polysaccharides

Review

Skin Health Promoting Effects of Natural Polysaccharides and Their Potential Application in the Cosmetic Industry

Yueying Yao [1,2] and Baojun Xu [1,*]

[1] Food Science and Technology Program, Department of Life Sciences, BNU-HKBU United International College, Zhuhai 519087, China
[2] Department of Food Science and Technology, National University of Singapore, Singapore 119077, Singapore
* Correspondence: baojunxu@uic.edu.cn; Tel.: +86-756-3620636

Abstract: Skincare is one of the most profitable product categories today. Consumers' demand for skin-friendly products has stimulated the development of natural-ingredient-based cosmeceutical preparations over synthetic chemicals. Thus, natural polysaccharides have gained much attention since the promising potent efficacy in wound healing, moisturizing, antiaging, and whitening. The challenge is to raise awareness of polysaccharides with excellent bioactivities from natural sources and consequently incorporate them in novel and safer cosmetics. This review highlights the benefits of natural polysaccharides from plants, algae, and fungi on skin health, and points out some obstacles in the application of natural polysaccharides.

Keywords: natural polysaccharides; skin health; cosmetics

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Citation: Yao, Y.; Xu, B. Skin Health Promoting Effects of Natural Polysaccharides and Their Potential Application in the Cosmetic Industry. *Polysaccharides* **2022**, *3*, 818–830. https://doi.org/10.3390/polysaccharides3040048

Academic Editor: Luminita Marin

Received: 18 September 2022
Accepted: 10 December 2022
Published: 14 December 2022

1. Introduction

The skin is the largest organ of the human body and is also the first line of defense from the external environment [1]. Due to its extensive area, it is easily exposed to and even damaged by a range of external factors such as ultraviolet radiation, which may lead to wounds, dehydration, skin aging, melanin deposition, microbial invasion, and skin barrier abnormalities [2]. Hence, different strategies to treat skin problems or promote skin health have been used, such as the use of skin care products or some physical therapies [3]. Among various treatments, natural skin care compounds are considered more skin-friendly from the perspective of consumers, so natural reagents are readily accepted and the demand for natural skin care products is increased [4]. Over the years, researchers have explored several natural compounds that can protect skin from damage, most of which are organically sourced macromolecules, including groups of proteins, lipids, polyesters, polysaccharides, and polyphenols [3]. In this review, special attention will be given to natural polysaccharides.

Naturally occurring polysaccharides can be obtained from plants, algae, and fungi through a series of steps of extraction, isolation, and purification [5]. They display distinct structural features, including their molecular weight, monosaccharide composition, glycosidic linkages, three-dimensional conformations, charge properties, and types and numbers of groups, which contribute to their functional properties and determine their extensive applications [6]. The application of some functional polysaccharides in cosmetics is based on their functionalities in the formulation technology, such as thickener, film former, conditioner, emulsifier, and gelling agent, which generally rely on their physicochemical properties [4]. On the other hand, bioactive polysaccharides are role by the ability of water retention, water absorption, anti-oxidant, anti-inflammation, anti-collagenase, anti-elastase, anti-melanogenic, or anti-tyrosinase [7]. Recently, the use of low-cost natural polysaccharides for skin applications has been gaining more attention because of their promising potent efficacy in wound healing, moisturizing, antiaging, and whitening, which in most cases depends not only on their physicochemical properties but also biological activities [7]. However, reliable natural reagents are still in short supply as many problems need to be solved before they can be converted into products, such as the instability of natural ingredients, low efficacy, and biosafety concerns [8,9].

Therefore, in addition to summarizing the latest advances in the topic of skin health benefits provided by polysaccharides from natural origin and their potential practical application in the cosmetic industry, this work will put forward some problems encountered in their application, to promote the development and application of natural polysaccharides in the field of skincare.

2. Skin Health Promoting Effects

2.1. Wound Healing

Wound healing is a complex dynamic process that is classically divided into four sequential and orchestrated stages of hemostasis, inflammation, proliferation, and tissue remodeling [3]. Repair refers to the body's attempt to restore normal structure and function after injury, and its success mainly depends on the degree of injuries, necrotic tissue, tissue regeneration capacity, and foreign body infection [10,11]. In recent decades, various strategies have been developed to improve healing and to limit scar formation by modulating wound healing processes, especially using natural polysaccharides as wound healing agents regarding their biodegradable, biocompatibility, and low toxicity characteristics compared with synthetic polymers [12]. More recently, several studies suggested that polysaccharides produced from *Gracilaria lemaneiformis* [13], *Ganoderma amboinense* [14], *Nostoc commune* [9], and *Phellinus igniarius* [15] exert efficient anti-oxidant and anti-inflammatory activities, as well as a good cell wound-healing effect, thereby having high potential to be regarded as a new resource for the development of wound-healing cosmetics.

