

Review Article

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## A Review on Probiotic and Health Benefits of Probiotics

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### ABSTRACT

Probiotics are kind of live and beneficial microorganisms that reside in the gastrointestinal tract of human and rodent and also naturally found in the fermented milk products. The probiotic correlation between consumption of probiotic and amelioration of metabolic problems has been confirmed by various studies. The microbes most commonly used as probiotic are lactic acid bacteria. Moreover, numerous strains of probiotic are belonging to genus *Lactobacillus bifidobacterium*. Moreover effects of probiotic has been reported to be strain dependent, although plethora of studies are coming throughout The world on health benefits of probiotics, still there is confusion about specific and accurate way by which probiotic influence the metabolism in general disorder. Therefore probiotics bacteria improve health by different mechanism such as improve hypercholesterolemia by binding of cholesterol to cell surface, assimilation of cholesterol, co-precipitation of cholesterol and finally lower the blood cholesterol. Probiotics have impact on obesity by lowering body weight, regulating lipid and glucose metabolism, have improvement of diabetes by improving insulin resistance, blood glucose level and also probiotics have role on improvement of colon cancer. This review more focuses on advantage effective of probiotics on health.

#### Keywords

Probiotics, Hypercholesterolemia, Obesity, Diabetes

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### Introduction

About  $10^{14}$  bacteria live in the colon of humans. Imbalance in gut microbiota may result in numerous metabolic disorder viz. obesity, diabetes, heart ailment, Dysbiosis in gut microbiota, results in to oxidation of more energy from undigested food (Turnbaugh *et al.*, 2009). Initiation of fat storage (Suppressing Fiaf) altering the gut peptides synthesis related to homeostasis of energy for example glucagon like peptide YY and peptide-1 and metabolic endotoxemia

(higher LPS imbalance). Metabolic endotoxemia, low grade inflammation, insulin resistant and other metabolic disorders. Therefore function and structure of the intestinal microbiota should be normalized, the ultimate method for normalizing the gut microbiota is by oral intake of probiotic (Kopp *et al.*, 2009).

*Bifidobacterium* and *Lactobacillus* are the genera of bacteria mostly used as probiotics. *Lactobacillus* are lactic acid bacteria which are used for food preservation and fermentation for thousands years. Lactic acid

bacteria are Gram positive, non-toxic, non-pathogenic fermentative bacteria, which produces the lactic acid from carbohydrates during fermentation of food. *Saccharomyces boulardii* which is a yeast also used as probiotic. But some other species of bacteria such as *Bacillus* and *E. coli* are also being used as probiotic (Hütt *et al.*, 2006).

### **History of probiotic**

Probiotics are kind of microorganisms, generally reside in the gastrointestinal tract of host. These are symbiotic microorganism, according to studies and investigation they have beneficial effect on host. The probiotic word derivative from the Latin (*pro*) and Greek (*bio*) literally meaning “for life”. History of probiotics is as old as human history, as it is firmly related to the utilization of fermented food. Metchnikoff known as father of probiotics at the starting of 20<sup>th</sup> century, he was the first conceptualize of probiotics. Metchnikoff in 1907 suggested that there are some kinds of bacteria present in the fermented milk products that produce acids, if consumed habitually, lead to healthier and long life. The probiotic (*Lactobacillus bulgaricus*) discovered by Metchnikoff was involved in the combination of fermented milk.

In 1953 probiotics introduced by the German scientist Werner Kollath “are kind of active substances that are essential for health development.” In 1954 Vergin introduced term of probiotics for the first time, while he was working on the antibiotic and other microbial compound detrimental impact on the gut microbiota. He found “probiotika” which is favorable for the gut microbiota. In 1965, Stillwell and Lilly defined probiotics as “substances secreted by one organism which stimulate the growth of another organism.” More specifically, Fuller in (1992) defined probiotic as “a live microbial food supplement which usefully impacts the host by

improving intestinal microbial balance.” (Gasbarrini *et al.*, 2016) And there were also other researcher which had their own different definition for probiotic. In 2001 World Health Organization (WHO) and Food and Agriculture Organization (FAO) of the United Nation developed well-defined probiotic, as probiotics are “live microorganism, which, when administrated in adequate amounts, confer health benefit on the host.” These kind of microbe can be bacteria, yeast or viral and generally can be seen under microscope (Gasbarrini *et al.*, 2016) (Table 1).

