Microbiology Discovery
ISSN 2052-6180 | Volume 3 | Article 5

HOAJ
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Special Section | Industrial Microbiology | Review
Open Access

Probiotics in personal care products

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Abstract

In recent years, probiotics have attained popularity among consumers worldwide as a natural approach to maintain or restore human health. As a billion dollar industry, many products are already available in the market place with even more potential candidates in development. Knowledge gained from the Human Microbiome Project supports the utility of probiotics to achieve a balanced microbial community and potentially reduce or alleviate certain disorders. Most of the research studies and commercial probiotic products have focused on the human gastrointestinal tract; however, in the last few years interests and applications have extended to other physiological systems. Personal care products, which consist of over-the-counter drugs, cosmetics, and other consumer products, are used by almost everyone on a daily basis. Although the understanding and development of probiotics in personal care products is lagging behind the rapid progress that has been made in food products, recent studies have reported their potential uses in this market sector. This paper reviews recent findings related to microbial communities in the skin and oral cavity, where a large number of personal care products are applied, and discusses the opportunities and challenges of probiotics in these products.

Keywords: Probiotics, microbiome in skin, personal care products, microbiome in oral cavity

Introduction

The concept of probiotics was proposed in the early 20th century by Elie Metchnikoff who postulated that ingested microorganisms could confer health benefits for humans [1]. These friendly or helpful bacteria may be the same or similar to species already residing in the human body. The World Health Organization has defined probiotics as *live microorganisms that, when administered in adequate amounts, confer a health benefit* [2]. Probiotics have been available in yogurts, dietary supplements, and other products for years. Recent interest by consumers, in promoting health naturally, has boosted sales and a new generation of products worldwide. Currently, probiotics are a multi-billion dollar industry with an estimated 7% growth projected globally [3,4].

While commercial products and applications of probiotics continue to expand, scientific evidence and clinical studies supporting various health claims have not kept up with their pace [1]. Many probiotic claims have been based on preliminary assessments, uncontrolled studies, and at times anecdotal observations or simply speculation [2]. There are myths and misconceptions regarding the definition and benefits of probiotics [5]. Furthermore, commercial probiotics for human and animal use are often labeled inaccurately, raising serious concerns among researchers and consumers [6].

Nevertheless, the past decade has witnessed many studies regarding the role of probiotics in treating gastrointestinal (GI) disorders. Advanced technologies in genome sequencing have enabled functional studies to identify a number of microbial communities in the human body and their roles in health and diseases. This knowledge augmented with various molecular studies has allowed a more comprehensive view of probiotics and their effects. Different mechanisms have been found to account for the possible health effects of probiotics; these include reducing harmful organisms, producing antimicrobial compounds, and stimulating the host's immune responses [1].

As studies on probiotics and products targeting GI microbial communities continue to grow, potential applications are being considered in personal care products, such as lotions, creams, and toothpastes [3]. For years the skin care industry has been investigating probiotics to enhance the function

 doi: 10.7243/2052-6180-3-5

and beauty of the skin, and researchers have been assessing whether probiotics could be used to treat certain skin conditions [4,7,8]. There are also reports indicating the potential of probiotics to combat tooth caries [2]. It is anticipated that the trend of including probiotics in personal care products will continue to grow.

According to the Office of Cosmetics and Colors in U. S. Food and Drug Administration (FDA), the term "personal care products" does not have a legal or regulatory definition, but usually refers to a wide variety of products found in the health and beauty departments of drug and department stores [9]. They may fall into a number of different categories (cosmetics, drugs, medical devices, and dietary supplements) that are regulated under the Federal Food, Drug, and Cosmetic Act (FD&C Act), or may be regulated as other types of consumer products under the Consumer Product Safety Act.

