

“Double-Edged Sword” Effect of the Gut Microbiota Biomodulator, Probiotics: A Key Player in Health and Disease

Md Abdul Alim Al-Bari¹ and Syed Rashel Kabir^{2*}

¹Department of Pharmacy, University of Rajshahi, Rajshahi, Bangladesh

²Department of Biochemistry and Molecular Biology, University of Rajshahi, Rajshahi, Bangladesh

***Corresponding Author:** Syed Rashel Kabir,
Department of Biochemistry and Molecular Biology,
University of Rajshahi, Rajshahi, Bangladesh; E-mail:
rashelkabir@gmail.com; rashelkabir@ru.ac.bd

Introduction

The human body as an excellent culture medium provides nutrients and supports environment for the growth of a wide variety of microorganisms. The constituents of microbial species are known as the human microbiota. The highest bacterial population is found in the colon (gut). Since the gut is essentially sterile at birth, a well-balanced microbial intestinal colonization in early postnatal life is necessary for the development of appropriate immune responses and to establish immune homeostasis later in life. Thus, the microbiota plays essential roles in the maintenance and development of the immune system, in the metabolism and in the body homeostasis. As a result, the microbial communities residing in the human gut microbiota play significant roles in human health maintenance. Although the components and functional characteristics of a 'healthy' gut microbiota remain to be elucidated, any perturbations in the microbial colonization have been associated with an increased risk of numerous diseases. Emerging published and ongoing experimental/clinical evidences suggest that gut microbiota biomodulators, such as probiotics, prebiotics, synbiotics, and postbiotics helps to prevent various disease conditions. Under different dysbiosis conditions, probiotics also act as 'surrogate' colonizers to

prevent numerous immune-, metabolic-, mediated diseases [1]. This editorial perspective aims to discuss on targeting the gut microbiota composition through the use of gut microbiota biomodulators, probiotics in the management of aberrant initial gut colonization and subsequent consequences for the health maintenance or disease conditions. Acquired knowledge and gathering experience on the specific roles of gut microbiota in acquisition, prevention and treatment of disease will help us to make up the possible alteration to maintain, re-establish and enhance health in the human host for a long time.

Manipulating the Gut Microbiota by Probiotics to maintain Health and Treat Disease

In the last decade, a vast number of evidences provide information about differences in gut microbiota composition between healthy and diseased individuals, and any alterations in gut microbiota composition associated with plenty disorders or syndromes. These diseases range from gastrointestinal diseases like inflammatory bowel diseases, chronic idiopathic constipation and colorectal cancer to metabolic diseases and potentially even to diseases like Alzheimer's disease, autistic spectrum disorders, chronic fatigue syndrome, Parkinson's disease, autoimmune diseases like rheumatoid arthritis and multiple sclerosis, allergic diseases and, more recently, in women related diseases such as vulvovaginitis and mastitis. The most studied disease conditions in relation to perturbation of intestinal microbiota are obesity, metabolic syndrome, type II diabetes and bowel diseases [2]. These diseases cause serious

public health problems that have reached epidemic proportions in many developed and middle-income countries. Hopefully, the uses of probiotics and prebiotics influence the balance of beneficial and detrimental bacterial species, and recover homeostasis of gut microbiota compositions in the diseased individuals.

In a "leaky gut", the passage of toxins, antigens or bacteria translocate into the body, which in turn, play pathogenic roles in advanced liver complications such as liver cirrhosis. The translocation of bacterial has close relations of endotoxemia to hyperdynamic circulation, portal hypertension, renal, cardiac, pulmonary, and coagulation disturbances [3]. As therapeutic management of the microbiota-gut-liver axis, prebiotics and probiotics may improve the clinical course of cirrhotic patients. Probiotics also act on nuclear receptors and different enzymes that up regulate oxidative metabolism, down regulate the synthesis of proinflammatory molecules, and restore or maintain a healthy symbiotic gut microbiota. Thus, the probiotics beneficially affects the host by improving the intestinal microbial balance.

It is essential to understand to what extent the intestinal microbiota is subjected to balance by probiotics with functional metabolic signatures and biomarkers. Substantiating the safety and mechanisms of action of probiotic/prebiotic formulations is also critical factor. However, beneficial modulation of the human microbiota by using probiotic strategies holds considerable promise as next-generation drugs, vaccinomics, and metabolic agents in novel drug discovery.

Microbiome Spectrum Disturbances and a of Renal Toxicity

The emerging recent clinical evidences suggest that the intestine and Chronic Kidney Disease (CKD) influence each other. In patients with CKD have a distinctly dysbiotic intestinal bacterial community which in turn drives a cascade of metabolic abnormalities, including uremic toxin production, inflammation, and immunosuppression, that ultimately promotes progressive kidney failure and cardiovascular disease. The uraemic status also affects the composition of intestinal microbiota and generates uraemic retention solutes and their precursors which

in turn, cause disturbances in the protective epithelial barrier of the intestine and the translocation of intestinal microbiota into the body, resultant the formation of uraemia [4]. Although the quality and the evidence based on the dietary measures of prebiotics, probiotics or synbiotics are debatable and contradictory especially in uraemia formation, intestinal uraemic metabolite generation remains an interesting target to obtain in the future as an alternative or additive to dialysis to decrease uraemic toxin generation. Some probiotics are able to change the enzymatic activities of the gut microbiota: e.g. the nitrogen metabolism as reflected by urinary concentration of p-cresol, or the glucosidases, or the bile salt hydrolases, or azoreductase. Thus, the use of probiotics is not completely implemented into the routine clinical practice for primary care physicians. There is still a great controversy with scarce scientific evidence, due to the diversity in the designs there of which justifies the variability in the efficacy results.

Conclusions

In this perspective, we focus on recent advances in the understanding of the role of prebiotics, probiotics, and synbiotics in functions of the gut and the induction and maintenance of numerous disease remissions. The economic and health costs of the disease conditions and their comorbidities such as obesity, systemic inflammation, metabolic dysfunction, fatty liver, insulin resistance/diabetes, or cardiovascular events are significant considerable [5]. Targeting microbiota, in order to restore/modulate the microbiota composition with antibiotics, probiotics, prebiotics, or even fecal transplants, is considered as a promising strategy for the development of new solutions for the treatment of these diseases. Here, off-course we emphasize the beneficial effects of probiotics in numerous diseases, the roles of probiotics in increasing the intestinal permeability and lipopolysaccharide-related endotoxemia must be considered during the course of treatment. Finally, we also consider the apparent roles of prebiotics and probiotics in ameliorating both systemic inflammation and metabolic dysfunction. Present information may be useful in the future design of novel therapies focused on

treating different diseases or symptoms by restoring the gut microbiota balance. As the gut microbiota is intimately influenced by diet, targeting the metabolic pathways involving dietary protein, fiber, prebiotics, probiotics, and synbiotics will be created new therapeutic opportunities for the management a series of diseases. The emerging nutritional interventions may ultimately lead to a paradigm shift in the conventional therapies for the treatment of different diseases.

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