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 ORIGINAL PAPERS

New insights into Skin Microbiota in Acne Pathophysiology

Gheorghe GIURGIU[1], Manole COJOCARU

[1] Deniplant-Aide Sante Medical Center, Biomedicine, Bucharest, 012371, Romania
[2] Titu Maiorescu University, Faculty of Medicine, Bucharest, 031593, Romania

Corresponding author e-mail: deniplant@gmail.com

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Abstract

The role of skin microbiota in acne remains to be fully elucidated. The emotions of stress (e.g., depression and anxiety), for instance, have been hypothesized to aggravate acne by altering the gut microbiota and increasing intestinal permeability, potentially contributing to skin inflammation. It is increasingly believed that the interaction between skin microbes and host immunity plays an important role in this disease, with perturbed microbial composition and activity found in acne patients. Acne also has close connections with the gastrointestinal tract, and many argue that the gut microbiota could be involved in the pathogenic process of acne. Diet also shapes the gut microbiota. Emerging data suggest that dietary factors (i.e., the Western diet) may influence acne development. Growing evidence indicates that probiotics modify the pathophysiologic factors that contribute to acne, potentially improving patient compliance. Probiotics also have immunomodulatory properties on keratinocytes and epithelial cells. Taken together, the findings suggest that the microbiota plays an important role in acne pathogenesis and can be modulated for clinical improvement, but efforts should be made to identify the exact mechanisms and therapeutic effects of oral/topical probiotics in acne. This presentation concentrates on the skin and gut microbes in acne, the role that the gut–brain–skin axis plays in the immunobiology of acne, and newly emerging microbiome-based therapies that can be applied to treat acne. With the help of Deniplant brand natural remedies, the authors have developed several products for acne that act as immunomodulators of the human microbiome.

Keywords: acne, microbiota, skin, gut, brain, therapeutic implications

Discussion

Acne is one of the most common skin diseases worldwide and results in major health care costs and significant morbidity to severely affected individuals.

Acne vulgaris is a chronic inflammatory disease affecting nearly 85% of young people. Acne is a highly prevalent inflammatory skin condition involving sebaceous sites. However, the pathophysiology of this disorder is not well understood (1).

The pathogenesis of acne is attributed to multiple factors. The skin is a reflection of the gut, and acne may be a sign of deeper imbalances in the gut, like inflammation and dysbiosis. The skin is the largest epithelial interface separating the human body from the outside environment, and its surface is colonized by a diverse community of bacteria, fungi, and viruses (2-5).

These commensal microorganisms play critical roles in lipid metabolism, colonization resistance to transient organisms, and regulation of the immune system. It is increasingly believed that the interaction between skin microbes and host immunity plays an important role in this disease, with perturbed microbial composition and activity found in acne patients. Host-microbiome interactions that affect both innate and adaptive immune homeostasis appear to be a central factor in this disease, with recent observations suggesting that the composition and activities of the microbiota in acne is perturbed (6).

In addition, the composition of skin microbiomes varies depending on internal and external factors such as skin integrity and physiological status, antibacterial therapy, and demographic characteristics. Dysregulation of both the innate and adaptive immune systems has been implicated in the pathogenesis of acne (7).

The chronic inflammatory and recurrent skin condition acne vulgaris, commonly referred to as acne, is a disease of the pilosebaceous unit (hair, hair follicle, erector pili muscle and sebaceous gland) and, strikingly, the eighth most prevalent disease globally, affecting approximately 10% of the world's population (8-10).

The disease has a multifactorial aetiology and is triggered initially during adrenarche in susceptible individuals, and can be mild to very severe with respect to symptoms. The emotions of stress (e.g., depression and anxiety), for instance, have been hypothesized to aggravate acne by altering the gut microbiota and increasing intestinal permeability, potentially contributing to skin inflammation and change in sebum production and fatty acid profiles (11).

