

Synbiotics: A Promising Approach For Improving Human Health

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Abstract

The present environmental condition and lifestyle are becoming the cause of an increase in health issues like diabetes, obesity, and intestinal disorders in a growing population. The demand for functional foods as nutritional and immunity-boosting supplements has increased due to people's increased health consciousness during the last few years, which has accelerated a number of clinical trials on the positive effects of combining probiotics and prebiotics as synbiotics on hosts. A healthy diet is extremely important in maintaining the health of an individual. There are multiple mechanisms that have proposed the effect of synbiotics in controlling various diseases. Hence present review focuses on the most recent finding regarding health benefits, formulation criteria, action mechanism, and future prospects of synbiotics with their positive effect on the host.

Keywords: Functional Foods, Probiotic, Prebiotic, Synbiotic

INTRODUCTION

Food product supplement that provides a positive effect on a host is becoming popular among health-conscious people and this contributes a major role in driving the market growth of functional food in coming years. Due to the increasing health problems, drug intake is increasing, as are healthy food intakes, to improve nutrition and enhance health and wellbeing, this leads to a high demand for functional foods to follow a healthy lifestyle without dependency on drugs. Therefore, the demand for probiotics, prebiotics, and synbiotics have more significant now a day. Many researchers evaluated that the combination of probiotic and prebiotic works more beneficially on the host rather than individual effect. Two health supplements with nutritive and immunity-boosting properties in one dose provide extra benefit to the host and thus increase the market demand. The market for synbiotics containing probiotics and prebiotics has increased in many countries. Multiple researchers have proposed the positive effect of synbiotic products in controlling various diseases.

The human gastrointestinal tract contains microbes that are responsible for maintaining human health. The host and intestinal microbiota must be in a healthy balance to perform good functioning of microorganisms in the human gut,

this imbalance leads to several disorders like irritable bowel disease, improper digestion, allergic diseases, gastrointestinal disorder, etc. Therefore, it is necessary to know the functioning of microflora and their mechanism of action to improve host health. The concept of food components known as probiotic and prebiotic and the combined action of both as synbiotic is introduced to help intestinal microflora for proper functioning and improved health benefits to the host. The present review discusses the various research done on the health benefit of synbiotics, their mechanism of action, formulation criteria, and future aspects.

SYNBIOTIC

Currently, synbiotic (combination of prebiotic and probiotic) production is mostly dependent on the well-characterized probiotic, belonging to genera *Lactobacillus* and *Bifidobacterium*, which ferment the non-digestible prebiotic in the human gut (Handan and Hutkins, 2000). It is found that the synergetic effect of prebiotics and probiotics significantly improve human health (Kerry et al., 2018). To develop synbiotic food products, it is important to choose probiotics and prebiotics carefully in order to have a favourable impact on the health of the host. The probiotic should be the only microbe that the prebiotic ingredient stimulates. (Markowiak and Slizewska, 2017). The synbiotic products improve the implantation of live microbes into the intestinal tract and stimulate the growth and/or activity of gut microbes and positively influence human health (Pandey et al., 2015). In concern with human health, synbiotic products show their potential in diseases related to inflammation and metabolism. The main components of a healthy gut are short chain fatty acids, acetate, propionate, and butyrate from the bacterial fermentation of non-digestible fibers in the colon (Rios Covian et al., 2016).

In recent years, many researchers are taking interest in finding the role of synbiotic products on human health. Several clinical trials are taking place on developing synbiotic food products by using different probiotic strains combining with prebiotic component and reported a beneficial effect on human health. Recent study shows that a staple food such as pasta can be converted into synbiotic food by using prebiotic fiber β -glucans and probiotic bacteria *Bacillus coagulans*. Consumption of synbiotic pasta shows positive effect on individual having Hyperglycemia, type-2 disease and obesity but it does not show much benefit on metabolic and inflammatory effect on host (Angelino et al., 2019). The increase number of viable cell count is observed in synbiotic litchi juice developed by using probiotic *Lactobacillus casei* microencapsulated by spray drying using whey protein concentrated powder (WPCP) in the combination with different prebiotic components- inulin, gum acacia and oligofructose among all these combinations, WPCP with inulin shows the best result (Prakash et al., 2017). A freeze-dried synbiotic product incorporating prebiotic component inulin, gum acacia, and probiotic *Lactobacillus plantarum* shows the promising result and the highest growth rate of bacteria is found in sample containing inulin followed by gum acacia and glucose (Dhewa et al., 2011). Table-1 shows the various synbiotic formulations.

