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A REVIEW ON GUT MICROBIOME: FOOTPRINT OF HUMAN HEALTH

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ABSTRACT

The human microbiome or microbiota consists of various microorganisms like bacteria, archaea, viruses and eukaryotes residing within and outside our bodies. The human gut possesses millions of microbes that defining a complex microbial community.Indigenous organisms in the human body are well adapted to the immune system, due to the biological interaction of the organisms with the immune system over the course of time. An alteration in the intestinal microbial community (Gut microbiome) plays a significant role in human health and disease development. These organisms have an influence on human physiology including good health and disease presenting to detriment metabolic and immune functions. Micro-organisms colonise different sites on and in the human body, where they acclimatize to distinct features of each niche. Researches have disclosed the influence of gut microbiome not only on human mind and health status, but also in extensive range of disease switching, ranging from cardio-metabolic diseases, allergies and obesities to life-threatening diseases such as cancer. The human gut microorganisms (mostly non-pathogenic) have symbiotic host relationships and are usually associated with the host's immunity to defend against pathogenic invasion. The mechanism leading to the disease development has a correlation with gut microbiota, metabolic products, and host immune response in humans. The understanding of mechanisms over gut microbiota exerts its positive or harmful impacts remains largely undefined. A comprehensive understanding of gut microbiota interactions, its role in health and disease, and recent updates on the subject are the striking topics of the current review.

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INTRODUCTION

The association of human health with the intestine has been long acknowledged as Hippocrates said, "Death sits in the bowls" in 400 B.C. Many studies worldwide have focused on the significant impact of intestinal microbiota on human health and disease (AboNahas *et al*., 2022). The human body is colonized by a diversity of bacteria, viruses, archaea, and unicellular eukaryotes. Microbes inhabit all human body surfaces, but a significant number of microbes live in the gastrointestinal tract/gut. The human gut possesses approximately more than one thousand microbial species that form a complex ecological community called gut microbiota (Lagier *et al.,* 2016). The human gut microbiota is carrying about 150 times more genes compared to the entire human genome. It is widely accepted that approximately a hundred trillion microbes live on and inside the human body having a key role in various biological processes including health and disease (Wang *et al.,* 2017). They are the primary mediators of body homeostasis, impacting various physiological activities, such as metabolism, inflammation, and haematopoiesis through both intestinal and extra-intestinal actions. The gut microbiota has currently been classified as a "vital organ" because of its multidirectional and communicational connection or axis with other organs through neural, endocrine, humoral, immunological, and metabolic pathways.

Any change in the microbial community not only causes gut-related issues but also influences other organs related diseases, though the actual interaction mechanism between the gut and the organs has yet to be fully understood (Ahlawat and Sharma, 2021). The interaction between host and microbes plays an important role in both health and disease. Gut microbiota diversity is greatly dependent on various host factors including diet, human lifestyle, age, and environmental factors. However, diet is currently considered one of the major factors (modifiers) in modulating the gut microbiota (Simoes *et al*., 2022). Human microbiota has promising potential in altering appetite, increasing nutrient harvest, and exerting energy from various food components. Microbes have also a fundamental role in xenobiotic metabolism. In xenobiotic metabolism, various gut microbes alter the chemical structures of various diet components, drugs, pollutants, and many pesticides (Nakov and Velikova, 2020). Many research studies have supported the concept that gut microbiota plays a key role in modulating immunity, weight gain or loss, energy homeostasis, and obesity-related disorders (Piccioni *et al*., 2022). Likewise, gut microbiota and their metabolites are associated with various non-alcoholic fatty liver diseases (NAFLDs), inflammatory bowels diseases (IBDs), hepatocellular carcinoma, cardiovascular diseases (CVDs), alcoholic liver disease (ALD), chronic kidney diseases (CKDs), and cirrhosis (Hsu *et al*., 2020; Jansen *et al*., 2021;

Ryma *et al.,* 2021; Wang *et al*., 2021; Zhou *et al*., 2021; Philips *et al*., 2022). The compositional difference in gut microbiota has been observed in health and disease conditions. Eubiosis conditions are effective in controlling various diseases caused by microbes. Proper intake of a healthy diet and the development of Eubiosisact in favour of human health. The high intake of antibiotics causes an imbalance in the gut microbiota and favours systemic diseases (Santacroce *et al*., 2021). Several population-based studies have revealed the highly beneficial role of human gut microbiota in healthy people, as well as the importance of well-understanding its structure and the factors that influence its composition, such as food, age, geography, systemic disorders, and drugs (Wang *et al*., 2017; Rowland *et al*., 2018). Phyla Firmicutes, Bacteroides, Actinobacteria, Proteobacteria, and Verrucomicrobia contribute to the significant resident bacterial populations in the gut microbiome (Fava *et al*., 2019). The microbes reside in a mutual association with the host in a healthy state, affecting the host's health by controlling nutrient metabolism, defending against pathogens, and delivering signals to immune cells to promote host physiology and immunity (Ribaldone*et al*., 2022). Bacteria and proteobacteria contribute to carbohydrate digestion, gut microbiota, regulation of the immune system, and defence against pathogen colonization (Rosser and Mauri, 2016; Fan and Pedersen, 2021). For survival, microbes in the intestine tract mainly depend on dietary substrates undigested in the upper digestive tract. Saccharolytic bacterial fermentation typically creates advantageous metabolites, while bacteria switch to an alternative energy source if there are insufficient carbohydrates, leading to the development of other metabolites that could be more disadvantageous to human health (Rowland *et al*., 2018).