Under the FD&C Act, a product's category is based primarily on intended use. For example, the term "cosmetics" is defined in section 201(i) of the FD&C Act in part as "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness or altering appearance"; "drug" is defined in 201(g) of the FD&C Act Section in part as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases" or "articles intended to affect the structure or any function of the body" [10]. Some products meet the definitions of both cosmetics and drugs when they have two intended uses. For example, a shampoo is a cosmetic because it is intended to cleanse the hair. An antidandruff treatment is a drug because its intended use is to treat dandruff. Consequently, an antidandruff shampoo is both a cosmetic and a drug. Another example is a mouthwash containing a microorganism (*Streptococcus salivarius*) is expected to reduce odor in individuals with bad breath.

This article provides an overview of probiotics use in personal care products. The discussion starts with a brief review of microbial communities in the skin and oral habitat. Their role in the health status of the host is further illustrated by examples of diseases associated with changes of microbial populations. The following section focuses on the potential of probiotics in personal care products, including those that may help to prevent disorders or restore health in the skin and oral cavity. In the last section of this review, we focus our discussion on the challenges (substantiating claims by research, differences in regulations applied to different product categories by different countries) and future directions which might be impacted by the increasing interest in probiotics in personal care products.

Review

Microbiota in health and diseases

The understanding of human microbiota, or the microbial community residing in the human body, has increased substantially as a result of the Human Microbiome Project (HMP) [11]. Realizing microbial populations outnumber human cells by a factor of 10 in our body, the National Institutes of Health (NIH) initiated HMP in 2007 to assess microbiota in GI tract, skin, oral cavity, nares, and vagina (in females) [12-14]. Advances in genomic technologies and computational methodologies allow a comprehensive characterization of microbial compositions, including those that cannot be cultivated on microbiological media [15-18]. The HMP concluded in 2012 with numerous findings published from this five-year study [14]. The overall microbial diversity is extensive regardless of the site surveyed, and each system has dominant groups of organisms reflecting its special niche [13]. The microbiota experience variations through life that are affected by internal (host health) and external (environmental) factors [19]. In general, microbial community differences within an individual (intrapersonal) are smaller than that between individuals (interpersonal) [16,20].

Among the goals of HMP, understanding the role of microbiota in the health status of the host is undoubtedly one of the top priorities [12,14,15,21]. In the past, microbial diseases focused on individual pathogens; the more recent approach is generally assessing microbial communities and their interactions with the host to gain a better understanding of the health condition of an individual. A number of studies have revealed that dysbiosis, a disturbance in the microbial ecosystem, is responsible for various diseases and disorders. The GI system is perhaps the best studied site in the HMP and yielded valuable scientific insights. Metagenomic analyses of gut microbiome demonstrated many incidences that link the shift of populations with illnesses and disorders; these include different types of diarrhea (e.g., acute, traveler's, and antibiotic-associated), irritable bowel syndrome, Crohn's disease, obesity, and other conditions [4,11,22-25]. On the other hand, microbiota from healthy individuals has been attributed to potentially fighting against obesity and playing a role insevere malnutrition conditions, as shown by recent research findings [26,27].

The skin microbiome

The skin is the largest organ in the human body. Its primary function is to protect our bodies from external harm by acting as a physical barrier, with additional roles that include regulation of body temperature, evaporation control, sensation, and storage of lipids and water [20,28]. As an interface between internal organs and the outside environment, the skin is always in contact with different substances. Microorganisms including bacteria, fungi, and viruses found everywhere often colonize the skin. They can generally be categorized into three groups: 1) transient microbes present intermittently, 2) temporary organisms that persist over a short period of time, and 3) residents that permanently inhabit the skin [9,29]. Additionally, skin continuously undergoes self-renewal, so resident microbial cells are shed in the process. Most of the microbes found on the skin are commensal organisms and harmless to healthy individuals; in fact, some are considered mutualistic

doi: 10.7243/2052-6180-3-5

organisms and confer health benefits to the skin by secreting antibacterial substances, preventing pathogen colonization, and influencing host immune responses [30]. On the other hand, commensal microorganisms can cause diseases and infections if the physical barrier has been compromised due to trauma or injuries [15,20]. Some are considered opportunistic pathogens that become infectious agents when the host is immunocompromised due to surgeries, treatment, or other confounding factors [31,32].