In addition to facilitating skin wound healing, their high film-forming ability and beneficial barrier properties contribute to their potential to be developed as an ideal biodegradable film to promote wound healing efficiency by providing a wound physiological environment [16,17]. Moreover, poly (vinyl alcohol) (PVA) is a non-toxic vinyl polymer with good chemical stability, biocompatibility, film-forming properties, and hydrophobicity, which is often used as a crosslinking agent to reinforce the functional properties of polysaccharide films [18]. For instance, Feki et al. [19] demonstrated that a biodegradable film based on the polysaccharides derived from fenugreek (*Trigonella foenum-graecum*), which is reinforced by PVA, could stimulate the surrounding healthy cells at the wound site by obtaining the growth factors required for wound healing, thus boosting re-epithelialization and accelerating skin wound closure in CO_2 laser fractional burn rats. Additionally, many other PVA-enhanced natural polysaccharide films have been shown to have potential wound-healing properties, as evidenced by their high anti-oxidant activity, anti-inflammatory property, and by histological evaluation, such as *Falkenbergia rufolanosa* polysaccharide [18], and *Hammada scoparia* leaves polysaccharide [16].

2.2. Moisturizing

Moisturizing is a critical part of skin care and has a positive effect on enhancing skin barrier function, metabolism, and appearance. From an aesthetic point of view, dryness of the skin can lead to some undesirable experiences that can undermine a person's confidence, such as painful, itchy, tingles, stings, and uncomfortable sensory feelings, or redness, dry white patches, crackers, and even fissures appearance, or the uneven and rough tactile feelings [4]. Additionally, if this skin condition persists for a long time, the skin will lose elasticity and wrinkles will gradually appear [4]. Thus, moisturizing products formulated with humectants or occlusive ingredients are used to retain the content of water in stratum corneum (SC) or suppress transepidermal water loss (TEWL) [7].

Lately, many researchers have discovered that several new sources of natural polysaccharides can achieve moisturizing effects from multiple perspectives, such as *Brasenia schreberi* Mucilage polysaccharide [20] and polysaccharide from fermented *Tremalla fuciformis* [21] can regulate gene expression and transcription to provide moisturizing and lubricating benefits, *Anadenanthera colubrina* polysaccharide imparts skin hydration effect by promoting the gene expression and immunoreactivity of several important aquaglyceroporin which facilitate the skin water passage [22], and galacturonans extracted from *Myrtus communis* leaves can form hydrogel to reduce TEWL because of its film-forming effect [23].

Although natural polysaccharides exhibit strong bioactivity, most studies demonstrated that the moisturizing effect of polysaccharides could be significantly improved through chemical structure modification [24,25]. Polysaccharides with a higher molecular weight are more likely to form a net-like structure to prevent water loss, resulting in better moisturizing retention properties [24]. Functional groups of polysaccharides, including pyruvate groups, glyoxylate groups, uronic acid groups, and sulfate groups, are potential factors for moisturizing retention [24]. For instance, when the polysaccharides derived from *Actinidia chinensis* roots were subjected to an SO_3-pyridine procedure to prepare sulfated polysaccharides, the moisturizing retention increased with the rise of substitution [25]. Hence, it is significant to explore the structure-activity relationships between bioactivities and the structure of polysaccharides to promote the application of natural polysaccharides.

2.3. Anti-Aging

Skin aging can be divided into endogenous and exogenous processes. The endogenous aging process is associated with reduced antioxidant status and cell proliferation capacity. Senescent cells express genes that produce inflammatory cytokines, growth factors, and degradative enzymes [7]. Exposure to nicotine or air pollution, sunlight through ultraviolet (UV) radiation, diet, and medication can be the main exogenous factors [26]. Both intrinsic and extrinsic aging can lead to the weakening of the skin's structural integrity and loss of physiological functions [27], which is manifested in the decrease of elasticity, appearance of wrinkles, dryness, changes in the thickness of the epidermis, dermal-epidermal junction, and dermis [28].