Criteria for formulating synbiotic

The synbiotic products improve the implantation of live microbes into the digestive tract and stimulate the proliferation and/or activity of gut flora and positively influence human health (Pandey et al., 2015). The most frequent and common probiotic strains used for formulating synbiotic are *Lactobacilli*, *Bifidobacteria* spp, *S. boulardii*, *B. coagulans*, and common prebiotics oligosaccharides like fructooligosaccharides, galactooligosaccharides, and xyloseoligosaccharide, inulin extracted from natural sources such as chicory and yacon roots. The development of synbiotic food products depends on various criteria as mentioned in figure 1, these criteria help to provide synbiotics with maximum health-promoting effect on the host.

Synbiotic: mechanism of action

The mechanism of synbiotic action is associated with the alteration of gut microbiota with the combination of probiotic strains and appropriate prebiotics as their substrates. Without a necessary prebiotic substrate, it is difficult for probiotic

microorganisms to survive in the environment of the digestive system and will not be able to tolerate oxygenation, pH, and temperature, as appropriate prebiotic flourishes the population of probiotic strain in the digestive system. There are two modes of action in which synbiotic works one is improved viability of probiotic strains and the other is provision of desired health effects (Manigandan et al., 2012). Figure 1 shows the detailed action mechanism of synbiotics.

The administration of synbiotic modulates the intestinal microbiota and significantly increases the short chain fatty acids, ketones, carbon disulfide, and methyl acetate and provides a potential health benefit to the host (Vitali et al., 2010). The therapeutic efficiency of synbiotic includes antimicrobial and anticarcinogenic qualities, antidiarrheal aspects, antiallergenic qualities, osteoporosis prevention, reduction in serum fats and blood sugars, regulation of the immune system, and treating liver-related brain dysfunction (Reddy et al., 2011). Synbiotic reduce the decomposition process in the intestine and prevents constipation and diarrhea. Synbiotic also work in preventing osteoporosis, reduction of blood fat and sugar levels, regulating the immunological system, and treatment of brain disorders associated with abnormal hepatic function (Pandey et al., 2015). Furthermore, the mechanism of synbiotic action in the digestive system, also needs to be investigated, which may have a positive impact on human health.

HEALTH EFFECTS OF SYNBIOTICS IN VARIOUS DISEASES

Synbiotics show various positive effects on human health improvement of liver function and immunomodulating ability, increased level of lactobacilli, Bifidobacteria, balanced gut microbiota, and prevention of bacterial translocation and reduced incidences of nosocomial infection in surgical patients (Zhang et al., 2010). Synbiotics' effects on various diseases are mentioned below in details:

Irritable bowel syndrome

Irritable bowel syndrome (IBS) is a common disorder related to the gastrointestinal tract, symptoms include abdominal pain, abdominal discomfort, and altered bowel habits (Lovell and Ford 2012). The notable positive effect of synbiotic containing six strains of *Lactobacillus* (*rhamnosus*, *acidophilus*, *casei*, *bulgaricus*, *platarum*, and *salivarius*), two strains of *Bifidobacterium* (*bifidum* and *longum*), and *Ulmusdavidiana* (Slippery elm bark powder), *Geumurbanum* (herb bennet powder), inulin powder as prebiotics were found in IBS patients not only on gastrointestinal symptoms and fatigue as well as improvement in abdominal bloating, frequency of stool (Lee et al., 2019). Synbiotic have the efficiency to improve the symptoms of IBS. However, more study is needed to understand the mechanism of synbiotic action. The short-course trial indicates that synbiotic may influence the gastrointestinal tract in Diarrhea-predominant IBS patients (Moser et al., 2019). Administration of synbiotic containing *Bifidobacterium lactis* and inulin in children with IBS show significant improvements in the initial phase of treatment as well as a higher rate of recovery when treated with synbiotics (Basturk et al., 2016).

