Prebiotics: A Carrier in The Development of Nutraceuticals Beverages

[1]Vaidehi Mande, [2]Dr Sneha V Karadbhajne, [3]Prashant Lungade
[1,2,3] Department of Food Technology
Laxminarayan Institute of Technology
Rashtrasant Tukdoji Maharaj Nagpur University
[a]vaidehimande@gmail.com [b]svklit@gmail.com [c]pslungade@gmail.com

Abstract
Prebiotics are short-chain carbohydrates that are non-digestible by enzymes and selectively stimulate the growth and activity of beneficial bacteria which are probiotic in nature. Prebiotics along with probiotic bacteria render many health benefits in the large intestine such as reduction of risk of cancer, control GIT infection, absorption of minerals like calcium and magnesium etc. Functional foods and nutraceuticals are now becoming a huge market globally. Nutraceuticals are food or part of food that plays a significant role in modifying and maintaining physiological functions in humans. Prebiotics, probiotics, dietary fibers, nutrients, herbal foods, and antioxidants are categorized under nutraceuticals. FOS and insulin are commonly used prebiotics in the market. This article aims to provide knowledge on prebiotics, their types, sources, industrial production, their benefits on human health, application in the food sector, and how prebiotics can be a source ingredient for the development of nutraceuticals beverages.

Keywords: prebiotics, Probiotics, Nutraceuticals, Health benefits.

1. Introduction

Industries are growing very fast, making a new era for industrial development globally. With a growing market with upcoming innovations in different sectors, their products are touching every field, leading to economic development for the countries. This also leads to pollution in all three forms mainly because of the extensive use of various chemicals, heavy metals, magnetic waves, and other harmful man-made items which supports an increase in different types of diseases, physiological problems etc. All these have raised demands for healthcare facilities, increasing medical expenditure with a high risk of side effects, toxicity, more reliance on food supplements for health improvement, etc. Due to these, pharmaceuticals and medicines failed in providing natural ingredients to humans for improving health. Due to these issues, scientists and researchers were forced to think about the addition of natural or alternative medicines with their application in the food sector. [1]. Our planet is surrounded by varieties of plant species that possess medicinal properties. A few of them are were used for a long-time for the immune building to prevent and treat diseases [2]. Herbal medicines have always been a form of therapy for livestock among resources poor marginal farmers [3]. They are used for the treatment of various diseases like hepatitis, arthritis, chronic heart diseases, cancer etc have been mentioned in our “Ayurveda” and proven scientifically by many researchers of modern times [4].

Nutraceutical and functional food products are becoming an important part of the diet as consumers are more aware of their contributions to general health and well-being. They are lifestyle-changing foods and have increased globally in the market. There is a number of unique and healthy foods which have been developed by combining food with herbal medicines fortified with micronutrients. Few countries follow and use traditional herbal products as medicine in dietary supplements, daily foods and functional foods, for replenishment and health promotion purposes. The term “nutraceutical” came from the words “nutrition” and “pharmaceutical” in 1989 by Stephen DeFelice. Nutraceuticals were defined as food or part of a food that provides medical or health benefits, including the prevention/treatment of a disease” [5]. They are available in the market in the form of capsules, pills, and powders, with a broad range of products covering the food areas like beverages, dietary supplements, fortified foods, herbal products and processed foods [6]. The functional foods are regular foods with naturally occurring bioactive substances (dietary fibre), foods supplemented with bioactive substances (probiotics, antioxidants), and derived food ingredients introduced to conventional foods (prebiotics). Nutraceuticals and functional foods together are becoming part of the human diet and provide health benefits with a lower risk of chronic diseases than those which provide good and adequate nutrition.

There is a wide range of products which are designed especially for health purposes like energy drinks, fibre-rich foods and supplements, mineral and vitamin-fortified RTE foods, prebiotic, probiotic and symbiotic supplements etc. Due to high demand, these industries are growing rapidly. Prebiotic, probiotic, and symbiotic industries play a significant role in nutraceutical and functional foods. Studies show that there is a link between probiotics, prebiotics and nutraceuticals for a good healthy gut and immunological function. Various types of microorganisms like gut microbiota, are inhabitants of the human gastrointestinal tract. Around 10^{10}–10^{12} per gram probiotic cultures in the human colon are crucial for health and gut conditions [7]. The majority of these microorganisms, which are mostly anaerobes, live in the large intestine [8]. In this review, we elaborate on different aspects of prebiotics, covering the definition of prebiotics, probiotics, nutraceuticals, types of prebiotics, their sources, mechanisms, application on food formulation, fermentation and selection criteria and covering an area of how prebiotics can be used as a food source for development of nutraceutical beverages.

2. Definitions

2.1 Prebiotics

Prebiotics are defined as food components which are non-digestible but selectively fermented compounds that stimulate the growth of beneficial gut microbiota providing health benefits to the host [9,10]. It consists of short-chain carbohydrates oligo-saccharides present in the large intestine helping them to modify their composition and function as gut microbiota. Healthy intestinal microbes like Bifidobacterium and lactobacillus ferment these non-digestible dietary substances and are called prebiotics [10]. They serve as substrates for selective enhancement and metabolic activity of gut microbiota. Prebiotics has the ability to degrade and decrease the growth of pathogens in healthy individuals by the addition of some immunomodulatory substances against pathogens by lactic acid produced by bifidobacterium and lactobacillus species which are probiotic bacteria. An ideal prebiotic should be 1) Resistant to acidic activity in the stomach, bile salts and enzyme hydroxylation in the stomach, 2) It should ferment in the large intestine by beneficial microbes, 3) should not be absorbed in upper GIT [11]. Prebiotics are more useful as functional food and nutraceuticals because of their ability to mix in all types of foods than probiotics [12]

Prebiotics travels from the small intestine and goes to the lower gut where it is accessible to probiotic bacteria without being utilised by other intestinal bacteria. Lactulose, galactooligosaccharides, fructooligosaccharides, inulin and its hydrolysates, malto-oligosaccharides, and resistant starch are frequently used prebiotics. The essential components of carbohydrate metabolism are short-chain fatty acids like acetic acid, propionic acid and butyric acid, used by the host as an energy source. It can also be found in different plant sources such as chicory, onion, garlic, asparagus, artichoke, leek, bananas, tomatoes and many other plants. Oligosaccharides are a combination of sugars with different degrees of polymerization [13]. Prebiotic oligosaccharides can be manufactured by three different methods: isolation from plant resources, microbiological production or enzymatic synthesis, and enzymatic degradation of polysaccharides [13,14]. Most of the prebiotic oligosaccharides are manufactured and are generally available in the markets. Mixtures of probiotics and prebiotics are used for their synergic effects in application to food products called symbiotics. A few other sources of prebiotics are raw oats, soya beans, unrefined barley, breast milk, non-digestible carbohydrates, non-digestible oligosaccharides, etc. [15]

2.2 Probiotics

Probiotics are live microorganisms, which when ingested improve the intestinal microbial balance. Bifidobacteria, Lactobacilli, and Eubacteria are microorganisms which have probiotics properties. They help in improving gastrointestinal health and inflammatory bowel diseases by protecting the digestive tract from pathogenic infection. They have the ability to stimulate immune functions, help in digestion, absorption of nutrients, and also synthesize some nutrients such as vitamins [16] Asian countries are very prone to gastrointestinal diseases, and probiotics are now becoming a trend as a functional health food for prevention against diseases. Probiotics are available in different forms of food like dairy products like yoghurt, buttermilk and cheese, and some bacterially fermented foods like Japanese miso, beer, sourdough, bread, chocolate, kimchi, olives, pickles, tempeh and sauerkraut. Out of these the dominant foods in probiotics are yoghurts and fermented milk, due to their relatively low pH environment for the survival of probiotic bacteria [17]. Lactobacillus and Bifidobacterium comprise the majority of probiotic microorganisms. Lactobacilli are non-spore-forming rod-shaped bacteria with complex nutritional requirements fermentative, anaerobic and acidophilic in nature [18]. Some of the popularly used probiotic microorganisms are Lactobacillus rhamnosus, Lactobacillus reuteri, bifidobacteria and certain strains of Lactobacillus casei, Lactobacillus acidophilus-group, and Bacillus coagulants. Other lactic acid bacteria such as Streptococcus, Lactococcus, Enterococcus, Leuconostoc, Propionibacterium and Pediococcus are also now included in probiotics [19].

