WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 7, 638-652. Review Article ISSN 2277– 7105

THE EFFECT OF PRESERVATIVES USED IN COSMETICS ON SKIN MICROBIOME, A REVIEW

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Article Received on
27 April 2020,

Revised on 18 May 2020,
Accepted on 08 June 2020,

DOI: 10.20959/wjpr20207-17830

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ABSTRACT

The biodiversity of the human skin acts as an indicator of skin health. The skin microbiota acts as the first line of defense against bacterial attacks. Bacteria are one of the dominant group of microbiota present on the human skin. The chemical ingredients in cosmetic formulations and the preservatives used to inhibit microbial contamination in the product either during manufacture, when in use or during its lifespan may be responsible for a change in the composition of the skin microflora. The other factors that affect the skin health are its pH, moisture present on the skin and the trans-epidermal water loss. This study includes the effect of commonly used preservatives in cosmetics on the composition of the skin microbiota. The main aim of this review is, to create awareness about the possible changes caused by preservatives used in personal care products of daily use on the skin microbiome.

KEYWORDS: Skin microbiota, skin microbiome, preservatives, personal care cosmetics, antimicrobial activity.

INTRODUCTION

Cosmetics are defined as mixtures, products or any substance that are applied externally to the human body.[1] They are applied on the skin or the epidermis, lips, hair, nails, etc. or as products intended to keep the oral cavity including the teeth and the mucous membrane lining the mouth clean and smelling fresh. Some cosmetic products are supposed to impart perfume while others are used to change the appearance of the wearer, cosmetics are also used for protecting the skin.[2]

Structure of the Skin

The skin is the largest organ of the human body. The skin covers a surface area of 1.6 m^2. The thickness of the skin is depends on the age, sex and location of the individual. The female skin is thin as compared to the males. The outer layer of the skin is made up of the epidermis, the dermis and the subcutaneous tissues.[3] The skin's environment is composed of 1.8m^2 of habitat which includes different microorganisms present in the folds, invaginations and specialized grooves that support them.[4] The skin acts as a first line of defense or a physical barrier, protecting us from any possible damage by microorganisms or environmental pollution. The skin serves as an intermediate membrane between the outside environments and its surface, and is helped by the presence of the collection of microorganism like bacteria, fungi, molds and viruses.[5-11]

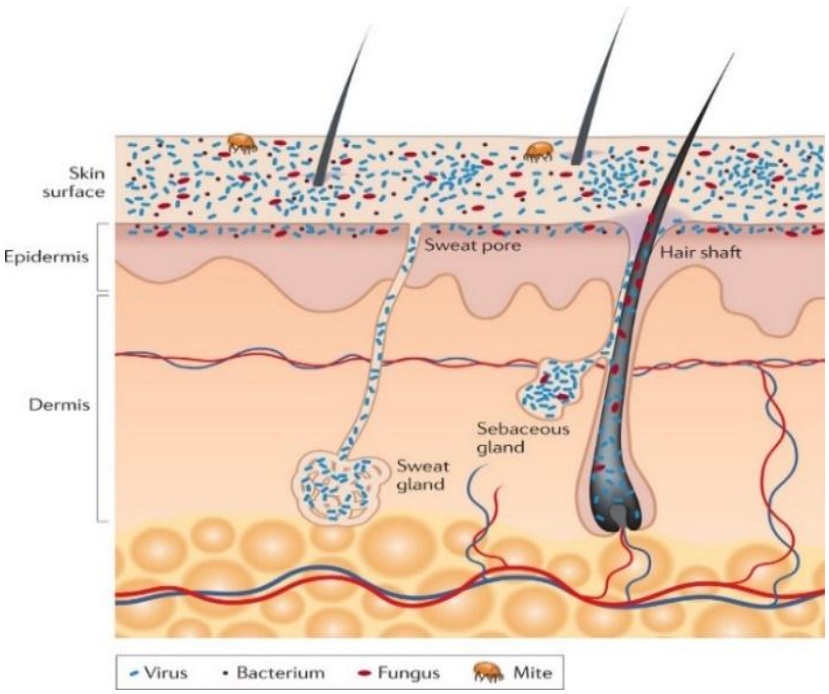

Fig. 1 Structure of Skin.[4]

Skin Flora

In a healthy human being, microorganisms are not found in the internal tissues, e.g. blood, brain, muscle, etc. However, the external tissues, like the skin and mucous membranes, are constantly exposed to the environment and organisms in it are readily colonized by various microorganisms. The mixture of organisms regularly found at site is referred to as the normal flora or "indigenous microbiota". The normal flora of humans consists of a few eukaryotic fungi and protists, but bacteria are the most numerous and obvious microbial components of the normal flora.[12]