Hypercholesterolemia

Hypercholesterolemia is the presence of a high level of cholesterol in the blood. The serum total cholesterol and LDL-Cholesterol were decreased in rats, fed with synbiotic containing probiotic *Bacillus coagulans* and prebiotic inulin (Abhari et al., 2015). The combination of probiotic and prebiotic can alter the AST (aspartate transaminase) and ALT (alanine aminotransferase) values in rats and also improve the lipid metabolism in hypercholesterolemia. The probiotic, prebiotic, and synbiotic significantly reduced total cholesterol, LDL cholesterol, and Tg levels in hypercholesterolemia-induced rats. The impact of synbiotic is more in LDL-Cholesterol value (Aktimur et al., 2017). The synbiotic formulation containing *Lactobacillus acidophilus*, *Lactobacillus casei*, and *Bifidobacterium bifidum* with natural prebiotic substances viz. banana powder, maltodextrin, and honey, enhance the efficiency to decrease the blood cholesterol level in albino rats (Kumar et al., 2019).

Obesity

Overweight and Obesity are the results of excess fat accumulation and this condition leads to increased health risk (Purnell et al., 2018). The synbiotic supplement contains *Lactobacillus acidophilus*, *Bifidobacterium lactis*, *Bifidobacterium longum*, and *Bifidobacterium bifidum* and the prebiotic component galacto oligosaccharide mixture effectively improves the obesity-induced disruption of gut microbiota and increases the abundance of intestinal microbiota associated with positive health effect (Sergeev et al., 2020). The synbiotic helps in decreasing waist circumference in overweight or obese children (Kianifar et al., 2018). An oral probiotic or synbiotic supplement has a small effect in decreasing waist circumference but does not alter body weight or BMI (Suzumura et al., 2019). Administration of synbiotic prepared using *Bifidobacterium animalis* and *Lactobacillus paracasei* and prebiotic oat β -glucan significantly reduce body weight gain and metabolic complications in the high fat diet fed mice and also restore intestinal microbiota (Ke et al., 2019). A synbiotic supplement containing selected strains like *Lactobacillus gasseri* and prebiotic component galactomannan and/or inulin fibers shows a positive effect in reducing weight and anti-inflammatory activity and also has a synergetic effect on short-chain fatty acid production due to which increased weight management becomes more effective (Ferrarese et al., 2018).

Diabetes

Type 2 diabetes is a common metabolic disorder. Several studies reported the positive effect of probiotics and prebiotics in chronic diseases including Diabetes Mellitus. Synbiotic diet supplement also shows a positive effect in improving lipid metabolism and glucose homeostasis in type 2 diabetic patients (Mahboobi et al., 2018). The daily consumption of synbiotic bread containing beta-glucan, *Bacillus coagulans*, inulin, and lactic acid reported a positive effect on hemoglobin A1c, plasma Superoxide dismutases, and Glutathione peroxidase among type 2 diabetic patients but it does not show any effect on Fasting Plasma Glucose, serum insulin, homeostatic model assessment of Insulin Resistance, high-sensitivity C-reactive protein, and total antioxidant capacity. However, further studies are required to confirm these effects of synbiotic bread (Ghafouri et al., 2019). Short-term supplementation of Synbiotic consisting of *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Lactobacillus fermentum*, *Lactobacillus gasseri*, and fructo oligosaccharide may affect the lipid profile and total antioxidant capacity in pregnant women with Gestational Diabetes Mellitus, it is also effective in decreasing blood pressure and useful in managing Gestational Diabetes Mellitus complication in pregnant women. However, it does not affect the Fasting Plasma Glucose and insulin resistance indices (Nabhani et al., 2018). The synbiotic supplements could decrease the concentration of serum triglycerides in pre-diabetic adults who are at risk of diabetes and cardiovascular diseases. However, further studies are needed to determine the therapeutic effects of synbiotic supplements in prediabetic individuals (Kassaian et al., 2019).

Oral health

Dental demineralization and carious lesions occur due to an acidic environment, predominantly created by *Streptococcus mutans* in the oral cavity. Probiotic *Lactobacillus acidophilus* combined with galactooligosaccharides and fructooligosaccharides significantly decreases the growth rate of *Streptococcus mutans* (Nunpan et al., 2019). More studies are needed to be done to understand the use of synbiotic for the oral microbiota (Kojima et al., 2016). There is some limitation associated with the use of synbiotic in oral health. Probiotics alone may not be able to quickly colonize adult oral cavities to maintain good oral hygiene (Lazarevic et al., 2010, Tiihonen et al., 2010). Therefore, the administration of synbiotic i.e. appropriate prebiotic along with probiotic is more effective and may prevent the growth of oral candidiasis (Ohshima et al., 2016). More studies are therefore required to determine the effect of synbiotic that help to suppress candida infection in the human oral cavity. The new synbiotic developed against oral pathogens shows that arabinose, xylose, and xylitol can be used as prebiotics, and five lactobacilli isolates from the oral cavity can be used as probiotics and inhibit the growth of *Candida albicans* and *Porphyromonas*

gingivalis and inhibit the production of insoluble glucan by *Streptococcus mutans*. This indicates that novel synbiotic can be developed by using an appropriate combination of probiotic and prebiotic in future (Kojima et al., 2019).

