

Functionality analysis of special active ingredients from skincare products: Seaweed extract, Yeast ferment filtrates and Probiotics

Sophia Ting Sun *

Shanghai American School-Pudong, Shanghai, China

* Corresponding Author Email: 100852@yzpc.edu.cn

Abstract. This paper is a comparative study for three of the most popular ingredients used within different skincare products for particular conditioning purposes. Those of which include seaweed and kelp extracts (phlorotannins) and yeast ferment filtrates. A special case for a newly discovered treatment--topical probiotic use--will also be discussed. The origin and use, as well as the experimental effectiveness of these ingredients will be examined and introduced in the paper. Main skin conditions each one of them targets will be briefly discussed in small sections. The paper will also examine the benefits of each ingredient as well as their advantage over other products. Concerns around the topics of new and developing skincare formulas, as well as their ingredient's extraction, will be discussed. Such concerns include, but are not limited to, environmental damage, ethical conflicts, social controversy.

Keywords: Active ingredient, Skincare, Yeast ferment filtrate, Probiotic.

1. Introduction

With developing technologies and advancements in new discoveries, skincare companies have raised their abilities in treating different conditions with many different forms of active ingredients. Many more forms of extracts from foods, plants, and the environment have been tested to be effective in the increase of protection or repairing of the skin. The skin is the first gate of defense for the body against any form of physical contact with the exterior environment. With the most fragile and sensitive layer on the face, people have been finding ways to strengthen the defense through different ways of enhancing its integrity as well as the visual appearance. Such methods include: hydration, minimizing of pores, anti-inflammatory processes, and support for the repair system. To investigate some of the most commonly used and effective active ingredients, the effect, use, and mechanism of seaweed extract, yeast extract, as well as a special case for probiotic will be discussed in this paper.

2. Seaweed, Kelp, and Seaweed Extract

Seaweed extract (or macroalgae) [1], like the name suggests, is one type of active ingredient extracted from plants in the ocean, otherwise known as *Laminaria japonica* [2]. This extract can be found in edible species of seaweed that include Chlorophyta, Phaeophyta, and Rhodophyta. It works to preserve the crucial equilibrium between the stratum corneum's and the skin's surface's water concentration (which is the outermost layer of the epidermis). Only at a minimum of 10% concentration for water present in the skin can maintain a flexible keratin for the skin that demonstrates glow, smoothness, and youth. The seaweed extracts can be responsible for the smoothing, soothing, and protecting of the skin [3]. Lastly for the Giant Kelp, or *Macrocystis Pyrifera*, can also be used as an active ingredient in skincare products for its anti-aging properties through the mechanism of phlorotannin. Though many other oils like jojoba oil and vitamin E oil do help moisturize the skin, they struggle to provide the user a fresh skin feel as well as a minimal number of side-effects (pimples resulting from excessive oil covering the pores) [2]. However, dose is always the real question as to whether or not the substance can exhibit a certain degree of effect.

2.1. Substance Activity and Chemical Property of Ingredient

Seaweeds include a variety of bioactive compounds, such as carotenoids, phytosterols, phycobiliproteins, phloroglucinol, and sulphated polysaccharides. [4]. Some of the bioactive compounds useful for skincare that are found within the seaweeds contain fucoidan, fucoxanthin, and phlorotannins, all of which are capable of presenting antioxidative properties. One important source of effect on the skin from seaweed and its similar substances is the substance—phlorotannin. It has many different possible bioactive traits including antioxidant, anti-allergic, anti-inflammatory, and antimicrobial if administrated in the right concentration with the right combination of formula.

Phlorotannins, which account for 5–12 percent of the dry weight of marine brown algae, are a crucial class of polyphenolic chemicals [5]. Polymerized phloroglucinol units make up the structures of phlorotannins (1,3,5-trihydroxybenzene—as shown in figure 1). They are naturally hydrophilic, with a molecular weight around 126 Da–650 kDa [6.]. The phlorotannins can be divided into six main classes based on structural diversity and varying amounts of polymerization: phloroethols, fuhalols, fucophloroethols, fucols, eckols, and carmalols. Phlorotannins are secondary metabolites that algae make as a kind of defense. The main purpose of this defense is to help the algae survive in differing ocean conditions, therefore meaning that the specific structures of these substances may change due to differing temperature, salinity, incidence of solar radiation etc. [7].

