

Synbiotics: Necessity of Today's Meal

Narnoliya LK¹ and Jadaun JS^{2*}

¹Center of Innovative and Applied Bioprocessing (CIAB), Department of Biotechnology (DBT), Sector-81 (Knowledge City), SAS Nagar, Mohali, Punjab 140306, India

²Dyanand Girls Post Graduate College, 13/394, Parwati Bagla Rd, Kanpur, Uttar Pradesh 208001, India

*Corresponding author: Jadaun JS, Dyanand Girls Post Graduate College, 13/394, Parwati Bagla Rd, Kanpur, Uttar Pradesh 208001, India, Tel: +91-512-3202435; E-mail: jsjdgpg2017@gmail.com

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Abstract

Synbiotic therapy is a powerful tool of modern medication practices for achieving quick recovery against a vast number of ailments. Synbiotics are the mixed product of prebiotics or dietary fiber and probiotic culture in living form. In clinical trials synbiotics provided superior results over individual treatment of prebiotic and probiotic substances. So these days this is the easiest and cheapest way to modulate the gut microbiome in the favor of good health. Administration of synbiotics is helpful for individuals of all age groups under different kind of disease conditions such as cancer, trauma, allergy, and inflammatory bowel disease and post-surgery infections. Many synbiotic formulations are available in market for public use and research is continue for manufacturing more better of the existing ones for superior activity.

Keywords: Disease; Microbiome; Synbiotics; Inflammatory

Introduction

A typical animal body especially human being, requires a perfect diet for maintaining the homeostasis. By following the dietplan, suitable for a particular age group, we can avoid major menaces caused by the diseases. Most of the sever or sometime lethal diseases are the outcomes of continual imbalance at nutritional level, intake of higher or lower quantity of any element or component in diet can cause flaws in the host body. Due to fast moving and modern life style we are lacking in consumption of good and healthy food, therefore, keeping human health in mind we are compelled to take some supplements in addition to our regular meal. Actually, nutritional status of meal directly or indirectly affect the microbial population of gastro-intestinal tract (GIT) up to major extent, because health of host is majorly depend on the ratio of beneficial microbe to harmful one [1].

There are a large number of microbes, approximately ten times higher than the total cells present in human body, were inhabitant on human GIT and mainly these are the members of phyla Bacteroidetes, Firmicutes, and Actinobacteria and collectively these are called as "microbiota" or "microflora" [2,3]. Diversity of microflora of GIT depends on several factors such as intestinal environment, primarily pH, nutritional level of host body, age and health status. Besides these factors abundance of micro flora is also affected by genotypic and environmental factors [4-6]. It is prerequisite, to prevent gut dysbiosis (imbalance of gut microbiota) to reduce the risks of several complications such as gastrointestinal diseases, metabolic disorders, obesity, malnutrition, anemia and food intolerance [7-9]. Colon is the most preferable site for colonization of microbes in GIT tract (from stomach to anus) here more than 70% of total microbes of body are present [10]. Modulation of gut microbiome could be performed by taking additional supplements and experts suggest administration of prebiotic and probiotics for balancing the micro biota [11]. Probiotics are the living organism either in viable culture or in lyophilized powder form which they positively influence the number of beneficial

microbes in gut. Prebiotics were termed for any dietary constituent, which were non digestible carbohydrates; provide growth promoting effect on limited species of gut microbiota [12]. A probiotic may be defined as a pure culture of bacteria, which is one of the member of gut microbiota and its presence should promote the beneficial species and limit the growth of harmful species.

Earlier, probiotic and prebiotic are consumed by the host separately but recent progress in this research area suggest that use of prebiotic and probiotic in combination possess more promising growth promoting effect on gut microbiome, this type of combination therapy termed as synbiotics [13,14].

What are synbiotics?

A large number of combinations of prebiotic and probiotic can be tried for making the best fusion product having the superior beneficial effects on intestinal environment. Synbiotic therapy fastens the growth rate of useful microbes and simultaneously reduces the abundance of harmful bacteria because prebiotics are the substances which encourage the growth of probiotic microbes as number of probiotic organisms increase density of harmful species goes down. Bacteria of Lactobacillus and Bifid bacterium group are the dominants in gut microbiome and these are able to show some beneficial activities for maintaining the good host physiology [15]. Application of probiotics lead to several advantageous functions such as reduction in frequency of antibiotic associated diarrhea, minimizes the side effects of chemotherapy, lessen the chances of rotavirus infection, modulation of hormonal and immune response, detoxification of compounds, improved lactose intolerance, ant hypertension, production of hypocholesteremic substances, and biotransformation of metabolites [16-20].

Problem associated with probiotics is that their low survival during passages through GIT hence combination with prebiotic could protect them against the enzymatic and chemical reactions of pancreatic juice, bile juice and intestinal fluid. In 1995, Gibson and Roberfroid used the term 'Synbiotic' to describe this combination study of probiotic and

prebiotic. Here, we reviewed about symbiotic availability in market, their beneficial role against several diseases and its limitations.