### **Mechanism of action of probiotics**

Have competition for nutrients.

Antimicrobial compounds such as organic acid, dipicolinic acid, bacteriosin and hydrogen peroxide are yielded by which the development of disease causing microbes is hampered.

Have competition for adhesion sites (colonization resistance) and Alters the pathogenic bacteria through development of biofilm.

Reducing the yield of molecules related to inflammation (IL-6, TNF- $\alpha$ ).

It normalizes the intestinal gut microbiota.

Calcium and other minerals absorption is enhanced.

Intestinal gut permeability is improved

By reducing luminal pH, it acts as a barrier to the development of disease causing enteric bacteria.

Its metabolic product reduces the toxigenic and mutagenic reaction.

Production of Butyric acid, Butyric acid is consumed by enterocytes.

Enhance the fat oxidation.

Enhance the level of adiponecetin. (Faujdar *et al.*, 2016)

### **Health benefits of probiotics**

In the recent years researchers are more interest to work on role of probiotics on



**Table.1** Different strains of probiotics bacteria which have different beneficial effects

No.	Probiotics Used	Model	Beneficial effects	References
1	<i>L. plantarum</i>	Human	Reduced $\gamma$ -glutamyltranspeptidase, T-cholesterol, glucose and LDL	(Barreto <i>et al.</i> , 2014)
2	<i>B. lactis</i> HN019	Human	Reduced T cholesterol, body weight, LDL, interleukin-6proinflammatory factor and tumor necrosis factor	(Bernini <i>et al.</i> , 2016)
3	<i>L. acidophilus</i> NCFM	Human	Insulin sensitivity improve in type2 diabetes	(Andreasen <i>et al.</i> , 2010)
4	<i>L. gasseri</i> BNR17	db/db mice	Improved diabetes, suppressing blood glucose level	(Yun <i>et al.</i> , 2009)
5	<i>L. reuteri</i> GMN 32	Rats	Prevent DC in DM rats and regulate blood glucose level	(Lin <i>et al.</i> , 2014)
6	<i>L. casei</i> Supplementation	Human	Type 2 diabetes	(Khalili <i>et al.</i> , 2019)
7	<i>L. rhamnosus</i> GG	Rats	Hypercholesterolemia	(Sangwan <i>et al.</i> , 2018)
8	<i>L. fermentum</i> FTDC 8312	Mice	Hypercholesterolemia, decrease T-cholesterol and LDL-C, increase HDL-C	(Lye <i>et al.</i> , 2017)
9	<i>L. rhamnosus</i> GG	Mice <i>C57BL/6J</i>	Non-alcoholic fatty liver disease and dyslipidemia	(Kim <i>et al.</i> , 2016)
10	<i>L. plantarum</i> LRCC 5273	Mice <i>C57BL/6</i>	Hypercholesterolemia and cardiovascular disease	(Heo <i>et al.</i> , 2018)
11	<i>L. plantarum</i> CUL 66	In vitro	BSH, lowering cholesterol and cholesterol metabolism (cholesterol homeostasis)	(Michael <i>et al.</i> , 2016)
12	<i>L. gasseri</i> SBT 2055	<i>Sprague</i> <i>Dawley</i> Rats	Glucose tolerance and anti-obesity effect	(Shirouchi <i>et al.</i> , 2016)
13	<i>L. rhamnosus</i> NCDC 17	Rats	Type 2 diabetes	(Singh <i>et al.</i> , 2017)
14	<i>L. plantarum</i> SCS2	Mice	Hypoglycemic effect	(Meng <i>et al.</i> , 2016)
15	<i>L. plantarum</i> MTCC 5690 and <i>L. fermentum</i> MTCC 5689	<i>C57BL/6J</i> Mice	Insulin resistance and type 2 diabetes	(Balakumar <i>et al.</i> , 2018)
16	<i>L. casei</i> CCFM 419	<i>C57BL/6J</i> Mice	Hyperglycemic in type 2 diabetes and insulin resistance	(Li <i>et al.</i> , 2017)

