

Gut-oral microbiome axis – Role in oral health and pathogenesis



Alka Sahu, Tripti Kshatri, Preeti K. Suresh*

University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur (Chhattisgarh)

Email: suresh.preeti@gmail.com

Abstract

The gut contains different type of microbiome which significantly control immune system and metabolism of body. These gut microbiomes have bidirectional connection with oral cavity known as gut-oral microbiome axis. So, disturbance in gut microbiome cause several oral diseases such as oral candidiasis, periodontal disease and OLP (oral lichen planus). The understanding of gut-oral microbiome axis provides new therapeutic and preventive strategies. This article mainly includes the composition, function, interaction of microbes and role of microbiome therapy, dietary modulation, prebiotics and probiotics to maintain oral wellness by gut microbiome balance.

Keyword: gut-oral microbiome axis, oral disease, gut dysbiosis

1. Introduction

Human body contain trillions microbiome that distributed in the gut, skin and oral cavity. This microbiome plays important role to maintain physiological homeostasis (1). Gut has maximum number of microbes including bacteria, fungi, viruses and archaea. They regulate metabolism, neurological and immunological function of body. Additionally oral microbes affect local and systemic wellness (2). Some clinical evidence confirms the bidirectional connection between gut and oral cavity (3). Imbalance in gut microbiome affect immunological, inflammatory and metabolic function of oral cavity (4). This imbalance causes oral disease like oral candidiasis, periodontal disease and OLP. Conversely, some oral microbiomes can translocate in gastrointestinal tract, colonize in gut and damage microbial ecology (5), (6). This article explores gut-oral microbiome axis, their bidirectional mechanism and management of oral health (7).

2. Composition and Functions of Gut Microbiome

The gut microbiome ecology is mainly influenced by Bacteroidetes and phyla Firmicutes ratio. This balanced ratio characterized as healthy gut (8). Other microbiomes like *actinobacteria* and *proteobacteria* affect intestinal and systemic equilibrium. Key genera that populate the gut include *Bifidobacterium*, *Fusobacterium*, *Enterococcus faecalis*, *Escherichia coli*, *Akkermansia muciniphila*, *Lactobacillus*, *Clostridium*, alongside fungi like *Candida* species (9).

The metabolism is a main function of gut microbiome where the dietary fibres fermented and converted into short chain acids. These metabolites are the main energy source, reduce inflammation and maintain epithelial barrier integrity (10). They also regulate the host immune system by controlling cytokine production and T-cell differentiation. Gut microbiome assists

in maintaining a robust epithelium and mucosa, thereby preventing the translocation of toxins and LPS (liposaccharides) into systemic circulation (11).

3. Gut–Oral Microbiome Axis

The gut-oral microbiome axis defines the bidirectional pathway where microbes can translocate from the oral cavity to the GIT. Conversely, gut microbiome metabolites, immune signals and microbial composition influence oral health (12). The various gut microbiomes that influence oral health are presented in Table 1.

Table 1. Gut microbiomes influencing oral health

Gut microbiome	Mechanism of action	Effect on oral wellness	Clinical evidence	Reference
<i>Lactobacillus spp.</i>	Release lactic acid, regulate immune response and restrict microbiomes	Decreases oral inflammation, prevent periodontitis	Probiotics improve oral microbiome balance	(13), (14)
<i>Prevotella spp.</i>	Overgrowth of microbes support systemic inflammation and increase endotoxin level	Combine with mucosal inflammation and periodontitis	Affect gut dysbiosis and oral disease	(15)
<i>Bifidobacterium spp.</i>	Improve gut barrier and minimize systemic inflammation	Indirectly minimize mucosal and gingival inflammation	Probiotics enhance periodontal wellness	(16)
<i>Candida spp.</i>	Gut derived fungal translocation and suppressed immune	Cause oral candidiasis	General immunocompromised	(17)
<i>Clostridium spp.</i>	Release toxins, promotes systemic inflammatory pathway	Cause oral mucosal inflammation and tissue damage	Combine with oral ulcer and IBD (inflammatory bowel disease)	(18)
<i>Escherichia coli</i>	Produce lipopolysaccharides and enhance oxidative stress	Cause periodontal breakdown and gingival inflammation	Oral inflammation due to gut dysbiosis	(19)
<i>Bacteroides fragilis</i>	Develop short chain fatty acids	Modulate oral immune homeostasis and minimize inflammation	Maintain gut-oral microbiome axis	(20)