2.3 Synbiotics

Symbiotic is a combination of prebiotics and probiotics which provides an additional health benefit [19]. Symbiotic beneficially affects the host by improving their survival and also selectively stimulate the growth and activity of health-promoting bacteria in the gastrointestinal tract. The products in which the prebiotic compound selectively favours the probiotic organism are true symbiotic [20]. Survival of probiotic bacteria becomes easy. Fermented milk is considered synbiotics as it provides both live beneficial bacteria (probiotics) and products of fermentation that may affect the intestinal microflora in a positive way [21]. For symbiotic products, probiotic strains like Lactobacillus, Bifidobacterium spp., Saccharomyces boulardii, Bacillus coagulants, etc. are used, and prebiotics in form of oligosaccharides like fructooligosaccharide (FOS), galactooligosaccharides (GOS) and xylose-oligosaccharide (XOS), inulin are mostly used. Prebiotics from natural sources like chicory; and artichokes are also used. Symbiotic benefits include (1) an increase in the balance of gut microbiota, (2) an improvement of liver function in humans (3) an increased ability for the immune building. [22]

2.4 Nutraceuticals:

The term Nutraceutical came from "nutrition" and "pharmaceutical" in 1989 by Stephen DeFelice. He defined nutraceuticals as "a food that provides medical or health benefits, including the prevention or treatment against disease" [6]. Nutraceuticals are classified into basic categories 1) dietary supplements, 2) functional foods and beverages and 3) nutraceutical ingredients (raw minerals or oils) [6]. They are in the form of capsules, pills and powders. Products like beverages, dietary supplements, fortified foods, herbal products and processed foods are said to have nutraceutical contents. [6]

Nutraceutical foods combine both nutritional and pharmaceutical effects while providing medical or health benefits prevention or treatment against diseases. Nutraceuticals consist of a naturally originated compound that positively affects the human body with nutritional value. Nutraceuticals can be naturally nutrient-rich food such as garlic, oats, onion etc or a specific component of food like omega-3 from salmon [23]. They are known also known as medical foods, nutritional supplements and dietary supplements. Herbal foods, dietary foods and supplements, genetically engineered foods, processed foods, and therapeutic foods come under the category of nutraceuticals [24]. Mostly all functional foods are said to have nutraceuticals present in them. Nutraceuticals are composed of groups of molecules, macronutrients, and micronutrients which are responsible for the beneficial effects on the host. The food sources used as nutraceuticals are all natural they are categorized as polyphenols, Dietary fibres, Probiotics, prebiotics, poly saturated fatty acids, antioxidants, minerals, vitamins, and spices [23].

Types	Examples
Vitamins and mineral supplements	Vitamins and inorganic minerals
Digestive enzymes	Enzymes
Probiotics	LAB, Bifidobacteria
Prebiotics	Digestive enzymes
Cereals, grains and dietary Fibres	Fibres
Health drinks	Fruit and vegetable beverages
Antioxidants	Vitamin C, Vitamin B
Phytochemicals	Carotenoids

Table-1 Classification of nutraceuticals as per chemical composition: [25]

Nutraceuticals are classified into 3 groups based on their source:

- **Herbal products*:*** Herbal products in old days were considered a part of medicine and were used in the pharmaceutical industry it also helped in reducing the risk of allergies and side effects of antibiotics. They are mostly used as concentrates. Ayurveda in India has the oldest written natural remedies with effective means for good health.
- **Nutrients:** A feed constituent in a form and at a level that will help support the life of an animal. Functional foods and beverages give nutrients in form of proteins, fats, carbohydrates, minerals and vitamins.
- **Dietary Supplement**: Dietary supplements are basically defined as products which are supplied with the diet and contain one or more ingredients like vitamins, minerals, proteins, herbs or other botanicals, probiotics, prebiotics, antioxidants, and enzyme.

3. Types and sources of prebiotics:

Carbohydrates which are non-digestible can be considered as prebiotic if they are {26}

(a) resistance to gastric acidity

(b) susceptible to fermentation by gut bacteria, and

(c) Have the ability to enhance the activity of beneficial microorganisms

Prebiotics are divided into categories:

1) Naturally occurring in plants such as bananas, asparagus, beans, and cereals

2) Synthesized from enzymatic digestion of polysaccharides like starch.

Type of prebiotics	**Source of prebiotics**	**Benefits**	**References**
FOS	Beet sugar, garlic, Asparagus, chicory, onion, honey, banana, barley, tomatoes and rye	Improve mineral absorption, decreases triglycerides, immunity improvement, inhibits pathogenic growth, prevents cancer and controls diabetes.	[27]
Isomaltulose	Sugarcane, honey	Improve gastrointestinal flora	[28]

Galactooligosaccharide	Milk from humans and cow	Increase Bifidogenic activity	[29]
Cyclodextrin	Water soluble glucans	They are dietary fibres useful for controlling body weight and lipid profile in the blood	[30]
Raffinose oligosaccharide	Legumes, lentils, peas, chickpeas, Mustard	Oligosaccharides	[31]
Soyabean Oligosaccharides	Soyabean	Prevents constipation with an increase in the production of SCFA, increases gut activity with the of vitamins protects the liver by reducing the production of toxic metabolites, and colon cancer risk is less and improves the absorption rate of calcium and other minerals.	[32]
Lactulose	Milk lactose	Being a synthetic sugar it is used to treat constipation. Helps to break down the colon with products that pull water out from the body and into the colon. It softens the stools. Lactulose is also used to reduce the ammonia content in the blood of patients with liver disease	[33]
Palatinose	Sucrose	Being called a low GI carbohydrate it helps to balance and sustain the energy supply to the body, it improves metabolism and promotes fat burning.	[28]
Maltooligosaccharides	Starch	They are functional oligosaccharides used in the food, beverage, cosmetic, and pharmaceutical industries.	[34]

		Used as an ingredient in functional foods for treating constipation or improving intestinal health giving beneficial effects on GIT.	
Isomaltooligosaccharide	Starch	IMO is a functional oligosaccharide, and it can modulate the composition and metabolic activity of gut microbiota improving the health of the host.	[34]

Table-2 Types of prebiotics and their sources:

3.1 **Naturally occurring prebiotics:** Various non-digestible carbohydrates are naturally found in different plants [26]

3.1.1. Chicory Roots

Chicory is a member of the Asteraceae family has excellent medicinal value and scientifically is known as Cichorium intybus. [35]. Fresh chicory contains slightly less amount of inulin compared to sucrose, protein, cellulose, ash, and other compounds in contrast to dried chicory, which contains more inulin than other compounds [36]. Other than phenolic compounds, chicory leaves also contain minerals and vitamins [37]. The non-digestible prebiotic found in chicory root is inulin. Being a polymer of fructose it is linked through the β (2-1) glycosidic linkage and helps in nourishing probiotic bacteria [38]. FOS and insulin differ only in chemical structure i.e. the molecular chains of FOS are shorter than those of inulin [39]. Inulin has become a replacement for sugar and fat in different food products [40].

3.1.2. Chia Seeds

Chia seeds scientifically known as *Salvia hispanica*; come under the Lamiaceae family. It is an annual herb plant [41]. These seeds provide a rich source of proteins and fats and have a high content of amino acids and dietary fibres [42]. The dietary fibre in chia seeds is higher than in cereals, dry fruits and nuts [43]. They contain α-linolenic acid, and other fatty acids such as oleic, palmitic, and linoleic acids are found in significantly lower amounts [44]. Studies have proven that chia seeds help in increasing the growth of gut microbes. [45]. Incorporating chia seeds into the diet can directly enhance gut health and functionality, as well as increase the absorption of minerals like zinc and iron [46].