## **Probiotics and hypercholesterolemia**

As per WHO cardiovascular diseases (CVD) will affect around 23.6 million individuals around the world by 2030 and will be the lead cause of death (WHO). In CVD cholesterol accumulates abnormally (hypercholesterolemia) in the veins as well as arteries, and this accumulation leads to obstruction in the flow of blood (atherosclerosis). Higher level of LDL-C is correlated with the higher risk of hypercholesterolemia. Probability of heart attack is observed to be three times more in hypercholesterolemic person than those who have normal blood lipid profile (Ebel *et al.*, 2014). Exact cause of hypercholesterolemia is not known till now. But eating habits along with sedentary lifestyle could be considered as one of the putative cause in occurrence of hypercholesterolemia.

Many drugs such as statin (simvastatins, atorvastatins, pitavastatins) are available in the market for lowering the cholesterol levels in the blood. Statins inhibit the activity of the enzyme involved in cholesterol biosynthesis in the liver (Bellosta *et al.*, 2004) but some researchers have reported the side effects (muscular pain and muscle weakness) of statin (Kim *et al.*, 2017). Now-days many reports are available indicating the beneficial effects of probiotics on hypercholesterolemia both in humans and rodents without side effects (Cavallini *et al.*, 2009; Yin *et al.*, 2010). Different mechanisms for lowering cholesterol by probiotics have been reported by different workers. Probiotics *L. rhamnosus* BFE5264 lowers the cholesterol levels in blood by incorporating the cholesterol in their plasma membrane and increased cholesterol excretion through faeces (Mathara *et al.*, 2008).

*L. casei* LC2WL probiotics bacteria degrades the bile salts by their BSH activity (Xiong *et*

*al.*, 2017), Probiotic *L. plantarum* NCU116 increases the LDL-C receptor (or by development of expression of LDL-c gene) in the liver (Li *et al.*, 2014). *L. plantarum* CA16 alone or in combination with *L. rhamnosus* GG exhibited the hypocholesterolemic effects in mice fed high fat diet supplemented with cholesterol (Kumar *et al.*, 2013; Wang *et al.*, 2013). *L. rhamnosus* GG exhibited the beneficial effects in hyperlipidemic rats through modulation of gastrointestinal gut microbiota (Kumar *et al.*, 2013). Yogurts containing *B. longum* BB536 have been reported to decrease levels of TG, LDL-C and TC in hypercholesterolemic albino rats (Al-Sheraji *et al.*, 2012). *B. longum* SPM1207 fermented yoghurt improved the dyslipidemia in humans (Kurpadet *et al.*, 2018). Mixture of few probiotics was observed to be more effective in improving the hypercholesterolemia than single strain of probiotic (Chang *et al.*, 2017). Mixture of five probiotics were reported to be more effective in the treatment of nonalcoholic fatty liver disease (NAFLD), improvement of dyslipidemia, inflammatory markers and liver function (Al-muzafar *et al.*, 2017). Similarly mixture of two *Lactobacillus* strains (*L. plantarum* and *L. reuteri*) and mixture of three *bifidobacterial* strains (*B. breve*, *B. longum* and *B. lactis*) have significant effect in decreasing serum TG, LDL-cholesterol and TC in hypercholesterolemic rats (Chang *et al.*, 2017).

## **Probiotics and obesity**

Obesity and its associated metabolic disorders viz. diabetes, hypertension, cardiovascular disease, non-alcoholic fatty liver disease and insulin resistance are increasing epidemically throughout the world. In 2008 approximately one-third of adult population in the world (1.46 billion people) was overweight as well as obese, and obesity had been reported to more in females than males (Frühbeck *et al.*,

2013). Many factors viz. environmental, host genome, diets, modern societies were reported to be the cause of the obesity. In addition dysbiosis of gut microbiota is also considered as additional factor in occurrence of type II diabetes mellitus and obesity (Moreno-Indias *et al.*, 2014).

