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Switching from Probiotics to Postbiotics: The Future for Better Health

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Abstract

Probiotics, live bacteria that boost the host's health, have garnered increasing attention in recent years as a way to enhance gut health and general welfare. Postbiotics, the metabolic by-products of probiotics, may be an even more efficient way to accomplish these objectives, according to a recent trend in microbiome research. The use of postbiotics instead of standard probiotics is growing in popularity as research indicates that postbiotics may have a number of benefits over them. Postbiotics can offer many of the same health advantages as probiotics, according to research. Postbiotics have been demonstrated to have a variety of benefits, including immune system modulation, enhanced gut barrier performance, and inflammation reduction. Postbiotics may also have advantages over probiotics, such as the capacity to operate as antioxidants, anti-inflammatory, and anti-cancer agents, in addition to probiotic advantages. Overall, the switch from probiotics to postbiotics offers an intriguing new area of study in the field of the microbiome that has the potential to completely change how we approach gut health and disease prevention. The review summarizes the advantages and disadvantages of dairy probiotics, Non-dairy probiotics and postbiotics in relation to human health.

Keywords: Probiotics, Postbiotics, Dairy, Non-dairy

1. Introduction

Recent years have seen a dramatic change in the field of nutrition, with more attention being paid to the role of the gut microbiota in health and disease. The gut microbiota is essential for preserving general health and wellbeing. The gastrointestinal system is home to trillions of microorganisms, including bacteria, fungi, viruses, and other germs [1]. Any alteration to the gut microbiota has been linked to inflammatory bowel disease, obesity, and cancer, among other health issues. Keeping a healthy gut microbiota is therefore essential for achieving optimal health.

Using probiotics and postbiotics is one strategy to keep the gut microbiome in good shape [2]. As a result, a variety of dairy and non-dairy products have been created and enhanced with these bioactive ingredients. In this context, the phrases probiotics and postbiotics have drawn a lot of interest. Probiotics are live microorganisms that, when taken in sufficient quantities, boost the host's health [3]. On the other side, postbiotics are non-viable microbial compounds or metabolic by-products that promote the host's health. Fermented foods and beverages, which have been enjoyed for thousands of years and are currently gaining favour as functional foods, frequently include these bioactive compounds [4].

Foods containing probiotics and postbiotics are being created to provide a practical and efficient method of supplying the human gut with these advantageous microbes and metabolites [5]. The demand for probiotic and postbiotic products is rising. As a result, there has been an increase in research and

development in this area, with food producers looking at different ways to include these bioactive substances into their goods.

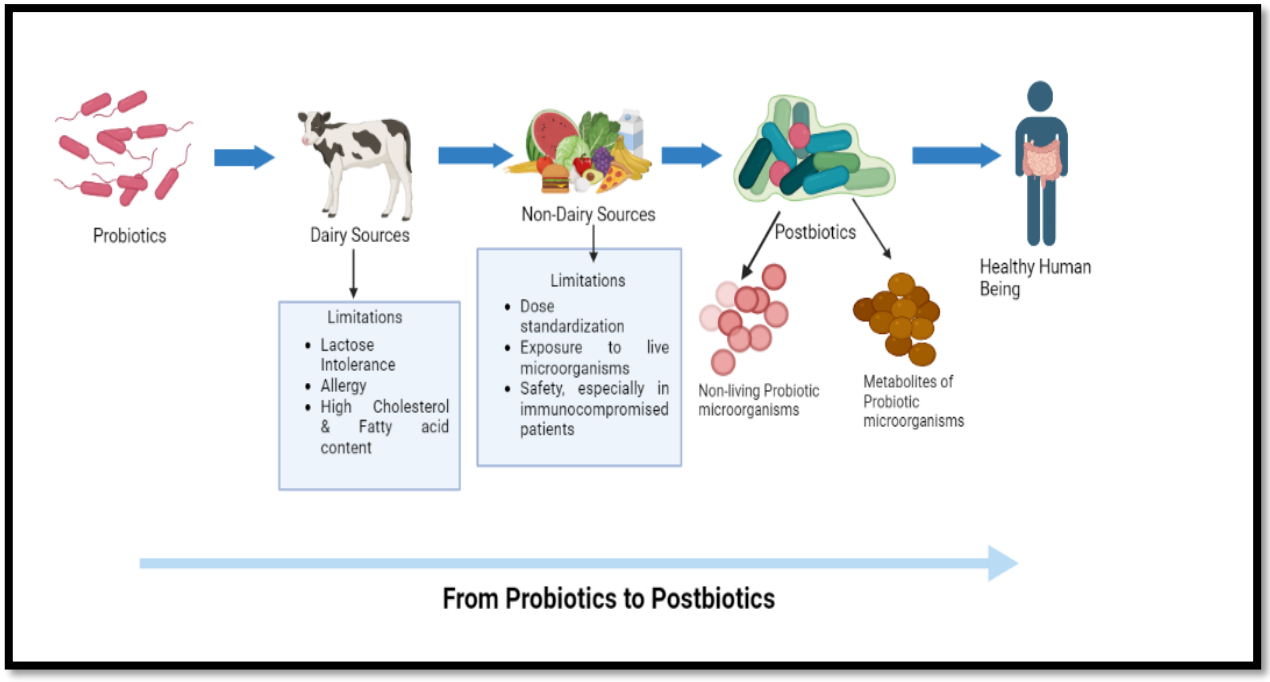

Figure1: Switching from probiotics to postbiotics

Microorganisms including *Lactobacillus*, *Bifidobacterium*, and *Streptococcus* are used in the creation of probiotic and postbiotic meals, among others. These bacteria are carefully chosen for their capacity to last in the gastrointestinal tract and offer the host particular health benefits [6]. On the other hand, probiotic bacteria that are involved in fermentation or biotransformation activities produce postbiotics as a result of their metabolic activity [4]. In order to ensure the viability and stability of the microorganisms, it is crucial to choose the right bacteria, optimise the fermentation conditions, and produce the right formulations for creating probiotic and postbiotic foods. In order to be sure that probiotic and postbiotic foods are safe for consumption by humans and offer the desired health advantages, they must also be thoroughly tested for safety and efficacy [7].

This review seeks to present a summary of the most recent developments in probiotic and postbiotic dietary trends, theories, and products. It will go through the various probiotic and postbiotic species, health advantages and disadvantages of dairy and non-dairy probiotic products, as well as the advantages of postbiotics over probiotics. Ultimately, this analysis will offer a thorough understanding of the development of probiotic and postbiotic foods as well as their potential to enhance human health.

2. Probiotics

According to WHO- probiotics are considered as “non-pathogenic live microbes that when administered in adequate amount confers a health benefit on host” [8]. Ferdinand vergin was the first scientist who introduced the term probiotics in 1954.

The administration of probiotic microbes should be sufficient and regular to a minimum value of 10^6 cfu/ml for its health benefits. Probiotics are broadly categorized into three categories namely Generally regarded as safe (GRAS). These include the microorganisms such as *Lactobacillus bulgaricus* and

Streptococcus thermophilus which are not related to health claims. Food supplements which are linked with health claims to enhance normal microflora e.g., *Lactobacillus rhamnosus GG*. Drugs that are used to cure various diseases such as acute paediatric diarrhoea and the microbes included into this category are *Lactobacillus acidophilus*. A capable strain of probiotic must be the one which is acid tolerant, oxygen tolerant, heat tolerant, bile tolerant, through which it can survive the gastrointestinal tract, should be easily grown and be suitable for industrial production in large scale [9].