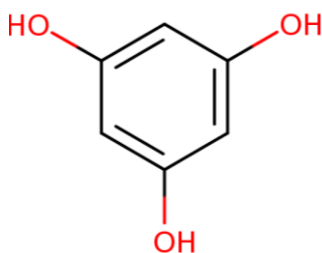


Figure 1. 1, 3, 5-trihydroxybenzene

As the previous introduction mentioned, phlorotannins exhibit many different types of bioactivities including antioxidant, anti-inflammatory, and antimicrobial. To achieve the aforementioned antioxidative qualities, they are able to block the generation of thiobarbituric acid reactive chemicals and reactive oxygen species [4]. According to a zebra fish embryo model study, the presence of phlorotannins was shown to be able to reduce oxidative stress while also being nontoxic at the measured quantities, which later assured its safety and efficacy. With the exploration of this property, increasing amounts of companies and research institutes have been looking for new opportunities in developing marketable products and beneficial usages of this bioactive substance.

2.2. Phlorotannin's Anti-allergy Properties

One common disease or discomfort that people experience on their skin is allergic reactions that differ in levels. Allergies are the most common immunological conditions found worldwide. The most popular approach employed by scientists to address this problem is to reduce the production of immunoglobulin E (IgE), which limits both the development of mediators and their eventual release from mast cells. In one study, the purported anti-allergic activities of phlorotannins were investigated using human basophilic leukemia (KU812F) and rat basophilic leukemia (RBL-2H3) cell lines [8]. By measuring the amount of histamine and -hexosaminidase released from the aforementioned cell lines with extracted and purified phlorotannins (from *Ecklonia cava*) present, the substance's anti-allergenicity was evaluated. The results from the tests showed that dieckol had the highest inhibitory activity on KU812 cells and 6,6'-bieckol demonstrated the most efficient inhibitory activity on the degranulation level of RBL-2H3 cells (both dieckol and 6,6'-bieckol are specific phlorotannins found within seaweeds). Results also pointed to a connection between phlorotannins' capacity to maintain cell membrane by lowering intracellular Ca^{2+} levels and their impact on the suppression of histamine release. Histamine is an organic nitrogenous compound found within the body that is involved in immunological responses. The release of this particular substance is the main reason for itching,

which is a common symptom of allergic reactions, including those resulted from application of a foreign stimulus (face cream, serum, lotion, etc.).

2.3. Phlorotannin's Anti-inflammatory Properties

Human bodies will respond to all forms of foreign stimulus (including exterior application of different substances on the skin) with inflammation as its natural defense system [4]. In order to form an inflammatory response, many different types of inflammatory mediators have to be present (these include lipoxygenases, leukotrienes, cytokines, platelet-activating factor, prostaglandins etc.). The inflammatory mediators are produced by the mast cells, neutrophils, and macrophages. One study examined the anti-inflammatory properties of three classes of phlorotannins: phloroglucinol, eckol, and dieckol. The three were examined to determine how well they inhibited pro-inflammatory responses in mouse and human umbilical vein endothelial cells [9]. Phlorotannins are capable of preserving the integrity of the specimens' vascular barriers, according to the test results. It was also effective in negatively regulating the adhesion and migration of leukocytes (high levels of leukocytes—which is a compound present within the immune system—found within the body indicates high levels of white blood cells, which is evidence for inflammation). Such responses from the application of phlorotannin further strengthened the proposed anti-inflammatory properties of the substance. Similar studies using *E. cava*'s extract further supported the anti-inflammatory purposes of phlorotannin. The extracts were capable of attenuating the expression of particular receptors that are responsible for inflammatory reactions [10]. Aforementioned studies all suggest the validity of the effectiveness of anti-inflammation for phlorotannins.

3. Yeast Ferment Filtrate

The second active ingredient introduced is the yeast ferment filtrate (or galactomyces ferment filtrate) [11]. This kind of bioactive chemical is obtained from the live fermentation of yeasts, as the name would imply. A unique genus of fungi belonging to the Dipodascaceae family is called *Galactomyces* [12]. Unlike how seaweed extract contains many different classes of phlorotannins and fucoidans (as well as other active chemicals) that work to rehabilitate the skin's original conditions, or even further strengthen them, yeast extracts can be very limited, to specifically the galactomyces ferment filtrate. This special type of yeast is nutrient dense in nature. It can often be found as a byproduct of the fermentation process for sake. The main purpose of this filtrate in skincare products is to act as a moisturizing agent, working to minimize pores, redness, and help protect the skin from potential environmental stress [13]. Though many different skincare brands attempt to use this substance as a moisturizing agent, only SKII have worked to perfect their technique in extracting the material and have patented their technique in using this substance, namely PITERA.

