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Review Article

PROBING PROBIOTICS: EXPLORING THEIR ROLE IN COSMETICS AND PERSONAL CARE INNOVATIONS

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Abstract:

Probiotics are gaining popularity and commercial viability. They are characterized as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host." But far too many of the goods on the market today that are marketed as probiotics don't meet the qualifying requirements. The number of items categorized as probiotics has expanded in the cosmetics market in recent years. Probiotics have a number of potential uses in personal care products, particularly for skin, oral, and intimate care. However, appropriate regulation of labelling and marketing standards is still necessary to ensure that consumers are, in fact, buying probiotic goods. This research examines probiotics' present market, regulatory issues, and possible uses in the personal care sector. Probiotics, defined as live microorganisms conferring health benefits when administered adequately, have gained substantial popularity and commercial presence. However, concerns arise as many products marketed as probiotics do not meet these qualifying standards. In recent years, the cosmetics market has witnessed a notable increase in items labelled as probiotics, despite uncertainties regarding their efficacy and adherence to regulatory criteria. This study investigates the current state of probiotics in the market, focusing on regulatory challenges and potential applications in the personal care sector, specifically in skin, oral, and intimate care products. Probiotics offer promising opportunities due to their purported beneficial effects, yet ensuring accurate labelling and marketing practices remains paramount. Effective regulation is essential to validate the probiotic content of products and to maintain consumer confidence. Key findings underscore the necessity for rigorous standards that verify the presence and efficacy of probiotics in personal care goods. Such measures are crucial not only for consumer protection but also for fostering transparency and credibility within the industry. By addressing these regulatory issues, this research aims to contribute to a clearer understanding of probiotics' role in personal care and to advocate for policies that uphold product integrity and consumer trust in the marketplace.

Keywords: probiotics; cosmetics; skin; personal care; intimate care

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INTRODUCTION:

A cosmetic is "any product (excluding pure soap) intended to be applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance", according to the US Food and Drug Administration (FDA)^[1]. This definition covers cosmetics, hair care products, and dental care items. It's vital to remember that no health claims are made in this description. There have been numerous research trying to alter the micro biome in a particular niche to promote health due to the growing interest in bacteria that colonize the human body rather than just those that infect it. The field of probiotics has expanded significantly as a result of the use of beneficial bacteria for this purpose. Probiotic uses vary significantly in form and are defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host" [2]. This includes applications in cosmetics, where the probiotics market is expected to increase at a 12% annual pace over the next ten years, led by North America [3]. This piece will examine the state of the art research on probiotics and their possible uses in personal care and cosmetics, as well as the current state of the "probiotic cosmetics" industry.

A) Types of Probiotics

There are several different types of probiotics, each with different benefits:

- 1. Lactobacillus: The most common probiotic, found in yogurt and other fermented foods. It can help with diarrhea and may help people who can't digest lactose, the sugar in milk.
- **2. Bifidobacterium:** Found in some dairy products. It may help ease the symptoms of irritable bowel syndrome (IBS) and other conditions.
- **3. Saccharomyces boulardii:** A yeast found in probiotics that can help fight diarrhea and other digestive problems.

B) Mechanisms of Probiotics

1. Competitive Exclusion of Pathogens

- Colonization Resistance: Probiotics occupy niches in the gut, preventing pathogenic bacteria from colonizing and proliferating.
- **Nutrient Competition:** Probiotics consume nutrients required by pathogens, thus starving them and limiting their growth.

2. Modulation of the Gut Microbiota

• **Balancing Microbiota:** Probiotics help maintain a healthy balance of gut bacteria by

- promoting the growth of beneficial bacteria and inhibiting harmful bacteria.
- Production of Antimicrobial Substances:
 Some probiotics produce bacteriocins and other antimicrobial compounds that can directly kill or inhibit the growth of pathogens.

3. Enhancement of Mucosal Barrier Function

- Strengthening Epithelial Tight Junctions: Probiotics can enhance the integrity of the gut epithelial barrier, preventing the translocation of pathogens and toxins into the bloodstream.
- Mucus Production: Probiotics stimulate the production of mucus, which acts as a physical barrier protecting the gut lining.