Many LAB (Lactic Acid Bacteria) like *Lactobacillus*, *Bifidobacterium longum*, *Streptococcus*, *Lactococcus*, *Escherichia coli* strain, yeast like *Saccharomyces boulardii* etc are categorised under probiotics. Microbes which are identified as probiotics are exploited in various fermentation processes for preparation of beverages [10]. If the source of probiotic is agricultural source, and have fibre and oligosaccharides, then it is considered as prebiotics. They are undigestible carbohydrates so they travel to lower digestive tract, there they provide food to the healthy bacteria. Prebiotics helps in growth of probiotics by providing energy to the microbes [11].

Probiotics works by various mechanism of action. It lowers the pH of intestine, reduces the apoptosis of epithelial cells and accelerate the mucin production, decrease the colonization of harmful microorganisms and helps in restoring or balancing the microbiota of gut [12]. Probiotics have various health benefits such as, it reduces the risk of necrotizing enterocolitis which is a disorder which affect the intestine of premature babies (from 2 weeks to 2 months) in which the intestine fails to hold waste and this can be lethal for the infants [13].

They also help in curing acute diarrhoea which can be caused by bacterial infection, food allergy, inflammatory bowel disease etc. *Lactobacillus rhamnosus GG* and *Lactobacillus reuteri* decreases the time duration of this acute diarrhoea by one day and also helps in decreasing the severity. *Saccharomyces boulardii* is also effective in acute diarrhoea [14]. Probiotic strain such as *Lactobacillus rhamnosus* improves the symptom of many allergic diseases, one of which is atopic dermatitis (AD) [15]. Therefore, by supplying these bacteria as probiotics for a long time, the intestinal malady can be cured to some extent.

Probiotics help in manufacture of nutrients which include amino acids, vitamins etc inside the host and also elevate the short chain fatty acid (SCFA) content in lumen of intestine. Butyrate, acetate etc are included under SCFA which helps in maintaining low pH inside the intestine to hinder the pathogenic microbial growth [16]. Also, the probiotics compete with other pathogens for nutrients and space which results in decreased number of pathogens in intestine. Maximum probiotics decreases the scoring atopic dermatitis (SCORAD) index score, hence assist in curing AD [17]. Probiotics comfort in periodontal disease, that include Gingivitis and periodontitis which damage the tissues of gum which are responsible for holding the teeth. These periodontal probiotics subdue the growth and colonization of pathogens, and also hinder the virulence gene expression by controlling the inflammatory cell number and induction of antimicrobial peptides expression [18].

3. Dairy sources of probiotics

Dairy products are one of the common sources of probiotics. Initially probiotics were ingested through dairy products such as curd, yogurt, acidophilus milk, cheese, ice cream, frozen symbiotic dessert, non-fermented goat's milk etc as they simplify the ingestion of probiotics inside the gut. Table 1 summarizes the list of probiotic microorganisms found in dairy products with their mechanism of action against diseases or disorders.

3.1. Yogurt

It is produced by fermentation of milk, containing Lactic acid bacteria which aid in fermentation of lactose and also have on effect on the proteins and milk peptides. It contains high amount of minerals like magnesium, calcium, zinc, and potassium, it is also a source of vitamin B [19]. During fermentation of yogurt various by products are produced such as enzymes. They provide functionalities to yogurt by activating the milk proteins such as casein and albumin to bioactive peptides. Non fermented dairy products lack this property. It contains various probiotic strains such as *Bifidobacterium bifidum*, *Lactobacillus acidophilus*, *Lactobacillus delbrueckii* etc which confer various health benefits [20]. Some of its health benefits includes the improvement in lactose intolerance, boost immunity, anti-allergic effect, relief of constipation and reduction of cholesterol, lowering of blood pressure [21]. Main disadvantage of fermented milk and yogurt is the survival of probiotics in the low pH, as the probiotics grows optimally between the pH 5.5-6.5.

3.2. Cheese

Cheese is also having various advantageous characteristics including, high content of fat, pH, viability of probiotic strains presents and increase their shelf life. Some researchers concluded that cottage cheese having *Lactobacillus planetarium* Lb4 contains 9 cfu/ml and can survive up to 28 days in refrigerated temperature [22]. Cheese is considered as an appropriate dairy product for transferring the probiotics into the gut because it possesses high amount of fat which is helpful in shielding the bacteria from the low pH environment inside the gut [23].

Cheese is a good vehicle for delivery of probiotic because of dense matrix and high fat content which protect the probiotic in the stomach also it fabricates a favourable condition for survival of probiotic by creating buffer against the low pH of gastrointestinal tract [24]. The growth of *bifidobacteria* and *lactobacilli* is promoted because of the presence of inulin and oligofructose in the form of prebiotics [25].

3.3. Ice cream

Ice cream has approximately neutral pH, and total solid level is high which provide shielding for the probiotics microbes [26].

The probiotic bacteria such as *Lactobacillus casei*, and *Bifidobacterium longum* can be incorporated in both of fermented as well as unfermented mixture and they are most resistance against the alkaline and acidic conditions as compared to other strains, making them appropriate to be used in probiotic ice cream. The high amount of fat and milk solids present in ice cream protects the probiotic strains [27].

But as the production of ice cream require various steps, it could negatively affect the viability of probiotics. Because of this, many strategies like incorporation of prebiotics, selection of strain, microencapsulation, adjustment of pH and cream fermentation, inoculation of optimum amount of probiotics, freezing control, aids to enhance the viability of probiotic strain in ice cream [28].

3.4. Kefir

It has creamy texture and acidic taste which is processed from different milk for example buffalo, goat, camel, sheep etc through microbial fermentation of kefir grains. It contains a high amount of vitamin C, B1, B2 and B5, along with minerals and amino acids. *Propionibacterium pituitosum* and *Propionibacterium peterssoni* synthesise B12, *Propionibacterium shermanii* produces B6 [29]. According to reports, kefir has as anti-tumour, anti-microbial, anti-diabetic, anti-hypertensive, immunomodulatory activity and also helps in digestion of lactose [30].

3.5. Probiotic milk

As *Lactobacillus acidophilus* is an acid-loving bacteria therefore it does not grow in the milk rapidly, so

maintaining the inoculum active is necessary, for that the mother culture in transferred to the acidophilus milk. Traditionally acidophilus milk, was heated for 1 hour at 95° C or for 15 min at 125° C. Because of this high temperature the growth of the *Lactobacillus acidophilus* is stimulated as the proteins gets denatured and peptides are released. Now this milk is kept at 37° C for 3-4 hours to let the spores to germinate and then resterilised to kill the all the vegetative cells. The *Lactobacillus acidophilus* is inoculated in heat treated milk, approximately 2-5% and it is kept for fermentation (18-24 hours) until the pH reaches to 5.5-6 or until 1% of the lactic acid is produced without alcohol [31].

3.6. Fermented whey dairy beverage

Whey is the main by-product of cheese or casein, generally yellow-greenish in colour containing 50% of the milk solids which include whey protein, lactose, mineral compound etc. Whey can be classified into two major types: sweet whey and acid whey. Sweet whey is characterized by a titratable acidity in the range of 0.10-0.2% lactic acid (LA) and a pH range of 5.8-6.6. Acid whey, on the other hand, has a higher titratable acidity percentage (>0.40% LA) and a pH value above 5.0. [32]**.** Its beneficial properties include antioxidant property, anticancer, antimicrobial and also immune stimulating features. It provides a suitable medium for the growth of yoghurt bacteria, kefir grain and various probiotics like *Lactobacillus* and *Bifidobacterium* also it increases the viability of these probiotic bacteria inside the gastrointestinal tract. Nutritional quality of whey can be improved by the addition of probiotic bacteria to it [33].