Historically, microorganisms that colonized the skin were thought to be limited in their types based on culturing methods [9]; these were primarily *Staphylococcus epidermidis* and other coagulase negative staphylococci as well as species of *Corynebacterium* and *Propionibacterium* [28,33]. The development of molecular techniques, such as metagenomic analyses, since revolutionized the ability to determine microbial composition on the skin, including those that cannot be cultivated on microbiological media [15,16,19].

Various factors affect the microbial flora of the skin and they can be generally categorized into host and environmental factors [28]. The skin microbiome is highly dependent on the microenvironment of sampled site, a reflection on the physiology of skin [16,28]. Sebaceous sites such as the forehead have the lowest diversity, and *Propionibacterium* species are the dominant organisms. On the other hand, moist areas (e.g., armpits, navel, groin) constitute higher diversity of microbiota, with *Staphylococcus* and *Corynebacterium* species as the predominant members [16,28]. Moreover, skin sites with greater bacterial diversity (e.g., forearm, hand, buttock) can harbor diversity as high as or higher than that of the gut microbiome. The acidic condition resulting from sebum degradation discourages pathogens from invading and establishing in the skin [28]. Personal hygiene is another environmental factor that has a direct effect on the skin's microbial flora. Soaps, makeup, and skincare products (e.g., moisturizers) alter skin conditions that in turn may influence the types of microbes residing on the skin. More discussion on this topic is covered in Probiotics and Skin Health section.

Among the host factors are age, sex, and anatomic sites. Skin microbiota differ among various age groups, with significantly different bacterial communities between the youngest and the oldest groups [19]. A newborn acquires resident bacteria on the skin soon after birth, and their composition is affected by birth delivery methods [20,30]. Hormonal changes during puberty stimulate the growth of lipophilic (or lipid-loving) bacteria due to sebum production [19]. Physiological changes and anatomic differences also contribute to microbial community variance between genders [16].

Altered lipid composition and organization can cause skin diseases when commensal bacteria become infectious agents. One such example is acne, an inflammatory malady that affects 80% of adolescents in the U.S. [31]. The change of lipid composition during puberty encourages lipophilic organisms, such as *Propionibacterium acnes,* to proliferate [25]. As these bacteria derive energy from metabolizing fatty acids in the sebum, a variety of enzymes are secreted that injure the tissue lining of sebaceous glands. In conjunction with activated immune responses, this results in a skin condition termed acne vulgaris [28]. In addition, the investigators noticed younger children had a higher abundance of *Staphylococcus (S.) aureus,* which were later replaced by lipophilic and other bacteria. This finding may have important implications for skin disorders, such as atopic dermatitis (or eczema), which are more prevalent among children but often resolves by adolescence and adulthood [34]. Further,diseases of the skin often result from reduced barrier function [20]. *S. aureus* is one of the most commonly cited skin pathogens, and it is responsible for several cutaneous infections such as impetigo, furuncles, subcutaneous abscesses, ulcers, and other more serious systemic infections when penetrating into the blood stream (e.g., toxic shock syndrome) [20,31,33]. Burn victims whose epidermis (and at times dermis as well) have been destroyed are exposed to various assaults. During the first 48 hours, Gram positive bacteria (e.g., *S. aureus*) are the main colonizers. A shift then occurs and Gram negative opportunistic organisms predominate, some with virulent properties that can cause life threatening infections [35]. In addition, there are dermatological disorders that have been associated with skin microbiota [15,25,28,34]. Atopic dermatitis (AD) is a chronic and intensely inflammatory skin disorder that has more than doubled in industrialized countries in the past three decades without a clear cause [28]. AD patients frequently acquire cutaneous infections with *S. aureus* as the main colonizing organism. A study that analyzed microbiome from three groups of people found a strong association between disease severity and bacterial diversity [34]. In general, the disease was most severe when community diversity was low; as microbiota increased after treatment, they approached a level of diversity similar to those from healthy skin. The shift of relative abundance of microbial community members was a complex process, further stressing the importance of a comprehensive assessment in treating AD cases [25,34].