4. Immune System Modulation

- **Stimulation of Immune Cells:** Probiotics can activate various immune cells, such as macrophages, dendritic cells, and T-cells, enhancing the body's immune response.
- Anti-inflammatory Effects: Some probiotics can produce anti-inflammatory cytokines and reduce pro-inflammatory cytokines, helping to modulate immune responses and reduce inflammation.

5. Production of Short-Chain Fatty Acids (SCFAs)

- Fermentation of Dietary Fiber: Probiotics ferment dietary fibers into SCFAs like acetate, propionate, and butyrate, which have various beneficial effects, including providing energy to colon cells and maintaining gut health.
- **Regulation of pH:** SCFAs lower the pH of the gut, creating an environment that is less favourable for the growth of harmful bacteria.

6. Interaction with the Host Metabolism

- **Lipid Metabolism:** Probiotics can influence lipid metabolism, helping to lower cholesterol levels and improve lipid profiles.
- Insulin Sensitivity: Some probiotics can improve insulin sensitivity and glucose metabolism, which can be beneficial for managing diabetes and metabolic syndrome.

COSMETICS FOR SKIN

The proliferation of products labeled as probiotics on the market does not always mean that science, business, and consumers should rejoice. Too many products do not meet the requirements necessary to be called probiotics. A lot of misleading statements and widespread misuse of the term have led to mainstream consumer channels giving consumers incorrect information. Probiotics are not found in fermented food, they are not found inside of us, and their viability does not always increase with the number of species present. Formulations are being developed based not on research evidence but rather on marketing and what the consumer might find appealing. For instance, products are purportedly composed of molecules.

The internet, the use of words to rank highly on search engines, and the use of pseudo-experts for product promotion allow these products to be highly rated and appear to be the best clinically documented for preventing or curing bacterial or yeast infections in the vagina. The net result is misleading and

confusing to consumers, as well as making healthcare professionals wary of the whole field of probiotics. To counter this, we need to re-state important facts. For a product to be considered probiotic, it must

For a product to be considered probiotic, it must comply with three main criteria.

- 1. The strain(s) must be described for the intended usage, including genetic and phenotypic characteristics, and a justification based on verified tests published in peer-reviewed publications must be provided.
- 2. To provide a benefit to the intended target site, the product must have an equal number of live microorganisms at the time of usage as when it was demonstrated in clinical research.
- 3. If humans are the intended receiver, the mode of administration, dosage, and length of use should be determined by scientific evidence in humans.

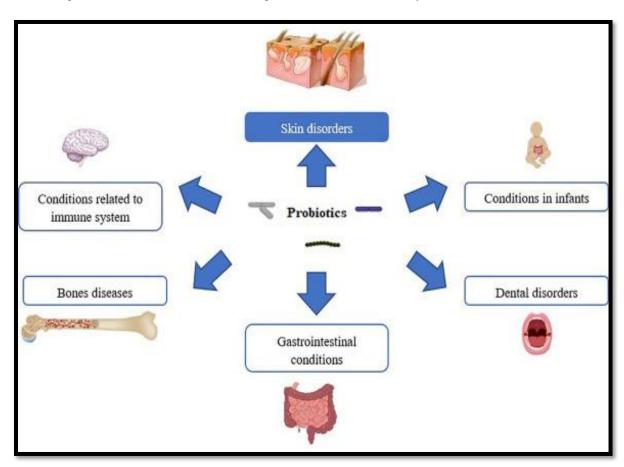


Figure 1. Flowchart of Probiotic used in cosmetic for skin

The cosmetics industry has ventured into this space by focusing its efforts towards skincare. There are several areas of opportunity and great value in this concept. A search of the websites of two major retailers of cosmetics in North America revealed that at least 50 products are already being commercialized with a claim to contain probiotics ^[4,5]. The most common claims are that the product contains ferments, lysed bacteria, or filtered extracts. Therefore, the product is not probiotic and the term should not have been used oriented towards "balancing" the skin Microbiota, improving the skin barrier, and increasing the skin's general look.