Table 1: Bacteria commonly found on the surfaces of the human body.[12]

Bacterium	Present on Skin
Staphylococcus epidermidis	++ (100% present)
Staphylococcus aureus	+ (commonly found)
Streptococcus pyogenes	+/-(Rarely found)
Corynebacteria	++ (100% present)
Mycobacteria	+(commonly found)

Staphylococci and *Corynebacteria* can be found all over the surface of the skin. While S*taphylococcus epidermidis* adapts easily to the diverse environments of the human body. *Staphylococcus aureus* is a potential pathogen and is the primary cause of bacterial disease in humans. Many of the normal flora are either pathogens or opportunistic pathogens. *Pseudomonas aeruginosa* is known to causes Gram-negative infections and *Corynebacteria*, and certain related propionic acid bacteria may be the cause of acne. *Streptococcus mutans* is the primary bacterium causing plaque leading to the formation dental caries.

Microbiota

Microbiota refers to the specific microorganisms present in the particular environment. Microorganisms like bacteria, viruses, fungi present in specific environment make up the microbiota of that environment. This means that different people have different composition of microbiota. This difference depends upon the area or region of the body that the sample of microbiota are collected. The microbiota from the gut and that present on the skin can be different in the same individual.

Microbiome

A microbiome refers to the collection of genomes of all the microorganisms found in a particular environment. All living beings including humans, plants, and other animals have microbiomes. The microorganisms can be similar on the entire living being or may have different compositions depending upon its location on the living being. This means there is extreme variation in the composition of the microbiome present on the same human or among different humans.

Preservatives

These are substances added to cosmetic preparations to slow down the growth of microorganisms and to prevent the deterioration of the manufactured product during its journey from the manufacturing floor to the complete use of the product by the consumer.[13] They also ensure that the consumer is protected from any possible infection. Many of the raw

materials used in cosmetics are added to the aqueous phase of the emulsion and hence susceptible to microbial attack and product degradation. Some commonly used ingredients like the esters, hydrocarbons or the soluble polymers provide nutrition with the carbon and nitrogen present in them which helps the growth of microorganism. This can happen at any of the stages encountered from manufacture to actual use by the consumer. Adequate care needs to be taken to make sure the product is free of any contamination during its lifecycle from the production floor till it reaches the end user. To achieve this objective the cosmetic products generally contain one of the most commonly used preservative ingredients like the alkyl esters of P-hydroxybenzoic acid (parabens), due to their strong stability, lack of volatility and low irritability,[14] benzoic acid, salicylic acid, sorbic acid, dehydroacetic acid and phenoxyethanol. The contamination of the product can be physically determined as the change in opacity, change in pH, colour and appearance of the product. The toxins secreted by the microorganisms not only affect the physical changes in the product but can also be harmful to the skin. The commonly found microbes in cosmetic products are the Gram +ve and gram –ve bacteria, yeast and mold. Some microbes are harmless, but some like *Staphylococcus aureus*, *Pseudomonas aeruginosa* are greatly harmful to human beings.

Mechanism of Preservative Action

Different preservatives act differently in inhibiting microbial growth. Some may interfere with the fatty acid metabolism by the microorganism while others may disturb the biological functions of the cell by associating with the cell wall of the bacteria still others may cause leakage of the contents of the microbial cell and thus destroy them. Some preservatives may interfere with the metabolism, inhibit respiration or have a direct effect on the enzyme system of the microorganism.[15]

Causes For Skin Allergies

The human gut microbiome in developed countries has undergone a catastrophic loss in microbial diversity due to exposure to Western world practices. A rapid increase has also been observed in food allergies in the last 75 years.[16] Similarly, it is observed in the last 5–10 years that the rate of deterioration has accelerated even in the case of skin microbiome,[17-25] leading to it being termed as a “skin allergy epidemic”. Multiple factors like the environment also contribute to this, but it is also been attributed to the use of synthetic additives in cosmetics.[26-31] The over exposure of normal, Western skin to cosmetics, soap, showering/washing, antibiotics, etc.[32] under the hygiene routine, does standup as one of the

reasons leading to the altered natural microbiota environment of human skin, especially in the developed world.[19,33-39] Natural ingredients found in nature, used in products, are seen as "friends" for the skin's natural environment unlike synthetic ingredients, which has been used in the last 60 years of their 200,000 years of existence.[19] This alteration, in many cases, has been linked to decrease in immunity to resist diseases and infection.[35,40,41] There is a complete lack of conclusive evidence which can link a particular dominating type of bacteria with skin health or disease, as humans possess a high intra- and interpersonal variation in skin microbial composition[18,42-44] where each individual has a "virtually unique microbiota".[19,45,46]