Reactive oxygen species (ROS) are continuously produced as a by-product of mitochondrial aerobic metabolism and have been proven to play a beneficial role in maintaining the body or cell health when present in a small amount [29]. However, excessive ROS in the body can induce and accelerate the intrinsic aging process, especially in skin that is usually present in areas that are not exposed to sunlight. In addition, the occurrence of photoaging relates to the production of ROS as well. Repeated exposure to solar UV can cause an increase in ROS, damage the cell structure and function, and mediate inflammatory responses [30,31]. Consequently, excessive ROS can activate numerous signaling pathways, leading to decreased skin collagen production, stimulate the production of senescence-associated secretory phenotype (SASP), and promote synthesis and activation of matrix metalloproteinases (MMPs), which ultimately accelerate the aging process of skin [32] (Figure 1). In this context, many natural polysaccharides, which have been reported to combat different causes of skin aging through multiple routes, can be viewed as potential alternatives to synthetic chemical compounds used in the cosmetic industry.

First of all, several natural polysaccharides, which show anti-oxidant and anti-inflammatory potential based on their ability to scavenge free radicals and reduce the production of inflammatory mediators, are valuable in treating or alleviating ROS-induced intrinsic aging. Barbosa et al. [33] have proved that *Pleurotus ostreatus* polysaccharides can protect the cell against oxidative damage triggered by H_2O_2 due to its anti-oxidant property. Luo et al. [15] have indicated that a polysaccharide from selenium-enriched *Phellinus igniarius* can clean up ROS and further enhance the ROS clearance ability via improving the activity of glutathione peroxidase (GSH-PX); Mao et al. [34] extracted a polysaccharide from *Grifola frondose* (Dicks.) Gray, which can effectively prevent RAW264.7 cells from H_2O_2-induced damage via reducing the release of ROS, and enhancing the levels of GSH-PX; Tseng et al. [9] have suggested that the polysaccharides extracted from *Nostoc commune* have the ability to inhibit IL-6. Thus, all these natural polysaccharides can promise an antiaging function due to their excellent anti-oxidant and anti-inflammatory properties.