Table 1: List of probiotic Microorganisms from dairy products.

Dairy product	Probiotic Microorganisms	Mechanism	Disease/Disorder	Reference
whey drink	*Lactobacillus rhamnosus*	It increases the anti-inflammatory cytokines which helps to tolerate the inflammation induced by colitis.	Ulcerative colitis	[34]
Fermented milk	*Lactobacillus fermentum*	Enhance the hypercholesterolemic effect	Hypercholesterolemic	[35]
Cream cheese	*Lactobacillus chungangensis CAU28*	It helps to decreases the IgE antibody which is related to immune homeostasis and also maintain the balance of Th1 and Th2.	Atopic dermatiotis	[36]
Fermented milk	*Lactobacillus spp*	Helps in absorption of amino acid which results in enhancement of postprandial MPS	Skeletal muscle protein anabolism	[37]
Kefir drink	*Commercial starter culture of kefir*	The fermented kefir reduces the symptoms induced by colitis and helps in relieving diarrhoea and mucosal wall damage	Inflammatory bowel disease (IBD)	[38]

4. Advantages of dairy probiotics products

4.1. Long viability of probiotics

It is one of the most important criteria for a probiotic food. The probiotics should remain viable till the product's shelf life. Different factors that affect viability of probiotics microbes are the strain of probiotic, temperature during processing, the procedure, condition during storage. Now as the process of fermentation maximises viability of microbes, the dairy products are considered suitable for the probiotics [39].

4.2. High sensory quality

This quality in food product increases its marketability of the product. Dairy industry is able to produce hybrid dairy product by combining fruit and dairy product, which makes the food product more tempting to consumers. Many authors recorded that when the yoghurt is fortified with fruits like strawberry, carrot etc, the sensory and physiochemical property of yoghurt is enhanced [40].

4.3. Symbiotic application

In food possessing both the prebiotics like insulin, oligosaccharide etc and probiotics are considered as symbiotic food. It increases the viability of good microbes in the gastrointestinal tract (GIT). According to some authors, the regular intake of symbiotic yoghurt was beneficial for the gut of any individual [41]. Also, kulka et al recorded that the probiotic bacteria like *Streptococcus thermophilus, Bacillus animalis, bulgaricus, Lactobacillus delbrueckii lactis BB-12* and insulin in symbiotic yoghurt, reduces the fever duration [42].

5. Limitations of dairy products

5.1. Lactose intolerance

Also called as lactose malabsorption. It is characterised by the inability of body to break lactose into galactose and glucose because of production of reduced amount of enzyme- lactase. The activity of lactase enzyme is maximum at birth but declines with time. The undigested lactose is then consumed by the other microorganisms in the intestine which produce several gases like hydrogen, methane etc. This results in watery stool, bloating, cramps, or sometimes irritability bowel syndrome [10].

5.2. Allergy

One of the best examples of allergies with milk protein is Atopic dermatitis (AD) which is associated with skin allergy in children. Cow's milk allergy (CMA) is also a type of allergy associated with infants and its cases have increased latterly. It induces a body's reaction towards cow's milk protein (CMP) like casein, beta-lactoglobulin and various soluble proteins like whey protein. CMA is subdivided into two categories based on its immunological mechanism. First is mediated by immunoglobulin (IgE) and second is non IgE mediated. Most of the allergies are IgE mediated. CMA mostly affect the children below the age of 2 [43].

5.3 High cholesterol and fatty acid content

As the milk contains both the fatty acids- saturated and polyunsaturated in the ratio- 0.05, so by ingesting a huge volume of milk, the amount of cholesterol in body increases which results in high risk of cardiovascular disease (CVD), stroke, coronary heart disease (CHD). So, the consumption of low fat or fat free milk is recommended by the health authorities [44].

Because of all these problems, associated with the dairy products, there was a need to switch to the non-dairy probiotic products such as fermented fruits, cereals, vegetables etc.

6. Non-dairy sources of probiotics

A number of non-dairy probiotic food products are manufactured worldwide. This include fermented and non-fermented products both, such as cereals, fruits and vegetables like banana, apple, pineapple, pomegranate, carrot etc. Fruits can be consumed in various forms such as juices, pulp, whole fruit, powdered fruit etc. Meat and fish are also non-dairy probiotic source.

6.1. Fruits and vegetables

They are considered as a good alternative to dairy based products. Two major microorganisms used for this purpose are- *Lactobacillus acidophilus* and *Lactobacillus casei* [45]. Fruit juices are majorly used, as their nutrient content is high in contrast to dairy products. Acidulants are also added in non-dairy sources which enhance the shelf life as they provide anaerobic condition for probiotics by utilizing the available oxygen. Sugar present in fruits help in the growth of probiotics and these juices remain in the stomach for shorter period of time [46]**.** Therefore, the probiotic microbes are exposed to the harsh acidic environment for shorter time. Along with all this, fruits have good sweet taste.

6.2. Sauerkraut

It is produced spontaneously after fermentation of cabbage after addition of salt under anaerobic condition. The microbes involved in the fermentation process takes few weeks at temperature approximately 15-20°C which is characterised by heterofermentative and homofermentative phase. These phases are dominated by *Leuconostoc mesenteroides* and *Lactobacillus plantarum* respectively. Few other important microbes which are present in lesser number include other species of *Lactobacillus, Leuconostoc, Weissella* and *Pediococcu* [47].

6.3. Meat

Meat is also used in sausage form. Fermented meat products can be considered as a source of probiotics with beneficial health effects. The ingestion of fermented sausage, having *Lacticaseibacillus paracasei* resulted in its colonization in gut after consumption for 3 days. After more experiments with this probiotic strain, a little induction of immunological response was also observed. Microbes used in development of products from fermented meat are *Bifidobacterium longum* and *Lacticaseibacillus casei, Lactobacillus rhamnosus* LOCK900, *lactobacillus plantarum* 299v, *Lactobacillus sakei* 23K, *Staphylococcus simulans* NJ201 etc [48].

6.4. Kombucha tea

Kombucha tea, also called as “Elixir of life or “tea of immortality” [49]**.** It is sweet, bubbly and slightly acidic which is produced by soaking leaves of black tea in boiling water and sugar is also added along with it. After that, the symbiotic culture of bacteria and yeast (SCOBY) is added in the mixture. The yeast and bacteria present in SCOBY produce cellulose and cellulosic portion. The pH of tea decreased by the symbiotic action of microbes in SCOBY which promote the fermentation of gas bubble [50]. Osmophilic strain of yeast which include *Bretanomyces spp., Candida spp., Lanchancea spp., Pichia spp., Saccharomyces spp.,* etc and few acetic acid bacteria such as *Gluconobacter spp., Acetobacter spp., Komagataeibacter spp.,* etc is present in kombucha tea. This tea has various therapeutic benefits, have anti- inflammatory, anti-carcinogenic, antimicrobial, anti-proliferative, anti-diabetic and antioxidant properties. It is also helpful in coronary heart disease [51].

