

A Note on Prebiotics Strategy to Cope with Current Health Challenges in Human Beings

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Abstract

The current widely used practices of processed food have resulted in elimination of healthy microflora from human gut leading several health issues like chronic constipation, irritable bowel syndrome, colon cancer, obesity, heart diseases and high cholesterol etc. Amongst others, prebiotic approaches have been developed to promote the growth of beneficial bacteria in the gut to treat gut related disorders and improve human health. Importance of prebiotics in maintaining gut microbial diversity, need of novel prebiotics having varied functional properties and their production strategies for commercial applications have been highlighted in this article.

Keywords: Prebiotics, Fructosyltransferase, Probiotics, Oligosaccharides, Non-digestible dietary fiber.

Introduction

Now a day's good health and balanced diet are the leading issues among all human beings. Therefore, great enthusiasm has been observed for the development of new variety of food [1]. Different bioactive nutrients including prebiotics (fructooligosaccharides, galactooligosaccharides, xylooligosaccharides, lactulose) are available as supplements or have been added in the variety of commercially available foods like yogurts and juices. Prebiotics are oligosaccharides and are known as non-digestible dietary fibers, which sustain a healthy microbiome by regulating gut microbiota and by modifying microbiota composition as well [2]. They are also used to restore bacterial homeostasis due to any health hazard in terms of disease [3].

Prebiotics/non-digestible fiber could usually be obtained from several natural foods like cereals, legumes, nuts, many fruits and vegetables [4]. However, because of frequent use of processed and junk food in the whole world, non-digestible fiber has been

eliminated from our daily life food. Consequently, gut microflora altered in the gut, which results number of gut disorders in every age group of the humans. Growing research literature shows that dietary fiber not only prevents gut diseases but also reduces the risk of heart disease, diabetes, colon cancer and involved in lowering cholesterol [5,6]. The recommended dose of dietary fiber is 25-30g/day; however, a careful estimation is that dietary fiber consumption by an American adult is 15g/day, which is less than half of the recommended dose. Regardless of using different methods to encourage the use of healthy food, the young generation seems trapped in the taste of junk food, which leads obesity, high cholesterol, heart problems and gut issues like constipation, irritable bowel syndrome and colon cancer in early age [7]. These health issues could be improved by adding non-digestible fiber in the food. In this article we are highlighting the importance, challenges and potential solutions of production of novel prebiotics at commercial level (Figure 1).