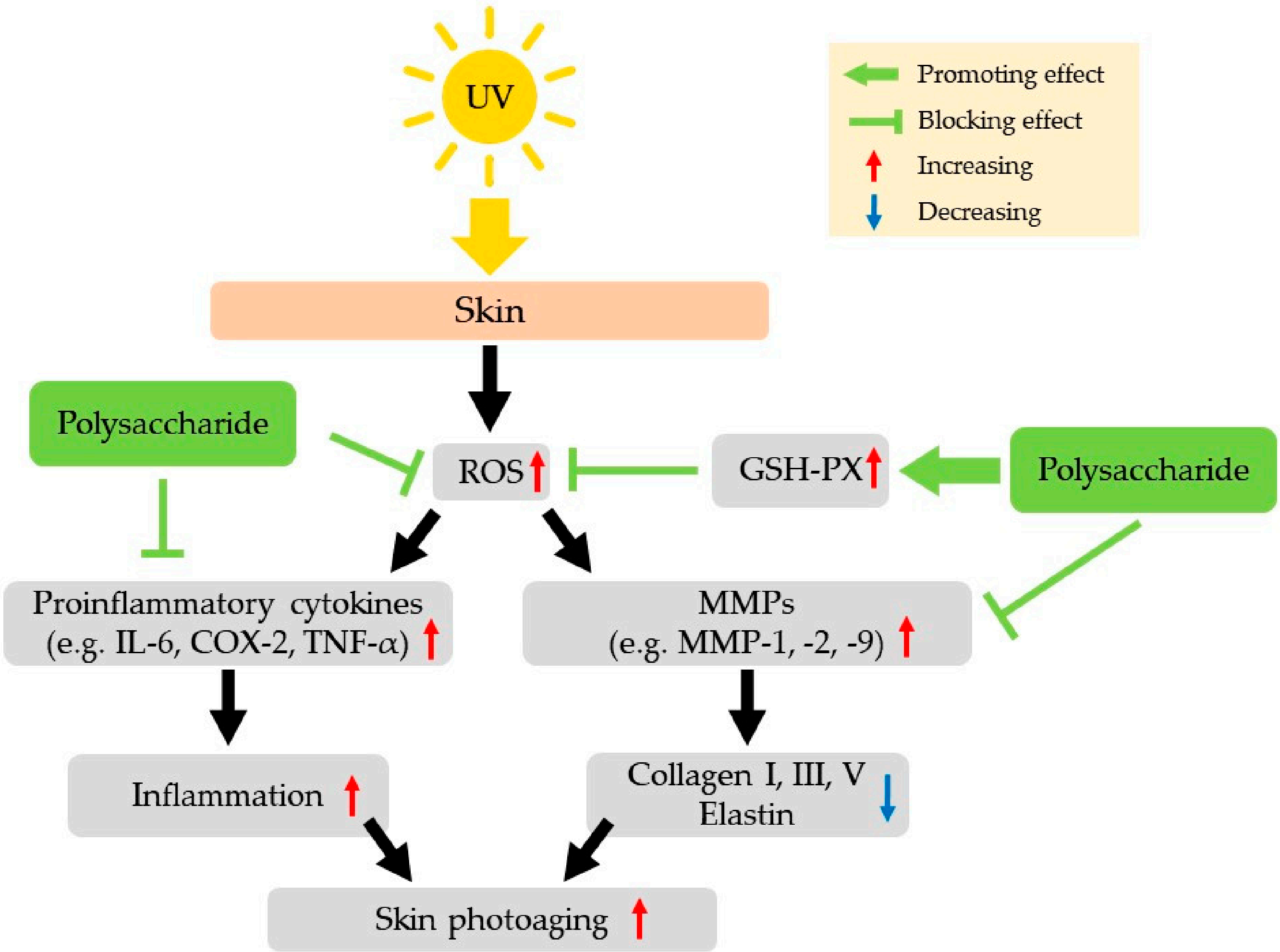

Figure 1. The schematic diagram of UV irradiation-induced skin aging and polysaccharides acting for skin protection.

Secondly, some botanical polysaccharides have been proven to counteract skin photoaging. For instance, a polysaccharide extracted from *Panax ginseng* C. A Meyer by-product can inhibit the gene expression of matrix metalloproteinase-1 (MMP-1), a UV-induced enzyme that contributes to skin damage and aging, to play an anti-photoaging role [35]. Besides, the polysaccharide fraction isolated from *Lycium barbarum* fruit can provide anti-photoaging action by protecting against collagen degradation and increased epidermis thickness.

Thirdly, some polysaccharides with excellent anti-collagenase or anti-elastase activity can delay the skin aging process as well, such as *Nostoc commune* polysaccharides can upregulate Type I collagen production to improve skin elasticity, flexibility, and tension [9], *Volvariella volvacea* aqueous extract which is rich in polysaccharides can stimulate the biosynthesis of collagen, thus providing skin firming and elasticity benefits [36], and *Brasenia schreberi* Mucilage polysaccharide shows collagen synthesis-promoting effect as well [20].

2.4. Whitening

Melanin, the dominant pigment responsible for skin color, derives from tyrosine through a series of oxidative reactions in melanosomes. The first period of melanogenesis is called the Raper-Mason pathway, which depends on tyrosinase (TYR), the rate-limiting enzyme [37]. Moreover, some proteins are involved in the maturation of melanosomes, like tyrosinase-related proteins (TRP1 and TRP2) [38]. After that, melanosomes are transported to nearby keratinocytes and deposited around the nucleus, where they work and eventually degrade [8]. Thus, the whole process of melanogenesis includes melanin synthesis, transport, and degradation.

Melanin synthesis is the most studied area in the regulation of melanogenesis rather than the transport and degradation [39]. First and foremost, according to the melanogenesis pathway, the expression and activation of tyrosinase have the most direct impact on the synthesis of melanin. Secondly, oxidative stress triggered by ROS is another crucial factor in stimulating melanin synthesis [40]. Besides, the Microphthalmia-associated transcription factor (MITF) is a critical transcription factor that can increase the expression of TYR, TRP1, and TRP2. Several signaling pathways can modulate MITF, such as the cAMP/PKA/CREB signaling pathway [41], and the MAPFs signaling pathway [42].

To date, numerous skin-whitening agents promise an anti-melanogenic effect by down-regulating TYR expression or suppressing TYR activity. Meanwhile, antioxidant status and free radical content in cells also affect melanin production. Therefore, natural polysaccharides which can act as tyrosinase inhibitors or antioxidants are usually selected as skin whitening agents [8]. For example, *Ganoderma lucidum* polysaccharides can reduce melanogenesis by inhibiting cAMP/PKA and ROS/MAPK signaling pathways, as well as inhibiting paracrine effects [43,44], and polysaccharides from enzymatically hydrolyzed *Cuscuta chinensis* Lam. seeds not only exerts superior anti-melanogenic activity by inhibiting the expression of TYR, MITF, and TRP-1 in B16F10 melanoma cells but also shows excellent free-radical scavenging ability [38].