6.5. Sourdough bread

It is considered as one of the oldest leavened breads prepared by fermenting grain. When cereals, legumes or pseudo-cereals are grinded and water is added, dough is formed which is then converted into sourdough with time. Sourdough have various benefits as it improves the texture, odour, and nutritional value of food

product. Also, it protects the bread from spoilage and enhance the shelf life because of its acidic nature, due to the presence of caproic, acetic, butyric acid etc. Lactic acid fermentation is induced in sourdough by the help of yeast (mainly *Saccharomyces cerevisiae*) and lactic acid bacteria forming symbiotic colony. It contains various microbes which include *Lactiplantibacillus plantarum, Levilactobacillus brevis, Fructilactobacillus sanfranciscensis* etc [52].

6.6. Other products

Other products include cereals, contain high nutrient content and are consumed globally are also observed as substitute vehicle. Several other advantages of consuming cereals include the presence of fibre and indigestible carbohydrates such as oligosaccharides that enhance the probiotic Lactic acid bacteria growth. Also, cereal based probiotic drink containing *Lactobacillus acidophilus* and *Lactobacillus plantarum* are made, which decreases the chances of type 2 diabetes, various heart disease, cancers etc.

Probiotic beverages which are made from fermented cereal have approximately 10^6 and 10^7 cfu/g viable probiotic bacteria. Microbes which are involved in this fermentation are mainly yeast and *Lactobacillus spp* (*9*)**.** Cereals such as millet, oats, barley have high content of beta-glucans and arabinoxylans which are considered as prebiotic fibre [53]**.** This is the same for other grains such as emmer, which is a type of awned wheat, having higher nutritional value as compared to other cereals as it contains beta-carotene 3 to 4 times more, double amount of vitamin A, lutein and riboflavin. It eliminates the risk of allergy, diabetes, sensitivity and intolerance [54]**.** Apart from cereals, pseudocereals can also be a source of probiotics. “Pseudo” means false or resembling and “cereal” means grains. Some of the well-known pseudocereals are chia (lamiaceae), amaranth, quinoa (amaranthaceae) [55].

Table 2: List of probiotic Microorganisms from Non-dairy products.

Non-dairy product	Probiotic Microorganisms	Reference
Non fermented probiotic beverage blended with banana, strawberry, and palmiteiro fruit	*Lactobacillus plantarum, Bifidobacterium animalis, L. casei*	[56]
Sweet orange fruit juice	*Lactobacillus casei*	[57]
Cashew apple juice	*Lactobacillus plantarum*	[58]
Malt, oat, and barley	*Lactobacillus fermentum* *Lactobacillus plantarum* *Lactobacillus reuteri*	[59]
Mustard leaf	*L. plantarum*	[60]

There are various limitations of probiotics that have led to the emergence of postbiotics include their instability under varying conditions, the potential risk of infection associated with live microorganisms, the variability of effects based on individual gut microbiota composition, and the need for a standardized approach. Postbiotics, being more stable, non-viable, and providing a consistent mechanism of action, offer an alternative that addresses these limitations and holds promise for various health benefits.

7. Postbiotics

They are non-viable, tyndallized, heat killed probiotics, which are basically inanimate microbes and their components such as Short Chain Fatty Acids, vitamins, organic acids, amino acids, cell wall etc [61]**.**

International Scientific Association for Probiotics and Prebiotics (ISAPP) elucidated a postbiotic as a preparation of inanimate microbe and or their components that confers a health benefit on host [62].
Generally, the postbiotic products are more stable and due to the presence of non-viable microbes as compared to probiotic products. Some examples of postbiotic microbes are *Bifidobacterium bifidium MIMBb75* which is a heat inactivated culture and provide relief in irritable bowel syndrome [63]**.** *Akkermansia muciniphila ATTCCBAA-831* can be inactivated, pasteurized or alive and is helpful in obesity [64].
One of the examples of postbiotic food is ambient yoghurt. It is a thermally treated yoghurt in which the starter culture is inactivated. There is no necessity to store this yoghurt in cold conditions. This is gaining popularity across different parts of the globe such as Asia, Africa, America, and it first appeared on the market in 2010 in China [62].

7.1. Classification of postbiotics

They are classified on the basis of the metabolites produced by the microbes such as cell wall, enzymes, exopolysaccharides, proteins etc [65]**.** They are also classified on the basis of the composition which include lipids, vitamins (majorly vitamin B), organic acid (propionic acid), carbohydrate etc. Their classification is also on the basis of their physiological function such as antioxidants, anti-hypersensitive, anti-obesogenic, anti-inflammatory, anti-proliferative outcome [66].

7.1.1. Short chain fatty acids (SCFAs)

SCFAs are the metabolites produced through the process of fermentation of plant polysaccharides by the bacteria present in intestine. SCFAs include butyrate, acetate, propionate which are present in the ratio 20:60:20 in feces and also colon [67]. The most abundant SCFA is acetate produced by fermentation process of enteric bacteria *Acetobactobacterium woodie* [65]**.** Butyrate helps in regeneration of the epithelium lining of the intestine also it is anti-inflammatory. Propionate act as a substrate for gluconeogenesis which take place in liver, and also have anti-inflammatory characteristics. SCFAs also modify the cell signalling, metabolism, regulations etc by affecting the immune cells [68].

7.1.2. Exopolysaccharides

Exopolysaccharides (EPS) are sugars and its derivatives having high molecular weight and are produced by lactic acid bacteria. EPS are homopolysaccharides having monosaccharide unit of only one type. Some of the examples of homopolysaccharides are dextran, cellulose, curdlan, levan etc [69]**.** EPS can prevent the cholesterol absorption by improving the lipid metabolism, also it has antioxidant and antimicrobial property exerted by *Lactobacillus* strains [70].

7.1.3. Enzymes

Enzymes are proteins which can act as catalyst in various biochemical reactions. They are mainly produced by bacterial strains such as *Bacillus licheniformis* and *Bacillus subtilis*. High amount of glutathione peroxidase having antioxidant property was found in *Lactobacillus fermentum*; fungal strains such as *Aspergillus niger* also produce certain enzymes and proteins [71].

7.1.4. Cell wall fragments

It includes lipoteichoic acids, techoic acids, peptidoglycan etc which are released during metabolic activities or fermentation process of some probiotic bacteria and can generate on immune response hence are immunogenic [72]**.** These two call wall components are present in the cell wall of gram-positive bacteria and have the properties like anticancer, antioxidant, antibiotic resistance etc [73].

7.1.5. Bacterial lysate

It refers to the broken bacterial cells and are acquired by the degradation of either Gram- positive or Gram-negative bacteria by physical or chemical method. It is helpful in decreasing chances of recurrency of respiratory tract infection mainly in children [74]. Apart from this, it helps in reducing the chronic obstructive pulmonary disease [75].

7.2. Methods to produce probiotics

Various technologies have been developed for postbiotic production. These technologies can be categorised into thermal and non-thermal strategies for postbiotics production. Thermal treatment includes the process of pasteurization conducted at a temperature range between 60-121℃ for about 60 minutes. Another process is sterilization which is a process of either killing or deactivation of microorganisms. These thermal techniques disrupt the cell membrane, also they cause nutrient and ion loss, inactivate the enzymes, coagulate proteins & ruptures the DNA [76].

Various non-thermal techniques include the use of ionizing radiations such as Cesium 137 and cobalt 60 gamma radiations for about 20 hours having the capacity to penetrate the microorganisms and cause DNA damage (Jadhav et al.,2021). Ultraviolet radiation comes under the category of non-ionizing radiations that denatures the protein and also cause mutation in DNA of the cell. Cells are exposed under UV radiations for 30 minutes [77].