Determination of skin microbiota was conducted for psoriasis, another cutaneous disorder. The cause for this chronic inflammatory condition of the skin affecting approximately 2% of the population worldwide is largely unknown. Applying molecular techniques, differences in colonization patterns between psoriasis lesions and uninvolved skin sites were noted [30]. The distributions of the three major skin microflora differed significantly in their representations, suggesting a substantial ecological disturbance of microbial population contributed to the psoriasis condition in patients.

Chronic non-healing wounds are a frequent challenge for people, because prolonged healing increases the risk of bacterial colonization with possible deleterious effects. A longitudinal study on microbiota in diabetic mice indicated a qualitative and quantitative shift in bacterial species colonizing the diabetic skin, and this change favored species such as *Staphylococcus* [33]. Not surprisingly, this shift in bacterial community coincided with impaired healing of the wound, and *Staphylococcus* species have been implicated in both impaired wound healing and leg ulcers [36].

These examples illustrate that dysbiosis in the skin habitat is a key player in shifting from a healthy condition to some type of disorder. Restoring homeostasis is a holistic approach to treat certain skin diseases.

Oral microbiome

Similar to the skin, the oral cavity actively interacts and connects with the external environment. As a major gateway to the human body, food enters the mouth and air passes through on its way to the lung. Unique to the oral cavity are two types of surfaces for bacteria to colonize: the hard surface of the teeth and the soft tissue of the oral mucosa [37]. Distinct habitats include teeth, gingival sulcus, tongue, cheeks, hard and soft palates and tonsils. Each niche provides surfaces and functions, atmospheric conditions, and nutrients for certain microbial population to flourish and establish [37,38]. As a result, the oral bacterial communities are complex and harbor approximately 1000 species with the majority identified by molecular methods (i.e., 16S rRNA sequencing) [39], making this habitat one of the most diverse microbiomes in human body [40].

The dynamic interaction with the external environment makes oral microbiota unique in facing certain challenges not present in other human systems; the multiple functions (e.g., eating, talking, smoking) carried out in the oral cavity may affect bacterial growth and persistence [38]. Certain foods rich in carbohydrates contribute to biofilm formation on both hard and mucosal surfaces of the oral cavities that can shelter both pathogens and commensal microflora. Saliva supports the dynamic flow of nutrients and other ingested materials (such as antimicrobials) in the oral cavity. Additionally, hygiene practices such as tooth brushing and mouth rinsing disrupt microbiomes due to agitation and dislodging from their adhesion sites [37,40].

Not surprisingly, microbial communities play an important role in oral health. Studies have indicated that biodiversity is crucial to maintaining good dental health, as demonstrated by comparing microbiomes in plaque and saliva between healthy and symptomatic individuals [40,42]. In general, oral health is achieved by balanced and diverse microbial communities that interact in mutualism with its host [38]. The higher diversity indicates that different species are responsible for certain functions required to maintain homeostasis within the oral cavity [20,37,40,42].

As with other ecosystems in the human body, shifts in oral microbial populations favor pathogens to predominate or result in decreased biodiversity. Factors contributing to ecological shifts include poor oral hygiene, immunological disorders, and certain genetic compositions that predispose individuals to infections [37]. Diseases resulting from oral ecosystem change include dental caries (tooth decay), periodontitis (gum inflammation), endodontic (root canal) infections, alveolar osteitis (dry socket) and tonsillitis [37,39,41]. Although halitosis (bad breath) is not a serious medical condition, the source could be anaerobes flourishing in the tongue mucosal area and producing volatile sulfur compounds [38,43]. Additionally, there are associations between oral pathogens and systematic diseases, such as diabetes, stroke, and cardiovascular disease [37,39]. All these undesired conditions underscore the key role the oral microbiome plays in human health.