Probiotics have been reported to exert anti-obesity effects (Alard *et al.*, 2016), and different probiotics have been reported to have different mechanism in lowering body weight (Park and Bae *et al.*, 2015). *L. plantarum* 9-41-A and *L. fermentum* M1-16 probiotics have been reported to have beneficial effects by regulating lipid and glucose metabolism (Xie *et al.*, 2011), *L. GG* lowers endotoxaemia (Bajaj *et al.*, 2014), some probiotic for instance *L. plantarum* produces the conjugated linoleic acid (Dahiya and Puniya *et al.*, 2017), some probiotics like *L. gasseri* SBT2055 reduces the cell size (hypertrophy) and increases the cell number (hyperplasia) in white adipose tissue (Hamad *et al.*, 2008) and some like *L. casei* NCDC19 even increases the energy expenditure by increases the expression of genes related to the metabolism of lipid (Jangra *et al.*, 2019; Miyoshi *et al.*, 2014).

Whereas supplementation of *L. plantarum* LG42 decrease, the expression of lipogenic genes (ACC, LXR- $\alpha$ , and SREBP-1) in liver tissue, expression of PPAR- $\alpha$  and CTP-1, responsible for beta-oxidation of fatty acid, increases in mice. Also *L. plantarum* decreases the expression of C/EBP- $\alpha$  and PPAR- $\gamma$  genes (Park *et al.*, 2014). Lowering of PPAR gamma could be correlated with reduced differentiation of adipocytes and reduced storage of fats under such conditions. *Lactobacillus paracasei* F19 exhibited the antiobesity effects in mice by increasing the levels of ANGPTL4, an inhibitor of lipoprotein lipase (LPL). Low LPL activity has been correlated with reduced fat storage

in adipocytes (Tanida *et al.*, 2008). Some probiotics improves the insulin resistance in mice through increasing the natural killer cells (Ma, *et al.*, 2008). Some probiotics increases the bifodobacterial numeral in the colon (Rather *et al.*, 2014). Some probiotics produces short chain fatty acids such as butyrate, propionate and acetate and these fatty acids have been reported to regulate food intake and induces the satiety through gut peptides (GLP-1, PYY) (Torres-Fuentes *et al.*, 2015). VSL#3 has been reported to increase the GLP-1 production through butyrate produced by colonic fermentation. GLP-1 decreased the food intake, reduced adiposity and improve glucose tolerance in mice (Liang *et al.*, 2014). But health benefits of probiotics had been conveyed to be strains dependent. Some researchers had conducted probiotic don't have effect on body weight (Jangra *et al.*, 2019) and even some have reported gain in body weight due to consumption of probiotics (Stenman *et al.*, 2016).

### **Probiotics and diabetes**

Recent studies have shown that more than 382 million individuals are suffering from diabetes around the globe. Diabetes mellitus is of two kinds, diabetes mellitus type 1 and diabetes mellitus type 2. Pancreas do not synthesizes the insulin in T1DM. But in T2DM body do not respond to the insulin produced by pancreas (insulin resistance). Probiotics have been reported to be effective in improving the insulin resistance, and different mechanisms have been proposed by different researchers. Beneficial effects on blood glucose levels are considered as one of the reasons in improving insulin resistance. Glucose levels in the blood is considered directly proportional to blood insulin levels (Hsieh *et al.*, 2013). Reduced body weights were considered another possible mechanism in improving insulin resistance and diabetes.

There are many reports suggesting the positive correlation in between insulin resistance and body weight (Alemzadeh *et al.*, 2008).

