Types of Indigenous Skin Bacteria and Their Effects

Subjects: Dermatology

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The skin is inhabited by about 10^2–10^7 cells/cm^2 and 1000 species of commensal bacteria, fungi, viruses, and other microorganisms. In particular, metabolites such as fatty acids and glycerol released by indigenous skin bacteria have been reported to have functional properties for the health of the skin. Therefore, skin-domesticating bacteria and the metabolites derived from those bacteria are used in many skincare product ingredients and function as probiotic cosmetics.

Keywords: fermentation ; skin microbiota ; cosmetics

1. Structure of Skin

The skin covers our entire body and is said to be the “largest organ of the human body”. It covers an area of about 1.6 square meters (adult) and comprises approximately 15–16% of the body weight [1][2]. The skin consists of three layers (epidermis, dermis, and subcutaneous tissue) and skin appendages.

The epidermis, the outermost layer of the skin, has an average thickness of 0.2 mm and consists of four layers: basal layer, spinous layer, granular layer, and stratum corneum (five layers, including a transparent layer only on the palms and soles) ([3], pp. 13–20).

The basal layer, the lowest layer of the epidermis, is the only layer of epidermal cells capable of cell division. New cells are created in this layer and are pushed up to the upper layers through repeated cell division. The cells in the stratum corneum are eventually exfoliated and peeled off. This cycle is called turnover and when it is in order, healthy skin is maintained [4]. In addition, the basement membrane, which exists in the lowest part of the skin, serves as a connection with the dermis and exchanges waste products and nutrients. The spinous layer forms the thickest layer (8–10 layers), and comprises the majority of the epidermis. On the lower side, polygonal cells become flattened as they ascend. The stratum granulosum consists of one or two flattened layers of cells; the keratohyalin granules present in this layer prevent ultraviolet light from entering the skin and being absorbed deeply. The stratum corneum, the outermost layer of cells, serves as the boundary between the inside and outside of the organism, preventing bacteria, UV rays, and other chemicals from entering the body from the outside and retaining water within the body [5][6].

The dermis averages 1 to 2 mm in thickness and consists of three layers: papillary layer, subpapillary layer, and reticular layer. Blood vessels, nerves, and lymphatic vessels pass through it, with mast cells related to inflammation and histiocytes related to immunity also present. A jelly-like matrix called hyaluronic acid is laid down between the fibrous proteins called collagen and elastin. Since blood vessels are not distributed in the epidermis, capillaries in the dermis provide nutrients, oxygen, and water to the epidermis, carry away waste products and carbon dioxide, and support cell division [5], ([6], pp. 27–29).

The thickness of the subcutaneous tissue averages from 4 to 9 mm. It is mostly composed of adipose tissue, also known as subcutaneous adipose tissue. Connecting the skin to muscles and bones, it acts as a buffer to protect them from external forces. It also functions to metabolize energy and maintain body temperature ([6], pp. 29–32).

Skin appendages include hair, hair follicles, sweat glands, and sebaceous glands [5], ([6], pp. 29–32).

2. Types of Indigenous Skin Bacteria and Their Effects on Health

2.1. Indigenous Skin Bacteria

The human skin harbors approximately 10^2–10^7 cells/cm^2 per person and 1000 species of bacteria, fungi, viruses, and other microorganisms [2][7]. The skin is in direct contact with the outside world. Therefore, aerobic bacteria are mainly found on the surface layer, while anaerobic bacteria inhabit the hair follicles and sebaceous glands as commensal bacteria. *S. epidermidis*, *S. aureus*, and *Micrococcus*, which are aerobic, and *Cutibacterium acnes* (*anaerobic bacilli*) are the most widespread [8].

Although less abundant, the fungi *Malassezia*, *Candida*, and *Trichophyton* are also present.

Representative indigenous skin bacteria include *S. epidermidis*, *Micrococcus* genus bacteria, *C. acnes*, and a type of yeast [9].

2.2. Distribution of Indigenous Skin Bacteria

The composition of the microbial layer of human skin varies by site, as UV exposure, pH, temperature, moisture, sebum content, and topography differ depending on the location. The types of microorganisms indigenous to the skin were recently investigated by the U.S. National Human Genome Research Institute [10]. The results showed that the microorganisms with the highest abundance were bacteria. In seborrheic areas (forehead, back, etc.), bacteria of the genus *Cutibacterium*, such as Acne bacillus, were found, while in dry areas (forearms and buttocks), bacteria of the phylum *Actinobacteria*, *Proteobacteria*, *Firmicutes*, and *Bacteroidetes* were most abundant. In moist areas (axillae, groin, navel, and soles), bacteria of the genera *Staphylococcus* and *Corynebacterium*, including *S. epidermidis* and *S. aureus*, were detected.

In addition, across the entire skin body, the four major phyla of commensal bacteria were *Actinobacteria*, *Proteobacteria*, *Firmicutes*, and *Bacteroidetes*, while at least 19 phyla were found to be part of the bacterial skin microbiome.

2.3. Classification of Skin-Associated Bacteria (Favorable, Hazardous, and Opportunistic Bacteria)

These commensal skin bacteria form a stable flora by using cutaneous lipids and amino acids on the skin as a source of nutrients for their growth, and by establishing a competitive and harmonious relationship among themselves. Microorganisms in the skin flora are classified into those that contribute to health (favorable bacteria), those that contribute to disease (hazardous bacteria), and those that can be either (opportunistic bacteria) depending on the situation.

