Biological Times

Volume No. 5 | Issue No. 7 | Pages 2-3

The Brain–Gut-Skin Axis: Neuroimmune and Microbial Crosstalk and Role of Postbiotics in Skin Health and Disease

Nadia Noreen[1*], Hifza Qamar[2], Ahmad Raza[3] and Fakhra Muqaddas[4]

1. Punjab university college of pharmacy, Lahore, Pakistan
2. Faculty of pharmaceutical sciences Government college university Faisalabad, Pakistan
3. Faculty of Veterinary Science, University of Agriculture Faisalabad, Pakistan
4. University of Veterinary and Animal Sciences Lahore, Pakistan

*Corresponding Author: **nnaaddiiaanoreen1094@gmail.com**

ABSTRACT

The Brain-Gut-Skin Axis (BGSA) is a complex bidirectional communication network in which psychological well-being and intestinal health directly influence skin health. There exists a strong connection between mental conditions, gut microbiome composition, and skin disorders. Studies have shown that people with skin inflammatory conditions also experience mental conditions like depression, along with gastrointestinal (GI)tract issues like bloating, constipation, etc. These clinical signs highlight the connection between brain, gut, and skin conditions. Dysbiosis disrupts normal physiology; thus, to maintain it, therapeutic interventions are suggested in this article. Postbiotics are emerging as a more stable and safer therapeutic alternative. Examples of the compounds that act as postbiotics and have shown promising results in treating inflammatory conditions such as atopic dermatitis (AD) and acne are short-chain fatty acids (SCFAs), extracellular polysaccharides, microbial cell fragments, cell lysates, vitamins, and teichoic acid. In recent years, a thorough understanding of BGSA and the use of emerging compounds like postbiotics is essential for eradicating the inflammatory skin conditions from their root.

Keywords: Neuroimmune system; neuroendocrine system; gut–microbiome; skin inflammation diseases; and postbiotics

To cite this article: Noreen N, H Qamar, A Raza & F Muqaddas. The Brain–Gut-Skin Axis: Neuroimmune and Microbial Crosstalk and Role of Postbiotics in Skin Health and Disease. Biological Times. 2026. July 5(7): 2-3.

Introduction

Stokes and Pillsbury first presented the concept of the brain-gut-skin axis (BGSA) in the 1930s [1]. They correlated emotional stress, gut physiology, and skin conditions on the basis of clinical observations and experimental findings. In 2010, the BGSA was defined as a complex bidirectional communication network that interrelates neural, endocrine, metabolic, immune, and microbial signaling pathways [1]. Firstly, researchers found that the circulation of hormones and neurotransmitters is the reason for the exclusive communication between the nervous system and immune system. Prolactin, growth hormone, and cortisol are the hormones that are secreted by the neuroendocrine system. Among the neurotransmitters, epinephrine and norepinephrine are released by nerve endings of immune cells [2]. Studies have also shown that dopamine, gamma-aminobutyric acid (GABA), and serotonin-like neurotransmitters can be produced and/or consumed by various types of bacteria. The brain-gut-skin axis explains that gut bacteria cause immune modulation, which affects skin inflammation [3].

Disfiguring skin conditions such as psoriasis, atopic dermatitis, acne vulgaris, and rosacea, once regarded as independent cutaneous disorders, are now declared as systemic and microbial dysregulations. The skin conditions are also influenced by the composition of the gastrointestinal (GI) microbiome; on the other hand, the GI microbiome is affected by these integumentary conditions [4]. A comprehensive understanding of BGSA may enable us to address the underlying cause of the skin diseases and suggest a more precise therapeutic approach [5]. The BGSA presents a triangular network of regulation, which implies that a tripartite dialogue maintains cutaneous homeostasis.[1]. Gastrointestinal microbial disturbance and cutaneous immune modulation are not independent triggers; they are actually correlated with the central nervous system, which determines disease manifestation, symptom appraisal, and clinical variability [6]. Postbiotics, i.e., Gut microbiota-derived metabolites, also influence the BGSA [7]. Thus, this article throws light on the internetworking between neuroimmune, endocrine, gut microbiome, and skin diseases.