Application of synbiotics for human health

Success of symbiotic formulae depends on the efficiency of both prebiotic and probiotic components used for production of particular synbiotic (Table 1). Till to date, many synbiotic combinations have

been prepared and tried in research for promoting the human health but only very few were successful and available in market. In the process of synbiotic products development, Professor Stig Bengmark did a milestone work and in the year 1999 he started a project with his colleagues for the formulation of one of best combination of prebiotic and probiotics [21].

Probiotics	Prebiotics	Synbiotics
Lactobacillus genus bacteria	Inulin	Lactobacillus genus bacteria+inulin
Lactobacillus and Bifidobacterium genus bacteria	Inulin	Lactobacillus and Bifidobacterium genus bacteria+inulin
Lactobacillus and Bifidobacterium genus bacteria	Oligofructose	Lactobacillus and Bifidobacterium genus bacteria+oligofructose
Lactobacillus, Bifidobacterium, Enterococcus genus bacteria	FOS	Lactobacillus, Bifidobacterium, Enterococcus genus bacteria+FOS
Lactobacillus, Streptococcus and Bifidobacterium genus bacteria	FOS	Lactobacillus, Streptococcus and Bifidobacterium genus bacteria+FOS
<i>Lactobacillus acidophilus</i> La5, <i>Bifidobacterium lactis</i> Bb-12, <i>Streptococcus thermophiles</i> and <i>Lactobacillus bulgaricus</i>	Oligofructose	<i>Lactobacillus acidophilus</i> La5, <i>Bifidobacterium lactis</i> Bb-12, <i>Streptococcus thermophiles</i> and <i>Lactobacillus bulgaricus</i> +Oligofructose
Bifidobacteria	FOS	Bifidobacteria+FOS
Lactobacilli	Lactitol (lactulose)	Lactobacilli+lactitol
Bifidobacteria	GOS	Bifidobacteria+GOS
<i>Lactobacillus acidophilus</i> P106	Oat	<i>Lactobacillus acidophilus</i> P106+Oat
Lactobacillus spp	Rice bran derivatives	Rice bran derivatives
<i>Lactobacillus paracasei</i> sp <i>paracasei</i> (FDDVS/ <i>Lactobacillus casei</i> -01 nutritis, Chr. Hansen, Hoersholm, Denmark)	FOS	<i>Lactobacillus paracasei</i> sp <i>paracasei</i> +FOS+Soya milk

Table 1: Table showing the prebiotic and probiotic component of synbiotic formulations studied under different clinical trial.

For development of this combination they screened more than 500 bacterial cultures, which have better ability to produce antioxidants, anti-inflammatory proteins, especially anti-inflammatory cytokines and more precious quality is to enhance the anti-inflammatory properties of other bacteria. They tested their ability under the simulated conditions of gastric juice i.e., at low pH 2.5 for two hour and also after exposure to 20% bile for onehour period. After screening test of bacterial strains, they finalized seven bacteria for further study as probiotics and these bacteria were *Pediococcus pentosaceus*, *Leuconostoc mesenteroides*, *Lactobacillus paracasei* F19, *Lactobacillus paracasei*, *Lactobacillus paracasei*, *Lactobacillus plantarum* F5 and *Lactobacillus plantarum* F26. These bacteria have remarkable characteristics for its application as synbiotics such as they can utilize inuline or amylopectin as solely carbon source, β -galactosidase producing, antigram positive microbial substances, antimicrobial activity against oral pathogen *Candida* and gastric pathogen *Helicobacter pylori* and also reduce symptoms of lactose intolerance.

Further, among these seven, total four strains were finalized for production of synbiotic and development of Synbiotic 2000 which was the concluding point of this study. It is a mixture of four bacteria of Lactobacillus group (*Pediococcus pentosaceus*, *Leuconostoc mesenteroides*, *L. paracasei* subsp. *paracasei* and *L. plantarum*) along with its prebiotic component which contains four fermentable fibers such as 2.5 g of each beta-glucan, inulin, pectin, and resistant starch (Medipharm AB, Kagerod, Sweden and Des Moines, IA). Recently,

Synbiotic 15, a variant of Synbiotic 2000, is also launched and it contains three bacterial strains (*L. Plantarum*, *L. Paracasei* and *Pediococcus*) instead of four bacterial strains as in Synbiotic 2000.

Synbiotic 2000 and its variant are proved very useful for those who suffer with obesity and chronic diseases. Another example of commercial synbiotic is SB3-Synbiotic marketed by an USA company PuoriApS. This is constituted by using strains of Bifidobacterium BB-12 and *Lactobacillus fermentum* PCC along with vitamin C for boosting of immune system. Protexin company also released a series of synbiotics for example Lepicol (psyllium husk, inulin and 5 strains of live bacteria), Bio-KultInfantis (7 strains of probiotics, high in omega-3 and vitamin D3, FOS and gum acacia as prebiotic), multi-strain Bio-Kult (14 strains of probiotics, soya and traces of milk), Bio-Kult Pro-Cyan (cranberry extract, probiotics and vitamin A) and Bio-KultCandéa (seven strains of probiotics, garlic and grape fruit seed extract). More details of these products were obtained from a web server.