3.1.3. Flaxseeds

Flaxseed also called linseed is a functional food. Its scientific name is *Linum usitatissimum* [47]. They are a rich source of nutrients like minerals, soluble fibres, proteins, and phenolic compounds which provides health benefits to humans [48]. Consumption of flaxseed decreases the growth of *Porphyromonadaceae* and *Proteobacteria* in the gut and may also positively affect the alcoholic liver condition [49]

3.1.4. Garlic

Allium sativum commonly known as Garlic; is high in FOS, which contributes to the protection of GUT and also the prevention of various diseases [50]. Garlic fructan is one of the significant components of garlic, almost 75% of its dry weight, possesses prebiotic potential and influences gut microbiota. The effect of Garlic fructan on gut microbiota stimulates the Bifidobacteria while suppressing Clostridia species which can support the growth of other pathogens. [51].

3.1.5. Onion

Onion is known as *Allium cepa* scientifically and is a member of the Liliaceae family [52]. It is a good source for giving good nutritional value, as well as medicinal properties [53]. The consumption of onion provides carbohydrates, dietary fibres, vitamins, and minerals [54]. Monosaccharides like glucose, fructose, sucrose and FOS are the chief soluble carbohydrates found in the dry matter of onion [55] which has an excellent prebiotic effect in improving the health of gut microflora [56].

3.1.6 Oats

Oats scientifically known as Avena *sativa* is a rich source of polysaccharides [57]. They are healthy cereals and contain a high amount of fibre, minerals, vitamins, and proteins [58]. The chief soluble constituent is non-starch called β-glucan [59]. β-glucan from raw oats can form highly viscous solutions providing health benefits to the human gut [60,61].

3.1.7 Barley

Barley is a crop with the scientific name *Hordeum vulgare*. It is a member of the *Poaceae* family [62]. It is a low-fat content crop with high fibre, proteins, and vitamin contents [63]. Wheat, barley, and oats are cereal grains having good probiotic properties and are used in a number of food products such as bread, biscuits, beverages, breakfast cereals, and cereal bars [64]. During fermentation, the probiotic microbes from these cereals convert them into a digestible form which helps to boost the proliferation of gut microbes [65]. Barley contains polysaccharides, oligosaccharides, vitamins, and minerals, like calcium, iron, and zinc [66]. β-glucan is one of the main components of barley and it exerts immunomodulatory effects by directly or indirectly regulating the gut microbes [67]. Barley crop has a tendency to lower cholesterol levels in the blood, regulate blood sugar level, and improve immunity [68]. Barley is one of the major raw materials for developing functional foods in the food industry [69].

3.2 Synthetic Prebiotics

3.2.1. Fructooligosaccharides (FOS)

Fructooligosaccharides also known as oligofructose or oligofructose are low-calorie-containing dietary fibres with prebiotic potential [70]. FOS are considered as natural food ingredients due to their various beneficial effects on animal and human health [71]. FOS is found naturally in plants, cereal grains (barley, wheat, oats), vegetables, and fruits (artichoke, asparagus, bananas, garlic, leeks, and onions) [72]. FOS is considered to have a significant class of bifidogenic oligosaccharides owing to their high production volume [73]. Pharmaceutical industries due to zero wastage have raised their FOS production and the waste feedstock is now converted into a nutraceutical product due to its prebiotic nature [74]. It can be used as an alternative sweetener Inulin and FOS increase calcium absorption in the gut of both humans and animals [75]. FOS have numerous beneficial properties; 1) It can be used as a low-intensity sweetener, 2) It is a dietary fibre with non-carcinogenic properties, control or stops the growth of pathogenic bacteria, improves immunity, enhances mineral absorption, decreases cholesterol levels, promotes vitamins synthesis, regulates obesity and diabetes, and prevent colon cancer progression [76]. FOS is also added to infant foods to give beneficial gut microbes and prevent the growth of pathogenic microbes [77].

The structure of FOS is made up of linear chains of fructose joined via β (2-1) bonds [78]. FOS are commercially produced and are added as a supplement in various food products, and used as nutraceuticals as they pass through GIT undigested and reach the large intestine where intestinal bacteria ferment them into SCFAs and lactate [79]. FOS are now available on the market as functional food ingredients because they seem to be an alternative to fat and prebiotic ingredients [80]. Besides this, FOS is also used in ice cream jam and confectionery product production as a sweetener [81].

Type of prebiotics	Method of production
Insulin(FOS)	Hot water extraction from chicory root followed by either enzymatic hydrolysis or polymerization of fructose monomers
Galactooligosaccharides(GOS)	Enzymatic lactose transgalactosylation
Xylooligosaccharides(XOS)	Enzymatic hydrolysis of plant xylans
Lactulose	Isomerization of lactose
Soybean oligosaccharides(SOS)	Enzymatic hydrolysis of soybean

Table-3 Illustration of types of prebiotics synthetically produced

3.1.2. Galactooligosaccharides (GOS)

Galactooligosaccharides are prebiotics which is not enzymatically digested but are fermented by probiotic *Bifidobacteria*. Oligolactose, oligogalactoses, and oligo galactosyl lactose are a few carbohydrates which come under GOS [82]. GOS helps to boost the multiplication of *Lactobacilli* and *Bifidobacteria* [83]. In infants, *Bifidobacteria* show high growth upon GOS ingestion [84]. Microbes like *Bacteroidetes*, and *Enterobacteria*, also show proliferation in the presence of GOS, but their growth is slower than that of *Bifidobacteria* [85]. Lactulose also shows GOS derivatives, since lactulose-derived GOS are considered as prebiotics [86]. GOS can be synthesized through electrophilic and nucleophilic displacement, but this method is not economical when employed on an industrial scale [87]. Enzymes galactosidase and galactosyl-transferase help to synthesize GOS in large quantities [88]. A catalytic reaction is involved for GOS, but it is an expensive approach [89]. To reduce costs, oligosaccharides from human milk and globotriose production are commonly used [90]. There are a number of techniques which are involved in increasing GOS production such as 1) increase in the number of acceptors and donors in the reaction, 2) reducing the water activity, 3) eliminating the intermediate molecules and direct shifting of the equilibrium reaction to the endpoint [91].

3.1.3. Xylooligosaccharides (XOS)

Xylooligosaccharides are formed through β-1-4 linkages with xylose molecules [92] They are mostly found in food materials like bran, fruits, honey, and vegetables [93]. With the ability to generate lactobacillus and Bifidobacteria and improve gut health

[94]. XOS is more beneficial than FOS, due to the improvement in the count of *Bifidobacteria* and reduced count of pathogenic microbes [95] The benefits of XOS include anti-freezing nature, high water activity, non-digestible and non-carcinogenic nature, positive effect on gut microbiota, and their applicability in pharmaceutical industries [96].

3.1.4. Fructans

Fructans are natural polymers found in different functional foods, in vegetables such as artichoke, asparagus, chicory roots, garlic, leek, and onion, and are widely used as prebiotics for improving human health [97]. They are formed from a polymer of fructose with β2-1 linkages [98]. Fructans help for improvement in gut physiology by enhancing the growth of *Bifidobacteria* and *Lactobacilli* with prevention from pathogenic microbes [99]. The consumption of fructans as prebiotics helps to substantially improve glucose levels and regulate lipid metabolism [100].

3.1.5. Soybean Oligosaccharides (SOS)

The oligosaccharides that are found in soybean are termed soybean oligosaccharides (SOS), which involve stachyose and raffinose. These oligosaccharides are not digested by the stomach or intestine enzymes but are hydrolysed by gut microbiota [101]. SOS enhances the proliferation of *Bifidobacteria* in the large intestine [102]. They are known as bifidogenic which shows the same effect as is [103]. SOS is also known as α-galactosyl sucrose derivatives, as they are obtained from soybeans. In soy germ powder these oligosaccharides are observed and their fermentation properties have been assessed with *Lactobacilli* along with inoculums of faecal bacteria [104].