<i>Enterococcus faecalis</i>	Limit bacterium migration	Contributes to biofilm formation and root canal infection	Use in gut infection and oral mucosal lesions.	(21)
<i>Akkermansia muciniphila</i>	Provide strength to gut barrier and decreases endotoxemia	Protect from oral inflammation by immune regulation	Provide information for microbiome studies	(22)
<i>Fusobacterium nucleatum</i>	This microbiome translocates and produces cytokine	Contributes to oral cancer and periodontitis	Bridging gut-oral dysbiosis	(23)

4. Significance of Gut Dysbiosis on Oral Wellness

The disturbance in gut microbiome by poor diet, chronic stress and use of antibiotics is known as gut dysbiosis. It can lead to decrease microbial diversity, immune dysregulation and systemic inflammation that is linked to oral disease as depicted in Figure 1 (6). For example, studies of clinical correlation of gut dysbiosis and periodontitis have been observed. Dysbiosis contributes to endotoxemia and produces inflammatory cells that target periodontal tissue. Studies have shown that oral cavity is affected by *Porphyromonas gingivalis*, which not only causes periodontitis but can also change the gut microbiome components and this phenomena is indicated as reciprocal dysbiosis (24). Dysbiosis often decreases *Bifidobacterium* and *Lactobacillus* species that defend against *Candida* species. Therefore, colonization of *Candida* species increases leading to causes oral candidiasis (25).