The gut environment, sequentially, can help reproduce, grow, and survive the microbial community (Browne *et al*., 2016). Carbohydrates are an essential and significant energy source; also, intestinal microbiota has provided a fermentation stage to deliver vital biomolecules to the host (Conlon and Bird, 2015). A normal balance between the host and gut flora is essential for human health, while disruption is linked with various human diseases, like hypertension, obesity, cardiovascular disorders, diabetes, and IBD (Von Martels*et al*., 2017; Kho and Lal, 2018). However, the human microbiome analysis is still at its initial phase in filling the knowledge gap in the microbiome-host relationship and its role in disease pathogenesis and therapeutical importance. Therefore, further in-depth research is needed to unravel this fascinating area of study. Gut microbiota in major human diseases from the findings of recent epidemiological, physiological and omics-based studies, supported by cellular and animal experiments, it is demonstrated that intestinal microbiota plays a significant role in both health and disease (Ding *et al*., 2019). Some promising studies have been reported and indicated an enormous potential for revolutionizing the pathogenesis of diseases and therapeutic approaches (Ding *et al*., 2019; Yin *et al*., 2019; Rajoka et al., 2020; Bangar *et al*., 2022). Several major human diseases are associated with an altered gastrointestinal microbiota, for example, obesity, diabetes, cardiovascular disorders, cancer, hypertension, and IBDs (Ding *et al*., 2019; Nie *et al*., 2019; Xu *et al*., 2019) It has been challenging to define an appropriate healthy microbiome composition because of inter-individual variation (Lloyd-Price *et al*., 2016). A well-balanced gut microbial community is essential for the host and the microbiome to co-exist in a mutually beneficial relationship.

Diabetes mellitus: Diabetes mellitus causes a significant adverse effect on the health condition of human populations worldwide. Diabetesrelated risk factors include aspects like a family history of diabetes, poor eating habits, and being overweight. Regarding the continuous rise of urbanization, shifts in diet, and the emergence of more unhealthy lifestyles, the growing incidence of diabetes is a global crisis. According to a report, about 463 million people globally reported diabetes in 2019, and future estimates predict that by 2045, the number of diabetic patients will exceed 700 million (Saeedi *et al*., 2019). Recent studies have demonstrated that the progression of diabetes is closely correlated to the alterations in the composition of intestinal microbiota (Sender *et al*., 2016; Gurung *et al.,* 2020). Diet is among the key determinants of the composition of the intestinal microbiota and a significant causal factor in the development of diabetes (Meijnikman *et al*., 2018). Human eating patterns have evolved over the past few decades, with fats preferred over fibers; in response to recent eating habits, intestinal microbiota has also changed. It has been indicated that the influence of microbiota on type 2 diabetes can be mediated through mechanisms involving changes in the butyrate and incretins secretions (Nohr *et al.,* 2013; Baothman *et al*., 2016). In patients with type 2 diabetes, a study showed a moderate degree of intestinal microbial dysbiosis, a decrease in bacteriaproducing universal butyrate, and an increase in opportunistic pathogens (Baothman *et al*., 2016).

Cancer: Cancer is the second most common cause of death globally (Fitzmaurice *et al*., 2017). There is a growing interest in the characterization and functionality of intestinal microbiota due to its complicated relationship with the host (Tao *et al*., 2020). Different studies have indicated that alteration of gut microbiota significantly contributes to developing colorectal carcinoma in genetic and carcinogenic tumorigenesis models (Arthur *et al*., 2012; Vivarelli*et al*., 2019). Metabolomics and metagenomics studies have demonstrated the dual role of gut microbiota in cancer risk reduction and tumour growth, and anti-cancer therapies (Bultman, 2014). A greater abundance of *Bacteroides massiliensis* was found in patients with prostate cancer, while *Eubacterium rectale* and *F. prausnitzii* have been identified in comparatively less abundance, indicating the potential contribution of these specific microorganisms in the pathogenesis of prostate cancer (Chung *et al*., 2018). It has also been found that the gut microbiota is linked with the development of colorectal cancer, with *Fusobacterium nucleatum*, *Bacteroides fragilis*, and *Peptostreptococcusanaerobic* being identified in its development as important players (Hsieh et al., 2018). Gut bacteria, especially *F. nucleatum* and *Clostridium colicanis*, were proposed as indicative markers in gastric cancer's carcinogenesis (Mehta *et al*., 2017). A deeper understanding of the influential role of gut microbiota in the development of cancer has increased the interest in research for microbiome-based therapeutics in cancer treatment. However, more studies involving human participants are required to deeply understand the mechanism of gut microbiota in the development of cancer and its anticarcinogenic characteristics.

CONCLUSION

The crucial role of probiotics in health, disease, and nutrition has increased their scientific and marketing significance across the globe. The attention has been shifted from prospective studies to clinical trials to have a better understanding of how microbiota can interplay in human health and disease. Eubiosis is important in exerting the health endorsing benefits of probiotics. An unhealthy diet intake, such low intakes of fruits and vegetables intakes and overuse of antibiotics can result in dysbiosis. In nutshell, probiotics aid in the treatment of various infectious diseases, dysfunctions of the GI tract, and inflammatory disorders as well as in controlling obesity and diabetes. The advances in gut microbiota modelling and analysis will enhance our knowledge of how they influence health and disease, allowing us to adapt current and forthcoming therapeutic and preventive strategies. Understanding the specific roles played by the gut microbiome in our growth and development, as well as how it functions in health and disease, holds the potential to improve many parts of our daily lives, from improving the formula for infants to offering new approaches in fighting obesity and cancer, among others. As gut microbiota is a complex topic, future research should focus on multidisciplinary approaches, taking into consideration recent innovations in various scientific fields.

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