4.0 Prebiotics on its selection, fermentability and digestion

Studies provide a theory that carbohydrates at the cecum work as substrates for fermentation by bacteria. It is not completely digested in the human gut and large intestine. Prebiotics like inulin and FOS in faeces are not detectable [105]. Studies and experiments prove that short-chain fatty acids enhance the survival of bacteria [106]. Growth of different strains of bifidobacteria on oligofructose extracts several prebiotics and examines their fermentation by different strains of Bifidobacterium, Clostridium, Bacteroides and Lactobacillus at different sugar levels. Results showed that the fermentation of oligosaccharides showed a change in the structure. Linear oligo-saccharides will break down to a larger extent than those with branched structures and bifidobacteria use a low degree of polymerization carbohydrates first whereas Bacteroides utilised those with a high degree of polymerization [107]. A Prebiotic is a selective substrate for one or a limited number of probiotics. The mechanism for probiotics is designed in a way that is stimulated to grow and produce short-chain fatty acids by prebiotics. The selectivity of prebiotics depends on the changes observed in faecal microbiota during supplements of prebiotics in vitro and in vivo experiments. [108]

The digestibility of prebiotics depends on their chemical structure. The prebiotics reaches the cecum without being digested and part of it which is not digested by pancreatic and small bowel enzymes reaches the large intestine. Improvement in lipid metabolism helps in the absorption of calcium ions which further improves bowel and immunological activities [99]. It remains ineffective in reducing the number of bacteria such as *Clostridia*, *Bacteroides*, *Enterococci*, and *Enterobacteria* in the gut, which have been shown to exhibit detrimental effects on the host’s health.

5.0 Industrial production of prebiotics:

Inulin and oligofructose are utilised in pure form as ingredients in many food products giving nutritional support [109]. Industrial production methods have been used to produce non-digestible carbohydrates from natural sources by means of hydrolysation of polysaccharides, enzymatic and chemical synthesis from disaccharides, and extraction methods to produce soybean oligosaccharides and raffinose [110]. Microencapsulation technology is an effective method for increasing the delivery of bioactive chemicals like probiotics, prebiotics, and nutraceuticals within the food are one of the most promising solutions in order to retain high viability levels etc.

6.0 Applications of prebiotics in food products:

Prebiotics in form of food components has multiple advantages. Their utilization is mostly to improve the sensory features of food, and to provide a well-balanced nutritional composition for humans [111]. They are used as fat replacers in bakery, beverage industries, etc. In bakery products and breakfast cereals, prebiotics gives a classic comparison with dietary fibre. The freshness in snacks and cereals with a good shelf life are also provided by prebiotics. They keep the moisture level in pieces of bread, cakes are maintained their freshness for a longer time. Their solubility allows fibre incorporation in liquid systems such as drinks, dairy products and table spreads. Prebiotics are often utilised as dietary fibre in form of tablets, and functional foods, such as dairy products, as prebiotic ingredients enhance the viability of healthy intestinal bacteria [112].

Having a good gelling property helps in the improvement of low-fat foods without any effect on taste and texture. This property of prebiotics is a boon for products like table spreads, butter-like products, dairy spreads, cream cheeses, and processed cheeses. Prebiotics in the diet is a replacement for fat and maintains the emulsion levels with a good spreadable texture. Exceptional results have been found in water-in-oil spreads [113]. The addition of prebiotics to fat-reduced meat products leads to a creamier, juicier mouthfeel and constancy because water hold is maintained. In the chocolate industry, prebiotics has also been added as fibre and a low-energy ingredient without the addition of sugar. The dairy market has shown huge development with these dietary products like fruit-based yoghurt which have prebiotic properties [114]. The addition of prebiotics in dairy products provides a good mouthfeel and gives a synergistic taste result in combination with non-sweeteners like aspartame and acesulfame K, without any increase in calories.

7.0 Application of prebiotics:

There is a number of ways for incorporating prebiotics as a source of energy in the food sector:

7.1. Food Beverages having prebiotics like inulin and oligo-fructose helps in improving the efficiency of the digestive system, as the addition of cereals in food helps in strengthening bones, and develops immunity against diseases.

7.2. Addition of prebiotics in infant food helps to improve the efficiency of the digestive system and it helps to increase immunity against diseases. Individual or combination of different types of prebiotics like inulin, oligofructose and galactooligosaccharides (GOS) in infant foods have shown an increase in the number of Bifidobacteria and Lactobacilli in the digestive system [115].

7.3. Probiotic products like dairy-based food and beverages have synbiotics when it fortified with prebiotics. It helps to increase mineral content.

7.4. Other than the pharmaceutical industry for providing nutrients and minerals in form of tablets or capsules nutraceuticals have become a category where with the addition of prebiotics and some probiotics it can also be made in form of tablets, capsules or powder. They are taken daily or are prescribed with a certain amount of dose to increase the amount of pro- and/or prebiotics in the gastrointestinal system. [6]

7.6. Prebiotics can be used as fat replacers. For diabetic patients or healthy living sugar can be replaced by prebiotics for sweetness. It can be used in different combinations of foods. [116]

7.7. Fruits and vegetables are good sources of prebiotics, antioxidants and phytochemicals. Combining the prebiotics with these antioxidants and phytochemicals like beta carotene, flavonoids provide additional nutrition to humans. [117]

8.0 Prebiotics as a source of energy for nutraceuticals:

Food nutrients which are isolated and purified are generally sold in form of medicine like capsules or tablets and not as food components. They are called nutraceuticals. It can be defined as a supplement to a regular diet that delivers a concentrated form of a biologically active component of food in a non-food matrix to improve health. A balanced intake of vegetables, fruit, beans, and grains can provide a variety of beneficial compounds. Prebiotics can be used in the development of nutraceuticals in form of beverages. Technologies like high-pressure processing, fermentation, extrusion, aseptic processing etc are the methods used for food processing in industries.

8.1 Use of plant-based products as a source of prebiotics to form nutraceuticals

There are a number of plant-based products like Chicory, flaxseeds, onion, garlic, chia seeds etc which are rich sources of prebiotics and dietary fibres and also enriched with minerals and nutrients. [118] Functional foods and nutraceuticals have a great demand globally for the usage of these products fortified with minerals and vitamins. It is now becoming a huge industry altogether with the promotion of probiotics, prebiotics and symbiotics in the market. The functional ingredient industry has become a large parallel industry producing nutraceutical and functional ingredients for the nutraceutical and functional industry. Prebiotic, probiotic, and symbiotic industries form a significant part of the nutraceutical and functional food industry [119]. Fruits and vegetables are a good source of vitamins and minerals which provides proper health. A balanced intake of vegetables, fruit, nuts and grains provides a variety of beneficial compounds consisting of antioxidants like carotenoids and flavonoids also known as phytochemicals. There are more than 1000 phytochemicals present in vegetables, fruits, beans and grains [120]. Common phytochemicals are Allyl sulphides, anthocyanidins, catechins, carotenoids, flavonoids, flavones, isoflavones, isothiocyanates, phytonutrients, and polyphenols. They are called powerful antioxidants which possess pharmacological properties making them attractive for the development of functional as well as nutraceuticals foods/beverages keeping probiotics, prebiotics and antioxidants as sources of energy.

8.2 Use of cereals, grains, and nuts as a source of nutraceuticals with prebiotics effect.

Barley, oats, millet, rice and nuts like almonds, and pistachio are good sources for prebiotics and probiotics foods. Prebiotics help beneficial bacteria to grow in the gut. Prebiotics works with probiotics providing healthful bacteria or yeasts, for good health and improvement. Mostly the majority of research around gut health is focused on probiotics and now prebiotics is a new area to focus on. More research is necessary to uncover all of the health benefits of prebiotics, but they are likely to be a valuable dietary component which can be the resourceful raw material for prebiotic nutraceutical foods.

8.3 Reutilization of fruits and vegetable waste and by-products as nutraceutical products:

Extraction and identification of dietary fibres and prebiotic compounds from food waste is a new area of interest. The by-products resulting from the processing of apples have 20-30% waste including seed, peel and pulp. [121] The apple pomace contains high content of dietary fibre compared to apples themselves. [122] Similarly, cactus fruit residues represent 25-30% of total fruit mass. [123] The residues contain a large intake of dietary fibre, phytochemicals and natural dyes. The fibres include cellulose, hemicellulose, simple sugars and pectin. Oligosaccharides from cactus fruit residues have prebiotic properties. Extraction methods for dietary fibre from pomace are achieved by multi-phase cleaning, grinding, micro ionization and pasteurization. The residues from vegetables like cabbage, artichokes, and black carrot have a good content of dietary fibres and prebiotic properties. [124]. Consumer demand growing drastically for the consumption of food enriched with natural supplements bringing health benefits to mankind. The consumption of dietary fibres in large amounts helps to prevent and reduce cardiovascular diseases with low cholesterol levels and GIT problems. The soluble and insoluble fibres is incorporated into the products with solid consistency and for liquid products, soluble fibres are most desirable.