Biological Architecture of BGSA:

The BGSA consists of three interlinked systems: (1) the central nervous system, including the hypothalamic–pituitary–adrenal (HPA) axis and autonomic pathways; (2) the gastrointestinal (GI) tract, including the intestinal microbiota and mucosal immune system; and (3) the skin, which serves both as a physical barrier and as an active neuroendocrine and immune organ. These systems are correlated with one another; neuroendocrine signals influence gastrointestinal physiology, changing microbial composition and inflammation, highlighting a mechanistic basis of BGSA interaction [8]. The BGSA works like a triangular connectivity between the parameters of the brain, gut, and skin together, rather than seeing these systems separately, which is critical in understanding why single-target therapies often fail in treating the skin inflammatory disorders. Individualized therapies fail because symptomatic treatment is suggested, while it is the hour of need to understand that all the organs are connected and have an influence on one another, having an eye on all of these will help to understand the disease from its core, and only then right treatment can be given [1].

Neuroimmune Mechanisms Linking Brain, Gut, and Skin Health:

Psychological strain triggers the hypothalamic–pituitary–adrenal (HPA) axis, increasing the release of corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and cortisol, which can influence the skin barrier and worsen inflammatory dermatoses. Simultaneously, gut microbiota alterations impact immune signaling, including cytokines such as Interleukin (IL)-1, IL-6, IL-23, Interferon(TNF)-α, C-reactive protein, and the availability of neurotransmitters [9]. The human GI tract hosts over 100 trillion microorganisms, which significantly exceeds the coding potential of the human genome[10]. *Bacteroidetes* , *Firmicutes* , *Actinobacteria* , and *Proteobacteria* are considered healthy microbes. *Akkermansia*, *Bifidobacterium*, and *Escherichia* are also important genera of bacteria[10]. Chronic cutaneous inflammatory diseases, such as atopic dermatitis (AD), rosacea, acne, and psoriasis, are linked with activation of the HPA axis, modulation of immune function, and emotional distress. As a result, of which skin produces cytokines and neuropeptides that influence gut function and psychological well –being [11].

Gut Microbiota as the Central Regulator in BGSA:

Gut and skin microbial populations play a significant role in skin health and immunity by strengthening the barrier and lowering inflammation. Skin inflammatory conditions are caused mainly due to dysbiosis [12]. Gut microbial flora primarily consists of six major phyla. [13]. The colon, part of the GI tract, is the largest harbor of bacteria, having more than five million different genes of 1000 to 1500 bacterial species. *Bacteroidetes*, *Firmicutes*, *Actinobacteria*, *Proteobacteria*, *Fusobacteria*, *Cyanobacteria*, and *Verrucomicrobia* are a few among them [14]. Disruption of these microbial communities triggers immunological modulation of local and/or systemic immune responses [15]. These flora play a role in digestion, immunity, mood, brain function, vitamin production, and preservation of the intact intestinal lining. Disruption of this delicate ecology, which is caused by poor diet, stress, and antibiotics, results in various health conditions [16]. In addition, researchers found that intestinal commensals affect vagus nerve function by producing neuroactive molecules and neurotransmitters [17].

Clinical Relevance of BGSA:

The co-morbidity of mental conditions like depression and abdominal bloating has been seen in patients with some chronic skin conditions like acne and psoriasis [18]. Take acne as an inflammatory skin condition, studies have shown that over 1300 adults with acne experienced GI symptoms like constipation, halitosis, and gastric reflux [19]. Thus, there exists a tripartite interaction under the BGSA whose understanding is crucial for maintaining physiological equilibrium [12]. Prevention and management of both psychiatric disorders and dermatological conditions is possible by understanding this axis [5]. Multiple studies have revealed that disruption of any aspect of BGSA can increase the risk of developing inflammatory conditions like acne [20]. By understanding the core concept of BGSA holds the strong promise of getting in-depth knowledge about mental illness, gut health, and skin conditions due to the intricate communication network it represents. By spotting out individualized variations in microbiota composition and metabolite profiles, clinicians can suggest the specific needs for specific patients [21].

