Chapter

Nut Phytonutrients for Healthy Gut: Prebiotic Potential

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Abstract

Nuts are a combination of prebiotic fiber and phytonutrients and have antioxidant, anti-inflammatory effects. According to 2005 "My Pyramid" it has been grouped with the meat and bean group. Bioactive compounds of nuts such as resveratrol, phytosterols, phenolic acids, flavonoids, and carotenoids display synergistic effects on preventing many age related pathologies. Resveratrol has been reported to extend the lifespan in model organisms such as yeast, *Drosophila* and mouse. Reports propose nuts as the best substitute for red meat to reduce mortality risk. Macadamia nuts with a rich source of monounsaturated fats (oleic and palmitoleic acids) imparts cholesterol lowering effects thereby preventing coronary artery disease. Anacardic acid, a phenolic lipid found in cashew nut shells, is specifically enriched in metastatic melanoma patients in response to immunotherapy. The non-bio-accessible materials of nuts serve as a substrate for human gut microbiota. Regular Walnut enriched diet improves lipid content and enhances probiotic and butyrate producing bacteria composition in healthy individuals. This also reduces cardiovascular risk factors by promoting beneficial bacteria. Gut microbiota diversity studies report an enrichment with genera capable of producing short chain fatty acids (SCFA) following consumption of nuts. The prebiotic effect of nuts can be partly from refining butyrate producing bacteria composition. Hence an optimized diet rich with nuts can be an intervention for promoting a healthy microbiota population and thereby improving overall physiology.

Keywords: lifespan, yeast, Macademia nut, immunotherapy, SCFA, prebiotic, microbiota

1. Introduction

The human gut microbiome consists of many microorganisms constituting bacteria corresponding to different species involving the collective genome consisting 100 times the genes present in the human genomes [1]. The existing microbial communities contribute towards the host health through different functions involving the probiotic properties along with the synthesis of the vitamins and important amino acids. Various changes have been observed in the constituents of the gut microbiota among all healthy individuals which has evolved correlation between the health, disease and diversity of the human gut microbiome. Also, the gut microbiota has been linked with pathogenesis involving intestinal and extra-intestinal disorders [2]. Hence, diet has been considered as the major determinants for the microbial composition in the gut that further influences the diversity, distribution and more of microbial populations from the early life stages [3]. The diet variations

Sl No.	Aim	Mediation	Study type	Study design	Findings	Reference
1.	Investigation of prebiotic effects of almonds using mixed fecal bacterial culture	Fine and defatted almonds	*In vitro*	In vitro gastric and duodenal digestion of the samples of almond has been used in the form of substrates for colonic model for evaluation of population, composition and metabolic activity of gut bacteria	For whole almond: *Bifidobacteri*, *Eubacterium rectale* and butyrate production increases	Mandalari et al. [17]
2.	Evaluation of the components of chestnut in the form of probiotic carriers by examining the effect on the viability of selected lactic acid bacteria (LAB)	Extracts of chestnut and its fiber	*In vitro*	Simulated gastric (with pepsin) and bile (with pancreatin) juices have been prepared for adding into the cultured LAB cells with chestnut fibers and extracts	*Lactobacillus paracasei GG*, *Lactobacillus rhamnosus* and *Lactobacillus casei* increases. *Streptococcus macedonicus* and *Streptococcus thermophilus* decreases.	Blaiotta et al. [20]
3.	Comparing the fermentation properties of raw and roasted almonds	Raw and roasted almonds	*In vitro*	Hydrolyzed raw and roasted almonds under simulated gastric and duodenal digestion have been added into cultured Lactobacillus acidophilus, Bifidobacterium breve, and *Escherichia coli* and incubation at 37°C for 48 h in anaerobic condition is done	*Lactobacillus acidophilus* and *Bifidobacterium breve* increases. *Escherichia coli* decreases.	Liu et al. [16]
4.	Analyzing prebiotic effects of raw and roasted almonds on fecal and caecal bacteria	Raw and roasted almonds	Animal model	Male specific-pathogen-free (SPF) Wistar rats of 10 weeks older are divided into three groups as per the feeding regime of raw and roasted almonds	*Lactobacillus spp.* and *Bifidobacterium ssp.* increases. *Enterococcus spp.* and *Escherichia coli* decreases.	Liu et al. [16]
5.	Investigating the walnuts modulation to be effective for gut microbiome and promoting health benefits	Walnuts	Animal model	Male Fischer rats divide into two groups as control diets and walnut diet. Fecal samples collected descending colon at the time of sacrifice	*Lactobacillus*, *Ruminococcaceae* and *Roseburia* increases. *Bacteroides*, *Anaerotruncus* and *Alphaproteobacteria* decreases.	Byerley et al. [26]

