International Journal of Nutrology
(Official Journal of the ABRAN - Brazilian Association of Nutrology)

REVIEW ARTICLE

DOI: 10.54448/ijn23223

Gut-Skin axis and healthy skin: a systematic review

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DOI: https://doi.org/10.54448/ijn23223
Received: 04-10-2023; Revised: 06-10-2023; Accepted: 06-14-2023; Published: 06-15-2023; IJN-id: e23223

Abstract

Introduction: The skin has a multifactorial aging process, both by intrinsic and extrinsic predictors. Skin diseases contributed almost 2.0% to the global burden of 308 diseases and injuries in recent years. The role of the gut microbiota (GM) in human aging is important. GM directly affects aging through the gastrointestinal system. The microbial impact on the skin is still not fully understood. **Objective:** The present study analyzed the major scientific evidence on the relationship between gut microbiota and the skin, emphasizing the importance of intestinal health for aesthetically healthy skin. **Methods:** The systematic review rules of the PRISMA Platform were followed. The research was carried out from February to May 2023 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 137 articles were found. A total of 47 articles were fully evaluated and 27 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 30 studies at high risk of bias and 13 studies that did not meet the GRADE. It was concluded that current scientific evidence reveals the existence of an important Skin-GM axis, highlighting the management of dermatoses through probiotics and prebiotics, as well as lifestyle changes. To establish aesthetically healthy skin, it is imperative to manipulate the gut microbiota to achieve balance. Thus, treatments that elevate or repair a bowel are essential as adjunctive therapy in the management of inflammatory skin diseases and may contribute to the effectiveness of standard dermal therapy.

Keywords: Skin. Gut microbiota. Gut-Skin axis. Probiotics. Prebiotics. Aesthetic.

Introduction

The skin has a multifactorial aging process, both by intrinsic and extrinsic predictors **[1]**. Skin diseases contributed almost 2.0% to the global burden of 308 diseases and injuries in recent years. In this context, the role of the gut microbiota (GM) in human aging is important. GM directly affects aging through the gastrointestinal system. However, the microbial impact on the skin is still not fully understood **[2-4]**. Cellular senescence is an intrinsic aging process that has recently been linked to microbial imbalance. With age, cells become senescent in stress response, where they suffer an irreversible growth arrest, maintaining high metabolic activity **[5-7]**.

In this sense, an accumulation of senescent cells has been associated with several chronic and aging pathologies due to an overexpression of the senescence-associated secretory phenotype composed of pro-inflammatory cytokines, chemokines, growth factors, proteases, lipids, and extracellular matrix components. Dermatological disorders can be promoted by senescence. GM influences cell senescence through the secretion of microbial metabolites **[6,7]**.

Also, metabolomics can be used to identify and quantify metabolites involved in senescence. Furthermore, new anti-senescent therapeutics are warranted due to the poor safety profiles of current pharmaceutical drugs. Probiotics and prebiotics can be effective alternatives, considering the relationship between the microbiome and healthy aging. However, more research on the composition of the intestine in a senescent state is needed to develop immunomodulatory therapies **[7,8]**.

In this context, it was found that the microbiota compositions of diseased lesional skin showed distinct differences compared to healthy skin. The role of microbial colonization in establishing immune system homeostasis has been reported, while host-microbe interactions and genetically determined variation in stratum corneum properties may be linked to skin dysbiosis. Both are relevant for skin disorders with aberrant immune responses and/or disturbed skin barrier function. Modulation of the skin microbiota composition to restore host-microbiota homeostasis may be a future strategy to treat or prevent the disease **[9-13]**.

Thus, the presence of bacteria in the intestine is mandatory for the development of various functions of the digestive system. In addition, GM is essential for activating the immune system, especially *Lactobacillus acidofilus*, *Lactobacillus bulgaricus*, and *Lactobacillus casei*, increasing IgA for the removal of antigens through a non-inflammatory path and increasing T and B lymphocytes. in the absence of GM, the motor function of the intestine is compromised. Lactobacilli and Bifidobacteria inhibit the growth of exogenous and/or harmful bacteria, stimulate immune functions, aid in the digestion and/or absorption of food ingredients and minerals, and contribute to the synthesis of vitamins **[14-19]**.

Therefore, the present study analyzed the major scientific evidence on the relationship between gut microbiota and the skin, emphasizing the importance of intestinal health for aesthetically healthy skin.

Methods

Study Design

The systematic review rules of the PRISMA Platform were followed. Available at: www.prisma-statement.org/. Accessed in: 06/02/2023.