Dental caries and periodontal diseases are the two most prevalent oral diseases worldwide [38,45]. Tooth decay affects all ages and is not limited to developed countries. As the primary cause of oral pain and tooth loss, this disease initiates when an individual repeatedly ingests high level of carbohydrates, resulting in oral microbiota shifted to acid producing microbes (e.g., species of *Lactobacillus* and *Streptococcus*) [40]. As biofilm matures on teeth, these organisms accumulate in dental plaque and lower the pH of the oral cavity. Opportunistic pathogens such as *Streptococcus mutans* take advantage of the environment and ferment carbohydrates, producing more acid by-products that further destroy the enamel and root of the tooth [37]. If left untreated, lesions can further progress into the pulp and cause it to become infected by anaerobic bacteria with proteolytic properties [40]. These endodontic infections are more serious and often are precursors to periodontal diseases.

Periodontal diseases are an inflammatory disorder of the periodontium, the specialized tissue that surrounds and supports the teeth. Gingivitis, the milder form, is perhaps the most commonly encountered oral diseases in adults [37,40,41]. Bacteria adhere to the tooth surface via dental plaque that is continuously being formed, and shifting from mostly Gram positive aerobes and facultative anaerobes to Gram negative anaerobes; this results in irritation and inflammation of the gum (gingiva). This disease, however, is reversible by removing dental plaques through good oral hygiene [40].

Once the attachment between gingivae and teeth is gone, periodontal pockets are formed that allow a number of anaerobic bacteria to colonize. As the infection progresses, tissue damage leads to teeth being motile in their sockets and eventually tooth loss [37]. Periodontitis can give rise to serious health concerns; left untreated, it may lead to systemic conditions with life-threatening consequences. Recent genome sequencing efforts have indicated that specific microbiota (e.g., *Porphyromonas gingivalis, Treponema denticoal, Tannerella forsythia*) are associated with advanced periodontitis [37,41].

Probiotics

With a better understanding of dysbiosis as the underlying cause for many diseases and disorders, restoring and maintaining a healthy microbiota is gaining wide support as a treatment and prevention approach in this post-antimicrobial era. The most noticeable development in this area is probiotics-beneficial microorganisms that, when administered in adequate

doi: 10.7243/2052-6180-3-5

amounts, can confer a health benefit on the host [1,2,6]. In recent years, numerous products containing probiotics have entered the marketplace; these include naturally fermented and not-fermented food products, dietary supplements, approved pharmaceutical products, cosmetics, hygiene items, and other products, such as household cleaners [1,3,45]. Although there is no generally accepted definition for the word "natural", promoting health in such a way is appealing to consumers worldwide with sales projected into the billions of dollars [3,4,46]. The users are not only limited to humans; probiotics have been applied regularly to animal feeds to boost livestock production, and the potential utility of probiotics in the aquaculture industryis also being explored [6,47,48].

Studies and clinical trials have been conducted to determine the effect of probiotics and the mechanisms of action in the GI system; these include strengthening and maintaining the intestinal barrier, modulating immune responses, enhancing microbial flora, producing antimicrobial substances, degrading toxins, and resisting pathogen colonization [31,42,43,49,50]. Most of the probiotics are lactic bacteria belonging to *Lactobacillus* and *Bifidobacterium*, as well as other bacterial genera and yeasts (e.g., *Saccharomyces*) [1,3,4,7,51]. The prophylactic effect of probiotics has been reported and encouraged after surgery to prevent *Clostridium difficile* infection [2]. Additionally, probiotics have met with some success in treating disorders such as acute diarrhea, pouchitis (recurrent inflammatory condition in the ileal pouch), irritable bowel syndrome, ulcerative colitis, cancer of the GI system (e.g., colorectal, bladder) and urogenital infections [3,25,31,47,52]. Due to the significant potential for treating GI disorders, a number of products are marketed with claims to promote GI health by balancing the microbiota in this system [5,53].