DOI: http://dx.doi.org/10.5772/intechopen.94864

Sl No.	Aim	Mediation	Study type	Study design	Findings	Reference
6.	Evaluating the effects of bacterial or fungal microbiota composition while consumption of nuts	Almond and Pistachio	Randomized, controlled, crossover trial	Healthy adults with 18 days feeding time interval being separated by a washout period of 2 weeks. Low-fiber American diet has been provided during these three treatment periods.	*Lactobacillus* and *Bifidobacteria* is maintained	Ukhanova et al. [14]
7.	Investigating the prebiotic effects of almond and almond skin intake in healthy humans	Roasted almond and almond skin	Randomized, controlled trial	Healthy adult volunteers consuming almonds and almonds skin, the diet being provided by the school canteens	*Lactobacillus spp.* and *Bifidobacterium spp.* increases. *Clostridium perfringens* decreases. *Escherichia coli* is maintained.	Liu et al. [18]
8.	Assessing the interrelationship of almond consumption and processing on the gastrointestinal microbiota(bacterial genera)	Whole almonds, whole, roasted almonds, roasted, chopped almonds and almond butter	Randomized, controlled, crossover trial	Healthy adults with controlled feeding	*Lachnospira*, *Roseburia*, *Oscillospira*, and *Dialister* increases.	Holscher et al. [33]
9.	Investigating the effect of walnut intake on the gut microbiome composition and microbial diversity	Walnut	Randomized, controlled, crossover trial	Healthy nonsmoking men and women of age above 50 years having different diet phases of walnut-enriched diet and nut-free control diet	Butyrate-producing bacteria, *Ruminococcaceae* and *Bifidobacteria* increase. *Clostridium spp.* decreases.	Bamberger et al. [34, 35]

Table 1.
Prebiotic prospects of consuming nuts phytonutrients for maintaining a healthy gut.

also evolve 57% of the total structural variations in the gut microbiota [4]. The acute alteration in the diet has shown variations in the microbial composition. All these variations contribute towards the modification of the gut microbiota for longer durability of health benefits.

Nut consumption has been found to be effective on the metabolic risk factors [5–7]. Nuts are a combination of prebiotic fiber and phytonutrients and have antioxidant, anti-inflammatory effects. Nuts also consist of high content of mono-saturated fatty acids, mainly in the hazelnuts along with consistency of lipophilic compounds such as tocopherols (almonds and hazelnuts) and high amount of phytosterols and carotenoids (pistachio) [8–10]. Phenolic compounds have been considered to be found in abundance in the form of phytochemicals in the nuts, mainly involving flavonoids and tannins that are basically found in walnuts and pecans. These diversity of compounds constituting antioxidant and anti-inflammatory effects have been proved to be beneficial concerning the health benefits. It further shows effects on the remodeling of the gut microbiota [11, 12]. The fibers along with the contents of the polyphenols plays an important role in mediating the profile of the gut microbiota resulting into the mechanism of health benefits such as generation of anti-inflammatory effects, maintaining the intestinal mechanisms and enteric barrier integrity. Hence, it has been revealed that the consumption of nut phytonutrients has been assisting the gut microbiome for the management of the inflammatory diseases (**Table 1**) [13, 14].

The potential prebiotic properties of the nut phytonutrients have been considered important for analyzing the mechanism of healthy gut. The nut phytonutrients have been effective in maintaining the health by activating the mechanisms in the gut due to the consistency of high fiber levels, antioxidants and anti-inflammatory properties. All the nut phytonutrients involving macadamias also contain fibers. These phytonutrients nuts are capable of feeding the gut bacteria as these nuts consist of prebiotic that are mainly involved in feeding the probiotic bacteria dwelling in the gut [15–17]. One of the studies has revealed that 56 g of almonds and 10 g of almond skins in a single day for continuity of six weeks have been shown to increase the growth of the important bacterial strains in the gut [18]. The similar results have been seen while using the pistachios [19]. The nut phytonutrients may also protect the proteobacteria present in the gut. Another major study in Food Microbiology has revealed that the extracts of the chestnuts and its flour has helped the different strains of lactobacilli bacteria in survival of the acids and bile present in the stomach [20]. Hence, this effectively proves that these nuts actively show mechanism in the large intestine and results in maintenance of a healthy gut. Also, the healthy bacteria present in our gut feed on the fiber of the nut phytonutrients resulting in the fermentation into the product of short-chain fatty acids. Hence, weight management is effectively maintained by these compounds.