9.0 Conclusion:

Prebiotics, probiotics and symbiotics have a significant role in human health. Their use is nutritionally very important in the area of research and development on various foodstuffs. Prebiotics works on fermentable carbohydrates which can stimulate the growth of probiotic bacteria and enhance the gastrointestinal system. Prebiotics are available naturally in plants, grains, seeds, nuts etc such as artichokes, garlic, and barley, as well as synthetically produced which when added to the food provide health benefits to the host. As nutraceuticals are huge in the market; they have the great possibility of incorporating a wide range of foods and beverages with prebiotics as their main source.

References

1. Hashemi, S.R., and Davoodi,H.2012.Herbal plants as new immune-stimulator in poultry industry: A review. Asian Journal of Animal and Veterinary Advances.7:105-116.
2. Mahima, A. K., Rahal, A., Deb, R., Latheef, S.K. and. Samad, H.A.2012. Immunomodulatory and therauptic potential of herbal, traditional/indigenous and ethnoveterinary medicine. Pakistan Journal of Biological Sciences.15:754-774.
3. Alamgir, M. and Uddin, S.J.2010. Recent advances on the ethnomedicinal plants as immunomodulatory agents p.227-244.In:D.Chattopadhyaye edited. Ethnomedicine: A sources of complementary therapeutics. Research signpost, Kerela, India.
4. Umashankar, M. and Shruti.S.2011. Traditional Indian herbal medicine used as antipyretic, antiulcer, antidiabetic and anticancer: A review. International Journal for Radiation Physics and Chemistry. 1:1152-1159.
5. Kalra EK. Nutraceutical- definition and introduction. AAPS PharmaSci.5(3),2003,E25.
6. 6. El Sohaimy SA(2012) Functional foods and nutraceuticals- modern approach to food science. World Appl Sci J 20:691-708
7. Collins, S.; Reid, G. Distant site effects of ingested prebiotics. Nutrients 2016,8,523.
8. Louis, P.; Flint, H.J.; Michel, C. How to manipulate the microbiota: Prebiotics. In Microbiotia of the Human body; Springer: Basel, Switzerland.2016;pp.119-142.
9. Gibson, G.R.; Probert, H.M.; Van Loo, J.; Rastall, R.A.; Roberfroid, M.B. Dietary modulation of the human colonic microbiota: Updating the concept of prebiotics. *Nutr. Res. Rev.* **2004**, *17*, 259–275. [CrossRef]
10. Gibson, G.R.; Scott, K.P.; Rastall, R.A.; Tuohy, K.M.; Hotchkiss, A.; Dubert-Ferrandon, A.; Gareau, M.; Murphy, E.F.; Saulnier, D.; Loh, G.; et al. Dietary prebiotics: Current status and new definition. *Food Sci. Technol. Bull. Funct. Foods* **2010**, *7*, 1–19. [CrossRef]
11. Kuo SM(2013) The interplay between fiber and the intestinal microbiome in the inflammatory response. Adv Nutr: Intern Rev J 4(1):16-28.
12. Vernazza, C.L. , Rabiu, B.A and Gibson, G.R.2006. Human colonic microbiology and the role of dietary intervention: Introduction to prebiotic. In prebiotics: Development & Application, G.R Gibbson and R.A Rastall editors, John Wiley & sons Ltd., West Sussex, pp-1-28
13. Crittenden, R.G., & Playne, M.J.(1996).Production, properties and application of food-grade oligosaccharides. Trends in Food Science and Technology, 7 ,353-361.
14. Gulewicz, P., Ciesiolka, D., Frias, J., Vidal-Valverde, C, Frejnagel., S., Trojanowska, K., & Gulewicz, K(2003). Dimple method of isolation and purification of T-galactosides from legumes. Journal of Agricultural and Food Chemistry, 48,3120-3123.
15. Swati S. Mishra, Prafulla K. Behera, Biswabandita Kar , Ramesh C. Ray (2018) Chapter 7 Advances in probiotics, prebiotics and nutraceuticals. Springer International Publishing AG, 121-141
16. Panitantum, V. 2004. The story of probiotics, prebiotics & synbiotics. A seminar presentation at Kasetsart University, Bangkok, under the auspices of BIOTEC, National Science and Technology Development Agency,

Bangkok, Thailand, January 26, 2004, 157-161.
17. Anandharaj M, Sivasankari B, Rani RP (2014) Effects of probiotics, prebiotics, and synbiotics on hypercholesterolemia: a review. Chin J Biol 2014: Article ID 572754
18. De Vrese M, Schrezenmeir J (2008) Probiotics, prebiotics, and synbiotics. In: Food biotechnology. Springer, Berlin, pp 1–66
19. Krasaekoopt W, Bhandari B, Deeth H (2003) Evaluation of encapsulation techniques of probiotics for yoghurt. Int Dairy J 13:3–13
20. Cencic A, Chingwaru W (2010) The role of functional foods, nutraceuticals, and food supplements in intestinal health. Forum Nutr 2(6):611–625
21. Famularo G, Simone C, Mettuzzi D, Pirovano F (1999) Traditional and high potency probiotic preparations for oral Bacteriotherapy. BioDrugs 12(6):455–470
22. Zhang MM, Cheng JQ, Lu YR, Yi ZH, Yang P, Wu XT (2010) Use of pre-, pro-and synbiotics in patients with acute pancreatitis: a metaanalysis. World J Gastroenterol 16(31):3970. https://doi org/10.3748/wjg.v16.i31.3970
23. Garima Verma et al.(2018) A review on nutraceuticals : Classification and its role in various diseases. International Journal of Pharmacy & Therapeutics,7(4),2016,152-160
24. Rajasekaran, A, Sivagnanam, G and Xavier R, Nutraceuticals as therapeutic agents. A Review. Res J Pharm Sci Technol, 1(4), 2008, 328-340.
25. Disket Dolkar, Parshant Bakshi , V.K. Wali, Vikas Sharma and Rafiq Ahmad Shah, Fruits as nutraceuticals, Article in Ecology, environment and conservation-march2017
26. Prado,S.B.R.D.; Castro-.Alves,V.C.;Ferreria,G.F.;Fabi, J.P. Ingestion of non-digestible carbohydrates from plant source foods and decreased risk of colorectal cancer: A review on the biological effects and mechanisms of action. Font.Nutr.2019,6,72.[cross Ref]
27. Sangeetha, P. T., Ramesh, M. N., & Prapulla, S. G. (2005). Recent trends in the microbial production, analysis and application of fructooligosaccharides. Trends in Food Science and Technology, 16, 442–457.
28. Lina, B. A. R., Jonker, D., & Kozianowsky, G. (2002). Isomaltulose (Palatinose): A review of biological and toxicological studies. Food and Chemical Toxicology, 40, 1375–1381.
29. Alander, M., Matto, J., Kneifel, W., Johansson, M., Kogler, B., & Crittenden, R. (2001). Effect of galacto-oligosaccharide supplementation on human faecal microflora and on survival and persistence of Bifidobacterium lactis Bb-12 in the gastrointestinal tract. International Dairy Journal, 11, 817–825.
30. Singh, M., Sharma, R., & Banerjee, V. C. (2002). Biotechnological applications of cyclodextrins. Biotechnology Advances, 20, 341–359.
31. Johansen, H. N., Glitso, V., & Knudsen, K. E. B. (1996). Influence of extraction solvent and temperature on the quantitative determination of oligosaccharides from plant materials by high-performance liquid chromatography. Journal of Agricultural and Food Chemistry, 44, 1470–1474.
32. Mussatto, S. I., & Mancilha, I. M. (2007). Non-digestible oligosaccharides: A review. Carbohydrate Polymers, 68, 587–597.
33. Villamiel, M., Corzo, N., Foda, M. I., Montes, F., & Olano, A. (2002).