Probiotics and skin care

Until recently, the beneficial effects of probiotics have been mostly focused on the GI system. In the last few years, however, there have been reports on the potential use of probiotics on the skin [7,51,53]. It has been suggested that probiotics ingested orally exerted their effects on the skin via mechanisms initiated in the gut, mostly due to changes in systemic immune responses such as modulating specific T-cells and stimulating toll-like receptors [4,7,31,47]. Atopic dermatitis and eczema are perhaps the most widely studied disorders in which probiotics have been used [2,3,51]. For instance, oral administration of *Lactobacillus* species was reported to be effective in managing inflammation [47,55,56]; however, the efficacy in infants and young children varied [2,57]. In the case of psoriasis where dysbiosis was associated with skin inflammation, probiotics have been suggested to restore commonly occurring resident microbes that were diminished when the disorder was present [30]. Other reported benefits to the skin from the ingestion of probiotics include the healing of burns and scars, rejuvenating skin tissues, protection against ultraviolet rays, and improving innate immunity of the skin [8,51,58].

Industries involved in personal care products have assessed probiotics as "bioactive ingredients" to help enhance the beauty as well as the function of the skin [4,10,59]. These products range from topical applications (e.g., body lotion, anti-aging serum, soap, aftershave, wipe) to ingestible products (e.g., probiotic drinks) [3,8,45]. *Lactobacillus* is the most common bacterial genus listed in the ingredients [4]; others with less specific descriptions (e.g., probiotic enzyme, ferment lysate, probiotic proteins) have implied association with some type of beneficial organisms. In a few cases bacterial metabolites (e.g., lactic acid, hyaluronic acid) are listed as ingredients [51]. The beneficial effects exerted by probiotic organisms via topical application are mostly circumstantial evidence [7]. Proposed mechanisms of action from scientific papers include improving barrier function of the epithelium layer and competitive exclusion (i.e., growth inhibition by limiting nutrients and producing antibiotics) of pathogens [47].

Safety limits for viable organisms in products other than food are usually very low. For example, the current FDA acceptable limits for total (not pathogenic) microorganisms in cosmetics are 500 colony forming units (cfu) per gram in eye-area products and 1000 cfu/g for other area products [60]. It is doubtful that such low number of live cells could exert beneficial effect, not to mention the technical challenge of maintaining viability after manufacturing and storage. The cosmetic formulas are usually complex containing a number of ingredients, including preservatives to discourage microbial growth. Typically, preservatives having broad-spectrum antimicrobial efficacy are combined with one or more compounds of more selective efficacy in order to deliver a broad antimicrobial effect against a wide range of potential contaminating microorganisms; and at the same time establish some degree of synergic activity [61]. Even if the safety limits are relaxed, concentrating cells and maintaining their long term viability in personal care products pose technical challenges for industries.

Because incorporating viable beneficial microorganisms adds complexity to the formulation and manufacturing processes, some cosmetic companies are addressing these issues by taking an alternative approach to probiotics. Instead of live microorganisms, only their "bio-active" molecules or metabolites may be used in cosmetic products. These so-called "novel technologies" draw from research on various fermentation-based proteins, filtrates, and lysates that reportedly retain beauty benefits without the presence of whole or live bacteria [8]. Papers have been published, suggesting possible effects of probiotics on the cellular activities of the skin, such as enhancement of respiration, energy generation, and stress responses [4]. A review by Lew and Liong summarized cellular components or microbial metabolites (i.e., bioactives) as probiotics in dermal applications. According to their review, lactic acid serves as a moisturizing factor, hyaluronic acid improves skin hydration and elasticity, and sphingomyelinase generates ceramide for skin barrier function.

In addition, lactic acid, acetic acid, and diacetyl are reported to have a preservative effect. However, claims for effects such as skin protection and cellular structure or function may render a product a drug under the FD&C Act, not a cosmetic, as noted in the introduction. Refer to Conclusion and future directions section for further discussion of product regulations [51].

Nevertheless, scientific evidence is generally lacking to support the overall benefits of probiotics in cosmetics. In contrast with the vast amount of literature addressing probiotic effects on GI disorders, research pertaining to probiotics in cosmetics is still in its infancy. The few clinical trials conducted by the cosmetic companies to address benefit have had limited value because the studies were performed either *in vitro* or only with a small sample size [1,58]. The use of probiotics in personal care products are anticipated to continue; collaboration between researchers, industries, and regulatory agencies is instrumental in making advances in this field [8].