Dehydration is another method to disrupt the cytoplasmic membrane, it also changes the structure of cell, ribosome, nucleic acid etc. Under dehydration, two techniques can be implemented that are Lyophilization which is also called freezes-drying technique and Spray-drying. For this, the temperature of product feeding is 60℃, outlet air is 90℃. But before freezing, some cryoprotectants are used in order to protect the cell injury. The most widely used cryoprotectants are peptides and carbohydrates [78].

Another method of cell membrane disruption through electroporation is Ohmic technology under which a frequency of 20-60 kHz is applied for 15 minutes. CO_2, along with pressure and temperature is also used which is known as Supercritical fluids-CO_2 technique. This results in enzyme inactivation, cell metabolism inhibition, cell membrane modification, imbalance of the intracellular electrolyte and pH [79].

Lactobacillus casei ATCC393 is given heat treatment for 40 min at 100℃ after which the cells are allowed for sonication at 50 W for about 10 min, followed by centrifugation for 40 min at 13000x g. during this process, postbiotic *L. casei* fractions are produced [80].

In another study, the cell suspension of *Lactobacillus, Bifidobacterium, Streptococcus, Lactococcus* etc was made and exposed to ultrasonic rays for disruption at 0℃ for 1 min, which is followed by removal of cell debris by centrifugation. For this, the supernatant is taken and tested.

There are several methods that uses chemicals for postbiotic production. The strains of *Bifidobacterium, Lactococcus, Issatchenkia, Lactobacillus, Enterococcus* etc were treated with chemicals such as 0.5 M ethanolic solution of potassium hydroxide. These cells are then sonicated at 300 W for about 2 min and then boiled for 1 hour. The solvent is extracted using diethyl ether. The cell fragments hence obtained are considered as postbiotics [81].

In another method, the postbiotics were obtained in the form of glycolipids from the bacterial strain of *Lactobacillus plantarum* B-01 after the application of CO_2 (known as supercritical fluid technology). By this method, the product yield was high as compared to solvent extraction that too in minimum time [82].

To obtain postbiotics, one technique is to treat it with enzymes. For that, *L. casei* CRL 431 at 42 kHZ for

30 min approximately. After that it is treated with enzymes like lysozyme or mutanolysin for 150 min at 37° [83].

The postbiotic extracts are processed in pharmaceutical and food industries by lyophilization or freeze-drying method and also spray drying method for their easy storage. But these processes can affect the composition of these postbiotics due to which their postbiotic activity reduces. For example, the hydrogen peroxide which shows antimicrobial activity is eliminated due to lyophilization [2].

8. Post-biotics over probiotics

Postbiotics are not live microorganisms, so they are not subject to the same limitations as probiotics, such as storage and transport issues. Additionally, postbiotics have long shelf life, more stability in wide temperature range and different pH, do not pass on the resistance for antibiotics, demarcate chemical composition, also they can be consumed by immunocompromised people [84].

As such, the development of postbiotic-based therapeutics may provide an attractive alternative to traditional probiotics, particularly for individuals who are unable to tolerate live microorganisms or who have concerns about their safety.

8.1. Stability

One of the main characters of post-biotics over probiotics is its stability during storage and even during industrial processes. As heat and oxygen can affect the live organisms (probiotics) therefore maintaining their stability is a difficult task but the dead microbe or their product remain comparatively stable [85].

8.2. Safety

Post-biotics are considered safer than the probiotics as they contain the microbes which do not have the ability to replicate so they would not give rise to fungaemia or bacteraemia [86].

Intellectual property protection

Post-biotics allows the product producer to have the patent of all the ingredients as we cannot get microbe from the commercial products. Apart from this, the country where the post-biotics is produced from any microbe, the country is allowed to have the control of that microbe under Nagoya Protocol [87].

8.3. Functionality

Post-biotics are considered beneficial for health which include anti-cancer effect, anti-infectious effect, wound healing capacity, detoxification etc. it is considered more effective than probiotics [88].

8.4. Regulatory considerations

Till date, there are no specific health claims regarding postbiotics based on Food for Specific Health Uses (FOSHU), but based on Food with Function Claims (FFC) some of them are associated with health claims therefore they are reported in Consumer Affair Agency situated at Japan. FFC require evidences that too scientific, for the application of these postbiotic products based on review and clinical studies [89].

Qualitative Presumption of Safety (QPS), developed an updated list of microbes which can be a potential postbiotics. It is developed by the European Food Safety Authority (EFSA). Those microbes require approval in Europe which are not mentioned in that list and can be used for postbiotic production. For example, a bacterial strain of *Bacillus xylanisolvens* was assessed and evaluated for safety purpose. This evaluation was done on inactivated and heat-treated bacteria [88].

9. Applications of postbiotics

9.1. Bio preservation of food

To increase the shelf life of the food and to prevent spoilage, these postbiotics are used. Postbiotics have

anti-microbial activity which affects the microbes involved in spoilage and pathogenic microbes through few mechanisms such as effect on proteins of cell wall, creation of pores in cell membrane, reducing the cytoplasmic pH**.** Phenolics and flavonoids are present in postbiotics from *Latilactobacillus sakei and Pediococcus acidilactici*, which helps in decreasing the population of *Salmonella typhimurium* in chicken drumstick [90]**.** Products containing *Saccharomyces cerevisiae* are included in diet of poultry which control the number of *Salmonella enterica* in foods obtained from poultry [91].

Postbiotics helps in preservation of vacuum-packed cooked sausages, as they contain preservatives. As the internal or external factors can influence the viability of probiotics, therefore postbiotics helps in preserving dairy products [92].

9.2. Food packaging

The food needs to interact with the packaging material as well as the surrounding environment this is called active packaging approach. This prevents the deterioration of food product by microbes when it is packed. For this, the food product is coated with postbiotics or by introducing in packaging matrix, or covalent linkage etc [93]**.** These postbiotics packaging are organic acid, bacteriocins and peptides based. Organic acids possess anti-microbial activity therefore is an important component of postbiotics. Various organic acids like lactic acid or acetic acid etc helps in reducing the pH of cytoplasm due to which the pathogenic microbes stop growing [93].

9.3. Cosmetics

Skin is a home to several microflora, and the alteration in the number of these microflora in skin cause diseases such as in case of acne which is generally caused by the increase in growth of *Staphylococcus epidermidis* and *Cutibacterium acnes*. Using topical postbiotics aids in decreasing the number of bacteria such as, *S. epidermis, S. pyogenes and C. acnes*, which cause skin acne [94].

10. Conclusion

Probiotics are consumed by human from time immemorable. Probiotics are easily consumed through various dairy sources and non-dairy sources and administer various health benefits to the host, by discrete mechanisms. One of the paramount mechanisms is to alter the gut microbiota. But from past few years the word postbiotics is more prominent as they are the metabolic by-product of the microbes or the inanimate microorganism unlike probiotics. Due to this, they are comparatively safe and have a long shelf life than probiotics. The storage and transport of postbiotics is quite unchallenging. Apart from this, they are generally stable over a wide range of pH and temperature, there is a futile chance of antibiotic resistance, and above all, it can be consumed by immunocompromised patients. Beside these positive health effects, post biotics have various applications like bio preservation of food, in food packaging, removal of biofilms, in cosmetics etc. Although further research is to be done to exploit these postbiotics in a better way.