3. Natural Polysaccharides

3.1. Polysaccharides Derived from Herbaceous Plants

Polysaccharides extracted from plants are part of the history of herbal ingredients and their pharmaceutical activities have been studied extensively around the world. Nowadays, more research studies are emerging that investigate the promoting effects of herbal plants on human skin health for external applications [5] (Summarized in Table 1).

Table 1. Summary of skin actions of polysaccharides extracted from herbaceous plants, algae, and fungi.

Polysaccharides	Actions	Mechanism	Type of Study	Ref.
		Polysaccharides derived from herbaceous plants		
Anadenanthera colubrina polysaccharide-rich dermocosmetic preparation (ACP)	Moisturizing	Boost the AQP3 gene expression and induce the formation and cohesion of involucrin and FLG	In vivo and clinical trial	[22]
Purified *Benincasa hispida* (Thunb.) Cogn. (Cucurbitaceae) polysaccharides (BPS) preparation	Moisturizing and Antiaging	Boost the AQP3 gene expression and reduce the generation of intracellular ROS	In vitro and in vivo	[45]
Polysaccharides from low-quality *Dendrobium* flowers	Moisturizing	Not mentioned	In vivo and clinical trail	[46]
Polysaccharides from red-ginseng (*Panax ginseng C.A Meyer*) by-product	Antiaging	Inhibit solar ultraviolet-induced MMP-1 protein through activator protein-1 (AP-1)	In vitro and in vivo	[35]

Table 1. *Cont.*

Polysaccharides	Actions	Mechanism	Type of Study	Ref.
		Polysaccharides derived from algae		
Polysaccharide fraction GLP-2 from *G. lemaneiformis*	Wound healing	Promote cell proliferation by activating the PI3 K/aPKC signaling pathway during human keratinocytes wound healing	In vitro and in vivo	[13]
Crude polysaccharides isolated from *Sargassum vachellianum*, *Sargassum horneri*, and *Sargassum hemiphyllum*	Whitening and Antiaging and Moisturizing	Not mentioned	In vitro	[47]
Enzyme-degraded fucoidan from *Laminaria japonica*	Whitening	Not mentioned	In vitro	[48]
Sulfated polysaccharides extracted from *Nostoc commune*	Wound healing and Anti-allergic abilities	Inhibit the production of IL-6, down-regulate the degranulation of RBL-2H3 basophilic leukemia cells, and promote the collagen I secretion	In vitro	[9]
		Polysaccharides derived from fungi		
Polysaccharide from mycelium of *Ganoderma amboinense* (GAMPS)	Wound healing	Not mentioned	In vitro	[14]
Fermented *Tremella fuciformis* polysaccharides (FTPS) purified components	Moisturizing	Promote the gene expression level of various moisturizing genes such as AQP3, TGM1, CASP14, HYAL2, and FLG.	In vitro and clinical trail	[21]
P. igniarius Selenium-rich mycelium Polysaccharides (PSeP)	Wound healing	Remove ROS and further enhance the ROS clearance ability by boosting the activity of GSH-PX	In vitro and in vivo	[15]

Anadenanthera colubrina (Vell.) Brenan is a tree rich in polysaccharides. Researchers obtained its hydro-glycolic extract and clinically confirmed its efficacy in maintaining skin hydration [49]. However, the fact that the *A. colubrina* extract contains abundant pigments had hindered its application in the cosmetic industry. Fortunately, Katekawa et al. [22] developed a pigment-free agent which contained *A. colubrina* polysaccharide-rich dermo-cosmetic preparation (ACP) and found that the TEWL in human subjects under treatment with 1% ACP and 3% ACP were significantly reduced. The mechanism behind its water retentions property is because it not only can facilitate the expression of aquaporin-3 (AQP3) gene, which is viewed to provide better distribution and maintenance of water, glycerol and other skin natural moisturizing factors, but also can induce the formation and cohesion of envelope proteins (involucrin and filaggrin (FLG)) to strengthen skin barrier function [49]. For this reason, this *A. colubrina* pigment-free polysaccharide-rich phytopharmaceutical preparation is considered to be an effective ingredient in skin hydration products. *Benincasa hispida* (Thunb.) Cogn. (Cucurbitaceae), also known as *wax gourd* in Asia, has various therapeutic uses in traditional medicine [45]. Wang et al. [45] developed its purified *B. hispida* polysaccharides (BPS) preparation and found its monosaccharide composition was arabinose, galactose, glucose, and GalA, with a molar ratio of 9.19:12.11:10.46:10.19. Also, researchers reported that BPS was an inhomogeneous acidic polysaccharide with a small amount of bound protein, which contributed to its favorable moisturizing and antiaging capability both in vitro and in vivo. Results showed that BPS could not only exert protective and antioxidant effects on H_2O_2-induced damage to human dermal fibroblasts (HDF-1) cells by reducing the generation of intracellular ROS, but also promise skin-hydration effect by boosting the AQP3 expression level in HDF-1 cells. This way, BPS might be considered as a favorable moisturizing and antiaging factor in cosmetics development.