Table 1. Percentage corresponding to the different types of products currently marketed as probiotic cosmetics.

TYPE OF PRODUCT TYPE OF PRODUCT	PROPORTION OF PRODUCTS
Deodorant	2%
Primer	2%
Balm	4%
Soap bar	4%
Foundation	6%
Cleanser	10%
Exfoliant	10%
Gel	10%
Mask	12%
Serum	16%
Cream	24%

Although improving the overall appearance of the skin can be a personal preference for the customer, there are some scientific guidelines involved. It is possible to quantify elements such skin colour, melanin, haemoglobin, and the absence of obvious age spots or markings ^[6].

These and other evaluations offer the way to produce measurable outcomes, which can subsequently give credence to assertions of advancements has been documented that some probiotic strains can enhance the function of the epithelial and epidermal barriers. The latter is extremely important to skin function and a popular target for consumer-pleasing promises. Experiments can be conducted to confirm if strains used as cosmetics really improve barrier function. In fact, studies conducted by scientists at a reputable cosmetic firm have demonstrated that a lysate from the probiotic Bacillus Subtilis Reuter strain demonstrated improvement with administration of the lysate containing product [7].

It could also reduce vasodilation, edema, mast cell degranulation, and TNF-alpha release by employing trans-epidermal water loss to Molecules 2021, 26, 1249 5 of 11assess barrier function. Certain items claim to contain a filtrate made from lysates or ferments. When it comes to filtrates, both living and dead bacterial cells are eliminated along with possibly some other heavier compounds (like peptides). This could eliminate some of the bacterial cell components and bioactive substances in the preparation that are necessary to see certain benefits. As a result, fats cannot be considered probiotics and

are not included in the definition of postbiotics. Cells that have had their outer membrane broken down by chemical or physical procedures are known as lysates [8]. Medical practice has made use of these preparations for half a century as immunomodulators. They are especially useful in treating respiratory tract infections because they may contain bacteria that stimulate the host cells' immune response [9]. By modifying protein components, Lacticaseibacillusrhamnosus GG and B. longum lysates have the ability to enhance tight-junction barrier resistance in vitro [10]. While employing these kinds of preparations has advantages, further research is still necessary before establishing generalizations and conclusions that depend on the particular strain. Even within the same species, different bacterial strains have different macrophage activation, flexibility, and cell composition [11].

In another investigation, lactobacillilysates changed their capacity to promote keratinocyte reepithelialization ^[12], underscoring the necessity of examining strain characteristics before asserting anything. Surprisingly, not much information has been released regarding the chemical makeup of the lysates utilized in cosmetics. This cell wall and analysis should be necessary, requiring the use of newer techniques like surface-enhanced Raman spectroscopy (SERS) or liquid chromatography—tandem mass spectrometry (LC-MS/MS)-based metabolomics ^[13]. In doing so, it will soon be extremely apparent that metabolite types and quantities differ between strains, and therefore their

application to human tissues would also differ. This again illustrates the need of performing tests in humans with whole microbial cells, lysates, or filtrates to show what activity is being promoted by the application of any given product; ideally to identify which component of the lysate is responsible. Several studies have demonstrated the benefits of particular probiotic strains for skin health [14 -17]. Additionally, the mechanisms of anti-aging operate [18]. But before making any promises, the cosmetics industry must focus its efforts on producing more scientific evidence and maintain consistency and transparency in its labelling processes.

TOPICAL ADMINISTRATION AND DESIGN OF PROBIOTICS

Not every skincare product for men or women needs to be used locally. Probiotics taken orally have been shown to impact the gut microbiota, which may help with skin disorders such atopic dermatitis, acne, and orrosacea^[19, 20]. Probiotic therapy throughout pregnancy and the first few years of life may be necessary to lower the incidence and severity of atopic dermatitis ^[21], implying immune modulation and enhancing the function of the developing gut barrier ^[22].