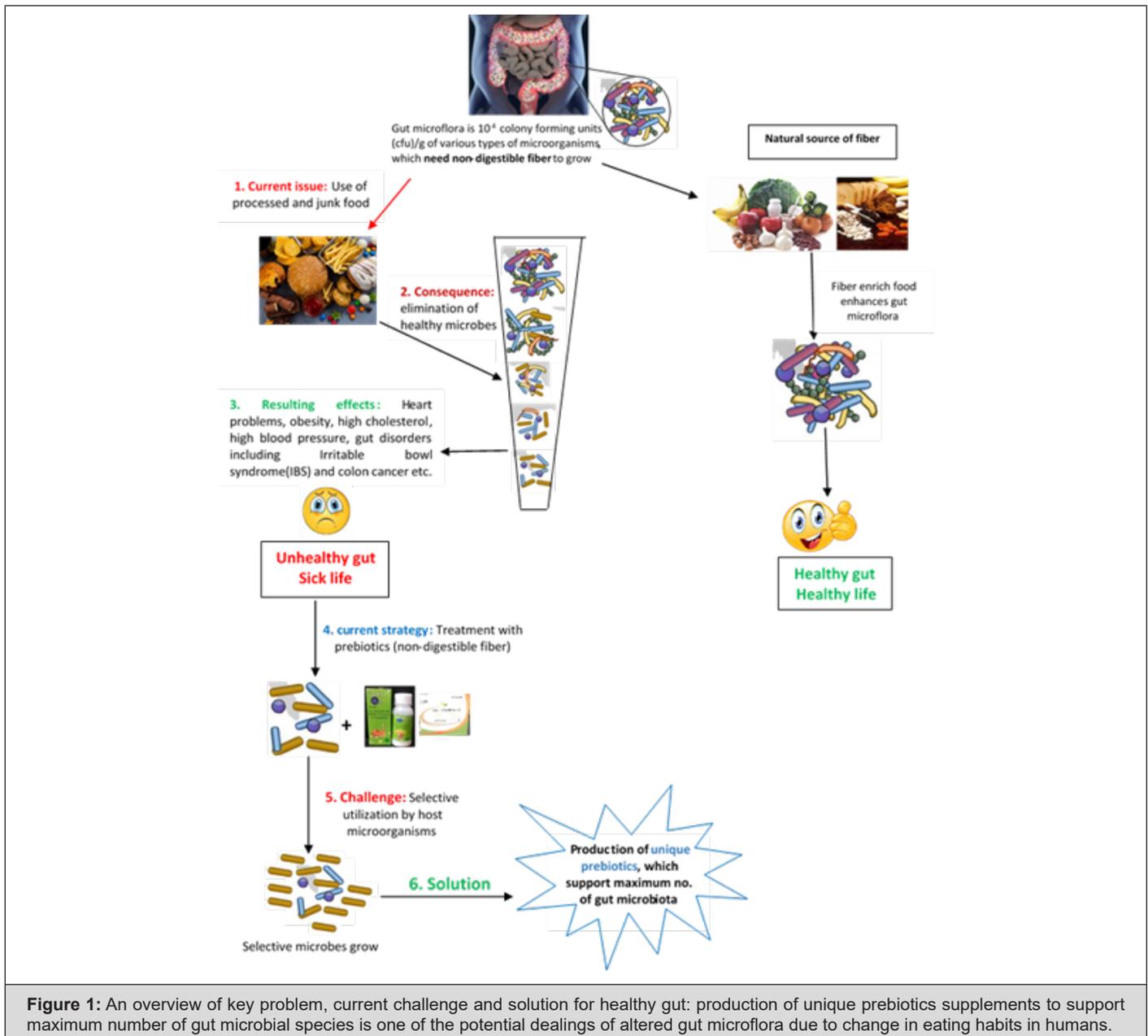


Figure 1: An overview of key problem, current challenge and solution for healthy gut: production of unique prebiotics supplements to support maximum number of gut microbial species is one of the potential dealings of altered gut microflora due to change in eating habits in humans.

Market of Prebiotics

As the importance of prebiotics has been highlighted by growing scientific literature, several researchers around the globe studied the source of natural non-digestible fibers and methods for their production in large quantity to add in the food. Prebiotics have grabbed the attention of pharmaceutical companies and became an important candidate in nutraceuticals to improve human health. Prebiotics market is expected to reach US \$ 5.485 billion by 2024, from US \$ 3.727 billion in 2018 according to global prebiotics market survey. Great health impact and intense research and innovation in the field are two major factors, which will enhance the market of prebiotics further in the near future.

Enzymes for Prebiotic Synthesis

Two groups of prebiotics/fructans, fructans/fructooligo

saccharides (FOS) and galactooligo saccharides (GOS) are well known for health benefits in humans [8-10]. Because of low amount of these oligosaccharides in natural food, it is required to synthesize these compounds in the laboratory for large scale applications. The pre-requisites for commercial production of oligosaccharides/prebiotics at industrial level requires an efficient method and economical raw material to make product cost effective. Biosynthesis of FOS is a preferred method over chemical methods to avoid the production of hazardous by products and low product during acid-catalyzed hydrolysis synthesis of FOS [11,12]. A wide variety of microorganisms and plants synthesize fructans. Several bacterial and fungal species are good sources of FOS producing enzymes, which have been divided into two classes: 1. β -D-fructofuranosidase and 2. Fructosyl transferase according to their enzymatic activity and the product they produced [13] (Figure 2).