Many reports showed that the oral take of probiotic have positive effects on oxidative stress, metabolic lipid profile and high sensitivity C-reactive protein in T2DM patients. Mixture of probiotics (*L. casei*, *L. acidophilus*, *L. bulgaricus*, *L. rhamnosus*, *Streptococcus thermophiles*, *B. longum*, *B. breve*) ingested for eight weeks exhibited the hypoglycaemic effects (Asemi *et al.*, 2013). Improvements in insulin resistance could be expected under hypoglycaemic conditions as glucose triggers the release of insulin from the beta cells of the pancreas. Recently, feeding of *L. casei*NCDC19 fermented milk along with sucrose and high fat diet to the c57bl/6 mice for 18 weeks have been reported to lower the glucose of blood, insulin serum and HOMA-IR score significantly when compared to group fed high-fat and sucrose diet only (Jangra *et al.*, 2019).

### **Probiotics and Dyslipidemia**

High fat diet has been reported to cause dyslipidemia. Many probiotics have been reported to improve the high fat diet associated dyslipidemia. Although many mechanisms have been suggested by different workers but exact mechanism of action is yet to be elucidated. Hypoglycemia is considered as important factor that leads to improvement of dyslipidemia because both glucose and insulin are considered as driver for lipogenesis (Basciano *et al.*, 2005). Probiotics hypoglycemic effects had been described by different workers (Al-Salami *et al.*, 2008). Decreased expression lipogenic genes (Sreb1/Srebp1c, Sreb1/Srebp1c, Mlxipl, Nr1h5, Fasn, Acacb, Scd1Gck) and increased expression of lipolytic genes (cpt1, ppar alpha) by

probiotics has also been reported by different workers (Jangra *et al.*, 2019), and that leads to improvement of dyslipidemia.

Improved insulin resistance, decreased tumor necrosis factor  $\alpha$  and total cholesterol in the serum of patients suffering from NAFLD has been reported and possible mechanism reported was decreased aspartate transaminase, aminotransferase activity. Combination of Streptococcus, *Lactobacillus* and *Bifidobacterium* was given these patients (Jain *et al.*, 2004), VSL#3 has also been reported to improve dyslipidemia (Alisi *et al.*, 2014; Jain *et al.*, 2004). *L. casei* NCDC19 has also been conveyed to improve dyslipidemia in mice fed high fat diet (Jangra *et al.*, 2019; Rather *et al.*, 2014). *Lactobacillus rhamnosus* GG (LGG) has shown protective effects against NAFLD in mice. In these mice beneficial bacteria number increased, gut barrier function improved and subsequently liver inflammation was decreased (Ritze *et al.*, 2014).

### **Probiotics and hyperglycemia**

High concentration of glucose leads to several metabolic disorders viz. obesity, cardiovascular disease and diabetes mellitus. Feeding of probiotics (*L. casei* and *L. acidophilus*) with high fructose diets improved diabetes, lipid and glucose metabolism, hyperglycemia, oxidative stress, dyslipidemia, hyperinsulinemia, and inhibited glucose intolerance in rats (Shewale *et al.*, 2014; Yadav *et al.*, 2008). Ingestion of *L. gasseri* BNR17 in *db/db* mice decreased the body weight and improved the glucose metabolism in type 2 diabetes (Yun *et al.*, 2009).

Mechanism of action of probiotics in lowering blood glucose is still not clear. Yadav and his colleagues (Yadav *et al.*, 2007). Reported feeding of yogurt containing

*L. casei* and *L. acidophilus* to animals inhibited the glucose intolerance, hyperinsulinemia, and hyperglycemia and oxidative stress was found to be reduced in these animals. Probiotics improved the low grade inflammation as well as immune responses (decreasing the cytokines numbers) (de LeBlanc *et al.*, 2010), by inhibiting the NF- $\kappa$  pathway (Shi *et al.*, 2006), Some of the specific strains of LAB improved the hyperglycemia through their antioxidant properties (Amaretti *et al.*, 2013). Feeding the *Lactobacillus johnsonii* (La1) for two weeks reduced the hyperglycemic and lowered the insulin resistance (Laitinen *et al.*, 2008). This probiotic reported to modulate the gut microbiota which obstructed the uptake of glucose, and more blood glucose absorption by liver (Mohammad-Shahi *et al.*, 2017). Hence, modulation of the gut microbiota by supplementing the probiotics could be another way of lowering blood glucose.