The prebiotic potential has been referred to as the growth of the selective microbial species found in the gut microbiota that provides benefits to the health in any individual with the mechanism of selective stimulation [21]. Limited research has been conducted on the prebiotic effects of nut phytonutrients and its impact on the gut microflora. But most of the studies have shown positive impact of nut phytonutrients for maintaining a healthy gut considering the prebiotic assistance.

2. Effects of nut phytonutrients on human gut microbiota

Natural fibers and phytochemicals are present in various nuts, and these components reach the proximal colon, providing substrates for the healthy maintenance of diverse microbiota. Nuts are food components rich in prebiotic fiber and polyphenols, and have proven benefits on human gut health and gut microbiota [22]. Specific nuts are rich in fiber and other phytonutrients, however, the effect of the increased consumption of nuts on human gut microbiota is yet to be investigated [23]. There has been a history of epidemiological studies and clinical trials, suggesting the metabolic and gut health benefits of nut consumption. In comparison to other nuts, pistachios have proven to have a balanced nutrition profile, with lower levels of polyunsaturated fatty acids (PUFAs) and monounsaturated fatty acids (MUFAs). Pistachios have higher levels of protein, soluble and insoluble fiber, potassium, vitamin K, phytosterols, xanthophyll carotenoids, γ-tocopherol, along with high antioxidant potential [24].

Nuts also play a role in reducing postprandial glucose fluctuations. Along with maintaining the gut health, nuts also help in potentially improving glucose homeostasis in patients suffering from gestational diabetes mellitus. GLP-1 and GIP are gut incretin hormones that possess strong glucose-dependent insulin regulatory properties and are released to lower blood sugar levels after having a meal. These hormones augment the glucose-dependent insulin secretion which plays a crucial role in controlling postprandial glucose excursions [24].

According to the reports by Emily et al. [22], there is increasing evidence showing the association of gut microbiota with different aspects of human health. Eight weeks of walnut consumption, approximately 43 g/day, has a significant improvement on lipid levels, and regular walnut consumption is linked with better gut health [25]. In a randomized, controlled, prospective, cross-over study by Charlotte et al. [25], 194 healthy individuals with 134 females aged 63 ± 7 years, and with BMI 25.1 ± 4.0 kg/m^2 were included to evaluate the gut microbiome. The results showed a significant decrease in *Clostridium sp.* cluster XIVa species with walnut consumption, proving the beneficial effect of nuts on the human gut. As reported in a study by Maria et al. [23], the effect of pistachio consumption on gut microbiota composition was much higher than that of almond consumption. The results also showed an increase in the number of potentially beneficial butyrate-producing bacteria. Nuts have proven efficacy to increase the good bacteria *Clostridium*, *Roseburia*, *Lachnospira* and *Dialister*, paving a way to yield a modulatory effect on the human gut [22]. Walnut consumption has evidently shown the enhancement in the probiotic- and butyric acid-producing species in healthy individuals [25]. *Lactobacillus, Ruminococcaceae,* and *Roseburia,* the probiotic-type bacteria significantly increased with walnut consumption, whereas Bacteroides, *Anaerotruncus*, and *Alphaproteobacteria* significantly decreased. **Figure 1** showing a schematic diagram showing prebiotic effects on host gastro-intestinal (GI) tract. Regular walnut consumption brought a drastic change in the gut microbiota, thereby suggesting a new mechanism that will further prove the beneficial health effects of walnut consumption [26].