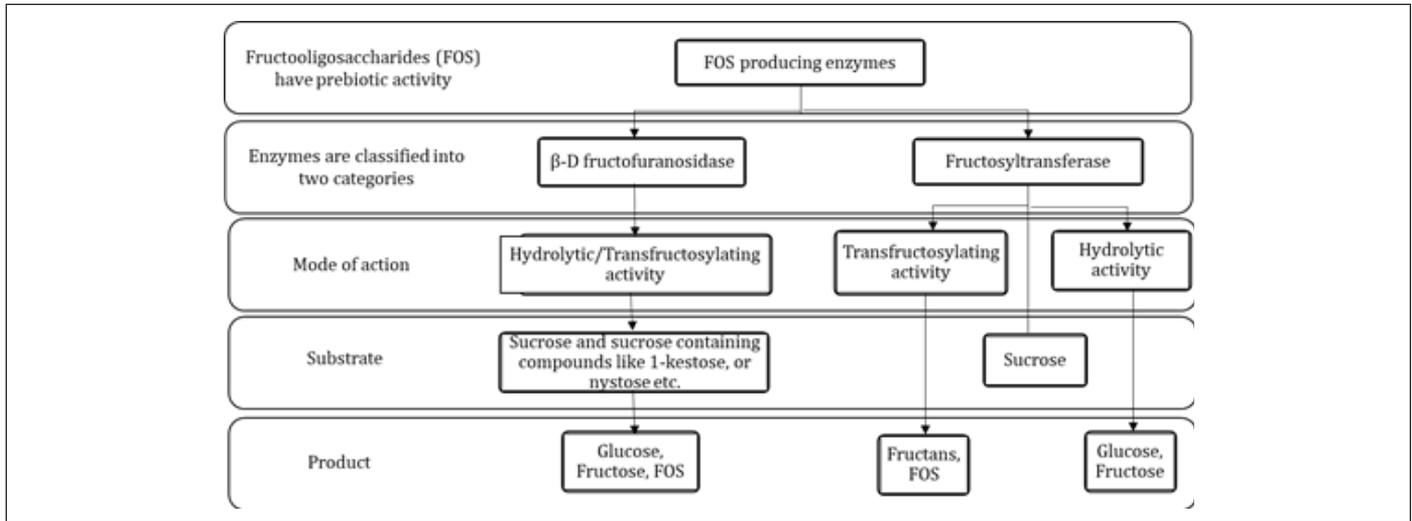


Figure 2: Mechanism of action of prebiotic producing enzymes: β-D fructofuranosidase has more hydrolytic activity than trans-fructosylating activity as compared to fructotransferases. Fructotransferases can produce variety of fructans using sucrose as substrate.

β-D-fructofuranosidase (FFase, EC 3.2.1.26) belong to GH32 family of glycoside hydrolases and involve in hydrolysis of α-1,4-glycosidic bonds of sucrose to produce equimolar mixture of monosaccharide D-glucose and D-fructose [14,15]. When subjected with sucrose containing substrates, these enzymes can be utilized for the production of plasticizing agents, fructooligosaccharides (FOS) and artificial honey [16]. On the other hand, fructosyltransferase (FTase, EC 2.4.1.9 and EC 2.4.1.10), which are grouped in family 68 of Glycoside Hydrolyzing enzymes (www.cazy.org), not only hydrolyze sucrose molecule to yield fructose and glucose but also transfer fructosyl group to sucrose acceptor and produce oligosaccharides/fructans. The fructans synthesized from sucrose contain a terminal glucose molecule [17] and are designated as GF_n, where G refers to the terminal glucose unit, F refers to fructose units and n is the number of fructosyl units per fructan molecule, also designated degree of polymerization [DP]. The products obtained by FTase enzymes have high biotechnological potential and have large number of applications in food and pharmaceutical industry [18].

FTase can be produced by different plants and microorganisms [15,19]. Because of easy handling, low cost and production of large quantity of enzyme, microbial FTase are preferred over plant FTase for prebiotics synthesis [20]. Therefore, fructosyltransferases have been isolated from different fungal and bacterial strains for commercial production of fructooligosaccharides [FOS] [21-25]. The type of FOS produced by different fructosyl transferases depend of the origin of the enzyme. Different enzymes are specific for the types of linkages that are synthesized in their respective FOS and polymer products.

Challenge in Prebiotic and Probiotic Relationship

Every FOS produced by plants, microorganisms or in the laboratory cannot be prebiotic. FOS should have certain properties to declare as prebiotic like

1. They should be resistant to stomach acidic pH and non-digestible by intestinal enzymes,
2. They must be hydrolyzed by gut microorganisms [probiotics],