In the synthesis of a novel synbiotic, rice bran derivatives like RiSolubles, RiceMucil, and Cea100 are used as prebiotic with Lactobacilli species as probiotic [22]. Formulation of 'Synbiotic Yoghurt' has been achieved by combining the *Lactobacillus acidophilus* P106 with oats and testing of this product on mice revealed that it as a safe and beneficial product [14]. Synbiotic fortified soya milk showed more useful effect on gut microbiome and for production of this product, prebiotic FOS/inulin and probiotic *Lactobacillus paracasei* sp

paracasei (FDDVS/*Lactobacillus casei*-01 nutrish, Chr. Hansen, Hoersholm, Denmark) were inoculated in soya-milk.

Mechanism of action of synbiotics

Two components of synbiotic are genuinely differ in their mode of action but their site of action is closely related, probiotic are functional in small and large intestine, although effect of prebiotics is observed mainly in large intestine, so synbiotics spread their effects synergistically [23]. Probiotics has the ability to alter the intestinal milieu by modifying the epithelial and mucosal barrier function through mucosal immunity. These also showed impact on cells of immunomodulation such as dendritic cells, monocytes, macrophages, B-cell, T -cell, epithelial cell [24,25]. Probiotic bacteria resist the growth of other pathogens by producing antimicrobial substances, which lower the luminal pH, preventing the translocation and adherence of bacteria and these antimicrobial substances are termed as bacteriocins. Several bacteriocins were produced by *Lactobacillus* sp., which restrict the growth of other gram positive bacteria and some gram negative bacteria [26,27]. Synergistic effect of probiotic and prebiotic is confirmed by Nemcova et al. [28] and host microbes presented an enhancement in number of *Lactobacilli* and *Bifidobacterium* counts and decrement in counts of *Escherichia coli*, *Clostridia*, *Enterobacteriaceae* bacteria etc. Prebiotics functions as selective growth promoting factor for a dedicated group of probiotic strains. Prebiotics support the growth of probiotics by providing adaptability against luminal environmental variations, whether it may be pH, temperature and oxygenations [29]. Another profit of synbiotic applications is that it reduces the level of toxic metabolites, leading to alleviation of nitrosamines and carcinogenic materials and increases the concentration of short chain fatty acids, ketones, carbon disulfide, and methyl acetates, propionate and butyrate [30,31]. However, mechanism of action of prebiotic on balancing of gut microbe is still not fully understood, although, consequently we can state that synbiotics lead to development of a favorable environment for the growth of selected microbe in intestinal lumen, which resulted in good health of host organism.

Beneficial effects of synbiotics

A number of clinical trials have been performed for the testing the efficacy of symbiotic treatment under variable level of chronic infections and other diseases. We summarized the achievement of synbiotic approach in medicinal research as follows-

- In control of acute pancreatitis [32,33],
- In reduction of inflammatory bowel disease (IBD) [34,35],
- In curing of trauma [36,37],
- In cancer prevention [38-41],
- In reduction of allergic symptoms [42,43],
- In reduction of incidence of ventilator-associated pneumonia [44],
- Influence on mineral absorption, bone mineral content [45],
- Prevent oral candidiasis [32],
- Reduction of incidence of septic morbidity and postsurgery infections [46,47],
- Improvement in inflammatory diseases [48].

Safety issue of synbiotics

The well-documented and studied synbiotic is synbiotic 2000. Till date, almost after 10 years of research on the synbiotic, it is highlighted

that it comes under safe category and its consumption upto 3 month displayed no side effects. Even there is no side effect reported when its administration was done in critically ill patient, such as HIV infected, liver transplanted, post-surgery and patient with ulcerative colitis [49,50]. Actually, both counterpart of synbiotic either *Lactobacillus* sp. or FOS are approved by FDA under GRAS (generally recognized as safe) category, so automatically the side effects of synbiotic became low. Although, a regularized research is required to observe each and every aspect related to the safety issue because probiotic are microbes and there are more chances of mutations so it is necessary to track their probiotic efficiency in each round of formulations.

Conclusions and Future Prospects

For living a healthy life, use of synbiotics became popular and need of daily life routine. If we want to maintain balance in microbial population of intestinal lumen, we have to supplement our food with additional probiotics and dietary fibers/prebiotics. It provides immunity against a wide range of infections and allergies. Simultaneously, it is very cheap and it is a natural way to enrich the most diverse and functional part of digestive tract like gut by beneficial microbiota. Any foodstuff, which we consider as prebiotic and each strain of probiotic bacteria have very unique mechanism of action in GIT to provide beneficial symptoms to host health. There is long time of research which is fully dedicated on this aspect but still we are on the periphery of the scientific investigations which is needed for its full understanding of interactions between prebiotic and probiotic to improve the host health. Although, a limited number of synbiotic formulations are available in market as product and also in reach of public domain and a large number of products are in trail but still meaningful research efforts are required to improve the efficacy of the synbiotic formulations.

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