2.1 Potential health benefits of nuts

Since the ancient times, nuts and dried fruits have been an important part of the human diet. Nuts are nutrient-rich foods and consist of excellent health-promoting and beneficial bioactive compounds [27]. According to a study by Rune et al. [28], nuts contain dietary antioxidants which are said to have a protective effect in chronic degenerative disease. Nuts possess antioxidants that reduce the oxidative stress which is common in chronic degenerative disease. Considering all the tree nuts, the highest amounts of antioxidants is present in walnuts, chestnuts, and pecans. Walnuts have a walnut pellicle, that contains more than 20 mmol antioxidants per 100 g, whereas peanuts contribute a significant number of antioxidants to the daily dietary intake. Nuts have shown strong and consistent reductions in

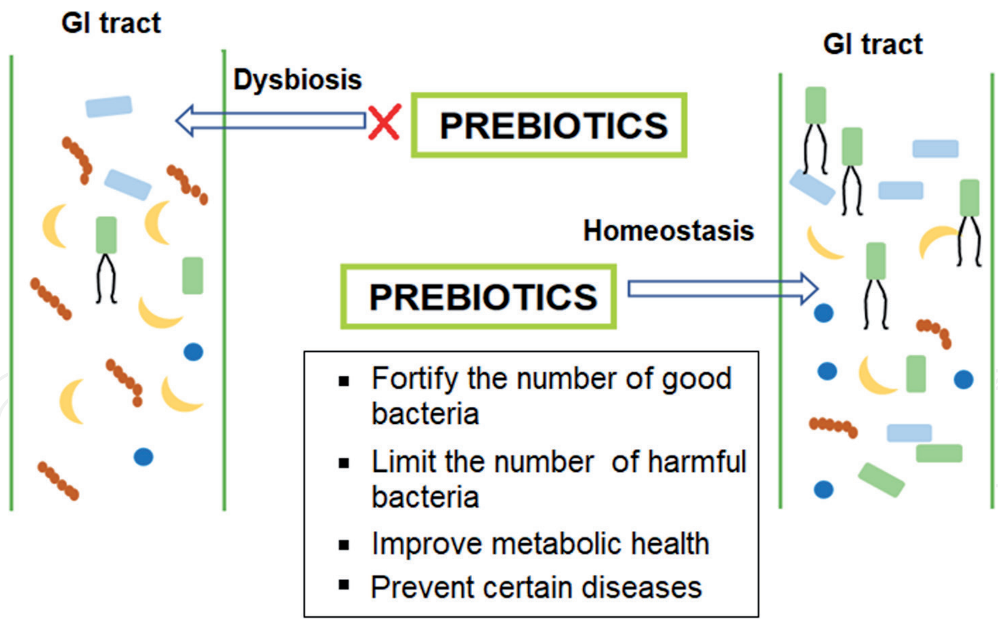

Figure 1.
Schematic diagram showing prebiotic effects on host gastro-intestinal (GI) tract.