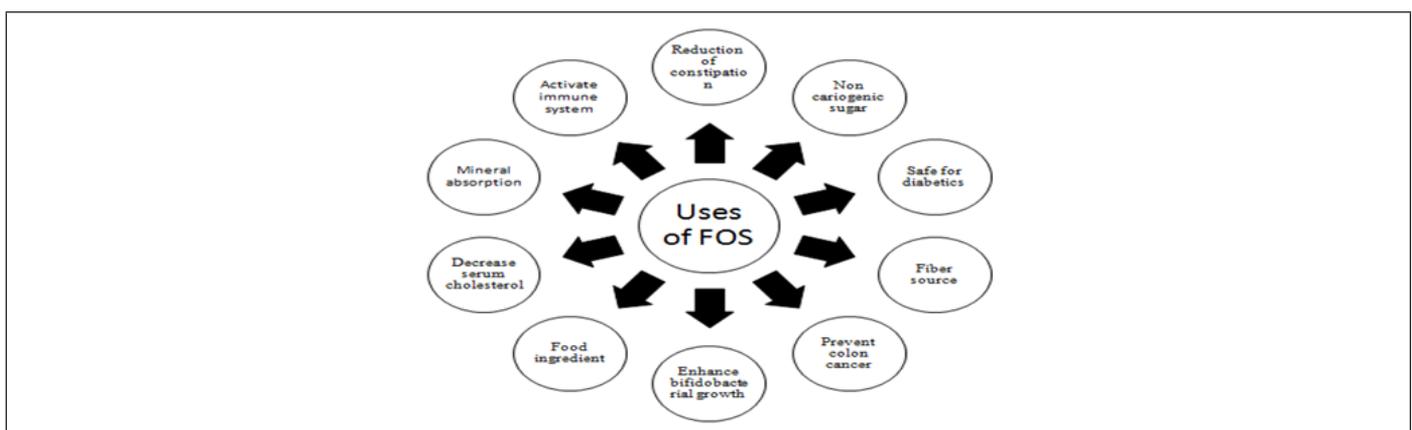


Figure 3: Health benefits of fructooligosaccharides (FOS)/prebiotics: prebiotics can not only be beneficial in gut disorders but also effective against common health problem, like obesity and diabetes, in young generation.

3. They should have positive health impact on host. Health benefits of prebiotics have been investigated and reviewed by several scientists around the globe [26-29] (Figure 3) Most of the prebiotics take part in health benefits by enhancing the growth of microbial species present in the gut. The normal human gut microflora is very diverse and dominated by anaerobic bacterial species like *Fusobacterium* spp., *Bacteroides* spp., *Clostridium* spp, additionally, *Bifidobacterium* spp. and *Lactobacillus* spp. [30]. All these microorganisms are important for healthy gut. However, gut microflora could be altered by changing life style and eating habits. Change in food from healthy, fiber rich [fruits and vegetables] to junk is one of the major reasons of alteration in gut microflora, which results in number of diseases in young age.

Diversity of gut microflora can be maintained by two ways; 1. By taking beneficial bacteria with food as probiotics however, all gut bacterial species are not culturable in the lab. 2. by continuous supply of variety of fiber [prebiotics] to enhance the growth of already existing bacterial species in the gut. Prebiotics produced from different plant, and bacterial sources are being added in yoghurts, juices and even baby formulas by many food companies these days [31]. Nevertheless, the gastrointestinal microflora consists of approximately 10¹⁴ colony forming units [cfu]/g of various types of both harmful and beneficial bacteria. It is not clear, which fructans are the most suitable substrates for the selective growth of specific beneficial species or strains. Therefore, there is huge need of understanding the relationship between prebiotics and probiotics to maintain the diversity of beneficial microbial species in the gut to get maximum health benefits from these microorganisms. Moreover, it is direly needed to explore diverse range of living systems to acquire variety of unique prebiotic compounds.

Novel Prebiotics

It has been observed that one type of fiber helps in growth of few microorganisms, which are not enough to maintain the diversity of gut microflora. Scientists are continuously looking for novel fructosyl transferases from plant and microbial species to produce variety of prebiotics for commercial applications. However, production of novel prebiotics which, could support the growth of large number of gut microbial species is need of the time. To this end we suggest to explore the fructosyltransferases from third domain of life (archaea). Several archaeal strains are annotated to harbour fructan synthesis genes in their genome sequences (www.cazy.org). So far, a few studies have been conducted to determine the role of archaeal or their enzymes in the synthesis of novel prebiotic compounds. These include a levansucrase from a halophilic microorganism *Halomonas mynensis* produced novel saccharides from raffinose, cellobiose, lactose and L-arabinose substrates [32]. In the other study, the GH68 genes from *Halorubrum saccharovororum* and *Natronococcus amylolyticus* were expressed in the heterologous host *E. coli*, and the two recombinant

enzymes displayed levan-forming activity [33]. Our research group is also involved in characterizing archaeal FTase genes that may code for novel prebiotic synthesizing enzymes. Thus, in addition to other sources of fructosyltransferases, archaea may also serve a source of novel fructosyltransferase enzymes for the production of unique prebiotics for nutraceutical market.

Conclusion

Prebiotics, also known as non-digestible dietary fiber, are vital for the nourishment of gut microbial species (probiotics) and can be obtained from fiber rich food. However, because of elimination of natural fiber from food, by frequent use of junk and processed food, gut microflora has been altered. Abolition of specific microbial species from gut thought to be a potent cause of several diseases in early age. Therefore, addition of prebiotics in food has been emerged as an influential way to maintain growth of gut microflora to contest current health challenges in young generation. All research efforts in the field so far directed at the production of novel oligosaccharides to enhance the growth of diverse population of gut microflora. However, an improved understanding of relation between prebiotics and probiotics is required for the synthesis of better oligosaccharides with varied functional properties. Moreover, sincere research efforts are recommended to explore the usefulness of archaeal fructosyltransferase enzymes for the production of novel multifunctional prebiotics supplements for good human health.

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Conflict of Interest

Authors declare there is no conflict of interests exists.

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