The representative good bacteria are *S. epidermidis*. In recent years, the use of *S. epidermidis* in the development of basic cosmetics tailored to individual skin conditions has attracted attention [11][12]. Forming indigenous flora on the skin surface and in the nasal cavity, *S. epidermidis* is known to produce glycerol and fatty acids by feeding on sebum and sweat (alkalinity) [12][13]. Glycerol moisturizes the skin and enhances the barrier function, while fatty acids keep the skin slightly acidic and prevent the growth of *S. aureus* by producing antimicrobial peptides [12][13]. Thus, *S. epidermidis* provides moisture to the skin, enhances the barrier function, and protects the skin from the proliferation of *Staphylococcus aureus.*

The typical hazardous bacteria are *S. aureus*. Present on skin surfaces and in pores, *S. aureus* is carried by about 30–50% of normal healthy adults [14].

Although normally harmless, it is highly pathogenic among staphylococci and is an important human bacterial pathogen responsible for a variety of conditions, ranging from asymptomatic inflammation to severe infections causing pneumonia, endocarditis, and sepsis [14]. Preferring an alkaline environment, it proliferates when there is a low level of beneficial bacteria that maintain the skin's mild acidity, causing itching, rough skin, and atopic dermatitis. In addition to their tendency to settle on the skin of atopic dermatitis patients, the enterotoxins (toxins in the bacteria) produced by the bacteria exacerbate skin inflammation, reduce the skin barrier function, and are said to be a contributing factor to the worsening of symptoms [15][16]. In addition, if the injured skin is left untreated, it can fester and worsen. Thus, *S. aureus*, although harmful to skin health when overabundant, is necessary to maintain a balance of commensal bacteria.

A typical opportunistic bacterium is *C. acnes*. Previously, it was called *Propionibacterium acnes* because of its propionic acid-producing ability. *C. acnes* is an anaerobic bacterium that can hardly proliferate in an oxygenated environment. It exists in pores and sebaceous glands where there is no oxygen, and because it prefers lipids, it is especially abundant in the fat layer at the back of hair follicles (pores) in the skin, where sebum secretion is high [17][18]. It feeds on sebum to produce propionic acid, fatty acids [19], and keep the skin surface slightly acidic, thereby inhibiting the growth of pathogenic bacteria that adhere to the skin. Acne bacilli are generally considered to be the cause of acne, but if they do not proliferate excessively, they are good for the skin. However, when pores become blocked due to increased sebum production, epidermal keratinization, or inflammation, acne rods proliferate excessively, causing inflammation and leading to acne. In healthy skin, acne rods play a beneficial role in the skin microflora of the sebaceous gland unit of the hair follicle, but when they proliferate excessively, they become the causative agent of acne.

From the above, it is thought that indigenous skin bacteria do not normally exhibit pathogenic properties, but rather exert a kind of barrier function that prevents the entry of pathogens from the outside. However, when the barrier is broken or the balance between symbiotic organisms and pathogens is disrupted, skin and systemic diseases may occur.

In recent years, products have been developed in the cosmetics field that assist in the treatment of skin diseases by selectively sterilizing, eliminating, or inhibiting the growth of specific bacteria among these indigenous skin bacteria.

2.4. Health Functionality of Metabolites Produced by Indigenous Bacteria

It has been shown that indigenous skin bacteria grow on the components present on the skin as a source of nutrients. Research suggests that their breakdown products and metabolites have a health-related functionality, although epidemiological evidence is still to be established. For example, *C. acnes* secretes short-chain fatty acids (SCFA) and glycerol as products of abundant triacylglycerol fermentation in sebum. The major SCFAs are acetic acid, propionic acid, and butyric acid. Although the role of propionic acid in the skin is not yet understood, it maintains the pH of follicular sebaceous-gland hair follicles at an acidic level and limits the growth of *S. aureus* (such as community-acquired methicillin-resistant *S. aureus*) [20].

Glycerol has strong hygroscopic properties, which allow it to retain moisture down to the skin's stratum corneum and strengthen the skin's barrier function [21]. Therefore, *S. epidermidis* and *C. acnes* utilize endogenous carbon sources such as glycerol to produce SCFAs, such as acetic acid, butyric acid, and lactic succinate [22][23][24]. SCFAs have been reported to exhibit antibacterial activity [25] and inhibit the growth of *C. acnes* [22]. In particular, succinic acid effectively inhibited the growth of *S. acnes* in vitro and in vivo [22].

Previous studies demonstrated that butyrate from glycerol fermentation of *S. epidermidis* ATCC 12228 can downregulate ultraviolet (UV)-induced IL-6 secretion via activation of short-chain fatty acid receptor 2 (FFAR2) [26]. Butyrate has also been shown to function as an inhibitor of histone deacetylase (HDAC), which confers anti-inflammatory activity [27].

Lactate produced by epidermal bacteria inactivates HDAC11 on monocytes in the dermis of the skin, thereby activating HDAC6 and the production of IL-10, which suppresses immunity [28]. Lactic acid is also one of the natural moisturizing factors (NMF) of the stratum corneum skin barrier, which helps to hydrate the skin surface and maintain a slightly acidic pH [29].

Free fatty acids in sebum are produced by the hydrolysis of triglycerides by lipases of indigenous skin bacteria. Sebum contains a variety of free fatty acids; oleic acid, linoleic acid, and linolenic acid are said to have antifungal effects on *Trichophyton rubrum*, while lauric acid and oleic acid inhibit the growth of *S. epidermidis* [30].

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