3.1. Examination of Galactomyces Ferment Filtrate's Effectiveness

With the availability of well-developed skincare products like SKII's PITERA essence (with a concentration of over 90% pure galactomyces ferment filtrate within the product, and with no other skin conditioning ingredient added), testing for the effectiveness of this particular active ingredient is much easier. One study examined the effect of the substance by applying different facial treatments to randomized group studies [11]. The clinical study involved two separate 8-week-long tracking of pore size, redness, and roughness. Subjects were asked to take pictures of their skin conditions after waking up, and after morning and evening face washes in order to keep the results fair (with an eMR pro). The hydration level of the skin was also measured with a craniometer at set intervals. Results indicated a consistent fluctuation of pore size due to face washes. The averaged results of the pore sizes were then collected in a table between the two treatment groups (as shown below in table 1 and 2).

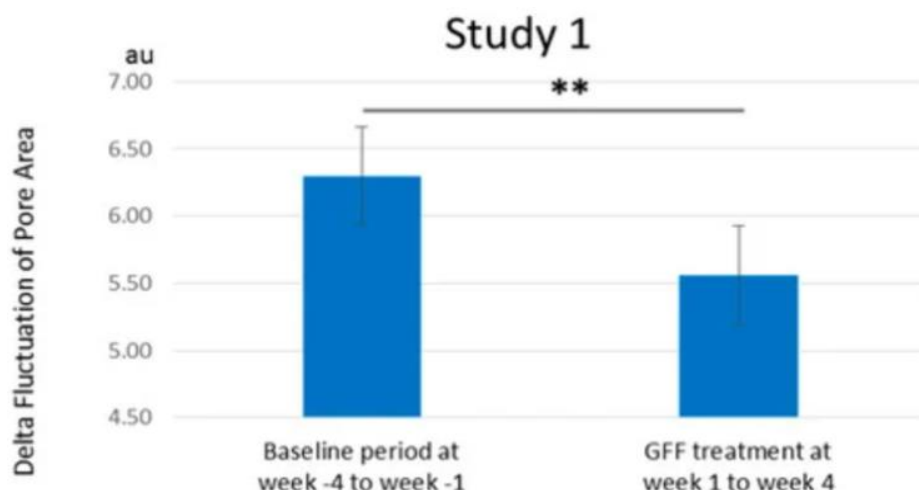


Table 1. Two treatment groups' averaged results of pore size measured in au for unit depicted (from study 1).

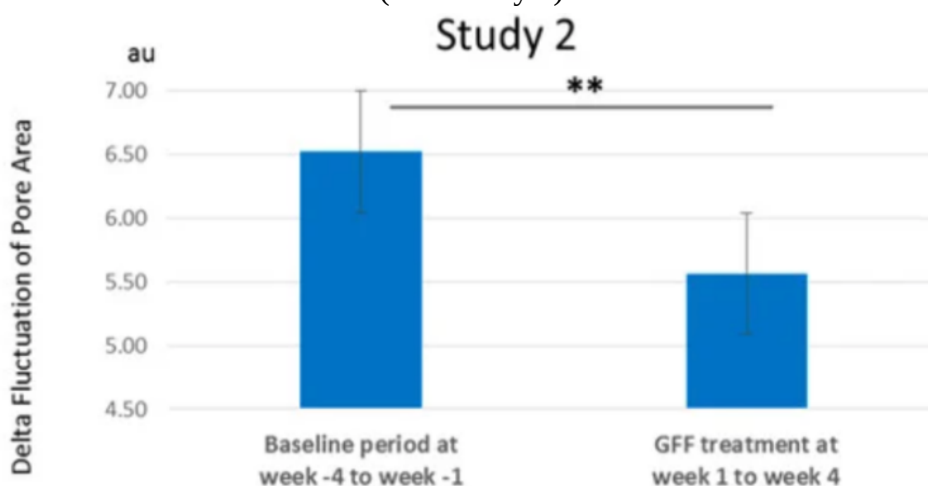


Table 2. Two treatment groups' averaged results of pore size measured in au for unit depicted (study2).