Role of Skin Microbiota

The majority of microbiota which are found on the surface of the skin are harmless or beneficial. Their presence is important as they act as a defense for the host. The relationship is "mutualistically symbiotic". On the contrary it is observed that pathogenicity only occurs when the skin's ecosystem is disturbed, and diversity of the microbiome is decreased as against the common belief that some microbes are inherently harmful. This deviation of the skin's microbiome, or "dysbiosis", is found to be responsible for many skin conditions.[47] Dysbiosis and decreased microbial biodiversity of the skin microbiome has been linked with many diseases, including acne, eczema,[48] dermatitis,[18] rosacea,[49] Malassezia folliculitis,[50] inflammation,[51] psoriasis,[52] general allergies,[53] sunburn,[54], athlete's foot and ringworm,[55] wound healing,[56] etc.

Probiotics and microbiome

In the early 20th century, Elie Metchnikoff introduced the concept of probiotics which postulated that ingested microorganisms could give health benefits for humans.[57] Probiotics may contain some friendly or helpful bacteria of the same or similar to species that already reside in the human body. The World Health Organization has defined probiotics as live microorganisms that, when administered in adequate amounts, confer a health benefit.[58]

The use of Soaps, makeup, and skincare products (e.g., moisturizers) for personal hygiene is one of the environmental factor that has a direct effect on the skin's microbial flora. The use of such products not only alters skin conditions but this in turn may influence the types of microbes residing on the skin. In the past decade many studies regarding the role of probiotics in treating gastrointestinal (GI) disorders have been carried out. 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.[57]

Probiotics and skin

Some industrial personal care products ranging from topical applications (e.g., body lotion, anti-aging serum, soap, aftershave, wipe) have certain "natural or synthetic actives" that work on the same lines as probiotics to help enhance the beauty as well as the function of the skin. There is no scientific evidence yet to support the overall benefits of probiotics in cosmetics.[59]

Table 2: Different types of cosmetic products having antimicrobial effects.[1]

Type	Product	Use	Active ingredient	Acts on
Face care products	Acne products & antiseptic cuticle treatment	Skin care; Cleaning and anti-acne treatments	Benzalkonium chloride	*Staphylococcus aureus, Staphylococcus epidermis, Propionibacterium* acnes
Skin care products	Antibacterial soap bars, Disinfectants & Antibacterial wipes	Cleaning and bacterial reduction	Alcohol, triclosan, natural ingredients and glycerin, Benzalkonium chloride	*Staphylococci, Mocrococcus, Corynebacterium sp., Streptococcus*
Leave-on Skin product	Deodorants	Inhibits bacterial metabolism responsible for the sweat degradation and body odor	Aluminum chlorohydrate, alcohol, triclosan, chlorhexidine	*Staphylococci and diphtheroids of the Corynebacteriaceae* family
	Antiperspirants	controls sweat and eliminates the bacteria responsible for body odor	Aluminum chlorohydrate, aluminum salts, zirconium-aluminum tetrachlorohydrex glycine complex	*Staphylococci and diphtheroids of the Corynebacteriaceae* family
Oral care products	Mouthwash	Prevention of bacterial growth and plaque formation	Alcohol &triclosan or alcohol &chlorhexidine	*Protobacteria, Actinobacteria,Spirochaetes*
	Toothpaste	Prevention of bacterial growth and plaque formation	Triclosan, chlorhexidine, natural extracts	*Protobacteria, Actinobacteria,Spirochaetes*
Rinse off hair product	Antidandruff shampoo	Reduces Pityrosporum; Inhibits growth of yeast and stops adhering of the dead cells to the scalp.	Zinc pyrithione, salicylic acid, imidazole derivatives, glycolic acid, steroids, coal tar and sulfur derivatives, piroctone olamine	*Genus Malassezia*

Effect of Preservatives on The Skin Microbiota

A study was conducted by Chintha Lalitha, P.V.V.Prasada Rao to study the changes on skin microbiota, to define the role of preservatives used in cosmetics and to determine the safe optimum concentration to be used in formulations to reduce its effect on skin flora as well as to reduce the risk of side effects.[60]

Bacteria from different skin donors was isolated and inoculated on Nutrient Agar. On identification of its cultural and biochemical characters test of its efficacy as antimicrobial and actual concentration used was performed using Kirby-Bauer's method and HPLC respectively. Efficacy of such preservatives in skin creams was tested using PET and USP methods. Microbial numbers (CFU/ml) were determined and compared against blank samples. Also challenge test with combination of preservatives for the testing of *Pseudomonas aeruginosa, Staphylococcus epidermidis, and Micrococcus luteus* were included. Effect at different pH were studied.