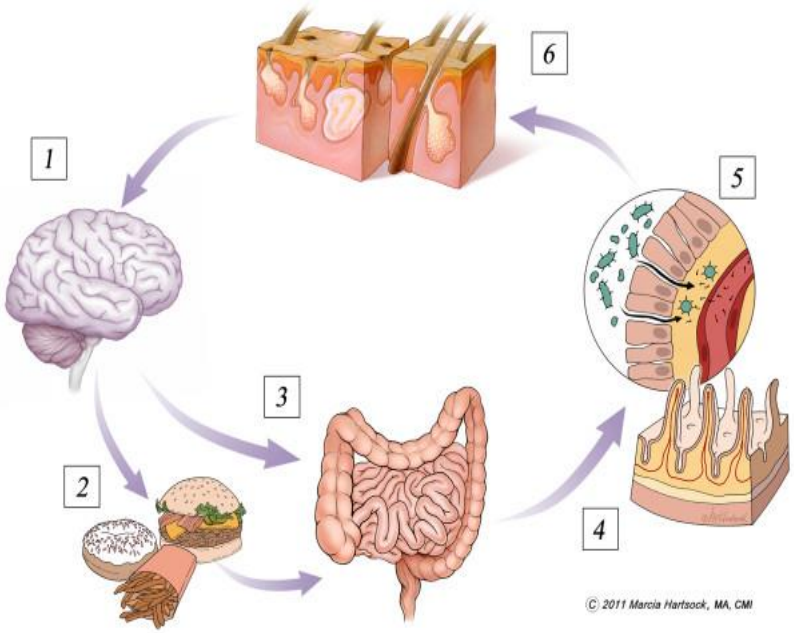

Fig. 1 Potential pathways of the gut-brain-skin axis in acne vulgaris **(11)**

In this article, we review recent developments in the interactions of skin microbes with host immunity, discussing the contribution of dysbiosis to the immunobiology of acne and newly emerging skin microbiome-based therapeutics to treat acne.

Many studies have confirmed that the skin bacterial microbiomes differ between young women and older women (12).

Acne also has close connections with the gastrointestinal tract, and many argue that the gut microbiota could be involved in the pathogenic process of acne. Few studies have examined the effects of antibiotics on the skin microbiota in acne (13).

Recent studies also showed that the gut microbiome is involved in acne, through interactions with the skin microbiome. The term 'microbiome' refers to microorganisms (bacteria, viruses and fungi) and their environment. A microbial imbalance or 'dysbiosis', compared with the normal distribution in healthy tissues, has been suggested to be involved in the pathophysiology of acne (14-16).

Staphylococcus epidermidis and Cutibacterium acnes (C. acnes; formerly Propionibacterium acnes) are two major inhabitants of the skin that are thought to contribute to the disease but are also known to promote health by inhibiting the growth and invasion of pathogens. The anaerobic bacterium Cutibacterium acnes

is believed to play an important role in the pathophysiology of the common skin disease acne vulgaris. It is understood that Cutibacterium acnes plays an important role in the synthesis of porphyrins on skin. It is alternatively possible that porphyrin levels (determined by the activity of specific Cutibacterium acnes strains) directly affect the presence of other bacteria (12).

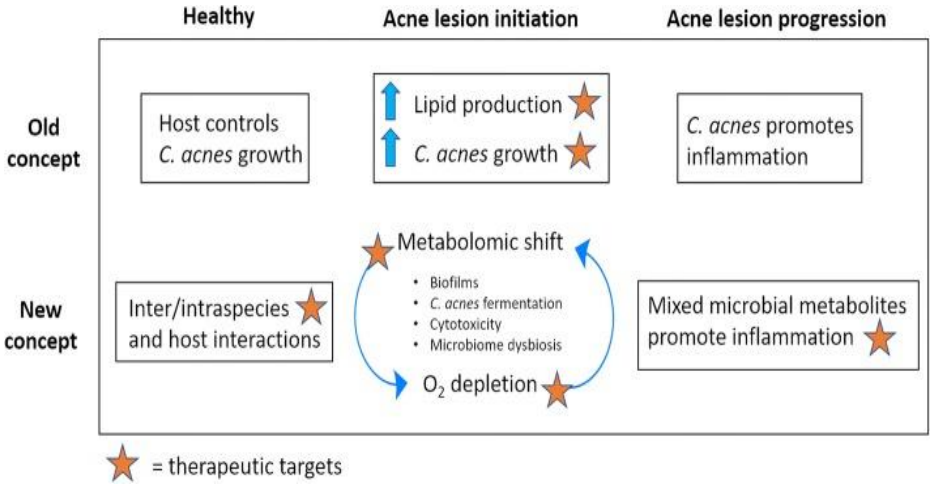

Fig. 2 Host-microbiome interactions and recent progress into understanding the biology of acne vulgaris **(17)**

In relation to acne pathogenesis, the perceived wisdom has always been that the condition develops within a follicle as a result of four main events: (1) androgen-induced hyperseborrhoea, (2) follicular hypercornification, (3) colonisation and proliferation of C. acnes and (4) stimulation of a local innate immune reaction (18).