11. Future prospectus

The market of probiotics and postbiotics is yet to be designed further. The notion of postbiotics is still unclear to common people. Postbiotics have a wide range of scope in food industry, due to which its commercialization will increase. Both the probiotic and postbiotics have a positive impact on host body but postbiotics have broad target area including skin, nasopharynx, oral cavity unlike probiotics. As these postbiotics are comparatively stable, various product including food, healthcare products, beverages, cosmetics can be produced. This review suggested that these postbiotics aid in ameliorating immune

system, allergies, diarrhoea, gastrointestinal disorders etc. However, there is confined attestations of treatment and prevention of disease by postbiotics, but it is expected that with the continuation of research, there will be more data availability which will prove the potency and effectiveness of postbiotics.

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17. References

1. Thursby E., Juge N., Introduction to the human gut microbiota, Biochem J, 2017, 474(11), 1823-1836.
2. Thorakkattu P., Khanashyam A.C., Shah K., Babu K.S., Mundanat A.S., Deliephan A., *et al*, Postbiotics: Current Trends in Food and Pharmaceutical Industry, Foods, 2022, 11(19), 3094.
3. Tridip K. Das, Shrabani Pradhan, Sudipta Chakrabarti, Keshab Chandra Mondal, Kuntal Ghosh, Current status of probiotic and related health benefits, Applied Food Research, 2022,2(2).
4. Wegh C.A.M., Geerlings S.Y., Knol J., Roeselers G., Belzer C., Postbiotics and Their Potential Applications in Early Life Nutrition and Beyond, Int J Mol Sci, 2019, 20(19), 4673.
5. Żółkiewicz J., Marzec A., Ruszczyński M., Feleszko W., Postbiotics-A Step Beyond Pre- and Probiotics, Nutrients, 2020, 12(8), 2189.
6. Fijan S. Microorganisms with claimed probiotic properties: an overview of recent literature. Int J Environ Res Public Health. 2014;11(5), 4745-67.
7. Zawistowska-Rojek A., Zaręba T., Tyski S., Microbiological Testing of Probiotic Preparations, Int J Environ Res Public Health, 2022, 19(9), 5701.
8. Piqué N., Berlanga M., Miñana-Galbis D., Health Benefits of Heat-Killed (Tyndallized) Probiotics, An Overview, Int J Mol Sci, 2019, 20(10), 2534.
9. Setta M.C., Matemu A., Mbega E.R., Potential of probiotics from fermented cereal-based beverages in improving health of poor people in Africa, J Food Sci Technol, 2020, 57(11), 3935-3946.
10. Vijaya Kumar B., Vijayendra S.V., Reddy O.V., Trends in dairy and non-dairy probiotic products - a review, J Food Sci Technol, 2015, 52(10), 6112-24

11. Davani-Davari D., Negahdaripour M., Karimzadeh I., Seifan M., Mohkam M., Masoumi S.J., Berenjian A., Ghasemi Y., Prebiotics: Definition, Types, Sources, Mechanisms, and Clinical Applications, Foods, 2019, 8(3), 92.
12. Bantayehu Addis Tegegne, Bekalu Kebede, Probiotics, their prophylactic and therapeutic applications in human health development: A review of the literature, Heliyon, 2022, 8(6).
13. Beghetti, I., Panizza, D., Lenzi, J., Gori, D., Martini, S., Corvaglia, L., Aceti A., Probiotics for Preventing Necrotizing Enterocolitis in Preterm Infants: A Network Meta-Analysis, Nutrients, 2021, 13(1), 192.
14. Allen S.J., Martinez E.G., Gregorio G.V., Dans L.F., Probiotics for treating acute infectious diarrhoea, Cochrane Database Syst Rev, 2010, 11: CD003048.
15. Rather I.A., Bajpai V.K., Kumar S,. Lim J., Paek W.K., Park Y.H., Probiotics and Atopic Dermatitis: An Overview, Front Microbio, 2016, 7:507.
16. Markowiak-Kopec P., Slizwska K., The Effect of Probiotics on the Production of Short-Chain Fatty Acids by Human Intestinal Microbiome, Nutrients, 2020, 12(4), 1107.
17. Umborowati M.A., Damayanti D., Anggraeni S., Endaryanto A., Surono I.S., Effendy I., The role of probiotics in the treatment of adult atopic dermatitis: a meta-analysis of randomized controlled trials, J Health Popul Nutr, 2022, 41(1), 37.
18. Gupta G., Probiotics and periodontal health, J Med Life. 2011, 4(4), 387-94.
19. Hadjimbei E., Botsaris G., Chrysostomou S., Beneficial Effects of Yoghurts and Probiotic Fermented Milks and Their Functional Food Potential, Foods, 2022, 11(17), 2691.
20. Gouda A.S., Adbelruhman F.G., Sabbah Alenezi H., Mégarbane B., Theoretical benefits of yogurt-derived bioactive peptides and probiotics in COVID-19 patients - A narrative review and hypotheses, Saudi J Biol Sci, 2021, 28(10), 5897-5905.
21. Kumar H., Bhardwaj K., Cruz-Martins N., Sharma R., Siddiqui S.A., Dhanjal D.S., Phyto-Enrichment of Yogurt to Control Hypercholesterolemia: A Functional Approach, Molecules, 2022, 27(11), 3479.
22. Jeon Eun Bi, Sung-Ho Son, Renda Kankanamge Chaturika Jeewanthi, Na-Kyoung Lee, Hyun-Dong Paik, Characterization of Lactobacillus plantarum Lb41, an isolate from kimchi and its application as a probiotic in cottage cheese, Food science and biotechnology, 2016, 25(4) 1129-1133.
23. Sherwani, Kishwer Fatima. Probiotics in Processed Dairy Products and Their Role in Gut Microbiota, Health, In: Hoda El-Sayed, editor, Effect of Microbiota on Health and Disease, *IntechOpen*, 2022
24. Bergamini C., V.Hynes E., R.Quiberoni A., Sua´rez V., B.Zalazar C., Probiotic bacteria as adjunct starters: influence of the addition methodology on their survival in a semi-hard Argentinean cheese, Food Research International, 2005, 38(5), 597-604.
25. Cardarelli, H. R., Saad, S. M. I., Gibson, G. R., and Vulevic, J, Functional petitsuisse cheese: Measure of the prebiotic effect, Anaerobe, 2007.
26. Mohammadi Reza, Amir M. Mortazavian, Roya Khosrokhavat, A. Gomes da Cruz, Probiotic ice cream: viability of probiotic bacteria and sensory properties, Annals of microbiology, 2011, 61, 411-424.
27. Homayouni, Aziz, Maedeh Alizadeh, Hossein Alikhah, and Vahid Zijah, Functional Dairy Probiotic Food Development: Trends, Concepts, and Products, In: Everlon Rigobelo, editor, Probiotics, InTech, 2012, p,197-212.