Lactulose formation catalysed by alkaline-substituted sepiolites in milk permeate. Food Chemistry, 76, 7–11.
34. Kaneko, T., Kohmoto, T., Kikuchi, H., Shiota, M., Iino, H., & Mitsuoka, T. (1994). Effects of isomaltooligosaccharides with different degrees of polymerization on human faecal bifidobacteria. Bioscience, Biotechnology, and Biochemistry, 58, 2288–2290.
35. Vasudeva,N.;Das,S.;Sharma,S.Cichoriumintybus:Aconcisereportonitsethnomedicinal,botanical,andphytopharmacological aspects. *Drug Dev. Ther.* **2016**, *7*, 1. [CrossRef]
36. Nwafor,I.C.;Shale,K.;Achilonu,M.C.Chemicalcompositionandnutritivebenefitsofchicory(*Cichoriumintybus*)asanideal complementary and/or alternative livestock feed supplement. *Sci. World J.* **2017**, *2017*, 1–11. [CrossRef]
37. Abbas,Z.K.;Saggu,S.;Sakeran,M.I.; Zidan,N.;Rehman,H.;Ansari,A.A.Phytochemical,antioxidantandmineralcomposition of hydroalcoholic extract of chicory (*Cichorium intybus* L.) leaves. *Saudi J. Biol. Sci.* **2015**, *22*, 322–326. [CrossRef]
38. ElKholy,W.M.;Aamer,R.A.;Ali,A.N.A.Utilizationofinulinextractedfromchicory(*Cichoriumintybus*L.)rootstoimprover the properties of low-fat synbiotic yoghurt. *Ann. Agric. Sci.* **2020**, *65*, 59–67. [CrossRef]
39. Chikkerur,J.;Samanta,A.K.;Kolte,A.P.;Dhali,A.;Roy,S.Productionofshortchainfructo-oligosaccharidesfrominulinofchicory root using fungal endoinulinase. *Appl. Biochem. Biotechnol.* **2019**, *191*, 695–715. [CrossRef] [PubMed]
40. RodríguezGarcía,J.;Salvador,A.;Hernando,I.Replacingfatandsugarwithinulinincakes:Bubblesizedistribution,physical and sensory properties. *Food Bioprocess Technol.* **2014**, *7*, 964–974. [CrossRef]
41. Kulczyn´ski,B.;Kobus-Cisowska,J.;Taczanowski,M.;Kmiecik,D.; GramzaMichałowska,A.Thechemicalcompositionandnutritional value of chia seeds—Current state of knowledge. *Nutrients* **2019**, *11*, 1242. [CrossRef]
42. Hrncˇicˇ,M.K.;Ivanovski,M.;Cör,D.;Knez,Ž.ChiaSeeds(*SalviaHispanica*L.):Anoverview-phytochemicalprofile,isolation methods, and application. *Molecules* **2020**, *25*, 11. [CrossRef]
43. Santillán-Álvarez,A.;Dublán-García,O.;López-Martínez,L.X.;Quintero-Salazar,B.;Gómez-Oliván,L.M.;Díaz-Bandera,D.; Hernández-Navarro, M.D. Effect of chia seed on physicochemical and sensory characteristics of common carp restructured as functional food. *J. Food Sci. Eng.* **2017**, *7*. [CrossRef]
44. Imran,M.;Nadeem,M.;Manzoor,M.F.;Javed,A.;Ali,Z.;Akhtar,M.N.;Ali,M.;Hussain,Y.Fattyacidscharacterizatioxdative perspectives and consumer acceptability of oil extracted from pre-treated chia (*Salvia hispanica* L.) seeds. *Lipids Health Dis.* **2016**, *15*, 162. [CrossRef] [PubMed]
45. Tamargo,A.;Cueva,C.;Laguna,L.; MorenoArribas,M.;Muñoz,L.A.Understandingtheimpactofchiaseedmucilageonhuman gut microbiota by using the dynamic gastrointestinal model simgi. *J. Funct. Foods* **2018**, *50*, 104–111. [CrossRef]
46. Da Silva, B.P.; Kolba, N.; Martino, H.S.D.; Hart, J.; Tako, E. Soluble extracts from chia seed (*Salvia hispanica* L.) affect brush border membrane functionality, morphology and intestinal bacterial populations in vivo (*Gallusgallus*). *Nutrients* **2019**, *11*, 2457. [CrossRef]
47. Goyal,A.;Sharma,V.;Upadhyay,N.; Gill,S.;Sihag,M.K.Flaxandflaxseedoil:Anancientmedicine&modernfunctionalood. *J.*

Food Sci. Technol. **2014**, *51*, 1633–1653. [CrossRef] [PubMed]
48. Kajla,P.;Sharma,A.;Sood,D.R.Flax seed—Apotentialfunctionalfoodsource.*J.FoodSci.Technol.***2015**,*52*,18571871.[CrossRef] [PubMed]
49. Zhang, X.; Wang, H.; Yin, P.; Fan, H.; Sun, L.; Liu, Y. Flaxseed oil ameliorates alcoholic liver disease via anti-inflammation and modulating gut microbiota in mice. *Lipids Health Dis.* **2017**, *16*, 1–10. [CrossRef]
50. Mikaili,P.;Maadirad,S.;Moloudizargari,M.;Aghajanshakeri,S.;Sarahroodi,S.Therapeuticusesandpharmacologicalproperties of garlic, shallot, and their biologically active compounds. *Iran. J. Basic Med. Sci.* **2013**, *16*, 1031–1048.
51. Zhang, N.; Huang, X.; Zeng, Y.; Wu, X.; Peng, X. Study on prebiotic effectiveness of neutral garlic fructan invitro. *Food Sci. Hum. Wellness* **2013**, *2*, 119–123. [CrossRef]
52. SinghBora,K.;Sharma,A.Phytoconstituentsandtherapeuticpotentialof*Alliumcepa*Linn.AReview.*Pharmacogn.Rev.***2009**, *3*, 170.
53. Nicastro,H.L.;Ross,S.A.;Milner,J. A.Garlicandonions:Theircancerprevention properties.*CancerPrev.Res.***2015**,*8*,181–189. [CrossRef] [PubMed]
54. Slavin,J.L.Carbohydrates,dietaryfiber,andresistantstarchinwhitevegetables:Linkstohealthoutcomes.*Adv.Nutr.***2013**,*4*, 351S–355S. [CrossRef] [PubMed]
55. Galdón,B.R.;Rodríguez,C.T.;Rodríguez,E.R.;Romero,C.D.Fructansandmajorcompoundsinonioncultivars(*Alliumcepa*). *J. Food Compos. Anal.* **2009**, *22*, 25–32. [CrossRef]
56. Vinke,P.C.;ElAidy,S.;VanDijk,G.Theroleofsupplementalcomplexdietarycarbohydratesandgutmicrobiotainpromoting cardiometabolic and immunological health in obesity: Lessons from healthy non-obese individuals.*Front. Nutr.* **2017**, *4*, 34. [CrossRef] [PubMed]
57. Sargautiene,V.;Nakurte,I.;Nikolajeva,V.Broadprebioticpotentialofnonstarchpolysaccharidesfromoats(*Avenasativa*L.): An in vitro Study. *Pol. J. Microbiol.* **2018**, *67*, 307–313. [CrossRef]
58. Rasane,P.;Jha,A.;Sabikhi,L.;Kumar,A.;Unnikrishnan,V.S.Nutritionaladvantagesofoatsandopportunitiesforitspro-cessing as value added foods—A review. *J. Food Sci. Technol.* **2013**, *52*, 662–675. [CrossRef]
59. Kaur,R.;Sharma,M.;Ji,D.;Xu,M.;Agyei,D.Structuralfeatures,modification,andfunctionalitiesofbetaglucan.*Fibers***2019**, *8*, 1. [CrossRef]
60. Henrion,M.;Francey,C.;Lê,K.A.;Lamothe,L.CerealBglucans:Theimpactofprocessingandhowitaffectsphysiological responses. *Nutrients* **2019**, *11*, 1729. [CrossRef]
61. El Khoury, D.; Cuda, C.; Luhovyy, B.L.; Anderson, G.H. Beta glucan: Health benefits in obesity and metabolic syndrome. *J. Nutr. Metab.* **2012**, *2012*, 1–28. [CrossRef]
62. Blattner,F.R.Taxonomyofthegenus hordeumandbarley(*Hordeumvulgare*).*Compend.PlantGenomes***2018**,11–23.[CrossRef]
63. Lahouar,L.;Ghrairi,F.;ElArem,A.; Medimagh,S.;ElFelah,M.;BenSalem,H.;Achour,L.Biochemicalcompositionandnutritional evaluation of barley rihane (*Hordeum vulgare* L.). *Afr. J. Tradit. Complement. Altern. Med.* **2016**, *14*, 310–317. [CrossRef]
64. Das,A.;Raychaudhuri,U.;Chakraborty,R.CerealbasedfunctionalfoodofIndiansubcontinent:Areview.*J.FoodSci.Technol.* **2011**, *49*, 665–672. [CrossRef]