Therapeutic Interventions Targeting BGSA:

Prebiotics alter both the composition and/or function of the gut microbiota and provide health benefits. They are indigestible dietary supplements that increase gut health by promoting the growth or activity of gut microbiota in the last part of the intestine, i.e., colon. Oligosaccharides (OSCs), fructans, resistant starches, galactooligosaccharides(GOS), and fructooligosaccharides (FOS) are the different forms of these dietary supplements that actually feed probiotics in the body and thus indirectly help to improve the skin barrier and lower inflammation [4]. Probiotics have potential benefits in mental and dermatological health, along with the GI tract. Dietary and microbial factors play a crucial role in the prevention and treatment of both mental and skin diseases. Probiotics show their mechanism of action by immune modulation, meaning by lowering proinflammatory cytokines and promoting anti-inflammatory ones [5]. But due to a high level of inter-individual heterogeneity, one strain of probiotics may be beneficial for one person but can be dangerous for another [22]. As the probiotics fall under the umbrella of food supplementation, they are manufactured under a less pharmaceutical-grade environment, and there are chances of substandard dosage forms and dosages of these products [23]. Moreover, to identify the best strain of bacteria, its dosages in colony-forming units(CFU), and the time (how long it should be taken), a more in-depth study is required [24].

Postbiotics are preparations of inanimate microorganisms and/or their components that confer a health benefit [25]. They contain inactivated microbial cells or cell fragments, with or without metabolites. They are light in weight, soluble chemical entities that are produced after the implication of a deliberate process to terminate cell viability. Examples of postbiotics that have been extensively researched are short-chain fatty acids (SCFAs), cellular lysates, vitamins, teichoic acid, microbial cell fragments, and extracellular polysaccharides [26]. They have demonstrated an effect in protecting the gut barrier. lowering inflammation, decolonizing the pathogens. They have researched evidence to be safely used even in the sensitive areas of the body, like the vagina and the mouth [27]. Essential microbial metabolites include butyrate, propionate, and acetate, which are SCFAs, indole derivatives, and tryptophan metabolites, which play a role in preserving gut barrier integrity, regulating inflammation, and affecting systemic physiology [26]. Among these, SCFAs, which are unbranched fatty acids, about 90%, are produced by the gut microbiome [28]. Around 5% SCFAs, like isobutyrate, isovalerate, and 2-methylbutanoate, are branched-chain (BCFAs) and are produced when amino acids like valine, leucine, and isoleucine are metabolized [29]. BCFAs in the gut decrease when people eat more insoluble fiber. High BCFAs levels are linked with mental diseases like depression, and high BCFAs levels are related to hypercholesterolemia [28].

Postbiotics are less likely to cause infections or immune reactions they are more beneficial for people with compromised immune systems and damaged skin barrier. Bioactive molecules among postbiotics have shown various therapeutic actions against acne, rosacea, psoriasis, atopic dermatitis (AD), and vitiligo problems. They exhibit wound healing, UV-protective, and immunomodulatory qualities. They are beneficial to balance and enhance skin resilience, and thus are used in topical formulations, such as moisturizers, cleansers, and serums for people with sensitive skin [26]. According to pre-clinical and clinical research, postbiotics have a potential therapeutic effect in treating skin disorders like atopic dermatitis and acne. Lipoteichoic acid (LTA), which is a crucial part of the Gram–positive bacterial cell wall, plays its role in the inhibition of melanogenesis [12]. The supplementation of butyrate-producing bacteria in experimental mouse models has elevated their serum butyrate levels, reduced inflammation, and improved skin conditions.[30].

Conclusion:

The brain-gut-skin axis is a critical triangle for understanding systemic and enteric systems' roles in dermatological diseases. By thoroughly digesting the concept of BGSA, more precise and individualized therapeutic techniques can be suggested. Gut dysbiosis can promote systemic inflammation and alter stress levels, which impacts skin disease severity. The skin, in turn, releases cytokines and neuropeptides that can impact both gut function and psychological well-being. This feedback loop mediated by hormones, neurotransmitters, immune factors, and microbial metabolites is central to the pathophysiology of psychodermatologic conditions such as acne, atopic dermatitis, psoriasis, and rosacea. These conditions can be improved by using prebiotics, probiotics, and postbiotics. They exhibit wound healing, UV-protective, and immunomodulatory qualities. They are beneficial to balance and enhance skin resilience. Fully unlocking the potential concept of BGSA will ultimately pave the way for safer, more accessible, and highly targeted interventions in chronic disease management.