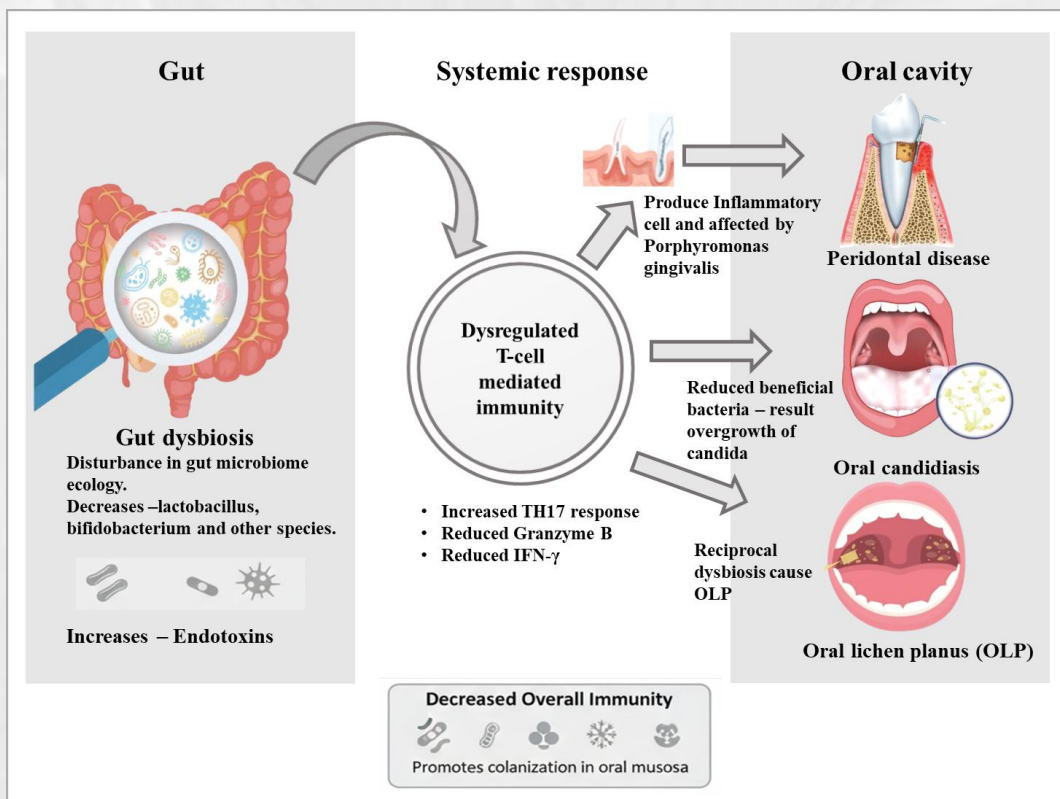


Figure 1. Impact of gut dysbiosis in oral disease

OLP is characterized by dysregulation of T-cell-mediated immune system. Gut dysbiosis increases the T-helper 17 (TH17)-mediated immune responses. These changes lead to the production of

cytotoxic molecules (e.g. Granzyme B, IFN- γ), resulting in keratinocyte apoptosis, ulceration, and the manifestation of OLP lesions (26), (27).

5. Strategies to Balance Oral Health via Gut Regulation

With the established connection between gut and oral cavity, restoration and maintenance of gut microbiome balance has emerged as a strategy to manage and prevent oral disease. Several therapies are employed, such as use of prebiotics and probiotics, dietary modulation, microbiome treatment and lifestyle (28).

Dietary modulation: A diet rich in fibre, fermented foods and polyphenols is reported to enhance the growth of beneficial bacteria and production of short-chain fatty acids. Whole grains, fruits and vegetables are fibre-rich foods, and improve gut barrier function and minimize systemic inflammation, which can affect periodontal tissue (29). Fermented foods introduce beneficial live cultures (probiotics) that modulate microbiome of both gut and oral cavity. It also decreases pathogen load and improves saliva buffering capacity. Additionally, polyphenol-rich foods includes apples, green tea, flaxseed, dark chocolate, extra virgin oil, berries, etc, have antioxidant and anti-inflammatory activities that are crucial to counteract gut dysbiosis(30).

Prebiotics and probiotics: Probiotics are alive yeast and bacteria which offer various health benefits when taken in sufficient quantity. These gut-oral probiotics (E.g., *Lactobacillus rhamnosus*, *Bifidobacterium longum*) have demonstrated efficacy in managing oral candidiasis, reduction in gingival bleeding and oral mucosal lesion disease. Prebiotics (e.g. fructo-oligosaccharides and inulin) are non-digestible compounds which selectively improve the growth and function of good gut bacteria (31).

Microbiome therapy: Microbiome-based therapies represent the backbone of personalized medicine. Fecal microbiome transplantation (FMT) though primarily developed for GIT disease, has shown potential to reduce systemic inflammation and improve oral health markers. Biologically designed probiotics are being engineered as highly precise antimicrobial or anti-inflammatory agents for periodontal disease. Moreover, postbiotics are non-viable microbial components that retain bioactivity. They offer a safe option for microbial modulation without introducing live bacteria (32).

6. Future Perspectives and direction

Future researchers must focus on delineating the gut-oral microbiome axis, immunological and molecular pathways. They should also explore the connection between gut dysbiosis and oral disease. The cutting-edge methods such as AI- based method and integrative omics is used to detect metabolic biomarkers and microbial growth that are responsible for oral disease. The personalization techniques are used for better therapeutic action. Moreover, rigorous clinical trials are necessary to validate safety and efficacy of treatment. A comprehensive collaboration of pharmaceutical science, gastroenterology, stomatology and AI offers controlled microbiome ecology as a standard element of future oral healthcare (33).