It showed various bacteria like *Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus saprophyticus, Staphylococcus sp., Bacillus cereus, Bacillus subtilis, Corynerbacterium sp.* and *Micrococcus lutes* were present in colonies. Biochemical characters of the identified bacteria were also carried out.

Antimicrobial Activity (AMA) of personal care products on skin isolates was done to ascertain their efficacy when applied topically in restricting the skin microbiota. The products were analyzed for their preservative compounds and found that preservatives at very lower concentrations are used to maintain their stability and reduce the spoilage without showing any inhibitory effect on the skin isolates.

The Minimum Inhibitory concentrations of the commonly used preservatives were determined.

The organic acids were also studied for the effect of pH on their efficacy to calculate the optimum dose of organic acids for the three test organisms at pH 5.5 in the personal care products like shampoos, face wash and other washing products and growth patterns of the three organisms were observed with the organic acids at pH of 5.5.

From the above it was concluded that, the antimicrobial activity with the three test organisms at various concentrations and time periods was proved by the preservatives. Also that a

combinations of preservatives are more effective than individual preservatives used at higher concentrations and the fact that lowering of pH to 5.5 in personal/skin care products not only addresses the reduction of the microbial growth but also reduces the pH of the skin to recommended levels by US and EU pharmacopeia.

Another study was conducted by Chintha Lalitha, P.V.V.Prasada Rao on three products; Talcum powder, deodorant spray and fairness cream to investigate the impact of preservatives on the skin microbiota. The three personal care products were procured from the local markets.[65]

On isolation and identification of skin microbiota done on swabs obtained from participants, it was found that the majority of the study samples were identified as both *Bacillus cereus* and *Bacillus subtilis* among the *Bacillus spp* present on the skin as a contaminant from surrounding soil and air. The remaining colonies belonging to the microbiota of human skin like *Micrococcus spp*., *Staphylococcus spp.*, *Corynebacterium spp*., and *Pseudomonas spp.* were identified.

Three samples were obtained from each participant by using all three products on the facial area and forearm of the participants and drawing swabs before and after use of the product. All colonies were incubated for 24 hrs. at 37^0 C and observed for growth of bacteria.

Test results showed that the topical application of the three personal care products; talcum powder, deo-spray and fairness cream are able to control the colonization of hostile and invading microorganisms on skin microbiota. But when the skin conditions are changed by the use of topical applications of cosmetic products the preservatives may affect a change in the population of skin biota. This change can also change the structure of normal microbiota thus leading to the disease.

DISCUSSION AND CONCLUSION

The human skin is a complex ecosystem comprising of the hosts co-existing with various other microorganisms. When the bacterial ecosystem is balanced and varied, the skin remains healthy. However, several environmental factors like pollution, trans-epidermal water loss, pH of the skin and the use of cosmetics containing preservatives can change this balance. Therefore, the influence of such cosmetics on microbial diversity and their relation to skin diseases has been explored more extensively in recent years. Though there is no concrete

evidence which points that the preservatives used in such preparations cause a change in the ecology of the skin by hampering the balance of the skin microbiota, it is observed that such change in the balance may be one of the reasons for the infections to manifest the skin. Alternatives like essential oils can be used as antimicrobials to reduce the effect of synthetic preservatives in cosmetics. Other cosmetic ingredients including carbohydrates, proteins, and lipids, can promote microbial growth. It has also been shown, that cosmetic ingredients do influence the skin microbiome and that microbial diversity can significantly change with the use of cosmetics.[61-65] However, no systematic studies have been performed to date to establish this.

Further studies need to be initiated to ascertain the effect of preservatives used in cosmetic preparations on the skin microbiota.

ACKNOWLEDGEMENTS

Authors are thankful Principal of LAD College Dr. Deepali Kotwal, Dr. Deepak Wasule Head- Department of Cosmetic Technology, LAD & Smt. RP College for Women, Nagpur for providing facilities and sharing their pulse of wisdom during the preparation of this review article.

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