Cancer

Mammalian microbiota plays a role in tumourigenesis, metastasis, and propagation of tumour cells, and therefore these human microbiotas can affect the efficacy as well as the toxicity of cancer treatment. There is a growing appreciation of the potential role of probiotic, prebiotic, and synbiotic in the prevention and treatment of cancer. Many studies indicated the positive effect of prebiotic and probiotic against tumours of the colon in animals but human data is limited. The preoperative administration of synbiotic containing *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus casei*, *Bifidobacterium*, and fructooligosaccharide significantly decreases postoperative infection rates in a patient undergoing colorectal cancer surgery (Flesch et al., 2017). The administration of synbiotic containing probiotic *Lactobacillus acidophilus*, *Bifidobacterium* sp., *Streptococcus thermophilus*, *Lactobacillus casei*, *L. delbrueckii* subsp. *bulgaricus* and *Bifidobacterium longum* and a prebiotic: chicory fructooligosaccharides exert significant antimutagenic properties and protection against the development of preneoplastic lesions in rats (Gavresea et al., 2018). Perioperative administration of synbiotics containing *Lactobacillus acidophilus*, *Lactobacillus rhamnosus*, *Lactobacillus casei*, *Bifidobacterium bifidum*, and fructooligosaccharides decreases postoperative mortality and complication rates and also could protect the intestinal barrier to prevent bacterial translocation and infection in patients undergoing surgery for periampullary neoplasms tumors (Sommecal et al., 2015). The administration of synbiotic (inulin + *Lactobacillus plantarum*) on Azoxymethane mediated colorectal cancer-induced rat model, showed that synbiotic diet effectively decreases pathogenic bacteria like *Salmonella* spp. and *Escherichia coli*, microbial enzymes, and the colonic aberrant crypt foci (one of the markers for colon cancer development in rodents and human) and increases the abundance of probiotic (Chaiyasut et al., 2016). The synbiotic product Kefir has beneficial effects on cancer prevention and treatment. Kefir contains bioactive component such as peptides, polysaccharides, and sphingolipids which has a protective role in many oncologic diseases (Rafie et al., 2015). Moreover, additional research is required to confirm the beneficial effect of synbiotic in controlling and treatment of cancer.

Diarrhea

Several clinical trials reported a positive effect of synbiotic in the management of acute diarrhea in children which includes a decrease in diarrhea duration, fast improvement in stool consistency, normalization of gut microflora, decreases in the use of antibiotics, antiemetics, and antipyretics, and enhance the efficacy against diarrhea originated from rotavirus (Jog, 2018). The early administration of synbiotic with antibiotic therapy could prevent antibiotic-associated diarrhea in children. However, synbiotic do not work on duration, stool consistency, and the frequency of defecation if antibiotic-associated diarrhea already occurs (Goli et al., 2019). The synbiotic containing *Lactobacillus* sp., *Streptococcus* sp., *Bifidobacterium* sp., and fructooligosaccharides decreases the duration of diarrhea in children with acute rotaviral diarrhea (Dewi et al., 2016).

Respiratory tract infection

Respiratory tract infection is an infectious disease that affects the upper and lower respiratory tract. The meta-analysis suggested that the administration of synbiotic could show a notable positive effect among adults than infants and children for preventing respiratory tract infections. However, more investigation is needed for strain-specific and dose-specific approaches (Chan et al., 2020). The occurrence of viral infection in children having asthma may reduce by the administration of synbiotic containing *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Streptococcus thermophilus*, *Bifidobacterium breve*, *Lactobacillus acidophilus*, *Bifidobacterium infantis*, *Lactobacillus bulgaricus*, and Fructooligosaccharide (Ahanchian et al., 2016). The occurrence, duration, and severity of upper respiratory tract viral infection may reduce by using a synbiotic strategy (Hamid and Jafari, 2016). Early intervention of synbiotic mixture

containing a mixture of *Bifidobacterium breve* and a galacto or/and fructooligosaccharide prevents symptoms of asthma and frequent wheezing and/or noisy breathing in infants having atopic dermatitis (Van der Aa et al., 2011).