Additionally, many natural polysaccharides from new resources with eco-friendly and sustainable properties have been developed. For example, *Dendrobium* spp. is rich in polysaccharides with bioactivities, and has been widely used in Chinese medicine because of its health-enhancing functions [50]. However, most research has only focused on the stem polysaccharide of *Dendrobium* orchid; its flower polysaccharide is neglected. Moreover, only 40% of the total orchid flower is qualified for commercial use and the rest of the low-grade flowers are abandoned [46]. Given this scenario, Kanlayavattanakul et al. [46] have developed an eco-friendly extraction method using green solvents to extract polysaccharides from low-quality *Dendrobium* flowers and proved that white *Dendrobium* can be used in the formulation of cosmetic products due to its efficient profile for skin dryness therapy without toxicity. Similarly, Kim et al. [35] have extracted polysaccharides from red-ginseng (*Panax ginseng C.A Meyer*) by-product via hot water extraction and demonstrated that polysaccharides from ginseng by-product can effectively prevent skin aging caused by UV light and suppress atopic dermatitis induced by house dust mites. Thus, around 8000 tons (per year) of by-product from red ginseng production can be further utilized in cosmetics rather than discarded [51].

3.2. Polysaccharides Derived from Algae

3.2.1. Red Algae

Numerous studies have shown that seaweed polysaccharides can be applied in cosmetic applications because of their excellent antioxidant and antimicrobial activities [7,52]. Apart from those well-defined polysaccharides such as carrageenan, some new polysaccharides from red algae with skin health benefits have been discovered and received increased attention as ingredients of cosmeceutical formulations [53,54]. However, purification and characterization are the key steps in developing a functional agent from marine polysaccharides, which have been ignored in the past [13]. Gracefully, some purified and well-characterized marine polysaccharides have been gradually developed in recent years (summarized in Table 1). For instance, *Gracilaria lemaneiformis* is a red alga that belongs to the family *Gracilariaceae*, and is widely distributed in the coastal areas of Asian countries. It is rich in sulfated galactan and consists mainly of repeated units of D-galactose and 3,6-anhydrous galactose with sulfate residues. In addition to the anti-tumor and prebiotic activities of the polysaccharide fractions of *G. lemaneiformis* (GLP-1, GLP-2, and GLP-3), Veeraperumal et al. [13] have also reported their wound healing activities for cosmetic applications. Among these fractions, GLP-2 has been characterized by a homogenous and repeating structure of alternating 4-linked 3,6-anhydro-α-*L*-galactopyranosyl and 3-linked β-D-galactopyranosyl units with sulfate residues, which shows the greatest ability to promote cell proliferation by activating the PI3 K/aPKC signaling pathway during human keratinocytes wound healing [13]. Therefore, the purified GLP-2 fraction can be further developed into cosmetic products for wound management and skin barrier repair.

3.2.2. Brown Algae

At present, several polysaccharides extracted from brown seaweeds have been anticipated for pharmaceutical and cosmeceutical formulations due to their anti-pigmentation, antioxidant, as well as their emulsifying, thickening, or other functional properties [55] (summarized in Table 1). As mentioned above, oxidative stress caused by excessive ROS can further results in skin disorders, such as hyperpigmentation, dark spots, freckles, and winkle formation [56]. A recent study demonstrated that crude polysaccharides isolated from *Sargassum vachellianum*, *S. horneri*, and *S. hemiphyllum* have potent antioxidant activity, tyrosinase and elastase inhibition, and moisturizing ability in vitro, thus having a good application prospect in the field of cosmetics [47]. Likewise, researchers found that the fucoidan from *Laminaria japonica*, a kind of sulfate polysaccharide with high molecular weight (MW) originally, showed the best antioxidant (48.3%), TYR activity inhibitory (62.0%) and anti-melanogenesis activities in B16 cells as MW reduced to 5–10 kDa by using bacterium *Flavobacteriaceae* RC2–3 to complete enzymatic degradation [48]. To this extent, low MW fucoidan can be a splendid candidate for the development of whitening skincare products.