7. Conclusion

The gut microbiome maintained oral health by modulating immune system, metabolism and microbial diversity. Gut dysbiosis is mainly caused by pharmacological factors (propagates inflammation and immune imbalance) and lifestyle. The oral diseases are linked to inflammatory factors that involve microbial translocation, cytokine signalling and short-chain fatty acids that recognized as gut-oral axis. The treatment of oral disease by regulating gut microbiome may be done by microbiome-based therapy, dietary modulation and use of probiotics and prebiotics. This therapy recovers microbiome balance and maintains gut-oral axis. Combining this advancement with personalized medicine, multi-disciplinary and integrative omics therapies will signify a transformative and scientifically critical path for future clinical pharmacy and oral healthcare.

8. References

1. Dekaboruah E, Suryavanshi MV, Chettri D, Verma AK. Human microbiome: an academic update on human body site specific surveillance and its possible role. *Archives of Microbiology* [Internet]. 2020 Oct 1;202(8):2147–67. Available from: <https://doi.org/10.1007/s00203-020-01931-x>
2. Khalil M, Di Ciaula A, Mahdi L, Jaber N, Di Palo DM, Graziani A, et al. Unraveling the Role of the Human Gut Microbiome in Health and Diseases. *Microorganisms* [Internet]. 2024;12(11). Available from: <https://www.mdpi.com/2076-2607/12/11/2333>
3. Kunath BJ, De Rudder C, Laczny CC, Letellier E, Wilmes P. The oral–gut microbiome axis in health and disease. *Nature Reviews Microbiology* [Internet]. 2024 Dec 1;22(12):791–805. Available from: <https://doi.org/10.1038/s41579-024-01075-5>
4. Park SY, Hwang BO, Lim M, Ok SH, Lee SK, Chun KS, et al. Oral–Gut Microbiome Axis in Gastrointestinal Disease and Cancer. *Cancers (Basel)* [Internet]. 2021 Apr 28 [cited 2025 Oct 14];13(9):2124. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8125773/>
5. Yamazaki K. Oral-gut axis as a novel biological mechanism linking periodontitis and systemic diseases: A review. *Japanese Dental Science Review* [Internet]. 2023 Dec 1 [cited 2025 Oct 14];59:273–80. Available from: <https://www.sciencedirect.com/science/article/pii/S1882761623000224>
6. Shen Y, Fan N, Ma S, Cheng X, Yang X, Wang G. Gut Microbiota Dysbiosis: Pathogenesis, Diseases, Prevention, and Therapy. *MedComm (2020)* [Internet]. 2025 Apr 18 [cited 2025 Oct 14];6(5):e70168. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC12006732/>
7. Kitamoto S, Nagao-Kitamoto H, Hein R, Schmidt TM, Kamada N. The Bacterial Connection between the Oral Cavity and the Gut Diseases. *J Dent Res*. 2020 Aug;99(9):1021–9.