Atopic dermatitis

Atopic dermatitis is an allergic disorder that makes skin red and itchy, which may be associated with altered gut microbiota. The synbiotic supplement contains *Lactobacillus casei*, *Bifidobacterium lactis*, *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, fructooligosaccharide, galactooligosaccharide, and biotin shows prominent effect in improving atopic dermatitis in children (Ibanez et al., 2018). The meta-analysis suggested that a multi-strain synbiotic product shows a significantly more beneficial effect on the prevention and treatment of atopic dermatitis in children (Chang et al., 2016). The clinical and immunological effect of synbiotic containing *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Streptococcus thermophilus*, *Bifidobacterium breve*, *Lactobacillus acidophilus*, *Bifidobacterium infantis*, *Lactobacillus bulgaricus*, and Fructooligosaccharide, improves the severity of atopic dermatitis in infants and children and have potential for prevention and treatment of atopic dermatitis (Farid et al., 2011).

Helicobacter pylori infection

Helicobacter pylori infection is a common bacterial infection in humans. The meta-analysis showed that synbiotic might improve the eradication rate of *Helicobacter pylori* and significantly reduce the rate of antibiotic treatment (Pourmasoumi et al., 2019). The administration of a synbiotic containing *Bifidobacterium lactis* with clarithromycin-based triple eradication therapy shows positive effects in eradicating *Helicobacter pylori* infection, decreases the side effects of antibiotics, and helps reduce or eliminate dyspeptic symptoms such as abdominal pain, diarrhea, and vomiting (Sirvan et al., 2017). The synbiotic supplement improves the eradication rate and side effects such as anorexia when added with *Helicobacter pylori* quadruple therapy (Shafaghi et al., 2016).

The addition of synbiotic containing *Lactobacillus*, *bifidobacterium*, and *enterococcus* with clarithromycin-based triple therapy reduces the side effect intensity of antibiotics and significantly improves the eradication rate of *Helicobacter pylori* infection (Sahin et al., 2013).

4. Effect of synbiotic on infants

Most infants suffer from colic pain in the first three months of life. The synbiotic treatment contains *Lactobacillus casei*, *L. rhamnosus*, *Streptococcus thermophilus*, *Bifidobacterium breve*, *L. acidophilus*, *B. infantis*, *L. bulgaricus*, and fructooligosaccharide significantly improve the colic symptoms by manipulating intestinal microbiota and no complication recorded by using the synbiotic formula in infants (Kianifar et al., 2014). Several studies showed that probiotic and synbiotic beneficially affect in prevention and treatment of infantile colic symptoms like pain and fussiness (Ahanchian and Javid, 2017). The intervention of synbiotic containing *Streptococcus faecalis*, *Clostridium butyricum*, *Bacillus mesentericus*, and *Lactobacillus sporogenes* and fructooligosaccharide shows rapid improvements in infantile colic and is effective in managing colic pain and reduce the mean daily crying time in new born (Vijayalakshmi et al 2017). The synbiotic containing fructo-oligosaccharides and *Bifidobacterium breve* in combination with an amino-acid-based formula showed a positive effect on intestinal microbiota and are suitable for diet management in infants (Fox et al., 2019). The administration of synbiotic supplements containing short-chain galacto-oligosaccharides, long-chain fructo-oligosaccharides, and *Bifidobacterium breve* resulted in a reduction of *Enterobacteriaceae* and increment in early modulation of *Bifidobacterium* in cesarean-born babies (Chua et al., 2017). The infant formula supplemented with synbiotic containing fructooligosaccharides, galactooligosaccharides, and *Lactobacillus paracasei* shows a significant reduction in episodes of lower respiratory tract infection and no serious adverse events in new born babies (Szajewska et al., 2017). The intervention of synbiotic formula

containing *Bifidobacterium lactis* and fructooligosaccharides significantly reduces the incidence of functional constipation, infantile colic pain, and regurgitation and results in normal growth of infants (Vandenplas et al., 2017).

Synbiotic and Covid-19

In the present situation of the Covid-19 pandemic where data regarding nutrition required in coronavirus infection are still lacking. Individuals are relying on food supplements that can boost their immunity and protect them against COVID -19 virus infection. Coronavirus infection is showing different symptoms in different individuals according to the severity of the disease, diarrhea and respiratory infection are some of the common symptoms of the virus which occur due to disturbance in gut microbiota. The use of synbiotic supplements possibly can be one of the treatments for covid-19.