It is obvious that the substance is indeed capable of minimizing pore sizes. With up to 15.66% minimization in the size statistically. The presence of galactomyces on the skin can stimulate the epidermal cells in producing hyaluronic acid, which helps smoothen the skin, as well as hydrating it (subsequently causing minimization of pores as they are filled with moisture).

4. Probiotics

Probiotics are also common active ingredients found in skincare products. The property of this particular substance is defined as "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host" [14]. French chemist Louis Pasteur made the initial discovery of the bacteria causing fermentation. His observations included the ensuing benefits to the Bulgarian population's health brought forth by foods like yogurt (longevity in survival). The fact that "lactobacilli might counteract the putrefactive effects of gastrointestinal metabolism that contributed to sickness and aging" sums up his remark on such effects [15]. Recent clinical studies have proved the gut microbiome's extended spectrum of effect in terms of their regulation in inflammatory reactions on the skin, or in other organs. While research and development for such properties have been expanding, the mechanism, efficacy, and safety of this rather new active ingredient is still waiting to be revealed. The U.S. Foods and Drugs Administration have categorized probiotics into different groups (food additives, drugs, dietary supplements, cosmetics, foods). Topical probiotics

are yet to be approved by the FDA but are used in different skincare products to improve moisturizing and anti-inflammation properties. The property and extensive effect for the active ingredient had proven to be effective against acne and skin-aging. Probiotic treatment on the skin had also been tested to be able to reduce cellular damage and increase cellular renewal, all of which contributing to the healthier appearance of the skin [14]. The nature of probiotics, which naturally occur within and outside of our bodies, make this substance safer in a way for sensitive skin [16]. While the body will repel foreign organisms and chemicals, they seem to accept the entering of familiar compounds more smoothly. In this case for skincare, depending on the exact composition of the formula, probiotic products could be better than others that require foreign substances as a major ingredient.

4.1. Probiotics and Acne

Acne is a common skin ailment that has numerous potential causes [16]. While the reasons could be those that occur in daily lives (incorrect skincare, imbalanced diet, etc.), they all lead to the same result in the skin—an imbalance within the microorganism levels (including probiotics). The skin microbiome consists many different microorganisms. A disruption in the original levels of these microorganisms could cause acne, atopic dermatitis, psoriasis, and rosacea. The healthy skin microbiome environment has many different purposes in protecting the body. It can provide a first line of defense against any form of foreign pathogenic invasion. Additionally, the skin of humans is overrun with coagulase-negative staphylococci. The epidermal barrier environment, as well as the innate and adaptive immune systems found in the epidermis and dermis, are just a few of the ways this group of bacteria might use to spread. They can also produce advantageous compounds that boost host immunity by exhibiting carefully tailored antibacterial, anti-inflammatory, or anti-neoplastic action, depending on the particular species and strain for this (as well as promoting the broad adaptive and innate immune responses to combat the specific condition) [17]. This is just one of many bacterial species in the skin microbiome that may have an impact on and change the health of the skin. Acne's pathogenesis may involve hyperseborrhea, follicular hyperkeratinization, increased microbial colonization, and inflammation [18].

Acne is a skin disorder that has been linked to interactions between host immunity and skin microorganisms, according to scientific research. *Propionibacterium acnes* commonly develops in sebum-rich parts of the skin's microbiome and interacts with other widespread microbes like *Staphylococcus epidermidis*, *Streptococcus pyogenes*, and *Pseudomonas* species. Its excessive multiplication has long been believed to contribute to acne's start [19]. The topical treatments nowadays could cause disruptions in the skin barrier that could lead to dryness, skin-irritation, and such unpleasant effects. Topical probiotic treatment, on the other hand, can target the particular imbalance in microorganisms to alleviate the severity of the acne without causing significant discomfort and side effects. Di Marzio et al. expanded the research into the benefits of employing lactic acid bacteria on skin by finding that *Streptococcus thermophilus*, a component of yogurt, could increase the creation of ceramides when applied topically to the skin for seven days [20]. Bowe et al. emphasized the relevance of this research to the treatment of acne, especially in light of the fact that some ceramides, including Phyto sphingosine, have both antibacterial and anti-inflammatory properties that are effective against *P. acnes* [21]. An in vitro study looked at the ability of probiotic bacteria and konjac glucomannan hydrolysates (GMH) to inhibit the growth of *P. acnes*. According to the authors, adding the GMH prebiotic significantly boosted the probiotic bacteria strains' capacity to inhibit the proliferation of this skin bacterial species [22]. Probiotics can also function as a protective barrier when applied topically because they operate as a competitive inhibitor of binding sites, which prevents the colonization of the area by other potential pathogens. [23]. In short, probiotic topical treatment for the skin can relieve acne severity by inhibiting and regulating the growth of many different acne-causing bacterial groups. Even without heavy acne, the skin can still be protected with consistent application of such treatment that maintains a healthy balance in the skin microbiome.