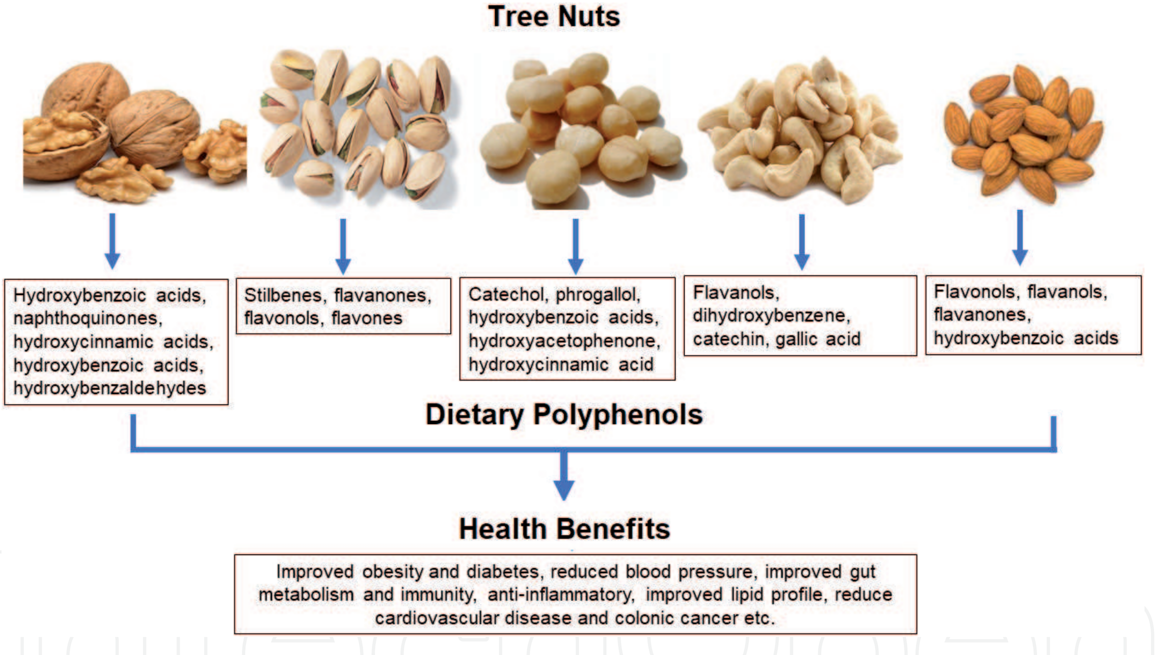

Figure 2.
The dietary polyphenols of different tree nuts and their health benefits.

the number of cardiovascular and coronary heart diseases death attributes. Nuts have played a major role in regulating the lipid and cholesterol level and maintain a healthy heart [28]. According to the German Nutrition Society, daily consumption of 25 g nuts is recommended as nuts are a rich source of nutrients for the healthy functioning of the heart and other organs. Nuts are a good source of all the important nutrients such as monounsaturated fatty acids (MUFA), polyunsaturated fatty acids (PUFA), dietary fiber, vitamins, antioxidants, and minerals. They have positive health effects even when consumed on a regular basis. Evidence states that regular nut consumption seems to have no negative impact on the body, heart, weight, healthy or obese patients. Nuts have shown proven benefits in the prevention of metabolic disorders, hyperlipidemia, atherosclerotic diseases, hyperglycemia, heart ailments, myocardial and coronary artery disease. Moreover, daily nut consumption has shown to reduce inflammatory processes in the body and increase the antioxidant capacity of the body [29]. The dietary polyphenols of different tree nuts and their health benefits are shown in **Figure 2**.

To obtain the full benefit of nutrients, bioactive compounds, and antioxidants present in nuts, frequent consumption of the same is highly recommended. Nuts are very flavourful, so consuming them on a daily basis will only give benefits. The risk of cardiometabolic and other non-communicable diseases can be modulated by the synergistical contribution of nuts and dried fruits that contain tremendous amounts of macronutrients, micronutrients, bioactive compounds, other health-promoting nutrients and flavor. The beneficial effects of nut consumption on various health outcomes have been reported by experimental research, prospective studies, and human clinical trials [27]. The dietary polyphenols of tree nut for health benefits.

3. *In-vitro* studies of prebiotic effects of nuts

The Dietary Guidelines for Americans has revealed that the intake of nut phytonutrients has given positive outcomes with effective health benefits. The health benefits of intaking these nuts have been found due to the presence of fatty acid, vegetable proteins, phenolics and vitamin phytosterols. Nut the most important attribute of the nut phytonutrients have been found due to the high content of dietary fiber and polymerized polyphenols that contribute towards the prebiotic properties. These components are further metabolized by the gut microbiota in the presence of the bioactive molecules that have been helpful in benefiting the health of the individuals. The *in vitro* studies by Blaiotta et al. [20] and Mandalari et al. [17] have shown the prebiotic effects of chestnuts and almonds. Liu et al. [18] and Ukhanova et al. [19] have also shown similar prebiotic effects concerning the various interventions of human clinical trials. The studies have proved that the butyrate production has been observed in both the groups revealing the effects of almonds and pistachios on the fecal bacterial and fungal microbiota. Also, the conclusion has been derived that neither almond nor pistachio intake have been efficient in increasing the *Lactobacillus* or *Bifidobacterium* strains. But the study by Liu et al. [18] has been capable of showing efficient increase of *Bifidobacterium* spp. and *Lactobacillus* spp. Among the almond and its skin along with the little variations in the population of *Escherichia coli* and *Clostridium perfringens*. Also, some bacterial enzymes have shown significant variations such as β-galactosidase activity has been observed to increase and fecal β-glucuronidase, nitroreductase and azoreductase activities have been found to show reduced effect.

The nut phytonutrients have been found to be rich in complex polyphenols, tannins to be the major one and other dietary fibers that have shown prebiotic effects in the gut of the individuals. The studies have shown that the dietary polyphenols have been found to be partially absorbed in the small intestine for carrying out an effective digestion process. The complex polyphenols have been seen to be unabsorbed in the gut and later they get bioactivated in the colon by the microbiota. Hence, these microbiota metabolites derived from the complex polyphenols are smaller molecules which are easily absorbed through the colon barrier [30]. Ellagitannins (hydrolysable tannins) and proanthocyanins (condensed tannins) have been known to be the major constituents as phenolic compounds of the nut phytonutrients [31, 32]. These have been mainly found in the blood of the individual that shows potential prebiotic effects on the gut while maintaining the human metabolism and health.