28. Abghari, Ali, sheikh-zeinoddin, Mahmoud, Soleimanian-Zad, Sabihe, Nonfermented ice cream as a carrier for Lactobacillus acidophilus and Lactobacillus rhamnosus, International Journal of Food Science & Technology, 2010, 46(1), 84 – 92.
29. Farag M.A., Jomaa S.A., El-Wahed A.A., El-Seedi A.H.R., The Many Faces of Kefir Fermented Dairy Products: Quality Characteristics, Flavour Chemistry, Nutritional Value, Health Benefits, and Safety, Nutrients, 2020, 12(2), 346.
30. Azizi N.F., Kumar M.R., Yeap S.K., Abdullah J.O., Khalid M., Omar A.R., Kefir and Its Biological Activities, Foods, 2021, 10(6), 1210.
31. Subrota Hati, Sujit Das, Surajit Mandal, Technological advancement of Functional Fermented Dairy Beverages, In: Alexandru M.G., Alina M.H., editors, Engineering tools in beverage industry, India, Elsevier, 2019, p, 101-136
32. Rahul Mehra, Harish Kumar, Naveen Kumar, Suvartan Ranvir, Atanu Jana, Harpal Singh, Whey proteins processing and emergent derivatives: An insight perspective from constituents, bioactivities, functionalities to therapeutic applications, Journal of Functional Foods, 2021, 87, 104760.
33. Katarzyna Skryplonek, Izabela Dmytrów, Anna Mituniewicz-Małek, Probiotic fermented beverages based on acid whey, Journal of Dairy Science, 2019, 102(9), 7773-7780.
34. Kaur H., Gupta T., Kapila S., Kapila R., Protective effects of potential probiotic Lactobacillus rhamnosus (MTCC-5897) fermented whey on reinforcement of intestinal epithelial barrier function in a colitis-induced murine model, Food Funct, 2021, 12(13), 6102-6116.
35. Krushna Gawande, Mrugnayani Kolhekar, Manorama Kumari, Suman Kapila, Prateek Sharma, Syed Azmal Ali, Behare. Lactic acid bacteria based purified exopolysaccharide showed viscofying and hypercholesterolemic capabilities, Food Hydrocolloids for Health, 2021, 1, 100042.
36. Kim S.K., Guevarra R.B., Kim Y.T., Kwon J., Kim H., Cho J.H., Role of Probiotics in Human Gut Microbiome-Associated Diseases, J Microbiol Biotechnol, 2019, 29(9), 1335-1340.
37. Sumi K., Osada K., Sakuda M., Ashida K., Nakazato K., Fermented milk retains beneficial effects on skeletal muscle protein anabolism after processing by centrifugation and supernatant removal, J Dairy Sci, 2021, 104(2), 1336-1350.
38. Sevencan N.O., Isler M., Kapucuoglu F.N., Senol A., Kayhan B., Kiztanir S, Dose-dependent effects of kefir on colitis induced by trinitrobenzene sulfonic acid in rats, Food Sci Nutr, 2019, 7(9), 3110-3118.
39. Granato D., Nazzaro F., Pimentel T.C., Esmerino E.A., da Cruz A.G., Probiotic food development an updated review based on technological advancement, Reference module in food science, Amsterdam, Elsevier, 2019, p, 422-428
40. Kiros E., Seifu E., Bultosa G., Solomon W.K., Effect of carrot juice and stabilizer on the physicochemical and microbiological properties of yoghurt, LWT-Food Sci Technology, 2016, 69, 191–196.
41. Granata M., Brandi G., Borsari A., Gasbarri R., Gioia D.D.I., Synbiotic yogurt consumption by healthy adults and the elderly: the fate of bifidobacteria and LGG probiotic strain, Int J Food Sci Nut, 2013, 64(2), 162–168.
42. Kulka R.T., Kotch J.B., Jensen E.T., Savage E., Weber D.J., Randomized, double-blind, placebo-controlled study of synbiotic yogurt effect on the health of children, J Pediatr, 2015, 166(6), 1475–1481.

43. Maiello N., Giannetti A., Ricci G., Cinicola B., Carello R., Indolfi C., Atopic dermatitis and atopic march: which link? Acta Biomed, 2021, 92(S7).
44. Fontecha J., Calvo M.V., Juarez M., Gil A., Martínez-Vizcaino V, Milk and Dairy Product Consumption and Cardiovascular Diseases: An Overview of Systematic Reviews and Meta-Analyses, Adv Nutr, 2019, 10(2), S164-S189.
45. Krasaekoopt W., Watcharapoka S, Effect of addition of inulin and galacto-oligosaccharide on the survival of microencapsulated probiotics in alginate beads coated with chitosan in simulated digestive system, yogurt and fruit juice, LWT Food Sci Technol, 2014, 57(2), 761–766.
46. Ding W.K., Shah N.P., Survival of free and microencapsulated probiotic bacteria in orange and apple juices, Int Food Res J, 2008, 15(2), 19–232.
47. Touret T., Oliveira M., Semedo-Lemsaddek T., Putative probiotic lactic acid bacteria isolated from sauerkraut fermentations, PLoS One, 2018, 13(9).
48. Munekata P.E.S., Pateiro M., Tomasevic I., Domínguez R., da Silva Barretto A.C., Santos E.M., Functional fermented meat products with probiotics-A review, J Appl Microbiol, 2022, 133(1), 91-103.
49. M. Soltani, M. Farshadfar, H. Shirvani, A. Yaghotipoo, Evaluation of the antibacterial effect of a beneficial compound based on the probiotic kombucha and honey, Honeybee Science Journal, 2021, 11(21).
50. C. Dufresne, E. Farnworth Tea, Kombucha, and health: A review, Food Review International, 2000, 33(6), 409-421.
51. Selvaraj S., Gurumurthy K., An overview of probiotic health booster-kombucha tea, Chin Herb Med, 2022, 15(1), 27-32.
52. Lau S.W., Chong A.Q., Chin N.L., Talib R.A., Basha R.K., Sourdough Microbiome Comparison and Benefits, Microorganisms, 2021, 9(7), 1355.
53. Abdi R., Joye I.J., Prebiotic Potential of Cereal Components. Foods, 2021,10(10), 2338.
54. Hawkesford M.J., Zhao F.J., Strategies for increasing the selenium content of wheat, J. Cereal Sci, 2007, 46(3), 282–292.
55. Petrova P., Petrov K., Lactic Acid Fermentation of Cereals and Pseudocereals: Ancient Nutritional Biotechnologies with Modern Applications, Nutrients, 2020, 12(4), 1118.
56. Ester B., Noelia B., Laura C.J., Francesca P., Cristina B., Rosalba L., Probiotic survival and in vitro digestion of *L. salivarius* spp. salivarius encapsulated by high homogenization pressures and incorporated into a fruit matrix, LWT, 2019, 111, 883–888.
57. Miranda R.F., de Paula M.M., da Costa G.M., Barão C.E., da Silva A.C.R., Raices R.S.L., Orange juice added with L. casei: Is there an impact of the probiotic addition methodology on the quality parameters? LWT, 2019, 106, 186–193.
58. Kaprasob R., Kerdchoechuen O., Laohakunjit N., Thumthanaruk B., Shetty K, Changes in physico-chemical, astringency, volatile compounds and antioxidant activity of fresh and concentrated cashew apple juice fermented with Lactobacillus plantarum, J. Food Sci. Technol, 2018, 55(10), 3979–3990.
59. Rozada-Sánchez, R., Sattur, A.P., Thomas, K. and Pandiella, S.S., Evaluation of Bifidobacterium spp. for the production of a potentially probiotic malt- based beverage, Process Biochem, 2008, 43(8), 848– 854.
60. Tanasupawat S., Komagata K., Lactic acid bacteria in fermented foods in Thailand, World Journal of Microbiology and Biotechnology, 1995, 11(3), 253–256.