References

[1] Guo Z, Yang J, Zang R, Yang Y, Wang Q, Xu C. The brain–gut–skin axis in inflammatory and disfiguring skin diseases: mechanistic insights, clinical correlations, and therapeutic strategies. Frontiers in Immunology. 2026 Feb 27;17:1737303
[2] 2. Chen G, Chen ZM, Fan XY, Jin YL, Li X, Wu SR, Ge WW, Lv CH, Wang YK, Chen JG. Gut–brain–skin axis in psoriasis: a review. Dermatology and therapy. 2021 Feb;11(1):25-38.
[3] 3.Abdi A, Oroojzadeh P, Valivand N, Sambrani R, Lotfi H. Immunological aspects of probiotics for improving skin diseases: Influence on the Gut-Brain-Skin Axis. Biochemical and Biophysical Research Communications. 2024 Apr 2;702:149632.
[4] 4.Munteanu C, Turti S, Marza SM. Unraveling the Gut–Skin Axis: The Role of Microbiota in Skin Health and Disease. Cosmetics. 2025 Aug 8;12(4):167.
[5] 5.de Mello P, Pinheiro DF, dos Santos EF, Vieira DG, Eing KK, Schmitt V. Exploring the Bidirectional Skin-Brain Axis: Mental Health, Dermatology-Related Quality of Life, and the Role of Probiotics. Journal of Dermatologic Science and Cosmetic Technology. 2026 Jan 20:100147.
[6] 6. Lazić Mosler E, Vekić Mužević M, Karlović D, Tarle M, Raguž M. Revisiting Rosacea Through the Skin–Gut–Brain Axis: A Neuroimmune Perspective. Life. 2026 Feb 18;16(2):347.
[7] 7. Singh V, Hussain MS, Das J, Chellappan DK, Chaudhary P, Sridhar SB, Panigrahy UP, Ramzan M, Mondal M, Ashique S. Targeting the Gut Microbiota with Pro-and Postbiotics: Emerging Strategies against Alopecia. Probiotics and Antimicrobial Proteins. 2026 Feb 18:1-27.
[8] 8. Ali A, Jafferany M. Microbiota, mind, and skin: bridging the Gut-Brain-Skin axis in psychodermatology. Archives of Dermatological Research. 2025 Sep 17;317(1):875.
[9] 9. Lazić Mosler E, Vekić Mužević M, Karlović D, Tarle M, Raguž M. Revisiting Rosacea Through the Skin–Gut–Brain Axis: A Neuroimmune Perspective. Life. 2026 Feb 18;16(2):347.
[10] 10. Rithi AT, Mitra A, Banerjee A, Ilanchoorian D. Current Understating of Gut Microbiome Alterations and Therapeutic Approaches for Improving Human Health Rithi AT, Abhijit Mitra2, Antara Banerjee2, Divya Ilanchoorian3 and Arun Kumar Radhakrishnan1. Int. J. Exp. Res. Rev. 2023;36:253-64.
[11] 11. Ali A, Jafferany M. Microbiota, mind, and skin: bridging the Gut-Brain-Skin axis in psychodermatology. Archives of Dermatological Research. 2025 Sep 17;317(1):875.
[12] 12.Munteanu C, Turti S, Marza SM. Unraveling the Gut–Skin Axis: The Role of Microbiota in Skin Health and Disease. Cosmetics. 2025 Aug 8;12(4):167.
[13] 13. Hou K, Wu ZX, Chen XY, Wang JQ, Zhang D, Xiao C, Zhu D, Koya JB, Wei L, Li J, Chen ZS. Microbiota in health and diseases. Signal transduction and targeted therapy. 2022 Apr 23;7(1):135.
[14] 14. Jimenez-Sanchez M, Celiberto LS, Yang H, Sham HP, Vallance BA. The gut-skin axis: a bi-directional, microbiota-driven relationship with therapeutic potential. Gut Microbes. 2025 Dec 31;17(1):2473524.di