Probiotics and oral care

Good hygiene has been recognized as the most effective approach to control oral diseases. In developed countries, dental caries in children are preventable by proper oral hygiene, diet, and fluoride exposure. People worldwide understand that removing dental plaque, by brushing with toothpaste or using chewing sticks, is important for oral health [37,40,42].

Applying probiotics to improve oral health is a relatively new area that is gaining momentum in recent years by researching into its effectiveness and safety [37,44,62,64]. Some have followed the traditional GI probiotic approach by ingestion; others have considered applying probiotics to oral care products and hygiene practices to prevent tooth decay and other oral health problems, such as gingivitis and periodontitis [1,64]. Several studies have shown that directly adding probiotics to oral care products or practices had positive effects. For example, probiotic organisms have been included in toothpastes to target *Streptococcus (St.) mutans* responsible for dental caries and plaques around orthodontic brackets [63,65]. Meswak, a plant native to the Middle East that has an inhibitory effect on *St. mutans*, has been used for tooth cleaning in the region. In combination with *Lactobacillus rhamnosus*, it further reduced the level of *St. mutans* in saliva [42]. In another study, including indigenous species of *Streptococcus* in mouthwash reduced the level of pathogens in saliva and subgingival plaques. Because these organisms were part of the normal flora, rinsing regularly did not pose safety concerns [44]. Several studies have indicated that *St. salivarius* was effective in reducing the severity of malodor in individuals with halitosis [40,43].

Companies are working toward adding probiotics to toothpaste and other oral products, such as chewable tablets, gums, and lozenges, to fight tooth decay, gingivitis, and bad breath [3,62,65]. As with skin care products, scientific evidence of efficacy for probiotics in oral products is limited. A few hypothetical mechanisms of action have been proposed; these include guarding oral health by competing for nutrients, preventing pathogens colonization by secreting antimicrobial substances, modulating immune functions, and maintaining homeostasis in the oral cavity [47,65]. Some suggested that probiotics show promise as clinical application for dental caries [1,2]; if taken into effect,more evidence of efficacy will become available in the near future.

Conclusion and future directions

Probiotics continue to expand in applications and market share, and this exponential growth is not likely to subside. However, the biggest shortcoming in the use of probiotics is the lack of scientific evidence and clinical studies for specific health applications [1,52]. Many probiotic claims for food have lost credibility because they were based on preliminary assessments and anecdotal observations, and personal care products are not exempt from the same trends and misconceptions. Furthermore, the beneficial effects touted by industry and others making such claims appear to be strain-dependent [3,5]. Unfortunately, the positive outcomes have been generalized and conveyed to consumers (and even to health professionals) without adequate data [6]. To further complicate the matter, products on the market often contain multiple microorganisms; making the data and deciphering the role of each strain a challenge [3].

Additionally the data on safety, specifically the long-term impact of probiotic organisms on existing microbiomes and overall health, is lacking [3,29]. This raises a concern for young children and those with underlying health conditions who may be at risk of experiencing serious and unexpected consequences [1].

Regulatory requirements are another challenge in marketing personal care products containing probiotics. As mentioned earlier, these products may fall into a number of different product categories (cosmetics, drugs, medical devices, and dietary supplements) that are regulated differently under the FD&C Act, or be regulated as other types of consumer products. For example, drug products must generally either receive premarket approval by FDA through the New Drug Application (NDA) process or conform to a "monograph" for a particular drug category as established by FDA's Over-the-Counter (OTC) Drug Review, while cosmetic products are subject only to post-market surveillance [66].