The prebiotic effects have been observed in the gut mechanism due to the presence of the prebiotic compounds in the nuts that stimulate the growth of non-pathogenic gut bacterial species along with the inhibition of growth of the pathogenic ones. The in vitro studies have revealed that the whole and defatted almonds, raw and roasted almonds and fiber and extracts of chestnut have shown prebiotic effects on the human gut. One of the recent studies have revealed that the almonds processing has been affecting the composition of the gastrointestinal microbiota when the treatment of intake of 42 g per day of chopped almond or almond butter for 21 days is carried on that results in enhancing the beneficial bacterial genera [33]. Similar results have been seen in a study that involves the daily intake of walnuts of 43 g for 56 days, resulting in affecting the gut microbiome by enhancement of the probiotic butyric acid-producing bacteria in healthy individuals [34, 35].

4. Bioactive compounds and nutritional composition of nuts

Nut phytonutrients have been found to have a high energy density and high nutrient content along with the healthy profiles. Almond, cashew, pistachio, baru almond, and peanuts have been found to have lowest amounts while Brazil nut, hazelnut, pecan, and walnut have been found to have highest lipid concentrations. The major components of the fatty acids of the almond, cashew, pecan, edible seed and hazelnuts consist of monounsaturated fat acids (MUFA). The Brazil nut, pistachio and walnut consist of polyunsaturated fat acids (PUFA). The Brazil nut and cashew consist of considerable content of saturated fatty acids (SFA). Also, almond, hazelnut, and pecan have been observed to have the highest MUFA:SFA ratios. Hence consumption of these phytonutritional nuts provides health benefits of lower risk for cardiometabolic disorders, dyslipidemia, obesity, and insulin resistance [36].

The lipophilic compounds have been also found in the nut phytonutrients involving higher concentration of tocopherols in almond, hazelnut, baru almond and peanuts. It consists of nutritional attributes of vitamin E efficiency, antioxidative, anti-inflammatory, and antiobesity properties [37]. Phytosterols components have also been found in the nuts, mainly in pistachio. These components help in inhibiting the intestinal absorption of cholesterol and reduce the risk of hyperlipidemia [38, 39]. Carotenoids are another lipophilic compound that have been found in lower amounts in nuts. Lutein is another bioactive compound which shows antioxidant activity [40].

Phenolic compounds are majorly found in the nut phytonutrients. The polyphenolic compound resveratrol has been shown to extend lifespan in different organisms. Wang et al. (2013) investigated the effect of resveratrol on lifespan on both gender and dietary nutrient composition in *Drosophila melanogaster*. The lifespan extension by resveratrol was found to be associated with downregulation of genes in aging-related pathways, including antioxidant peroxiredoxins, insulin-like peptides involved in insulin-like signaling and several downstream genes in Jun-kinase signaling involved in oxidative stress response. Pecan, pistachio, walnut, and baru almond have been found to have the highest values among the nuts. Some of the oilseeds have been propounded to have high concentrations of flavonoids and tannin (pecan), flavonoids (walnut), and tannins (baru almond). Many other nuts have been found to have more concentration of tannins in them. Flavonoids and tannins show reduced pro-oxidant and proinflammatory conditions and hence decrease the risk of obesity and inflammatory diseases.

DOI: http://dx.doi.org/10.5772/intechopen.94864

5. Conclusion

Nuts are an important part of our diet. The enriching bioactive compounds of nuts have profound influence on human health. An optimum intake of these nut phytonutrients have prebiotic effect on our health. Different studies reveals the promoting effect of these nutrients on healthy gut microbiota population. These nut based phytonutrients acting as prebiotic to fortify the host probiotic bacteria and also limit the pathogenic bacteria maintaining a homeostasis condition in the host. With the advancing studies of prebiotics and probiotics on model organisms including *Drosophila*, mice new avenues are open to explore a beneficial diet plan with nut based prebiotics. In this new era of personalized medicine these prebiotic and probiotic supplements can provide a therapeutic target for different pathological condition. This will provide a basic understanding of the trilogue of diet, host and gut microbiota interactions.

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