Data Sources and Research Strategy

The search strategies for this systematic review were based on the keywords (MeSH Terms): *"Skin. Gut microbiota. Gut-Skin axis. Probiotics. Prebiotics. Aesthetic".* The research was carried out from February to May 2023 in Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. In addition, a combination of keywords with the Booleans "OR", "AND" and the operator "NOT" were used to target scientific articles of interest.

Study Quality and Risk of Bias

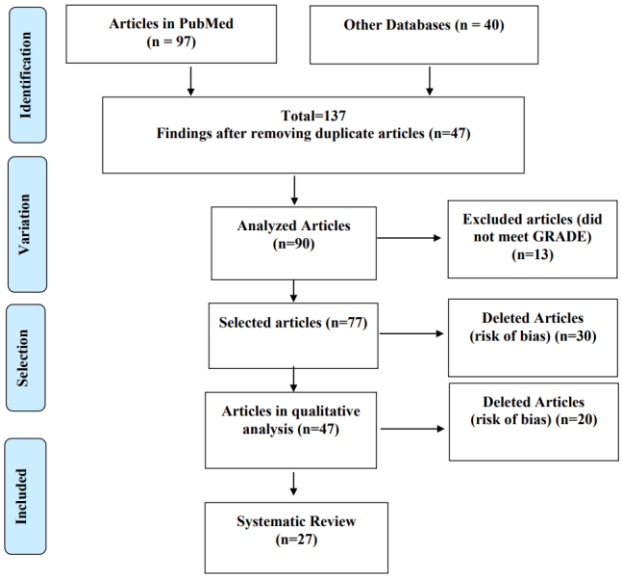
Study quality was based on the GRADE instrument. The highest ratings were for randomized controlled trials, prospective or retrospective observational trials, meta-analyses, and statistically significant sample sizes. The risk of bias was analyzed according to the Cochrane instrument, based on the effect size of each study versus the sample size.

Results and Discussion

Summary of Literary Findings

A total of 137 articles were found. Initially, duplication of articles was excluded. After this process, the abstracts were evaluated and a new exclusion was performed, removing the articles that did not include the theme of this article, resulting in 77 articles. A total of 47 articles were evaluated in full and 27 articles were included and developed in this systematic review study (Figure 1). Considering the Cochrane tool for risk of bias, the overall assessment resulted in 30 studies with a high risk of bias and 13 studies that did not meet GRADE.

Figure 1. Flowchart showing the article selection process.



Source: Own authorship.

Gut-Skin Axis - Clinical Findings

The skin and gut microbiota (GM) make many comparisons regarding purpose and function. Both act as the main interfaces of the body with the external environment and, therefore, must be maintained in homeostasis **[1]**. The physical barrier, as well as the commensal microbiota present in the skin and intestine, are essential components for proper maintenance. The skin is particularly vulnerable to damage from frequent exposure to environmental factors such as air pollution, tobacco smoke, nutrition, and personal care products **[2-4]**. As a result, premature aging of the skin can occur, which is accompanied by unwanted aesthetic indications and impaired skin function. This disruption of skin health can result in systemic damage. Previous

research suggests that the skin is the main source of serum inflammatory markers **[5,6]**.

Furthermore, a rapid increase in skin and serum cytokine levels following acute disruption of the epidermal permeability barrier. Furthermore, a significant reduction in inflammatory markers in the epidermis and serum was found after the correction of epidermal functional abnormalities with topical treatment. More recent research has extended the investigation to elderly humans with disruption of the epidermal barrier. Treatment with a lipid-based dermatologic agent successfully reduced levels of circulating cytokines, specifically IL-1β and IL-6, to levels comparable to young controls. An increase in these pro-inflammatory cytokines is associated with chronic aging disorders, including cardiovascular disease, Alzheimer's disease, and diabetes. Therefore, considering the epidermal dysfunction that accompanies age and its apparent relationship with systemic inflammation, the skin may play a role in the pathogenesis of agerelated chronic diseases **[20-22]**.

In this sense, the GM and its metabolites that enter the circulation can travel through the body and affect distant organs and tissues, including the skin. It is important to note that there is a two-way communication pathway between the GM and the integumentary system known as the gut-skin axis. Several cutaneous pathologies co-occur with gastrointestinal disorders, with disturbances in the GM associated with inflammatory dermatoses. Increased intestinal permeability resulting from dysbiosis can lead to the accumulation of bacterial metabolites (eg, aromatic amino acid phenols) in the skin and compromised epidermal differentiation and skin integrity. This circulation of metabolites gives rise to an association between skin diseases and metabolic or cardiovascular dysfunctions **[23,24]**.

