The Effect of Cleansers on the Skin Microbiome




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>> Human skin is a complex ecosystem with various microenvironmental conditions, and thus, skin microbial communities are very diverse and complex.[1] Skin structures, such as hair follicles, sebaceous glands, eccrine and apocrine sweat glands, as well as subepidermal skin compartments, provide distinct biological niches that are colonized by their own unique skin microbiota.[2] The current understanding is that most of these skin microbes are harmless or commensal organisms that play essential roles in inhibiting colonization by pathogenic microbes or modulating innate and adaptive immune systems. A disruption in the microbiome can create inflammation, irritation, dry, itchy skin, dermatitis, and even worsen some skin diseases. The importance of the microbiome in the GI (gastrointestinal) tract has been well established, and we are now learning about the importance of the microbiome for skin health. By reviewing cleansers and their mechanism of action on the skin's microbiome on the particular skin environment, we can gain insight on initial treatment of skin conditions and hopefully pathways for improvement of skin diseases.

CLEANSERS AND MICROBIOME

Cleansing requires a delicate balance between skin hygiene and stratum corneum barrier damage. The act of cleansing is a complex physical and chemical interaction between water, detergent, and the skin.[3] Products can shape specific skin microbial communities by changing their chemical environment.[3]

During cleansing, micelles are created with external hydrophilic groups surrounding an internal lipophilic pocket. These micelles can surround oily substances, such as sebum, dispersing the oil in water for removal and rinsing. Cleansers are effective at maintaining skin hygiene and a healthy biofilm but may cause skin barrier damage, worsening eczematous skin disease.[3] This arises because surfactants cannot distinguish between lipophilic skin debris requiring removal and the lipophilic intercellular lipids required for barrier maintenance.

The chemical soap component that causes barrier damage is the high charge density of the carboxyl head group, which promotes strong protein binding. This characteristic ensures excellent cleansing and removal of protein debris but damages the stratum corneum proteins, denatures enzymes, and alters corneocyte water-holding capability.

Barrier damage is also influenced by cleanser pH. For example, soap typically has an alkaline pH of 10-11, producing skin protein swelling and ionization of the lipid bilayers. Thus, synthetic detergents with more acidic to neutral pH of 5-7 minimize barrier damage and are the preferred cleanser for individuals with dermatologic diseases. High pH causes swelling of the stratum corneum, which allows unwanted deeper penetration of the soap into the skin, possibly causing irritation and itching. The soap also binds to stratum corneum proteins further inducing swelling and hyperhydration of the skin. Following the completion of washing, the excess water evaporates leading to skin tightness and dryness because the soap binding reduces the ability of the skin proteins to hold water. Cleansers are too often harsh and can result in excessive drying of the skin, which leads to overcompensation by the oil glands and ultimately to more oil on the surface of the skin.[4] Cleansers can then disrupt the stratum corneum which, in turn, perturbs the environment where good commensal bacteria thrive.

Keratinocytes continuously sample the microbiota colonizing the skin surface through pattern recognition receptors (PRRs), such as Toll-like receptors (TLRs), mannose receptors and the nucleotide binding oligomerization domain like (NOD-like) receptors. These receptors recognize pathogen-associated molecular patterns (PAMPs) including flagellin and nucleic acids, as well as lipopolysaccharide from Gram-negative bacteria, peptidoglycan and lipoteichoic acid from Gram-positive bacteria, and mannan and zymosin

from fungal cell walls. The activation of keratinocyte PRRs by PAMPs immediately initiates the innate immune response, resulting in the secretion of antimicrobial peptides (AMPs), cytokines and chemokines. Despite being constantly exposed to large numbers of microorganisms, the skin can discriminate between harmless commensal microorganisms and harmful pathogenic microorganisms.[5]

Dysregulation of the skin immune response is apparent in several skin disorders (for example, psoriasis, atopic dermatitis (AD), and contact dermatitis), but how dysregulation affects and/or results from changes in the microbiota remains unclear. AD lesions are characterized by low levels of AMP production as compared with levels from normal skin. This is in sharp contrast to psoriatic lesions, which produce abundant quantities of AMPs and are characterized by an activated innate immune response.[2] Therefore, there needs to be a fine balance on the skin microbiota environment in order to not dysregulate the skin's immune response.