[15] 15. Tang B, Zheng X, Luo Q, Li X, Yang Y, Bi Y, Chen Y, Han L, Chen H, Lu C. Network pharmacology and gut microbiota insights: unraveling Shenling Baizhu powder's role in psoriasis treatment. Frontiers in Pharmacology. 2024 Feb 14;15:1362
[16] 16. Zhang YJ, Li S, Gan RY, Zhou T, Xu DP, Li HB. Impacts of gut bacteria on human health and diseases. International journal of molecular sciences. 2015 Apr;16(4):7493-519.
[17] 17. Chen G, Chen ZM, Fan XY, Jin YL, Li X, Wu SR, Ge WW, Lv CH, Wang YK, Chen JG. Gut–brain–skin axis in psoriasis: a review. Dermatology and therapy. 2021 Feb;11(1):25-38.
[18] 18. Uhlenhake E, Yentzer BA, Feldman SR: Acne vulgaris and depression: a retrospective examination. J Cosmet Dermatol. 2010, 9: 59-63. 10.1111/j.1473-2165.2010.00478.x.
[19] 19. Bowe WP, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis-back to the future?. Gut pathogens. 2011 Jan 31;3(1):1.
[20] 20. Kiu LY. The Gut-brain-skin Axis and Acne Vulgaris: Current Understanding and the Management Implications. Clinical Dermatology Review. 2025 Jul 1;9(3):213-9.
[21] 21. Nagamine T. Gut-skin-brain axis in people suffering from sepsis with acute skin failure. World Journal of Psychiatry. 2025 Jul 19;15(7):106062.
[22] 22.Hills RD, Pontefract BA, Mishcon HR, Black CA, Sutton SC, Theberge CR. Gut microbiome: profound implications for diet and disease. Nutrients. 2019 Jul;11(7):1613.
[23] 23.Merenstein D, Pot B, Leyer G, Ouwehand AC, Preidis GA, Elkins CA, Hill C, Lewis ZT, Shane AL, Zmora N, Petrova MI. Emerging issues in probiotic safety: 2023 perspectives. Gut microbes. 2023 Dec 31;15(1):2185034.
[24] 24.Dudek-Wicher R, Junka A, Paleczny J, Bartoszewicz M. Clinical trials of probiotic strains in selected disease entities. International Journal of Microbiology. 2020;2020(1):8854119.
[25] 25. Salminen S, Collado MC, Endo A, Hill C, Lebeer S, Quigley EM, Sanders ME, Shamir R, Swann JR, Szajewska H, Vinderola G. The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. Nature reviews Gastroenterology & hepatology. 2021 Sep;18(9):649-67.
[26] 26. Thorakkattu P, Khanashyam AC, Shah K, Babu KS, Mundanat AS, Deliephan A et al (2022) Postbiotics: current trends in food and pharmaceutical industry. Foods 11(19):3094
[27] 27. Scott E, De Paepe K, Van de Wiele T. Postbiotics and their health modulatory biomolecules. Biomolecules. 2022 Nov 4;12(11):1640.
[28] 28. Mishra AK, Verma S, Mishra A, Khan G, Singh H. Unlocking the role of microbiome through gut-skin axis to alleviate aging: current perspectives and future scope. GeroScience. 2026 Mar 21:1-7
[29] 29. Rios-Covian D, González S, Nogacka AM, Arboleya S, Salazar N, Gueimonde M, de Los Reyes-Gavilán CG. An overview on fecal branched short-chain fatty acids along human life and as related with body mass index: associated dietary and anthropometric factors. Frontiers in microbiology. 2020 May 27;11:973..
[30] 30. Salazar N, Arboleya S, Fernandez-Navarro T, de Los Reyes-Gavilan CG, Gonzalez S, Gueimonde M. Age-associated changes in gut microbiota and dietary components related to the immune system in adulthood and old age: cross-sectional. Nutrients. 2019;11(8).