activities of moisturizing, whitening, anti-aging and repairing skin was described. The physicochemical properties and various activities of polysaccharide were summarized, and the structure-activity relationship of polysaccharide's cosmetic activities was analyzed. Studies have shown that there is no single way for polysaccharides to exert their cosmetic activity. The macromolecular structure of polysaccharides often contains more active fragments, and polysaccharides may promote the expression of the same activity through different ways. The molecular weight, monosaccharide composition and functional group of polysaccharides have significant influence on the aesthetic activity, and the optimal aesthetic activity will be obtained if the structural parameters are controlled within a certain range. these properties of polysaccharides can also be adjusted by changing the extraction method and polysaccharide modification, to explore methods to improve the cosmetic activity of polysaccharides.

At present, the research on the activity mechanism may not be comprehensive, and it needs to be further developed to study the monosaccharides, functional groups or structural fragments with the highest activity among polysaccharides, how the highly active polysaccharide binds to the receptor and finally acts on the cell, and then the regulated polysaccharide structure can be matched with the detection of aesthetic activity. It is believed that the most effective structural unit of polysaccharide in exerting aesthetic activity can be found eventually. Maximize the cosmetic activity, analyze the structure-activity relationship, and finally improve the application value of polysaccharide in the cosmetics industry.

CrediT authorship contribution statement

Qingyuan Wu: Investigation, Writing-Original draft preparation, Writing- Reviewing and Editing. **Na Cheng:** Writing-Original draft preparation, Writing- Reviewing and Editing. **Danjiao Fang:** Investigation. **Hao Wang**: Investigation. **Faiz-Ur Rahman:** Writing-Reviewing and Editing. **Huifang Hao:** Writing- Reviewing and Editing. **Yongmin Zhang:** Conceptualization, Funding acquisition, Writing- Reviewing and Editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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