Worldwide variations in regulatory framework regarding probiotics cause further complications for research and industry. The European Food Safety Authority (EFSA) rejected nearly all health claims for benefits of probiotic bacteria; consequently, companies cannot mention the health benefits of their products based on the probiotic content [3,46]. This action raised concerns among some scientists and clinical investigators that it sent negative messages to consumers and that years of research regarding the benefits of probiotics would thus be wasted. They communicated their objections to EFSA, and requested that EFSA consider a more realistic standard of evidence for these products [67,68]. Other countries may be more lenient in their regulations. For example, Canada recently approved a patented probiotic formula to treat *C. difficile* infections in hospitalized patients. South Africa is proactively reviewing regulations regarding probiotic-containing products to ensure that "the manufacturers… be held responsible for providing the consumer with scientifically sound and legally correct information" [69]. In Asia, the Indian Council of Medical Research came up with a set of guidelines for evaluating an influx of probiotic products into their country [70]. Although Japan has one of the largest functional food markets globally, it considers probiotics as Food for Specified Health Uses (FOSHU) and has approved relatively few products in the category of "foods to modify gastrointestinal conditions" [3,71]. Until recently China has been tolerant of products with various health claims; since the enactment of the Food Safety Law in 2009, regulation has tightened and explicitly required human clinical data. These examples indicate the international community's awareness of the importance of accurate health claims and realize the disparity of various probiotic products. The regulatory framework will undoubtedly become more stringent in the future, and products that lack scientific substantiation for their health claims are expected to be removed from the market [3].

Probiotic GI products, which are leading the way in clinical trials and marketing, can provide important lessons for use of probiotics in personal care products [5]. One example is the guidelines for probiotics in food generated by the Food and Agricultural Organization (FAO) and World Health Organization (WHO). After realizing the lack of consensus on the approach to determine efficiency and safety of probiotics, these international organizations convened to produce a guide that included recommendations on labeling and health claims for food products [72]. This is a resource that the stakeholders of personal care products can leverage while working through the various challenges mentioned above.

Cosmetics, which constitute a major component of the personal care industry, face a unique issue in complying with the definition of probiotics as viable organisms in their products. Under the legal framework of the FD&C Act, there are guidelines on the number of live organisms permitted in products. Some have suggested the term "probiotic" is outdated and have proposed "pharmabiotics" (including inactivated microbiota or its components) as the term is more comprehensive and reflects the nature of products currently on the market [3,5]. However, FDA does not currently have a regulatory definition for "probiotic". A dialogue among stregulatory agencies, research communities, and industries would be beneficial in order to address this issue, as cosmetics affect a large number of consumers.

The current consensus is that probiotics have great potential to contribute to the promotion of human health. Much progress has been made in their application to the GI system; however, scientific evidence from well-controlled studies is lagging behind the rapid rise of personal care products and consumers' interests. Collaboration and harmonization among stakeholders is paramount in moving this field forward. Some effort is already taking place; an example is the National Center for Complementary and Alternative Medicine, which is part of the National Institutes of Health's (NIH) Probiotic and Prebiotic Working Group, a trans-agency effort focused on identifying gaps and challenges in probiotic and prebiotic research [1]. The continued advance in knowledge and data from the HMP enables the development of innovative approaches to utilize certain biomarkers in assessing the effects of probiotics and allows clinical studies to be conducted on a larger scale [3]. Industry should work with researchers and regulatory authorities if they wish to gain credibility for their products by addressing accurate labeling, good manufacturing practices, and rigorous quality control [72]. Because personal care products are an integral part of people's routines and habits, the potential benefits of probiotics, if substantiated, could have a positive impact on human lives.

Disclaimer
The information and conclusions presented in this manuscript do not represent new FDA policy nor do they imply an imminent change in existing policy.

Competing interests
The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	JT	MJH
Research concept and design	✓	✓
Collection and/or assembly of data	✓	✓
Data analysis and interpretation	--	--
Writing the article	✓	✓
Critical revision of the article	✓	✓
Final approval of article	✓	✓
Statistical analysis	--	--

Publication history
Editor: Janet Donaldson, Mississippi State University, USA.
Senior Editor: Ester Grilli, University of Bologna, Italy.
Received: 26-May-2015 Final Revised: 09-Jul-2015
Accepted: 20-Jul-2015 Published: 25-Jul-2015

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Citation:
Huang M-CJ and Tang J. **Probiotics in personal care products**. *Microbiol Discov*. 2015; **3**:5.
http://dx.doi.org/10.7243/2052-6180-3-5