The stratum corneum is a layer supporting a complex ecosystem, a stratum ecologica. Skin barrier structure and function is essential to human health. It is well known that there is a balanced interplay between the host and the bacterial populations which is continuously exposed to host, intrinsic factors as well as environmental, and other extrinsic factors. A sustained imbalance in the microbial community composition, defined as dysbiosis, characterizes several skin disorders such as eczema, allergies, dandruff, or acne. Nevertheless, because of the huge inter- and intra-individual variability in skin microbiota composition, a healthy microbiota depends on the particular skin site.[7] An investigation carried out in 2013 by Fitz-Gibbon et al[8] highlighted that, rather than the entire species, certain *Cutibacterium* strains have been shown to be responsible for the occurrence of acne while other strains were not. Several studies suggest microbial diversity being a requisite for healthy skin. For example, *Staphylococcus aureus* colonization in AD patients was predominant in about 90 percent of the cases and this imbalance was associated with a loss of skin microbiota diversity. This suggests that dysbiosis with increased *Staph Aureus* colonization is an important factor exacerbating the pathogenesis of AD (Fig. 1).[7] Depending on the skin site, certain bacteria are commensal or pathogenic. The state of dysbiosis is typical of some chronic inflammatory skin diseases such as psoriasis, rosacea, or acne. When the skin barrier is weakened such as occurs in disease states or injury, skin pH raises, and water loss dramatically increases. Skin flaking and keratinocytes apoptosis also occur. All these changes are accompanied by a sustained inflammation with involvement of immune cells such as Langerhans cells, dendritic epidermal T cells (DETC), neutrophils, macrophages, and mast cells. Interestingly, it becomes more and more evident that the microbiota composition is affected by these biochemical and biophysical changes resulting in a decreased microbial diversity and increased colonization by pathogenic bacteria, as previously discussed, *Staphylococcus aureus* forming biofilms in skin disorders such as AD.[9]

It is globally accepted that commensal bacteria might become pathogenic in particular conditions. *Staphylococcus epidermidis* is widely classified as a bacterium beneficial to skin health. It is known to inhibit *Staphylococcus aureus* biofilm formation by production of the serine protease glutamyl endopeptidase (Esp) and also stimulates keratinocytes to produce antimicrobial peptides resulting in *Staph aureus* killing. However, despite these multiple beneficial functions, *Staph* epidermidis is still classified as one of the most important pathogens in nosocomial infections associated with catheters and other medical implants.[10] However, environmental stresses and other factors can cause a shift of our skin microorganisms from commensal to pathogenic, resulting in inflammation, itching, scaling, and other clinical signs of imbalance between our skin and the microbiota.

Understanding both temporal variations of the skin microbiome and chemistry is crucial for testing whether alterations in personal habits can influence the human skin ecosystem and, perhaps, host health. One study in *BioMed Central Biology*[6] showed that when the hygiene routine is modified, the skin microbiome can be altered, but that this alteration depends on product use and location on the body. The gut microbiome has unique responses to dietary changes depending on the individual and so too, the responses are individual-specific for the skin. A recent study carried out by Bouslimani et al[6] evaluated the influence of personal care products on the skin in terms of microbial and molecular composition. The key findings were the following: 1.) Molecules associated with personal skin and hygiene products last on the skin for weeks after their first use despite regular showering. 2.) Molecular and bacterial diversity were altered following beauty products usage. Some beauty product ingredients likely promote or inhibit the growth of specific bacteria: for example, lipid components of moisturizers could provide nutrients and promote the growth of lipophilic bacteria such as *Staphylococcus* and *Propionibacterium* (*Cutibacterium*).