Nevertheless, current studies have mainly focused on the extraction of crude polysaccharides or the proof of their effects on promoting skin health without considering the purification and characterization of polysaccharides, or discussing their potential action mechanisms.

3.2.3. Blue-Green Algae

Cyanobacteria (blue-green microalgae) are increasingly considered to be the ideal species for use in the cosmetic and cosmeceutical industries due to their content of special natural compounds, especially sulfated polysaccharides [57]. *Nostoc* is a genus of cyanobacteria, which is usually composed of a filamentous moniliform embedded in a mucinous matrix, a complex sulfated polysaccharide compound [58]. This complex compound has been proven to play a vital role in withstanding natural stresses, such as resistance to UV, heat, and desiccation [59]. Therefore, researchers have gradually revealed its efficacy in the field of medicine or cosmeceuticals in the last decade [59]. More recently, one research work has studied the biochemical compounds, safety, and effect on wound-healing and anti-allergic abilities of a *Nostoc* strain, *N. commune* (summarized in Table 1). This study has revealed that this polysaccharide-rich extract, which passed the cytotoxicity and heavy metal assays, can effectively inhibit the production of IL-6, down-regulate the degranulation of RBL-2H3 basophilic leukemia cells, and promote the collagen I secretion, thereby suppressing allergic inflammation and delaying the aging process [9]. Given these results, *Nostoc commune* polysaccharides may have promising applications in the field of wound-healing, anti-allergic, and anti-aging cosmetics, but further purification and other functional analyses should be investigated.

3.3. Polysaccharides Derived from Fungi

Fungal polysaccharides can be composed of different monosaccharides, and have a variety of skin health-promoting effects, such as anti-oxidant [60], antiaging [61], and regulating immune function [61]. Moreover, fungal polysaccharides are commonly non-cytotoxic components, especially those derived from edible mushrooms, which further indicates the great potential of fungal polysaccharides for cosmetic and cosmeceutical applications [15]. For this reason, an increasing number of studies focus on discovering new fungal polysaccharides with skin protection functions, and modifying the extraction methods or combining them with other substances to improve the yield of polysaccharides or increase efficacy, to promote the development and application of fungal polysaccharides in the cosmetic industry (summarized in Table 1).

First of all, some fungal polysaccharides with skin-promoting benefits have been developed by scholars in recent years. For instance, *Ganoderma amboinense* has been discovered to be a new resource for extracting polysaccharides that have wound-healing effects. *Ganoderma amboinense* is a common *Ganoderma lucidum*, a medicinal fungus belonging to the Polyporaceae family of *Basidiomycota phylum*. Zhao et al. [14] demonstrated that polysaccharide from mycelium of *G. amboinense* (GAMPS) had the proliferative ability and antioxidant activity on normal cells, and GAMPS at low concentration (0.1 μg/μL) could promote migration and repair scratch injury of NIH/3T3 cells. Thus, GAMPS is considered to have good wound-healing properties. Additionally, Yang et al. [21] have investigated the structure and moisture retention ability of fermented *Tremella fuciformis* polysaccharides (FTPS) purified components, and indicated that FTP-2 with 177,263 Da molecular weight could significantly raising the moisture content of the skin epidermis via promoting the gene expression level of various moisturizing genes such as AQP3, transglutaminase-1 (TGM1), non-apoptotic cysteine-aspartic protease-14 (CASP14), hyaluronan glucosidase-2 (HYAL2), and FLG. Hence, non-cytotoxic FTPS has great potential as a functional ingredient in cosmetics.

Furthermore, some scholars have been focusing on developing a new methodology to achieve higher content of active components in extracted fungal polysaccharides. The polysaccharides are normally extracted by hot water extraction technique [62], ultrasound-assisted extraction [57], acid and alkaline extraction [63], and microwave-assisted extraction [64]. Nevertheless, these processes generally have several drawbacks such as long extraction time, low extraction yield, or the need for multiple extractions to generate considerable amounts of crude polysaccharides. Given this, Barbosa et al. [33] have developed a novel methodology using a binary system with hot water and supercritical CO_2 to recover the antioxidant-rich polysaccharide of *Pleurotus ostreatus*. The optimal extraction condition was 25 MPa, 433.15 K, and 20% H_2O, with 30.69% of the total yield and 0.921 mg of CHO_3. Under this best-defined extraction condition, *P. ostreatus* polysaccharide had 80.83% antioxidant activity and no cytotoxic effect was shown in vitro. Overall, this efficient technology is ready to extract antioxidant-rich fungal polysaccharides with pharmacological or physiological potential, to make mass production possible.