### **Probiotics effects on colon cancer**

Probiotics have been reported to have beneficial effects on colon cancer (Liong *et al.*, 2008). There are many ways through which probiotic confers anti-carcinogenic effects (Gillissen *et al.*, 2018). These are as follows:

- Formation of compounds with anti-carcinogenic properties (short chain fatty acids and conjugated linoleic) (Uccello *et al.*, 2012).
- Inhibits the binding of mutation causing microorganisms in the colon.
- Decrease in the activity of enzymes involve in production of carcinogens. Probiotic suppresses the colon enzymes viz.  $\beta$ -glucosidase,  $\beta$ -glucuronidase, nitrate reductase, zoredutase and 7- $\alpha$ -dehydroxylase. These enzymes involved in the conversion of inactive carcinogens into active carcinogens

such as ammonia, cresols, phenols, and N-nitroso compounds (Kumar *et al.*, 2013).

Decrease the nephrotoxic, mycotoxins, and genotoxic immunosuppressive substances.

Physical binding between the cancer causing compounds and peptidoglycan some probiotic microorganisms could exhibit anti-carcinogenic activity (Gillissen *et al.*, 2018).

The efficacy of probiotic strains viz. *Lactobacillus fermentum* NCIMB5221 and *Lactobacillus fermentum* NCIMB8829 in hampering colorectal cancer cells, and increase the growth of normal epithelial colon cells with SCFAs (ferulic acid) have been shown by in vitro experiments (Tomaro-Duchesneau *et al.*, 2012). Some studies *in vitro* have reported the beneficial effects of probiotics on colon cancer. Though, further studies are necessary to delineate the pathway by which probiotics confers anti-cancerous effects. Moreover, more clinical and animal trials are needed in this regard.

### **Probiotics and gut microbiota**

Trillions of bacteria are residing in the human gut (Koboziev *et al.*, 2014). Gut microbiota has been reported to confer many functions to the host such as vitamin production, bioactive compounds production, immune modulation, degradation of carcinogens and toxins, maintenance of intestinal epithelia and inhibition of colonization of pathogens in the colon (Zhang *et al.*, 2015). Recent reports have correlated the dysbiosis of gut microbiota (low number of bifidobacteria and lactobacilli) with the occurrence of obesity (Daillère *et al.*, 2016). Many mechanisms for association of dysbiosis with lifestyle disorders have been proposed by different workers which are described below as:



Capability to extract more energy from the undigestible food (Turnbaugh *et al.*, 2006).

Suppressing intestinal Fiaf expression (LPL inhibitor) which leads to more fat storage in the adipocytes (Cani and Delzenne *et al.*, 2009).

Affecting gut peptides synthesis, involved in energy homeostasis such as glucagon like peptide I and peptide YY.

Increase in lipopolysaccharides level in circulation (metabolic endotoxaemia) which is supposed to cause insulin resistance and chronic low-grade inflammation.

The best way for controlling the flora balance in intestine is through intake of probiotics. There are many reports that show a direct relationship between the intake of probiotics and the improvement of metabolic disorders (Heczko *et al.*, 2006). Probiotics are defined by the WHO and FAO (WHO/FAO, 2002) as live microorganisms that confer health benefits upon the host when administered in adequate amounts. Intake of appropriate dose of a probiotic plays an important role in conferring the beneficial effects. Commonly used probiotics belong to *Lactobacillus*, *Bifidobacterium* and *Saccharomyces* genera. To confer health benefits, probiotics must colonize (even temporally) in the colon after oral intake (Goldin and Gorbach *et al.*, 2008).

Positive correlation between metabolic endotoxaemia and bifidobacterial counts in the colon of mice has been reported (Cani *et al.*, 2007). Bifidobacterial counts in the colon decreased with the intake of high fat diet, and that lead to metabolic endotoxaemia and other metabolic disorders in the mice. Oral intake of bifidobacteria with high fat diet restored the bifidobacterial counts in the colon, and negative effects of high fat diet were reversed (Moya-Pérez *et al.*, 2015). Higher number of bifidobacteria in the colon of mice fed high

fat diet along with *L. casei*NCDC19 fermented dahi has also been reported (Rather *et al.*, 2014).