65. Bell,V.;Ferrão,J.;Pimentel,L.;Pintado,M.;Fernandes,T.Onehealth,fermentedfoods,andgutmicrobiota.*Foods***2018**,*7*,195. [CrossRef] [PubMed]
66. McKevith,B.Nutritionalaspectsofcereals.*Nutr.Bull.***2004**,*29*,111–142.[CrossRef]
67. Jayachandran,M.;Chen,J.;Chung,S.S.M.;Xu,B.Acriticalreviewontheimpactsofβglucansongutmicrobiotaandhuman health. *J. Nutr. Biochem.* **2018**, *61*, 101–110. [CrossRef] [PubMed]
68. Salmerón,I.Fermentedcerealbeverages:Fromprobiotic,prebioticandsynbiotictowardsNanosciencedesignedhealthydrinks. *Lett. Appl. Microbiol.* **2017**, *65*, 114–124. [CrossRef]
69. Steele,K.;Dickin,E.;Keerio,M.;Samad,S.;Kambona,C.;Brook,R.;Thomas,W.;Frost,G.Breedinglowglycemicindexbarley for functional food. *Field Crop. Res.* **2013**, *154*, 31–39. [CrossRef]
70. Louis, P.; Flint, H.J.; Michel, C. How to manipulate the microbiota: Prebiotics. In *Advances in Experimental Medicine and Bi- ology*; Crusio, W.E., Dong, H., Lambris, J.D., Radeke, H.H., Rezaei, N., Eds.; Springer Science and Business Media LLC: Berlin/Heidelberg, Germany, 2016; Volume 902, pp. 119–142.
71. Kumar, C.G.; Sripada, S.; Poornachandra, Y. Status and future prospects of fructooligosaccharides as nutraceuticals. In *Role of Materials Science in Food Bioengineering*; Grumezescu, A.M., Holban, A.M., Eds.; Elsevier BV: Amsterdam, The Netherlands, 2018; pp. 451–503.
72. Sabater-Molina, M.; Larqué, E.; Torrella, F.; Zamora, S. Dietary fructooligosaccharides and potential benefits on health. *J. Physiol. Biochem.* **2009**, *65*, 315–328. [CrossRef]
73. Sánchez-Martínez, M.J.; Soto-Jover, S.; Antolinos, V.; Martínez-Hernández, G.B.; López-Gómez, A. Manufacturing of short-chain fructooligosaccharides: From laboratory to industrial scale. *Food Eng. Rev.* **2020**, *12*, 149–172. [CrossRef]
74. De La Rosa, O.; Flores-Gallegos, A.C.; Muñíz-Marquez, D.; Nobre, C.; Contreras-Esquivel, J.C.; Aguilar, C.N. Fructooligosaccha- rides production from agro-wastes as alternative low-cost source. *Trends Food Sci.Technol.* **2019**, *91*, 139–146. [CrossRef]
75. Bali, V.; Panesar, P.S.; Bera, M.B.; Panesar, R. Fructo-oligosaccharides: Production, purification and potentialapplications. *Crit. Rev. Food Sci. Nutr.* **2015**, *55*, 1475–1490. [CrossRef]
76. Martin, B.R.; Braun, M.M.; Wigertz, K.; Bryant, R.; Zhao, Y.; Lee, W.; Kempa-Steczko, A.; Weaver, C.M. Fructo-oligosaccharides and calcium absorption and retention in adolescent girls. *J. Am. Coll. Nutr.* **2010**, *29*, 382–386. [CrossRef] [PubMed]
77. Flores-Maltos, D.A.; Mussatto, S.I.; Contreras-Esquivel, J.C.; Rodríguez-Herrera, R.; Teixeira, J.A.; Aguilar, C.N. Biotechnological production and application of fructooligosaccharides. *Crit. Rev. Biotechnol.* **2016**, *36*, 259–267. [CrossRef] [PubMed]
78. Akkerman, R.; Faas, M.M.; De Vos, P. Non-digestible carbohydrates in infant formula as substitution for human milk oligosac- charide functions: Effects on microbiota and gut maturation. *Crit. Rev. Food Sci. Nutr.* **2019**, *59*, 1486–1497. [CrossRef] [PubMed]
79. Mutanda, T.; Mokoena, M.P.; Olaniran, A.O.; Wilhelmi, B.S.; Whiteley, C.G. Microbial enzymatic production and applica- tions of short-chain

fructooligosaccharides and inulooligosaccharides: Recent advances and current perspectives. *J. Ind. Microbiol. Biotechnol.* **2014**, *41*, 893–906. [CrossRef] [PubMed]

80. Besten, G.D.; van Eunen, K.; Groen, A.K.; Venema, K.; Reijngoud, D.-J.; Bakker, B.M. The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. *J. Lipid Res.* **2013**, *54*,2325–2340. [CrossRef] [PubMed]

81. Rolim, P.M. Development of prebiotic food products and health benefits. *Food Sci. Technol.* **2015**, *35*, 3–10.[CrossRef]

82. Martins, G.N.; Ureta, M.M.; Tymczyszyn, E.E.; Castilho, P.C.; Gomez-Zavaglia, A. Technological aspects of the production of fructo and galacto-oligosaccharides. Enzymatic synthesis and hydrolysis. *Front. Nutr.* **2019**, *6*,78. [CrossRef] [PubMed]

83. Macfarlane, G.T.; Steed, H.; Macfarlane, S. Bacterial metabolism and health-related effects of galacto-oligosaccharides and other prebiotics. *J. Appl. Microbiol.* **2007**, *104*, 305–344. [CrossRef]

84. O’Callaghan, A.; van Sinderen, D. Bifidobacteria and their role as members of the human gut microbiota. *Front. Microbiol.* **2016**, *7*, 925.

85. Rinninella, E.; Raoul, P.; Cintoni, M.; Franceschi, F.; Miggiano, G.A.D.; Gasbarrini, A.; Mele, M.C. What is the healthy gut microbiota composition? A Changing ecosystem across age, environment, diet, and diseases. *Microorganisms* **2019**, *7*, 14. [CrossRef]

86. Marín-Manzano, M.C.; Abecia, L.; Hernández-Hernández, O.; Sanz, M.L.; Montilla, A.; Olano, A.; Rubio, L.A.; Moreno, F.J.; Clemente, A. Galacto-oligosaccharides derived from lactulose exert a selective stimulation on the growth of bifidobacterium animalis in the large intestine of growing rats. *J. Agric. Food Chem.* **2013**, *61*, 7560–7567. [CrossRef]

87. Palcic, M.M. Biocatalytic synthesis of oligosaccharides. *Curr. Opin. Biotechnol.* **1999**, *10*, 616–624. [CrossRef]

88. Gänzle, M.G. Enzymatic synthesis of galacto-oligosaccharides and other lactose derivatives (hetero-oligosaccharides) from lactose. *Int. Dairy J.* **2012**, *22*, 116–122. [CrossRef]

89. Weijers, C.A.; Franssen, M.C.; Visser, G.M. Glycosyltransferase-catalyzed synthesis of bioactive oligosaccharides. *Biotechnol. Adv.* **2008**, *26*, 436–456. [CrossRef] [PubMed]

90. Oliveira, D.L.; Wilbey, R.A.; Grandison, A.S.; Roseiro, L.B. Milk oligosaccharides: A review. *Int. J. Dairy Technol.* **2015**, *68*, 305–321. [CrossRef]

91. Karlsson, E.N.; Schmitz, E.; Linares-Pastén, J.A.; Adlercreutz, P. Endo-xylanases as tools for production of substituted xylooligosaccharides with prebiotic properties. *Appl. Microbiol. Biotechnol.* **2018**, *102*, 9081–9088. [CrossRef]

92. Jain, I.; Kumar, V.; Satyanarayana, T. Xylooligosaccharides: An economical prebiotic from agroresidues and their health benefits. *Indian J. Exp. Boil.* **2015**, *53*, 131–142.