Apart from improving the technological process to increase the yield and the activity compounds of the polysaccharide product, some substances were combined with fungal polysaccharides to make the compound polysaccharides have better functional properties than the original one. *Phellinus igniarius* (*P. igniarius*) is a traditional Chinese medicine, which is also called forest gold [65]. The medical function of *P. igniarius* polysaccharides, such as anti-tumor [66], and immune regulation [67], has been studied extensively around the world. Howbeit, the efficacy or yield of active polysaccharides will fluctuate if different extraction methods or conditions are applied. To improve the efficacy, a recent study conducted by Luo et al. [15] has extracted the *P. igniarius* Selenium-rich mycelium Polysaccharides (PSeP) through the enrichment of inorganic selenium by *P. igniarius*, since both polysaccharides and selenium have antioxidant ability. Then, researchers found that enrichment of selenium in an appropriate amount could enhance the wound-healing function of *P. igniarius* polysaccharides because PSeP could remove ROS and further enhance the ROS clearance ability by boosting the activity of GSH-PX, a pathway that needed selenium as a critical coenzyme to clean up ROS [68]. For this reason, *P. igniarius* polysaccharide was endowed with a better role in accelerating the wound healing process.

4. Challenges and Prospects

In this study, we reviewed the various benefits of natural polysaccharides from new resources for skin health, but identified some problems as well.

Primarily, plenty of research has emerged in recent years on the skin benefits of natural polysaccharides, but few research findings have been translated into commercial products successfully. On the one hand, natural polysaccharides extracted from herbs, fungi, or alga are complex and difficult to purify, which can interfere with the study of natural formulas and extracts, and affect the reliability of the results. Besides, although natural ingredients are moderate, biosafety issues should be taken seriously, such as cytotoxicity or side effects, resulted in few clinical studies on the skin protection ability of active compounds from natural resources [8]. On the other hand, current studies mainly focus on discovering new ingredients without an in-depth exploration of their underlying mechanisms. For example, Jesumani et al. [47] have revealed that the crude polysaccharide extracted from *Sargassum horneri* has excellent tyrosinase inhibition ability, but the purification process and its mechanism have not been subsequently investigated. Further, the relationships between the functionalities and structural characteristics of polysaccharides from natural sources cannot be described and summarized until the structure of the purified polysaccharides is detected [24]. If the structure-activity relationships of wound-healing, moisturizing, anti-aging, and whitening with plants, algae, and fungi polysaccharides are well explored, it will provide a clear direction for researchers to generate modified polysaccharides with enhanced bioactive effects [24]. Thus, in-depth, comprehensive studies are encouraged in future research, that consider issues such as purification and characterization of natural polysaccharides, evaluation of toxicity and side effects, identification of the mechanism of action, exploration of structure-activity relationships, and analysis of clinical impacts.

Secondly, it is necessary to establish and implement some regulations for the utilization of novel natural resources before new products are put on the market or mass production begins [9]. For this reason, we strongly support further research in the areas of standardized culture systems, safe and optimal extraction processes, quality assurance, and quality control of extract production, especially for some fungi or alga resources, to evaluate their potential for sustainable and large-scale commercial applications.

Therefore, in order to promote the development and application of natural polysaccharides, all problems should be carefully addressed before they can be converted into products.

5. Conclusions

The application of natural polysaccharides as ingredients in skincare products could provide safer and better functional benefits than several synthetic ingredients. However, the difficulty in purification, the biosafety issue, the lack of in-depth exploration of their underlying mechanisms and structure-activity relationships, and the immature regulations are the major hindrances to the large-scale commercial application of natural polysaccharides. Thus, it is expected that in the future, after carefully addressing these issues, these polysaccharides can be translated into commercial skincare products with therapeutic and preventive properties.

Author Contributions: Y.Y.: Investigation, Writing—Original draft preparation. B.X.: Conceptualization, Methodology, Software, Supervision, Writing—Reviewing and Editing. All authors have read and agreed to the published version of the manuscript.

Funding: This project is jointly supported by two grants (project code: UIC202016 and UIC202107) from BNU-HKBU United International College.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data are available from the corresponding author upon request.

Conflicts of Interest: The authors declare no conflict of interest.

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