8. Rosenberg E. Diversity of bacteria within the human gut and its contribution to the functional unity of holobionts. *npj Biofilms and Microbiomes* [Internet]. 2024 Nov 23;10(1):134. Available from: <https://doi.org/10.1038/s41522-024-00580-y>
9. Ghosh S, Pramanik S. Structural diversity, functional aspects and future therapeutic applications of human gut microbiome. *Arch Microbiol* [Internet]. 2021 [cited 2025 Oct 14];203(9):5281–308. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC8370661/>
10. Mukhopadhyaya I, Louis P. Gut microbiota-derived short-chain fatty acids and their role in human health and disease. *Nature Reviews Microbiology* [Internet]. 2025 Oct 1;23(10):635–51. Available from: <https://doi.org/10.1038/s41579-025-01183-w>
11. Yoo JY, Groer M, Dutra SVO, Sarkar A, McSkimming DI. Gut Microbiota and Immune System Interactions. *Microorganisms* [Internet]. 2020 Oct 15 [cited 2025 Oct 14];8(10):1587. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7602490/>
12. Colombo APV, Lourenço TGB, de Oliveira AM, da Costa ALA. Link Between Oral and Gut Microbiomes: The Oral–Gut Axis. In: Dame-Teixeira N, Deng D, Do T, editors. *Oral Microbiome: Symbiosis, Dysbiosis and Microbiome Interventions for Maintaining Oral and Systemic Health* [Internet]. Cham: Springer Nature Switzerland; 2025. p. 71–87. Available from: https://doi.org/10.1007/978-3-031-79146-8_5
13. Huang Z, Xie L, Huang L. Regulation of host immune responses by *Lactobacillus* through aryl hydrocarbon receptors. *Medicine in Microecology* [Internet]. 2023 June 1 [cited 2025 Oct 15];16:100081. Available from: <https://www.sciencedirect.com/science/article/pii/S259009782300006X>
14. Camarena AH, Higuera NS, Cortez EGC, Rubio VP. Lactobacillus Probiotics and their Impact on Periodontal Diseases. *EAS J Dent Oral Med* [Internet]. 2023 Aug 10 [cited 2025 Oct 15];5(04):111–4. Available from: https://www.easpublisher.com/media/features_articles/EASJDOM_54_111-114.pdf
15. Iljazovic A, Roy U, Gálvez EJC, Lesker TR, Zhao B, Gronow A, et al. Perturbation of the gut microbiome by *Prevotella* spp. enhances host susceptibility to mucosal inflammation. *Mucosal Immunol* [Internet]. 2021 Jan [cited 2025 Oct 15];14(1):113–24. Available from: <https://www.nature.com/articles/s41385-020-0296-4>
16. Abdulqadir R, Engers J, Al-Sadi R. Role of Bifidobacterium in Modulating the Intestinal Epithelial Tight Junction Barrier: Current Knowledge and Perspectives. *Curr Dev Nutr* [Internet]. 2023 Oct 30 [cited 2025 Oct 15];7(12):102026. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10700415/>
17. Kreulen IAM, de Jonge WJ, van den Wijngaard RM, van Thiel IAM. *Candida* spp. in Human Intestinal Health and Disease: More than a Gut Feeling. *Mycopathologia* [Internet]. 2023 [cited 2025 Oct 15];188(6):845–62. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10687130/>