Probiotic strains are often freeze-dried. Nevertheless, final viability can differ based on the drying protectant that is used. Skim milk, serum, trehalose, glycerol, betaine, adonitol, sucrose, glucose, lactose, and polyethylene glycol are the most often utilized protectants; however, they might not be appropriate for the product's intended application or its physicochemical properties [23]. When the strains should not be exposed to water when employing this procedure as it will cause them to rehydrate too soon [24]. Probiotics can have their shelf life and viability increased by using microencapsulation. Its main purpose is to make sure that organisms can withstand the harsh conditions found in the digestive system [25], while topical treatments have also used it [26].

The bacteria are usually encapsulated in a lipid or biopolymer protective matrix. Many creams are not produced in sterile conditions; therefore preservatives are often added with bactericidal and/or bacteriostatic effects. These potentially can not only affect the probiotic strain viability but also inadvertently alter the Microbiota of the recipient. Regulation of probiotics is primarily concerned with safety. There is no specific requirement for commercializing

probiotics, and products are regulated according to their final use, whether it is as a drug, medical device, food, dietary supplement, or cosmetic. The descriptiveness and level of documentation required to claim a cosmetic probiotic is substantially less than for one making drug claims in Canada and elsewhere [27]

Unfortunately, in a bid to maximize profit, some companies make disease or illness-alleviation statements associated with their cosmetic products, when this should be reserved for drugs or clinically proven supplements. Cosmetic items are anticipated to contain minimal amounts of microorganisms (less than 500 colony forming units (CFU)/g for products intended for the eye area and 1000 CFU/g for other products) due to safety concerns [28]. There cannot be a cosmetic that is a true probiotic because it is not feasible for them to contain live bacteria. They may still, however, contain ingredients derived from probiotic strains that have potential advantages. As postbiotics, these can be defined as a "composition of inanimate microorganisms and/or their components that imparts a health benefit on the target host." They can also be made up of bacterial lysates, ferments, and fultrates^[29]."

Purified metabolites and components devoid of cells are not included in this definition; instead, they should be classified according to their chemical nomenclature. Postbiotics do not include filtrates that do not contain any cell components. However, lysates of bacteria and Ferments may fall under this category, depending on what makes them up. From a biochemical perspective, fermentation is an anaerobic metabolic process in which carbohydrates (like lactose) are partially oxidized to form lactic acid, which is then used by the cell as energy. "Foods made through desired microbial growth and enzymatic conversions of food components" is how fermented foods and beverages are defined [30]. This is not the same as the ferments that are applied topically. In that instance, fermentation has occurred, but not in relation to the use or conversion of food intended for human consumption. An aerobic or anaerobic process known as fermentation occurs when a living thing or its enzymes chemically alter a substrate to produce a product of interest [31]. Thus, if probiotic bacteria present in the fermentations contained in cosmetic products are viable and if they stay alive until these goods might be sold as probiotics once they get to the host target site.

Table 2. Properties of probiotics for cosmetic products.

Sr. No.	Probiotics	Properties	Cosmetic Products
1)	Lactobacillus acidophilus, Lactobacillus bulgaricus	Antiacne and antimicrobial properties.	Anti-acne creams, Anti-acne facewash.
	lysates and Lactobacillus plantarum		
2)	Lactobacillus delbreuckii and Lactobacillus casei lysates	Anti-inflammatory, soothing properties	Anti-acne cream, Anti-acne gels, Skin toner.
3)	Lactobacillus rhamnosus lysates	Prevent skin damage from UV radiation. Lactic acid has also been described as a very effective exfoliating and moisturizing agent.	Sunscreen creams, lotions and gels, Exfoliating scrubs, Moisturizing creams and lotions.
4)	Streptococcus thermophilus	Enables skin hydration, rendering an antioxidant effect and pH control.	Moisturising creams and lotions, Anti-aging creams and serums, Anti-wrinkle creams, Under eye creams.
5)	Bifidobacterium lysates longum sp.	Showed positive effect for reactive and skin at in vivo experiment, decreasing skin sensitivity	Skin hydrating gels, serums, soaps.
6)	Lactobacillus paracasei	Imparts antibacterial properties reducing dandruff	Antidandruff shampoos.
7)	Streptococcus thermophilus YIT 2084	It is capable to produce the hyaluronic acid by itself, this increases skin moisture and reduces the appearance of fine lines and wrinkles.	Moisturizing creams serums and Anti- wrinkle creams.