4.2. Probiotics and Atopic Dermatitis

Chronic inflammatory skin disease known as atopic dermatitis (AD) can result in severe itching and scaly lesions. Patients with AD are currently treated with moisturizers, anti-inflammatory drugs, antihistamines, biologics such as dupilumab, and topical or systemic antimicrobial therapy in order to restore and preserve the skin barrier [24]. Other nonpharmacological treatments, such as probiotics, are being studied to treat this skin problem because these conventional medicines may not be sufficient for some people or might have negative effects.

To further investigate the effects of probiotics on this skin disease, Di Marzio et al. looked into how the levels of ceramides in persons with AD's stratum corneum were altered by a cream that contained *Streptococcus thermophilus*. A significant and pertinent increase in the levels of skin ceramides was seen on the forearm skin of 11 patients after a 2-week application of a cream containing a sonicated preparation of the lactic acid bacterium *Streptococcus thermophilus*, possibly as a result of the bacterial sphingomyelinase's hydrolysis of sphingomyelin. The patients' erythema, scaling, and pruritus all improved as well [20]. A clinical trial also looked at the effect of a lotion containing the heat-treated probiotic strain *Lactobacillus johnsonii* NCC 533 on the colonization of *Staphylococcus aureus* in 31 AD patients. According to the trials, *S. aureus* colonization was controlled by using the lotion for three weeks, and according to SCORAD (SCORing Atopic Dermatitis tool), local clinical improvement was also present [25].

Similar to the former treatments used for acne conditions, the prior AD condition topical treatments were also flawed with unpleasant side-effect. Further research with probiotic topical treatments will hopefully avoid such problems and seek for a better alternative for patients with aforementioned condition, or even further beyond that limit.

5. Discussion & Conclusion

As technological advancements continue to prosper and improve, different methods focused on the exploitations in environmental resources have been initiated and executed. For skincare, with increasing amounts of consumer demand in the diverse effects of products, companies have been increasing their research funding to find potential sources of active ingredients that can be used in their products. However, the demand for such natural ingredients can lead to environmental concerns that could affect the stability of an entire ecosystem. Many of the active ingredients found in cosmetics are actually sourced within animals or plants that play an important role in their own special habitats. Taking seaweed extracts as an example, these sources are usually found in marine environments, and often act as the important primary producer that create the basis for a food chain. If companies choose to exploit natural regions for this original plant, the ecosystems will likely be disrupted as the imbalance in diet will be present. The direct impact could be on the smaller consumers that might not seem as important in the human eye. However, the prolonged situation in lack of food will cause species to die out, leading to the suffering of other consumers that play a larger role (both physically and theoretically).

Apart from the exploitation of natural resources, ethical problems with animal testing could occur with new formulas for products consisting new chemicals. For example, like the probiotic studies, countless trials would have to be presented in order for the formula to be approved and accepted by regulations and companies. The goal of such alternatives was to alleviate the pain, but if that represents exerting pain on other animals to test for success, it could result in controversy. Such trials and human effort put into the research and development of the product will also cause an inevitable rise in the price of the product. When affordability of the product becomes an issue, it would be unfair for citizens since they will not enjoy the same right in protecting their own skin's health. Though the experimentation and science behind the product itself is cold and concrete, the potential questions arising from the development of these products could be much more emotional and problematic. With increasing attention for animal protection, it would be increasingly difficult for companies to find

cheap method to test their products. The conflict between animal protection and profit will come into play when research develops and expands.

Question and concerns over skincare and the future of it are not limited to the aforementioned scenarios. In a time with increasing attention for ethical correctness as well as protection and equality for all, it is both important and difficult to make balanced decisions that satisfy all. For skincare companies, the effort and attention needed to create new formulas will certainly be inestimable and unpredictable. Skincare have been improving and have become better in terms of their limited side effects and refined formulas.