18. Pourliotopoulou E, Karampatakis T, Kachrimanidou M. Exploring the Toxin-Mediated Mechanisms in *Clostridioides difficile* Infection. *Microorganisms* [Internet]. 2024 May [cited 2025 Oct 15];12(5):1004. Available from: <https://www.mdpi.com/2076-2607/12/5/1004>
19. Shu S, Mi W. Regulatory mechanisms of lipopolysaccharide synthesis in *Escherichia coli*. *Nat Commun* [Internet]. 2022 Aug 5 [cited 2025 Oct 15];13:4576. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9356133/>
20. Yang Y, Cao X, Kato N, Wang Y. Gut *Bacteroides fragilis* in health and diseases: An updated review. *Journal of Future Foods* [Internet]. 2025 July 17 [cited 2025 Oct 15]; Available from: <https://www.sciencedirect.com/science/article/pii/S2772566925001429>
21. Sadanandan B, Yogendraiah KM. Enterococcus faecalis Biofilm: A Clinical and Environmental Hazard. *Medical Sciences Forum* [Internet]. 2025 [cited 2025 Oct 15];35(1):5. Available from: <https://www.mdpi.com/2673-9992/35/1/5>
22. Pellegrino A, Coppola G, Santopaolo F, Gasbarrini A, Ponziani FR. Role of Akkermansia in Human Diseases: From Causation to Therapeutic Properties. *Nutrients* [Internet]. 2023 Apr 8 [cited 2025 Oct 15];15(8):1815. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC10142179/>
23. Groeger S, Zhou Y, Ruf S, Meyle J. Pathogenic Mechanisms of *Fusobacterium nucleatum* on Oral Epithelial Cells. *Front Oral Health* [Internet]. 2022 Apr 5 [cited 2025 Oct 15];3:831607. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9037381/>
24. Kamer AR, Pushalkar S, Hamidi B, Janal MN, Tang V, Annam KRC, et al. Periodontal Inflammation and Dysbiosis Relate to Microbial Changes in the Gut. *Microorganisms* [Internet]. 2024 June [cited 2025 Oct 15];12(6):1225. Available from: <https://www.mdpi.com/2076-2607/12/6/1225>
25. Zangl I, Pap IJ, Aspöck C, Schüller C. The role of *Lactobacillus* species in the control of *Candida* via biotrophic interactions. *Microb Cell* [Internet]. [cited 2025 Oct 15];7(1):1–14. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC6946018/>
26. Yokomizo S, Kaneko N, Chen H, Yan L, Tsuji S, Akagawa S, et al. Dysbiosis of the gut microbiome may contribute to the pathogenesis of oral lichen planus through Treg dysregulation. *Mucosal Immunology* [Internet]. 2025 Oct 1 [cited 2025 Oct 15];18(5):1013–26. Available from: [https://www.mucosalimmunology.org/article/S1933-0219\(25\)00055-8/fulltext](https://www.mucosalimmunology.org/article/S1933-0219(25)00055-8/fulltext)
27. Beaty CS, Short AG, Mewar P. Oral Mucosal Lesions, Immunologic Diseases. In: *StatPearls* [Internet] [Internet]. StatPearls Publishing; 2023 [cited 2025 Oct 15]. Available from: <https://www.ncbi.nlm.nih.gov/sites/books/NBK597383/>
28. Khor B, Snow M, Herrman E, Ray N, Mansukhani K, Patel KA, et al. Interconnections between the Oral and Gut Microbiomes: Reversal of Microbial Dysbiosis and the Balance between Systemic Health and Disease. *Microorganisms* [Internet]. 2021 Feb 26 [cited 2025 Oct 15];9(3):496. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC7996936/>
29. Ross FC, Patangia D, Grimaud G, Lavelle A, Dempsey EM, Ross RP, et al. The interplay between diet and the gut microbiome: implications for health and disease. *Nature Reviews Microbiology* [Internet]. 2024 Nov 1;22(11):671–86. Available from: <https://doi.org/10.1038/s41579-024-01068-4>
30. Park I, Mannaa M. Fermented Foods as Functional Systems: Microbial Communities and Metabolites Influencing Gut Health and Systemic Outcomes. *Foods* [Internet]. 2025 Jan [cited 2025 Oct 15];14(13):2292. Available from: <https://www.mdpi.com/2304-8158/14/13/2292>
31. Chaudhari A, Dwivedi MK. Chapter 1 - The concept of probiotics, prebiotics, postbiotics, synbiotics, nutriprobiotics, and pharmabiotics. In: Dwivedi MK, Amaresan N, Sankaranarayanan A, Kemp EH, editors. *Probiotics in the Prevention and Management of Human Diseases* [Internet]. Academic Press; 2022. p. 1–11. Available from: <https://www.sciencedirect.com/science/article/pii/B9780128237335000131>
32. Sejbuk M, Siebieszuk A, Witkowska AM. The Role of Gut Microbiome in Sleep Quality and Health: Dietary Strategies for Microbiota Support. *Nutrients* [Internet]. 2024 Jan [cited 2025 Oct 15];16(14):2259. Available from: <https://www.mdpi.com/2072-6643/16/14/2259>
33. Pattapulavar V, Ramanujam S, Kini B, Christopher JG. Probiotic-derived postbiotics: a perspective on next-generation therapeutics. *Front Nutr*. 2025;12:1624539.