PROBIOTICS FOR INTIMATE CARE OF FEMALES

Lacto-bacilli are often abundant in a healthy vaginal environment. Numerous factors, such as the use of douches and medicines, having several sexual partners, and the introduction of pathogens into the region, can upset the body's natural balance and cause bacterial infections, UTIs, candidacies, and other illnesses. 48 years ago, this gave rise to a rationale for adding lactobacilli to the urogenital tract in order to restore health [32]. Since then, research has been done on the vaginal delivery of probiotic strains of Lactobacillus via suppositories or vaginal ovules. A variety of strains have been tested, starting with the instillation Lacticaseibacillus (formerly, of Lactobacillus) rhamnosus GR-1 into the vagina [33]. These strains have been shown to reduce the recurrence of urinary tract infections (UTI) [34,35], including Limosilactobacillus (formerly, Lactobacillus) reuteri RC-14 and Lactobacillus crispatus CTV05501 in conjunction with L. rhamnosus Lcr35 for BV and vulvovaginal candidacies [36,37] and Lactobacillus paracasei IMC 502 to preserve vaginal homeostasis [45].

Probiotic strains are showing promise in the new field of urogenital malodour reduction, which has a major negative influence on women's quality of life, particularly when combined with bacterial vaginosis [38]. Numerous non-probiotic products, like perfumes, vinegar rinses, and vaginal douches, make the claim that they can lessen body odor. Their effectiveness is questionable, though, and they may raise the risk of infection—including sexual acquisition—by upsetting the beneficial microorganisms [58,59]. An advantageous feature of a successful probiotic would be its capacity to proliferate and generate metabolites that break down or neutralize offensive substances [39,40]

A product of this kind could need to be registered as an over-the-counter medication rather than a cosmetic or personal care item, depending on its nature. Probiotic lactobacilli-containing topical gel is currently being developed, and the findings look promising for Candida in the vagina [41]. One could argue that procedures performed on the urogenital tract do not properly fit the description of cosmetic procedures, which are meant to enhance or restore a person's appearance. Similarly, treatments aimed at lessening halitosis [42-44] could not work either, depending on how "appearance" is defined and interpreted. On the other hand, using a topical

treatment to treat acne problems with lactobacilli would only be cosmetic [45].

CHARACTERISTICS OF PROBIOTICS AND HOW THEIR LYSATES ARE ADDED TO COSMETICS

Probiotics, particularly their lysates, have gained attention in cosmetic formulations due to their potential benefits for skin health. Here are some key properties and considerations regarding probiotics and their lysates in cosmetics, supported by references:

Moisturizing and Hydrating Properties: Probiotic lysates can enhance skin hydration by promoting the synthesis of ceramides and other moisturizing factors. This helps in maintaining skin barrier function and preventing transepidermal water loss (TEWL) [46]. Anti-inflammatory Effects: Lysates from probiotics have shown anti-inflammatory properties, which can be beneficial for soothing irritated or sensitive skin conditions [47].

Antioxidant Activity: Probiotic lysates contain antioxidants that can protect the skin from oxidative stress and environmental damage, thereby contributing to anti-aging effects [48]. Microbiome Balancing: Probiotics help in maintaining the balance of the skin microbiome by inhibiting the growth of harmful bacteria and promoting beneficial microorganisms [49].

Wound Healing and Repair: Some studies suggest that probiotics and their derivatives accelerate wound healing processes by promoting collagen production and epithelialisation. Incorporation of probiotic lysates into cosmetic products involves ensuring stability and efficacy. Manufacturers often use encapsulation technologies to protect probiotics from environmental factors and to ensure their delivery to the skin intact [50].