The skin surface varies topographically owing to regional differences in skin anatomy and, according to culture-based studies,[2] these regions are known to support distinct sets of microorganisms. Some regions of the skin are partially occluded, such as the groin, axillary vault and toe web. These regions are higher in temperature and humidity, which encourages the growth of microorganisms that thrive in moist conditions (for example, Gram-negative

TABLE 1. SKIN PROBLEMS SUSTAINED THAT RELATE TO MICROBIOME IMBALANCES[2,11,12]

Condition:	Examples of Microorganisms Involved:
Acne	P acnes, S epidermis
Atopic Dermatitis	S aureus
Rosacea	B oleronius, S epidermidis
Dandruff	Malassezia species
Psoriasis-Scalp	Malassezia
Psoriasis- Skin	Candida, S aureus
Diaper Rash	C albicans
Bear Irritation	Tinea, S aureus, Candida

bacilli, coryneforms and *S aureus*). The density of sebaceous glands is another factor that influences the skin microbiota, depending on the region. Areas with a high density of sebaceous glands, such as the face, chest, and back, encourage the growth of lipophilic microorganisms (for example, *Propionibacterium spp*. and *Malassezia spp*.). See Table 1.[2,11,12] Therefore depending on the patient's skin condition (oily versus dry etc) and skin location, the treatment will depend on what bacteria to target and what cleanser will be appropriate to not disrupt the commensal bacteria.

Various types of dermatoses and so-called "sensitive skin" are thought to be related to a dysfunctional skin barrier. This could be due to a number of conditions, such as AD, senile itch, eczema, allergic contact dermatitis, and cosmetic intolerance syndrome. A well-formulated cream for sensitive skin can enhance barrier repair, increase the water-holding capacity of the skin, and optimize healing. In one study, a larger population of female participants with sensitive skin, a gentle fragranced foaming cleanser with hydrophobically modified polymers (HMPs) to surfactants to create a polymer/surfactant complex that is functional, aesthetic, and mild was as effective as a leading dermatologist-recommended, fragrance-free, gentle, non-foaming cleanser.[13] HMPs interact with the hydrophobic tails of the surfactant, forming larger surfactant structures that cannot readily penetrate the stratum corneum. The binding of the HMPs also lowers the surfactant concentration in the micelles formed during cleansing decreasing protein damage. Finally, HMPs provide for increased foam formation, a cleanser trait consumers find desirable. This method basically increases cleanser mildness by reducing skin permeability.[13]

Data demonstrate that a proprietary combination of ceramide PC-104, palmitamide MEA, glycerrhetinic acid, and grape seed extract in a glycerin, dimethicone, and petrolatum vehicle was effective in reducing signs and symptoms of mild to moderate AD and other types of pruritic dermatoses (e.g., senile itch, cosmetic intolerance syndrome) in children and adults.[13]

Therefore, simply adding ceramides, fatty acids, cholesterol, and/or triglycerides to a cleanser hoping to replenish some of the components of lost intercellular lipids removed during cleansing may be only partly helpful. The problem with this approach is the short contact time between the cleanser and the skin. Cleansers should remain on the skin for as short a period as possible to minimize stratum corneum protein damage; however, this short contact does not allow time for ingredients to penetrate and remain in the skin. Further, since ceramides can penetrate into the stratum corneum from a cleanser, then possibly so too would the surfactants cause accelerated barrier damage. Not only is it then critical to choosing an appropriate cleanser but repairing the epidermis after cleansing with the proper moisturizer. There are trials[14] with cleansers using Sophorolipid, a glycolipid produced from fermentation that has prevented the overgrowth of candidae albicans in clinical trials, as well as a biosurfactant that is produced by bacteria, yeast, and fungi. Other companies are adding prebiotics to their skin care. Prebiotics are nutrients for bacteria that help to create a healthy environment for the skin microbiome.

CONCLUSION

We hope this review provides an overview of the current knowledge of the skin microbiome as well as the future challenges for the skincare industry. As discussed, imbalances in the skin microbiota composition (dysbiosis) are associated with several skin conditions, either pathological such as eczema, acne, allergies, or dandruff or non- pathological such as sensitive skin, irritated skin, or dry skin. Therefore, developing hygiene and/or beauty products that preserve or restore the natural, individual balance of the microbiota represents a novel opportunity not only for dermatologists treating skin disorders but scientist designing skincare cleansers and moisturizers to advance the individual's skin microbiome. Furthermore, skin sampling of an individual's skin microbiome before suggesting or prescribing treatments may be the future for designer skincare.

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