93. Zúñiga, M.; Monedero, V.; Yebra, M.J. Utilization of host-derived glycans by intestinal lactobacillus and bifidobacterium species. *Front. Microbiol.* **2018**, *9*, 1917. [CrossRef]

94. Markowiak, P.; Ślizewska, K. Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients***2017**, *9*, 1021. [CrossRef]

95. Bosscher, D. Fructan Prebiotics Derived from Inulin. In *Prebiotics and Probiotics Science and Technology*; Rastall, R.A., Charalampopoulos, D., Eds.; Springer International Publishing: Geneva, Switzerland, 2009; pp. 163–205.
96. Ende, W.V.D. Novel fructan exohydrolase: Unique properties and applications for human health. *J. Exp. Bot.***2018**, *69*, 4227–4231. [CrossRef] [PubMed]
97. Frances-Robles,E.; Lopez,M.G.Implication of Fructans in health: Immunomodulatory and antioxidant mechanism. Sci.World J. 2015,2015,1-15[CrossRef]
98. Delzenne, N.M.; Kok, N. Effects of fructans-type prebiotics on lipid metabolism. *Am. J. Clin. Nutr.* **2001**, *73*,456s–458s. [CrossRef] [PubMed]
99. Švejstil, R.; Musilová, S.; Rada, V. Raffinose-series oligosaccharides in soybean products. *Sci. Agric. Bohem.* **2015**, *46*, 73–77. [CrossRef]
100. González-Rodríguez, I.; Ruiz, L.; Gueimonde, M.; Margolles, A.; Sánchez, B. Factors involved in the colonization and survival of bifidobacteria in the gastrointestinal tract. *Fems Microbiol. Lett.* **2012**, *340*, 1–10. [CrossRef]
101. Niittynen, L.; Kajander, K.; Korpela, R. Galacto-oligosaccharides and bowel function. *Scand. J. Food Nutr*.**2007**, *51*, 62–66. [CrossRef]
102. Manderson, K.; Pinart, M.; Tuohy, K.M.; Grace, W.E.; Hotchkiss, A.T.; Widmer, W.; Yadhav, M.P.; Gibson, G.R.; Rastall, R.A. In vitro determination of prebiotic properties of oligosaccharides derived from an orange juicemanufacturing by-product stream. *Appl. Environ. Microbiol.* **2005**, *71*, 8383–8389. [CrossRef] [PubMed]
103. Molis, C. F., Lourie, B., & Ouarne, F. (1996). Digestion, excretion, and energy value of fructooligosaccharides in healthy humans. AmericanJournal of Clinical Nutrition, 64, 324–328.
104. Van Laere, K. M. J., Bosveld, M., Schols, H. A., Beldman, G., & Voragen, A. G. J. (1997). Fermentative degradation of plant cell wall derived oligosaccharides by intestinal bacteria. In R. Hartemink (Ed.), Non-digestible oligosaccharides: Healthy food for the colon? Proceedings ofthe international symposium (pp. 37–46). Wageningen Graduate School VLAG: Wageningen, Netherlands.
105. Cummings, J. H., Macfarlane, G. T., & Englyst, H. N. (2001). Prebiotic digestion and fermentation. American Journal of Clinical Nutrition, 73,415S–420S.
106. Kolida, S., & Gibson, G. R. (2011). Synbiotics in Health and Disease. Annual Review of Food Science and Technology, 2, 373–393.
107. Ellegard, L., Andersson, H., & Bosaeus, I. (1997). Inulin and oligofructose do not influence the absorption of cholesterol, or the excretion ofcholesterol, Ca, Mg, Zn, Fe, or bile acids but increases energy excretion in ileostomy subjects. European Journal of Clinical Nutrition, 51, 1–5.
108. Franck, A. (2002). Technological functionality of inulin and oligofructose. British Journal of Nutrition, 87, S287–S291.
109. Mussatto, S. I., & Mancilha, I. M. (2007). Non-digestible oligosaccharides: A review. Carbohydrate Polymers, 68, 587–597.
110. Franck, A., & Coussement, P. (1997). Multi-functional inulin. Food Ingredients and Analysis International, 8–10.

111. Walter, T. (1999). Bread goes prebiotic. International Food Ingredients, 2, 20–21.
112. Zimeri, J. E., & Kokini, J. L. (2003). Rheological properties of inulin- waxy maize starch systems. Carbohydrate Polymers, 52, 67–85.
113. Miremadi, F., & Shah, N. P. (2012). Applications of inulin and probiotics in health and nutrition. International Food Research Journal, 19, 1337–1350.
114. Anonymous.2007.Prebiotic in infant nutrition. Asia pacific food industry. 28,42-43
115. Sadeq Hasan Al-Sheraji Amin Ismail, Mohd Yazid Manap, Shuhaim Mustafa Rokiah Mohd Yusof, Fouad Abdulrahman Hassan ;Prebiotics as functional foods: A review; Journal of functional foods 5 (2013) 1542–1553
116. Amrit Pal Kaur , Sonali Bhardwaj , Daljeet Singh Dhanjal , Eugenie Nepovimova
Natália Cruz-Martins , Kamil Kuca , Chirag Chopra Reena Singh , Harsh Kumar , Fatih Şen ,Vinod Kumar , Rachna Verma and Dinesh Kumar *Review* Plant Prebiotics and Their Role in the Amelioration of Diseases *Biomolecules* 2021, *11*, 440. https://doi.org/10.3390/ biom11030440
117. Paiboon Thammarutwasik, Tipparat Hongpattarakere, Suphitchaya Chantachum, Kongkarn Kijroongrojana, Arunporn Itharat, Wantana Reanmongkol, Supinya Tewtrakul and Buncha Ooraikul Prebiotics – A Review Songklanakarin J. Sci. Technol. 31 (4), 401-408, Jul. - Aug. 2009 Bindels, L.B.; Delzenne, N.M.; Cani, P.; Walter, J. Towards a more comprehensive concept for prebiotics. *Nat. Rev. Gastroenterol. Hepatol.* **2015**, *12*, 303–310. [CrossRef] [PubMed]
118. Corina Pop , Ramona Suharoschi and Oana Lelia Pop *Review* Dietary Fiber and Prebiotic Compounds in Fruits and Vegetables Food Waste MDPI *Sustainability* 2021, *13*, 7219. https://doi.org/10.3390/su13137219
119. Fermoso, F.G.; Serrano, A.; Alonso-Fariñas, B.; Fernández-Bolaños, J.; Borja, R.; Rodríguez-Gutiérrez, G. Valuable Compound Extraction, Anaerobic Digestion, Composting: A Leading Biorefinery Approach for Agricultural Wastes. *J. Agri. Food Chem.* **2018**, *66*, 8451–8468. [CrossRef] [PubMed]
120. Skinner, R.C.; Gigliotti, J.C.; Ku, K.M.; Tou, J.C. A comprehensive analysis of the composition, health benefits, and safety of apple pomace. *Nutr. Rev.* **2018**, *76*, 893–909. [CrossRef]
121. Obidizinski, S.; Dolzynska, M.; Lewicka, S. *Analysis of Physical Properties of Dietary Fiber From Apple Waste*; Uniwersytet Przyrod- niczy w Lublinie: Lublin, Poland, 2017; pp. 272–277. [CrossRef]
122. Wichienchot, S.; Ishak, W.R.B.W. Prebiotics and Dietary Fibers from Food Processing By-Products. *Food Process. By-Prod. Util.* **2017**, 137–174. [CrossRef]
123. He, C.; Sampers, I.; Raes, K. Dietary fiber concentrates recovered from agro-industrial by-products: Functional properties and application as physical carriers for probiotics. *Food Hydrocoll.* **2021**, *111*, 106175. [CrossRef]