CONCLUSION

The understanding that some bacteria are beneficial to their hosts and that microorganisms are found in abundance on both the human body and the world has opened up new avenues for managing ecosystem and Businesses across various individual health. industries, including the cosmetics industry, have benefited from this knowledge by creating new products and boosting sales. Just twenty years ago, probiotics, prebiotics, and microbiome were unheard of terms in cosmetic products. If their use aligned with robust scientific studies substantiating assertions and elucidating the mechanisms of action of the strains and materials being marketed, that would be encouraging. Regretfully, this is not always the case. Despite being a foundational subject in the cosmetics industry, chemistry has not been sufficiently used to pinpoint the compounds that give the benefits by products of microbes.

The field of microbiome research is growing, thus more knowledge in microbiology and chemistry will be required to guarantee that customers may access high-quality cosmetics that comply to definitions (of a probiotic, prebiotic, etc.). It's undeniable that modifying microorganisms can result in new approaches to enhancing wellbeing and beauty. As a result, there will be regulatory obstacles as cosmetics enter the health market. Advocating for the necessity regulatory bodies update their frequently outdated systems and classifications, we also need to demand on clinical validation, product safety, and evidence of stringent protocols for the handling, storage, and application of products containing microorganisms and their metabolites or cell walls. Unfounded assertions benefit no one, yet thorough scientific research can yield findings that are extremely beneficial to human health and welfare.

REFFERENCES:

- US Food and Drug Administration. Cosmetics Overview [Internet]. Available from: https://www.fda.gov/industry/regulatedproducts/cosmetics-overview#cosmetic (accessed 2020 Nov 15).
- Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. Nat Rev Gastroenterol Hepatol. 2014;11:506–14.
- 3. Probiotic Cosmetic Products Market Forecast, Trend Analysis and Competition Tracking-Global Market Insights 2020 to 2030 [Internet]. Available from: https://www.futuremarketinsights.com/reports/probiotic-cosmetic-products-market (accessed 2020).
- 4. Ulta Beauty [Internet]. Available from: https://www.ulta.com/ (accessed 2021 Feb 19).
- 5. Sephora [Internet]. Available from: https://www.sephora.com (accessed 2021 Feb 19).
- Matts PJ. New insights into skin appearance and measurement. J Invest Dermatol Symp Proc. 2008;13:6–9.
- 7. Guéniche A, Bastien P, Ovigne JM, Kermici M, Courchay G, Chevalier V, et al. Bifidobacterium longum lysate, a new ingredient for reactive skin. Exp Dermatol. 2010;19:1–8.
- 8. Klein G, Schanstra JP, Hoffmann J, Mischak H, Siwy J, Zimmermann K. Proteomics as a quality control tool of pharmaceutical probiotic bacterial lysate products. PLoS One. 2013;8.