### **Other ways to increase health beneficial bacteria (Probiotic) in the colon**

#### **Prebiotics**

Prebiotics (generally oligosaccharides) are defined as indigestible part of the food that reaches the colon as such and selectively stimulates the activity of beneficial microorganisms (probiotics) in the colon of the host (Gibson *et al.*, 2004). Cereals (wheat, barley, oats etc.), vegetables (onion, garlic, tomato, leafy green vegetables etc.) and fruits (banana, apple etc.) are considered as potential source of prebiotic. Galactooligosaccharides (GOS), lactulose and maltooligosaccharides are artificial prebiotics, and most effective on stimulating the growth of probiotic (Patterson *et al.*, 2003). Many literatures have reported the increment in the amount of beneficial microorganisms in the colon upon consumption of prebiotics both in rodents and humans (Legette *et al.*, 2012; Messaoudi *et al.*, 2011). Selectively stimulating the growth of the beneficial microorganism in the colon is considered one of the mechanisms through which prebiotics confers their health benefits to the host (Pandey *et al.*, 2015). A prebiotic must possess some features in order to stimulate the growth of probiotics in the colon such as

- a) must not be absorb in intestinal
- b) indigestible or partially digestible
- c) should not be fermented in oral cavity by bacteria
- d) must be fermented selectively in colon to stimulate the growth of microorganisms

In the colon short chain fatty acids (mainly butyrate, propionate and acetate) are produced

when prebiotics is fermented in the colon (Fernández *et al.*, 2016). Butyrate is considered source of energy for the enterocytes of intestinal cells. Propionate is reported to protect against diet induced obesity (Barczynska *et al.*, 2015).

### **Synbiotics**

Synbiotic is considered another approach by which number of beneficial microorganisms can be increased in the gut. In this approach probiotics and prebiotics are used together in order to get synergistic effects (Kearney *et al.*, 2018). In synbiotic formulation substrate (prebiotic) for probiotics is readily available for the fermentation. This helps in improvement of survivability issues of probiotics as they pass through the harsh conditions of the gastrointestinal tract. A very few studies are available where health benefits of synbiotics were evaluated in high fat diet fed conditions.

In conclusion, the present review more focused on different beneficial effect of probiotics. Information obtained from the *in vivo* and *in vitro* studies exhibited probiotics are suitable option for treatment and prevention of diseases without side effects. Hypocholesterolemic effects of probiotics are one of the greatest health impacts of probiotics. That improve hypercholesterolemia through the binding of cholesterol to cell surface, cholesterol assimilation, co-precipitation of cholesterol, deconjugation of bile acids by BSH activity, and multi strains of probiotics more effective in the treatment of non-alcoholic fatty liver disease. Probiotics have been reported to exert anti-obesity and different probiotics have been reported to have different mechanism in lowering body weight through the regulating lipid and glucose metabolism, producing of the conjugated linoleic, reducing the cell size (hypertrophy) and increases the cell number

(hyperplasia) in white adipose tissue, increasing the energy expenditure by increases the expression of genes related to lipid metabolism. Probiotics have been reported to be effective in improving the insulin resistance. Beneficial effects on blood glucose levels are considered as one of the reasons in improving insulin resistance. Probiotic have positive effects on oxidative stress, metabolic lipid profile and high sensitivity C-reactive protein in T2DM patients. Many probiotics improve the high fat diet associated dyslipidemia through the decreasing of expression lipogenic genes (Srebf1/Srebp1c, Scd1/Gck) and increased expression of lipolytic genes (cpt1, ppar alpha) and that leads to improvement of dyslipidemia. Probiotics have beneficial effects on colon cancer, Through Formation of compounds with anti-carcinogenic. Inhibits the binding of mutation causing microorganisms in the colon. Decrease in the activity of enzymes involve in production of carcinogens. Still, more studies and scientific improvements are necessary to found the probiotics health benefits and potential application.

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