References

- [1] Pereira, L. (2018, November 22). *Seaweeds as source of bioactive substances and skin care therapy-cosmeceuticals, algotherapy, and Thalassotherapy*. MDPI. Retrieved September 20, 2022, from <https://doi.org/10.3390/cosmetics5040068>.
- [2] Choi, J.-S. (2013). *Effects of seaweed laminaria japonica extracts on skin moisturizing ...* ResearchGate. Retrieved September 20, 2022, from https://www.researchgate.net/publication/237096622_Effects_of_seaweed_Laminaria_japonica_extract_on_skin_moisturizing_activity_in_vivo.
- [3] Purcell-Meyerink, D., Packer, M. A., Wheeler, T. T., & Hayes, M. (2021, February 28). *Aquaculture production of the brown seaweeds laminaria digitata and macrocystis pyrifera: Applications in food and pharmaceuticals*. MDPI. Retrieved September 20, 2022, from <https://doi.org/10.3390/molecules26051306>.
- [4] Kumar, L. R. G., Paul, P. T., Anas, K. K., Tejpal, C. S., Chatterjee, N. S., Anupama, T. K., Mathew, S., & Ravishankar, C. N. (2022, May 17). *Phlorotannins–bioactivity and extraction perspectives - journal of applied phycology*. SpringerLink. Retrieved September 20, 2022, from <https://link.springer.com/article/10.1007/s10811-022-02749-4>.
- [5] Venkatesan, J., Keekan, K. K., Anil, S., Bhatnagar, I., & Kim, S.-K. (2019). *Phlorotannins*. Encyclopedia of Food Chemistry. Retrieved September 20, 2022, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7150275/>.
- [6] Barbosa, M., Lopes, G., Ferreres, F., Andrade, P. B., Pereira, D. M., Gil-Izquierdo, Á., & Valentão, P. (2017, October 12). *Phlorotannin extracts from Fucales: Marine polyphenols as bioregulators engaged in inflammation-related mediators and enzymes*. Algal Research. Retrieved September 20, 2022, from <https://www.sciencedirect.com/science/article/abs/pii/S2211926417304137>.
- [7] Kirke, D. A., Rai, D. K., Smyth, T. J., & Stengel, D. B. (2019, May 25). *An assessment of temporal variation in the low molecular weight phlorotannin profiles in four intertidal brown macroalgae*. Algal Research. Retrieved September 20, 2022, from <https://www.sciencedirect.com/science/article/abs/pii/S2211926418310968>.
- [8] Le, Q.-T., Li, Y., Qian, Z.-J., Kim, M.-M., & Kim, S.-K. (2008, October 14). *Inhibitory effects of polyphenols isolated from marine alga ecklonia cava on histamine release*. Process Biochemistry. Retrieved September 20, 2022, from <https://www.sciencedirect.com/science/article/abs/pii/S1359511308003140>.
- [9] Kim, T. H., Ku, S.-K., Lee, T., & Bae, J.-S. (2012, April 13). *Vascular barrier protective effects of phlorotannins on HMGB1-mediated proinflammatory responses in vitro and in vivo*. Food and Chemical Toxicology. Retrieved September 20, 2022, from <https://www.sciencedirect.com/science/article/abs/pii/S027869151200275X>.
- [10] Son, M. (n.d.). *The phlorotannin-rich fraction of Ecklonia cava extract attenuated the expressions of the markers related with inflammation and leptin resistance in adipose tissue*. The Phlorotannin-Rich Fraction of Ecklonia cava Extract Attenuated the Expressions of the Markers Related with Inflammation and Leptin Resistance in Adipose Tissue. Retrieved September 20, 2022, from <https://www.hindawi.com/journals/ije/2020/9142134/>.
- [11] Miyamoto, K., Dissanayake, B., Omotezako, T., Takemura, M., Tsuji, G., & Furue, M. (2021). Daily Fluctuation of Facial Pore Area, Roughness and Redness among Young Japanese Women; Beneficial