- 9. Villa E, Garelli V, Braido F, Melioli G, Canonica GW. May we strengthen the human natural defenses with bacterial lysates? World Allergy Organ J. 2010;3–23.
- Sultana R, McBain AJ, O'Neill CA. Straindependent augmentation of tight-junction barrier function in human primary epidermal keratinocytes by Lactobacillus and Bifidobacterium lysates. Appl Environ Microbiol. 2013;79:4887–94.
- Mokrozub VV, Lazarenko LM, Sichel LM, Babenko LP, Lytvyn PM, Demchenko OM, et al. The role of beneficial bacteria wall elasticity in regulating innate immune response. EPMA J. 2015;6:13.
- 12. Mohammedsaeed W, Cruickshank S, McBain AJ, O'Neill CA. Lactobacillus rhamnosus GG lysate increases re-epithelialization of keratinocyte scratch assays by promoting migration. Sci Rep. 2015;5:16147.
- 13. Ankrah NYD, May AL, Middleton JL, Jones DR, Hadden MK, Gooding JR, et al. Phage infection of an environmentally relevant marine bacterium alters host metabolism and lysate composition. ISME J. 2014;8:1089–100.
- 14. Genova E, Pelin M, Decorti G, Stocco G, Sergo V, Ventura A, et al. SERS of cells: What can we learn from cell lysates? Anal Chim Acta. 2018;1005:93–100.
- 15. Navarro-López V, Martínez-Andrés A, Ramírez-Boscá A, Ruzafa-Costas B, Núñez-Delegido E, Carrión-Gutiérrez MA, et al. Efficacy and safety of oral administration of a mixture of probiotic strains in patients with psoriasis: A randomized controlled clinical trial. ActaDermVenereol. 2019:99:1078–84.
- 16. Yu Y, Dunaway S, Champer J, Kim J, Alikhan A. Changing our microbiome: Probiotics in dermatology. Br J Dermatol. 2020;182:39–46.
- 17. Korpela K, Salonen A, Vepsäläinen O, Suomalainen M, Kolmeder C, Varjosalo M, et al. Probiotic supplementation restores normal microbiota composition and function in antibiotic-treated and in caesarian-born infants. Microbiome. 2018;6:182.
- 18. Sharma D, Kober MM, Bowe WP. Anti-aging effects of probiotics. J Drugs Dermatol. 2016;15:9–12.
- 19. Jung GW, Tse JE, Guiha I, Rao J. Prospective, randomized, open-label trial comparing the safety, efficacy, and tolerability of an acne treatment regimen with and without a probiotic supplement and minocycline in subjects with mild to moderate acne. J Cutan Med Surg. 2013;17:114–22.

- 20. Knackstedt R, Knackstedt T, Gatherwright J. The role of topical probiotics in skin conditions: A systematic review of animal and human studies and implications for future therapies. Exp Dermatol. 2020;29:15–21.
- 21. Kalliomäki M, Salminen S, Poussa T, Arvilommi H, Isolauri E. Probiotics and prevention of atopic disease: 4-year follow-up of a randomized placebo-controlled trial. Lancet. 2003;361:1869–71
- 22. Isolauri E, Kalliomaki M, Laitinen K, Salminen S. Modulation of the maturing gut barrier and microbiota: A novel target in allergic disease. Curr Pharm Des. 2008;14:1368–75.
- 23. Hubálek Z. Protectants used in the cryopreservation of microorganisms. Cryobiology. 2003;46:205–29.
- 24. Morgan CA, Herman N, White PA, Vesey G. Preservation of microorganisms by drying; a review. J Microbiol Methods. 2006;66:183–203.
- 25. Yao M, Xie J, Du H, McClements DJ, Xiao H, Li L. Progress in microencapsulation of probiotics: A review. Compr Rev Food Sci Food Saf. 2020;19:857–74.
- 26. Puebla-Barragan S, Reid G. Forty-five-year evolution of probiotic therapy. Microb Cell. 2019;6:184–96.
- 27. Government of Canada. Questions and Answers on Probiotics [Internet]. Available from: https://www.canada.ca/en/health-canada/services/food-nutrition/food-labelling/health-claims/questions-answers-probiotics.html (accessed on 20 November 2020).
- 28. US Food and Drug Administration. Methods for cosmetics. In: Bacteriological Analytical Manual.
- 29. Salminen S. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. Nat Rev Gastroenterol Hepatol.
- 30. Marco ML, Sanders ME, Gänzle M, Arrieta MC, Cotter PD, De Vuyst L, et al. The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on fermented foods.
- 31. Chojnacka K. Fermentation products. In: Pohorecki R, Bridgwater J, Molzahn M, Gani R, Gallegos C, editors. Chemical Engineering and Chemical Process Technology-Volume V: Chemical Engineering Education and Main Products. London, UK: Eolss Publishers Co. Ltd.; 2010. Volume 5.
- 32. Bruce AW, Chadwick P, Hassan A, VanCott GF. Recurrent urethritis in women. Can Med Assoc J. 1973;108:973–6.