As the old naturopathic medicine saying goes, “The skin is a reflection of the gut.” More recent studies evaluating the role of oral probiotics on acne have largely been published in foreign journals. Probiotics are live micro-organisms that provide a health benefit to the host. The term probiotic has been defined as “living microorganisms which, when consumed in adequate amounts, confer a health effect on the host”. Probiotics modify several factors in the pathophysiology of acne development and can potentially improve compliance as well. The immunomodulatory effects of probiotics on keratinocytes and epithelial cells suggest a physiologic mechanism to support the use of probiotics as an adjuvant treatment of acne (19).

A reduction on the inflammatory cascade again targets a factor in the pathogenesis of acne. People with acne may have more inflammation in their bodies. Oral probiotics can calm inflammation systemically (20).

The aim of this review article is to evaluate the role of pro- and prebiotics on the normal function of healthy skin as well as their role in the prevention and therapy of skin disease. Thankfully, oral probiotics can remedy this situation, improving both your gut and skin health.

Gut dysbiosis (or imbalance in your gut) has been linked to acne and other skin conditions. Oral probiotics like Lactobacillus acidophilus/Bifidobacterium bifidum can resolve dysbiosis. Acne patients were found to have a decrease in Lactobacillus and Bifidobacterium bacteria. Stress is associated with acne and also impairs Lactobacillus and Bifidobacterium. Besides helping your digestion, oral probiotics can also heal key issues linked to skin health and acne reduction. Hormone levels contribute to acne, and oral probiotics can improve hormonal balance, per a study of women with polycystic ovarian syndrome (21).

Propolis has been attracting the attention of researchers because of its antimicrobial, antioxidant, antiviral, and antifungal properties.

Researchers are also currently testing probiotics that contain healthy bacteria to be applied directly to your skin. These are known as topical probiotics **(**22).

Prebiotics are worth keeping an eye on for acne treatment (23).

There are many dermatological conditions associated with alteration of the intestinal microbiota and / or skin. In the last ten years there have been many researchers who have studied this connection. We can divide these diseases into two groups: The first includes all chronic inflammatory diseases such as psoriasis and atopic dermatitis and autoimmune diseases such as vitiligo and alopecia. In all these conditions, it is very important to explore intestinal inflammation and dysbiosis of the intestinal microbiome. In the second group we can list the diseases usually considered as infections such as acne, seborrheic dermatitis, rosacea and pityriasis versicolor. They are caused by microorganisms that normally live on the skin, even in healthy people. For this reason, we should begin to consider such diseases not as infections, but as a form of dysbiosis of the skin microbiome. The approach to the microbiome in dermatological problems is a 360° approach that assigns a very important role to the diet, but also includes the use of certain natural immunomodulators of the intestinal and skin microbiota. For example, Deniplant, a patented blend of medicinal plants with fruit tree buds, has been tested in dermatological conditions with psoriasis, atopic dermatitis and acne.

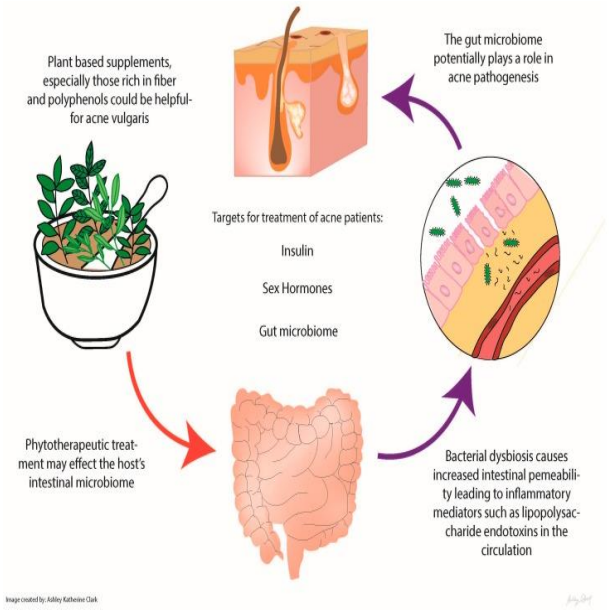

Fig. 3 Edible plants and their influence on the gut microbiome and acne **(1)**

Conclusion

Skin microbiota (bacteria, fungi, and viruses) are indispensable parts of the skin barrier; they regulate inflammatory processes and provide innate and adaptive immunity. The main inducer for this multifactorial disease is microbial fluctuation of common resident microbes on the skin with each microbe possessing their own purpose and style in protecting the human body. Oral administration of probiotics was found to constitute an adjuvant therapy to conventional modalities for treating mild to moderate acne vulgaris.

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