The effectiveness of targeting gut imbalance in COVID-19 is unknown. Research shows that synbiotic have a positive effect in modulating gut microbiota, therefore, they can help in improving the gastrointestinal symptoms of covid-19. A synbiotic formula enhanced antibody production against SARS-CoV-2 in patients with COVID, as well as decrease pro-inflammatory immune markers and restore gut imbalance (Zhang et al., 2022). The use of some vitamins, trace elements, nutraceuticals and probiotic could be useful in the prevention and management of covid -19 infections (Jayawardena et al., 2020). Nutrition supplements can be used to improve the gut microbiota and could be one of the ways to decrease the impact of covid-19 in elderly people (Dhar and Mohany 2020). A recent study shows that modification in gut microbiota can decrease the complication and intensity of upper respiratory tract infection which is one of the major effects of covid-19 (Gao et al., 2020).

Future prospects of Synbiotic

The expansion of clinically efficient synbiotic composition remains a challenge, and certain criteria must be satisfied. Knowledge of intestinal microbiota and environment will improve the ability to formulate a new synbiotic functional product for different uses and help to a well-demonstrate beneficial effect on the host. The synbiotic have the commercial and clinical potential to develop many economic opportunities and promising effects in solving health problems related to the digestive system and skin. There is a need to monitor the function of probiotic continuously to demonstrate the long-term effect of introduced strains (Kearney and Gibbons, 2018) and their prebiotic substrate. The formulation of synbiotic combination with effective doses of each ingredient that provide clinical benefit to the host is still a challenge. The criteria for probiotic and prebiotic selection and the combination should be logical and satisfy the entire requirement to confirm its synergistic effect on the host (Krumbeck et al., 2018). Every microorganism has a different carbohydrate utilization pattern which should be kept in mind before designing a new synbiotic food product. Complete knowledge about the mechanism of probiotics and prebiotic helps scientists to develop synbiotic functional food which modulates the intestinal microbiota in such a way that provides positive health effects in preventing and treating several diseases. Still, there is not much information on the action of prebiotics and synbiotic; furthermore, clinical trials are needed to be done to claim the health effect of synbiotics (Pandey et al., 2015).

Conclusion

From the above mention studies, it is clear that the synergistic effect of both probiotic and prebiotic as synbiotic have a more beneficial effect on the host rather than working individually. A probiotic and prebiotic component is selected in such a way that their combination offers the greatest therapeutic value to the host as well as able to prevent several diseases related to the digestive system. Prebiotic stimulates the growth and activity of probiotic in the colon which are either already presents in the gut or ingested and helps in controlling several diseases like obesity, gastrointestinal disorder, allergic disease, irritable bowel disease, etc. Research has been done on probiotics and their positive effects on the host, however, the combination of healthy microbes and non-digestive bioactive compounds, which have a

synergetic effect, requires further clinical trials to develop new synbiotic functional foods that could help to treat various digestive and skin problems.

Conflict of interest Statement

There is no conflict of interest.

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Table: 1. Details of various Synbiotic Combination

PROBIOTIC	PREBIOTIC	REFERENCE
Bifidobacterium, Lactobacilli, S. boulardii, B.coagulans	FOS, GOS, XOS, Inulin, fructans	(Pandey et al., 2015)
Bifidobacterium breve	Mixture of GOS and FOS	(Mazzola et al., 2015)
Bifidobacteria, Bacteroides fragilis, Peptostreptococcaceae, Klebsiellae	Fructo-oligosaccharides	(Hoseinifa et al., 2016)
Bifidobacteria lactis, Lactobacillus bulgaricus, L. acidophilus, L. rhamnosus	Lactulose	(Oliveira et al., 2011)
Bifidobacterium adolescentis, L. plantarum	Xylo-oligosaccharides	(Aachary and Prapulla, 2011)
Bifidobacterium longum, B. catenulatum	Galacto-oligosaccharides	(Macfarlane et al., 2008)
Bifidobacterium bifidum, B. lactis	Fructo-oligosaccharides	(Bartosch et al., 2005)
Lactobacillus caseimicroencapsulated by spray drying using whey protein concentrated powder (WPCP)	Inulin, Gum acacia and Oligofructose	Prakash et al., 2017)
Lactobacillus Plantarum	Inulin and Gum acacia	(Dhewa et al., 2011)
Lactobacillus rhamnosus	Inulin	(Szydłowska and Krajewska, 2019)
Bifidobacterium lactis	Oligosaccharide	(Sazawal et al., 2010)
Bifidobacterium	Inulin and Oligofructose, lactulose, and resistant starch	(Slavin, 2013)
Bacillus Coagulans	β-glucans	(Angelino et al., 2019)
Lactobacillus plantarum	Cacao pod husk pectin	(Kuo et al., 2021)
Lactiplantibacillus pentosus GSSK2	Isomalto-oligosaccharides	Khanna et al., 2021)