- Bruce AW, Reid G. Intravaginal instillation of lactobacilli for prevention of recurrent urinary tract infections. Can J Microbiol. 1988;34:339– 43.
- 34. Reid G, Bruce AW, Fraser N, Heinemann C, Owen J, Henning B. Oral probiotics can resolve urogenital infections. FEMS Immunol Med Microbiol. 2001;30:49–52.
- 35. Stapleton AE, Au-Yeung M, Hooton TM, Fredricks DN, Roberts PL, Czaja CA, et al. Randomized, placebo-controlled phase 2 trial of a Lactobacillus crispatus probiotic given intravaginally for prevention of recurrent urinary tract infection. Clin Infect Dis. 2011;52:1212–7.
- 36. Verdenelli MC, Cecchini C, Coman MM, Silvi S, Orpianesi C, Coata G, et al. Impact of probiotic SYNBIO® administered by vaginal suppositories in promoting vaginal health of apparently healthy women. CurrMicrobiol. 2016;73:483–90.
- 37. Rossi A, Rossi T, Bertini M, Caccia G. The use of Lactobacillus rhamnosus in the therapy of bacterial vaginosis. Evaluation of clinical efficacy in a population of 40 women treated for 24 months. Arch Gynecol Obstet. 2010;281:1065–9.
- 38. Petricevic L, Witt A. The role of Lactobacillus caseirhamnosus Lcr35 in restoring the normal vaginal flora after antibiotic treatment of bacterial vaginosis. Gen Gynaecol. 2008:1369–74.
- 39. Bilardi JE, Walker S, Temple-Smith M, McNair R, Mooney-Somers J, Bellhouse C, et al. The burden of bacterial vaginosis: Women's experience of the physical, emotional, sexual and social impact of living with recurrent bacterial vaginosis. PLoS ONE. 2013;8.
- 40. McMillan A, Rulisa S, Sumarah M, Macklaim JM, Renaud J, Bisanz JE, et al. A multi-platform metabolomics approach identifies highly specific biomarkers of bacterial diversity in the vagina of pregnant and non-pregnant women. Sci Rep. 2015;5:1–14.
- 41. Puebla-Barragan S, Renaud J, Sumarah M, Reid G. Malodorous biogenic amines in Escherichia coli-caused urinary tract infections in women—a metabolomics approach. Sci Rep. 2020;10:9703.
- 42. Donders G, Bellen G, Oerlemans E, Claes I, Ruban K, Henkens T, et al. The use of 3 selected lactobacillary strains in vaginal probiotic gel for the treatment of acute Candida vaginitis: A proof-of-concept study. Eur J ClinMicrobiol Infect Dis. 2020;39:1551–8.
- 43. Iwamoto T, Suzuki N, Tanabe K, Takeshita T, Hirofuji T. Effects of probiotic Lactobacillus salivarius WB21 on halitosis and oral health: An

- open-label pilot trial. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 2010;110:201–8. 45.
- 44. Masdea L, Kulik E, Hauser-Gerspach I, Ramseier A, Filippi A, Waltimo T, et al. Antimicrobial activity of Streptococcus salivarius K12 on bacteria involved in oral malodour. Arch Oral Biol. 2012;57:1041–7. doi: 10.1016/j.archoralbio.2012.02.011.
- 45. Lebeer S, Oerlemans E, Claes I, Wuyts S, Henkens T, Spacova I, et al. Topical cream with live lactobacilli modulates the skin microbiome and reduce acne symptoms. bioRxiv. 2018.
- 46. Vieira AT, et al. Influence of Oral and Gut Microbiota in the Health of Menopausal Women. Front Microbiol. 2017;8:1884.
- 47. Guéniche A, et al. Lactic acid bacteria secrete metabolites retaining anti-inflammatory properties after intestinal transport. Gut Microbes. 2010;1(4):299-306.
- 48. Kim HS, et al. A novel cosmetic strategy based on lactic acid bacteria-produced metabolites. PLoS One. 2014;9(12)
- 49. Jensen GS, et al. A Double-Blind Placebo-Controlled Clinical Study Evaluating the Effectiveness of a Probiotic and Prebiotic Skin Care Regimen. J Clin Aesthet Dermatol. 2021;14(5):28-32.
- 50. Fore J, et al. Probiotics, prebiotics and the gut microbiota. Transl Res. 2010;160(4):289-95