- Effects of Galactomyces Ferment Filtrate Containing Antioxidative Skin Care Formula. *Journal of Clinical Medicine*, 10 (11), 2502. <https://doi.org/10.3390/jcm10112502>.
- [12] Lumbsch, H., & Huhndorf, S. (1970, January 1). [PDF] *outline of ascomycota - 2007: Semantic scholar*. undefined. Retrieved September 20, 2022, from <https://www.semanticscholar.org/paper/Outline-of-Ascomycota-2007-Lumbsch-Huhndorf/ab8e0047672f67e93b8426ce5bac085a8bb35fbb>.
- [13] C., F., Jennifer, Emily, Jessica, Frida, Rita, Stella, MD, C. from, Hawwa, H, Rebecca, Rosie, Maha, Maria, Shawna, Pk, Sarah, Sy, Annie, & Chiili. (2020, April 18). *Cosrx Galactomyces 95 Whitening Power Essence Review: A horror story*. Simple Skincare Science. Retrieved September 20, 2022, from <https://simpleskincarescience.com/cosrx-galactomyces-95-essence-review/>.
- [14] Lee, G. R., Maarouf, M., Hendricks, A. J., Lee, D. E., & Shi, V. Y. (2019, June 10). *Topical probiotics: The unknowns behind their rising popularity*. *Dermatology Online Journal*. Retrieved September 20, 2022, from <https://doi.org/10.5070/D3255044062>.
- [15] Medicine, *E. of I. (n.d.). *Probiotics history: Journal of Clinical Gastroenterology*. LWW. Retrieved September 20, 2022, from <https://doi.org/10.1097/MCG.0000000000000697>.
- [16] Navarro-López, V., Núñez-Delegido, E., Ruzafa-Costas, B., Sánchez-Pellicer, P., Agüera-Santos, J., & Navarro-Moratalla, L. (2021, July 15). *Probiotics in the therapeutic arsenal of Dermatologists*. *Microorganisms*. Retrieved September 20, 2022, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8303240/>.
- [17] Williams, M. R., & Gallo, R. L. (2015, September 24). *The role of the skin microbiome in atopic dermatitis - current allergy and asthma reports*. SpringerLink. Retrieved September 20, 2022, from <https://link.springer.com/article/10.1007/s11882-015-0567-4>.
- [18] *The potential of probiotics for treating acne ... - wiley online library*. (n.d.). Retrieved September 20, 2022, from <https://onlinelibrary.wiley.com/doi/abs/10.1111/dth.13279>.
- [19] Platsidaki, E., & Dessinioti, C. (2018, December 19). *Recent advances in understanding Propionibacterium acnes cut bacterium acnes in acne*. F1000Research. Retrieved September 20, 2022, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6305227/>.
- [20] Di Marzio L;Cinque B;De Simone C;Cifone MG; (n.d.). *Effect of the lactic acid bacterium streptococcus thermophilus on ceramide levels in human keratinocytes in vitro and stratum corneum in vivo*. *The Journal of investigative dermatology*. Retrieved September 20, 2022, from <https://pubmed.ncbi.nlm.nih.gov/10417626/>.
- [21] AC; B. W. P. L. (n.d.). *Acne vulgaris, probiotics and the gut-brain-skin axis - back to the future? Gut pathogens*. Retrieved September 20, 2022, from <https://pubmed.ncbi.nlm.nih.gov/21281494/>.
- [22] Al-Ghazzewi FH; (n.d.). *Effect of Konjac glucomannan hydrolysates and probiotics on the growth ...* Retrieved September 20, 2022, from <https://onlinelibrary.wiley.com/doi/full/10.1111/j.1468-2494.2009.00555.x>.
- [23] Lee GR; Maarouf M; Hendricks AJ; Lee DE; Shi VY; (n.d.). *Topical probiotics: The unknowns behind their rising popularity*. *Dermatology online journal*. Retrieved September 20, 2022, from <https://pubmed.ncbi.nlm.nih.gov/31220895/>.
- [24] M. Catherine Mack Correa; Judith Nebus. (n.d.). *Management of patients with atopic dermatitis: The role of emollient therapy: Sciencegate*. *Dermatology Research and Practice*. Retrieved September 20, 2022, from <https://www.sciencegate.app/document/10.1155/2012/836931>.
- [25] Blanchet-Réthoré S; Bourdès V; Mercenier A; Haddar CH; Verhoeven PO; Andres P; (n.d.). *Effect of a lotion containing the heat-treated probiotic strain lactobacillus johnsonii NCC 533 on Staphylococcus aureus colonization in atopic dermatitis*. *Clinical, cosmetic and investigational dermatology*. Retrieved September 20, 2022, from <https://pubmed.ncbi.nlm.nih.gov/28721083/>.