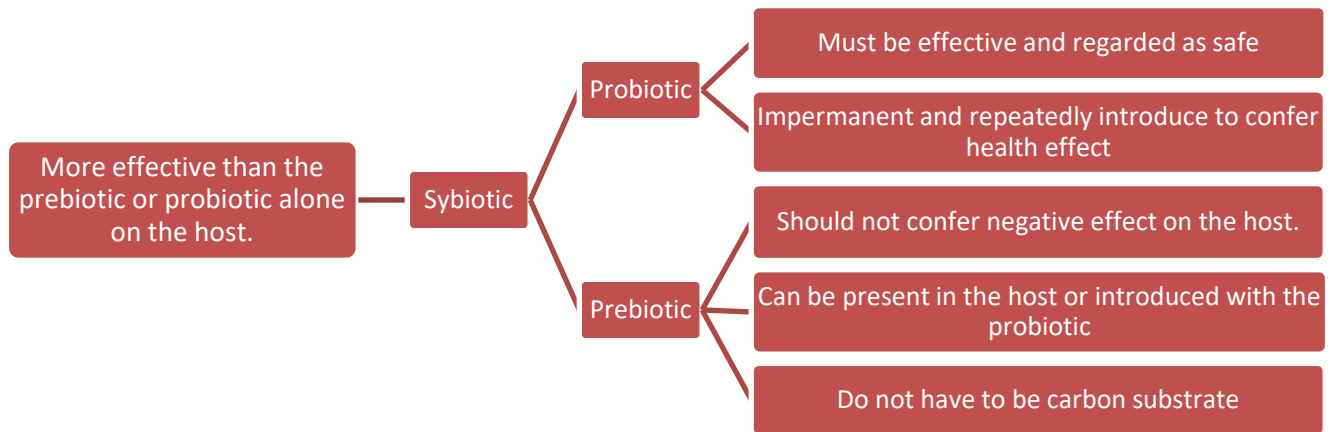


Fig. 1: Synbiotic: formulation criteria

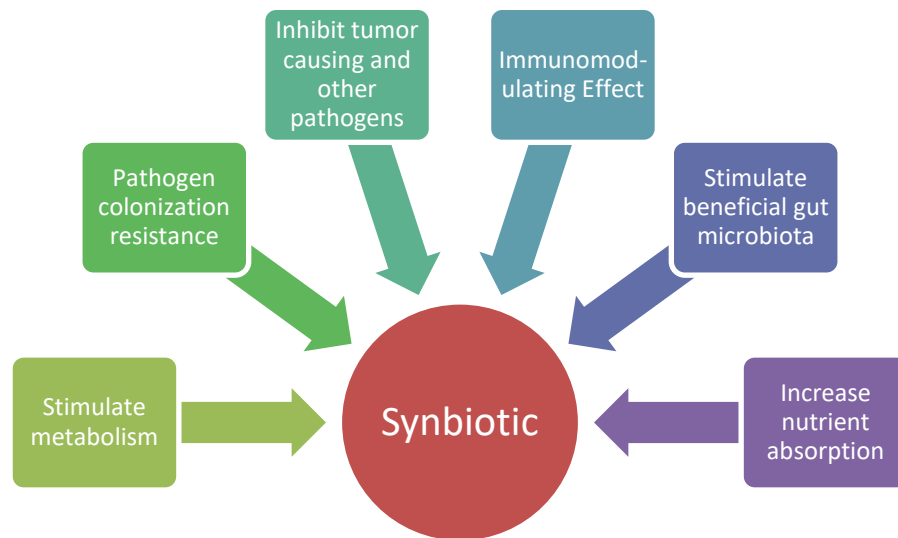


Fig. 2: Synbiotic: Mechanism of action