In particular, a bidirectional relationship was found between psoriasis and obesity, where psoriasis predisposes individuals to obesity and vice versa. Similar changes in the GM of psoriasis patients and obese individuals are observed, as well as shared pathophysiology, including an increase in microbial by-products (ie, adipocytes). Furthermore, patients with severe psoriasis have an increased risk of death from cardiovascular disease, neoplasms, diabetes, kidney disease, and other systemic diseases **[6,8,25]**.

In this regard, senescent cells commonly accumulate in the skin, triggering inflammation through the secretory phenotype associated with senescence and contributing to various types of cutaneous dysfunction. The unique interaction between the gut and skin presents an opportunity to target senescent skin cells in hopes of resolving skin breakdown and associated metabolic disruption simultaneously. Suppression of the senescence-associated secretory phenotype pathway can improve skin health and help restore microbial imbalance through gut-skin communication pathways. Likewise, directly modulating the intestinal microbiome is a promising approach for the treatment of skin diseases **[5,26]**.

Thus, prolonged underlying inflammatory responses induce keratinocyte apoptosis, contributing to the distinct cutaneous manifestations of these disorders. Current therapeutic approaches are arduous for the patient or have little effect. Probiotic bacteria with antiinflammatory properties have the potential to bring therapeutic benefits to people suffering from neurogenic skin inflammation or autoimmune skin diseases. However, more clinical evidence is needed to support its routine use in medical practice. Likewise, probiotics that protect keratinocytes from oxidative stress or induce skin re-epithelialization can be of inestimable importance for wounds that do not heal **[15,19,26]**.

In this scenario, it is not surprising that several intestinal pathologies have skin comorbidities. However, the reason for this remains underexplored, and neither major research in gastroenterology nor dermatology has systematically investigated the intestinal axis of the skin. Thus, several mechanistic levels at which the gut and skin may interact in physiological and pathological circumstances have been proposed. The GM has an enormous metabolic capacity along the gut-skin axis. Dietary or microbiota metabolites are accessible to the skin. Therefore, after defining open key questions about the nature of these metabolites, how they are detected, and what skin changes they can induce, understanding these pathways will lead to new therapeutic strategies based on targeting one organ to improve the health of the other **[8,22]**.

Furthermore, a low-glycemic-load diet rich in plant fiber and low in processed foods has been linked to an improvement in acne, possibly through intestinal changes or attenuation of insulin levels. While there is much interest in the human microbiome, there is much more unknown, especially along the skin axis. Collectively, the evidence suggests that approaches such as food and herbal supplements may be a viable alternative to the current standard of first-line care for moderate acne, which typically includes antibiotics. Although patient adherence to major changes in diet is probably much lower than with medication, it is a treatment route that deserves further study and development **[11,23]**.

Finally, probiotics and prebiotics are microorganisms that can improve gut health. They

target gastrointestinal effects via the gut. Over the last decade, research on the GM has rapidly accumulated and has been accompanied by a growing interest in probiotics and prebiotics as a way to modulate the GM. Given the public health importance of these approaches, it is timely to reiterate factual and supportive information about their clinical application and use for skin treatments. For example, Lactobacillus, Bifidobacterium, and Saccharomyces strains have a long history of safe and effective use as probiotics, but *Roseburia spp, Akkermansia spp, Propionibacterium spp*, and *Faecalibacterium spp* show promise for the future. For prebiotics, glucans and fructans are well established and there is evidence based on the prebiotic effects of other substances such as mannose oligomers, glucose, xylose, pectin, starches, human milk, and polyphenols. Thus, current scientific evidence reveals the existence of an important Skin-GM axis, highlighting the management of dermatoses through probiotics and prebiotics, as well as lifestyle changes **[11,24,27]**.

Conclusion

It was concluded that current scientific evidence reveals the existence of an important SkinGM axis, highlighting the management of dermatoses through probiotics and prebiotics, as well as lifestyle changes. To establish aesthetically healthy skin, it is imperative to manipulate the gut microbiota to achieve balance. Thus, treatments that elevate or repair a bowel are essential as adjunctive therapy in the management of inflammatory skin diseases and may contribute to the effectiveness of standard dermal therapy.

Acknowledgement

Not applicable.

Ethical Approval

Not applicable.

Informed consent

Not applicable.

Funding

Not applicable.

Data sharing statement

No additional data are available.

Conflict of interest

The authors declare no conflict of interest.

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