61. Basavaprabhu H.Nataraj, Syed Azmal Ali, Pradeep V, Behare, Hariom Yadav, Postbiotics-parabiotics: the new horizons in microbial biotherapy and functional foods, Microb Cell Fact, 2020, 19**,** 168.
62. Vinderola G., Sanders M.E., Salminen S., The Concept of Postbiotics, Foods, 2022, 11(8), 1077.
63. Andresen V., Gschossmann J., Layer P, Heat-inactivated Bifidobacterium bifidum MIMBb75 (SYN-HI-001) in the treatment of irritable bowel syndrome: a multicentre, randomised, double-blind, placebo-controlled clinical trial, Lancet Gastroenterol Hepatol, 2020, 5(7), 658-666.
64. Rodrigues V.F., Elias-Oliveira J., Pereira Í.S., Pereira J.A., Barbosa S.C., Machado M.S.G., *Akkermansia muciniphila* and Gut Immune System: A Good Friendship That Attenuates Inflammatory Bowel Disease, Obesity, and Diabetes, Front Immunol, 2022, 13, 934695.
65. María José Hernández-Granados, Elena Franco-Robles, Postbiotics in human health: Possible new functional ingredients? Food Research International, 2020, 137, 109660.
66. Haben Fesseha, Tadelech Yilma, Endale Mekonnen, Postbiotics and their role in healthy life, Journal of Life Science and Biomedicine, 2022, 12(4), 64-76.
67. Nogal A., Valdes A.M., Menni C., The role of short-chain fatty acids in the interplay between gut microbiota and diet in cardio-metabolic health, Gut Microbes, 2021, 13(1), 1-24.
68. Tedelind S., Westberg F., Kjerrulf M., Vidal A., Anti-inflammatory properties of the short-chain fatty acids acetate and propionate: a study with relevance to inflammatory bowel disease, World J Gastroenterol, 2007, 13(20), 2826-32.
69. Worraprat Chaisuwan, Kittisak Jantanasakulwong, Sutee Wangtueai, Yuthana Phimolsiripol, Thanongsak Chaiyaso, Charin Techapun, Microbial exopolysaccharides for immune enhancement: Fermentation, modifications and bioactivities, Food Bioscience, 2020, 35, 100564.
70. Khalil E.S., Abd Manap M.Y., Mustafa S., Alhelli A.M., Shokryazdan P., Probiotic Properties of Exopolysaccharide-Producing Lactobacillus Strains Isolated from Tempoyak, Molecules, 2018, 23(2), 398.
71. Kim H. S., H. S. Chae, S. G. Jeong, J. S. Ham, S. K. Im, In vitro Antioxidative Properties of Lactobacilli, Asian-Australasian Journal of Animal Sciences, 2005, 19(2), 262-265.
72. van der Es D., Hogendorf W.F., Overkleeft H.S., van der Marel G.A., Codée J.D., Teichoic acids: Synthesis and applications, Chem. Soc. Rev, 2017, 46(5), 1464–1482.
73. Lebeer S., Claes I., Tytgat H.L., Verhoeven T.L., Marien E., von Ossowski I., Functional analysis of Lactobacillus rhamnosus GG pili in relation to adhesion and immunomodulatory interactions with intestinal epithelial cells, Appl Environ Microbiol, 2012, 78(1), 185-93.
74. S Navarro, G Cossalter, C Chiavaroli, A Kanda, S Fleury, A Lazzari, The oral administration of bacterial extracts prevents asthma via the recruitment of regulatory T cells to the airways, Mucosal Immunology, 2011, 4(1), 53-65.
75. Kearney S.C., Dziekiewicz M., Feleszko W., Immunoregulatory and immunostimulatory responses of bacterial lysates in respiratory infections and asthma, Ann Allergy Asthma Immunol, 2015, 114(5), 364-9.
76. Monika, Anju, Rakesh gehlot, Rekha, Postbiotics; Novel Ingredient in Functional Foods, Journal of Science and Technology, 2022, 7(5), 160-178.
77. Sharifeh Shahi, Reza Khorvash, Mohammad Goli, Seyed Mohsen Ranjbaran, Afsaneh Najarian, Bbdorreza Mohammadi Nafchi. Review of proposed different irradiation methods to inactivate food-processing viruses and microorganisms, Food science & nutrition, 2021, 9(10), 5883-5896.

78. Fenster K., Freeburg B., Hollard C., Wong C., Rønhave Laursen R., Ouwehand A.C., The Production and Delivery of Probiotics: A Review of a Practical Approach, Microorganisms, 2019, 7(3), 83.
79. Dias A.L.B., de Aguiar A.C., Rostagno M.A., Extraction of natural products using supercritical fluids and pressurized liquids assisted by ultrasound: Current status and trends, Ultrason Sonochem, 2021, 74.
80. Tiptiri-Kourpeti A., Spyridopoulou K., Santarmaki V., Aindelis G., Tompoulidou E., Lamprianidou EE, Lactobacillus casei Exerts Anti-Proliferative Effects Accompanied by Apoptotic Cell Death and Up-Regulation of TRAIL in Colon Carcinoma Cells, PLoS One, 2016, 11(2).
81. Nakamura F., Ishida Y., Sawada D., Ashida N., Sugawara T., Sakai M., Fragmented Lactic Acid Bacterial Cells Activate Peroxisome Proliferator-Activated Receptors and Ameliorate Dyslipidemia in Obese Mice, J Agric Food Chem, 2016, 64(12), 2549-59.
82. Rakhuba, Dzianis, Galina Novik, and Estera Szwajcer Dey. Application of supercritical carbon dioxide (scCO2) for the extraction of glycolipids from Lactobacillus plantarum B-01, The Journal of Supercritical Fluids, 2009, 49(1), 45-51.
83. Aguilar-Toala J.E., Hall F.G., Urbizo-Reyes U.C., Garcia H.S., Vallejo-Cordoba B., Gonzalez-Cordova A.F., In Silico Prediction and In Vitro Assessment of Multifunctional Properties of Postbiotics Obtained from Two Probiotic Bacteria, Probiotics Antimicrob. Proteins, 2020, 12(2), 608–622.
84. da Silva Vale, A., de Melo Pereira, G.V., de Oliveira, A.C., de Carvalho Neto, Production, Formulation, and Application of Postbiotics in the Treatment of Skin Conditions, Fermentation, 2023, 9(3), 264.
85. Huber M., Mossmann H., Bessler W.G., Th1-orientated immunological properties of the bacterial extract OM-85-BV, Eur J Med Res, 2005, 10(5), 209-17.
86. Yelin I., Flett K.B., Merakou C., Mehrotra P., Stam J., Snesrud E., Genomic and epidemiological evidence of bacterial transmission from probiotic capsule to blood in ICU patients, Nat Med, 2019, 25(11), 1728-1732.
87. Salminen S., Collado M.C., Endo A., Hill C., Lebeer S., Quigley E.M.M., The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics, Nat Rev Gastroenterol Hepatol, 2021, 18(9), 649-667.
88. Scarpellini E., Rinninella E., Basilico M., Colomier E., Rasetti C., Larussa T., From Pre- and Probiotics to Post-Biotics: A Narrative Review, Int J Environ Res Public Health, 2021, 19(1), 37.
89. Maeda-Yamamoto, M. & Ohtani, T, Development of functional agricultural products utilizing the new health claim labeling system in Japan, Biosci. Biotechnol. Bioche, 2018, 82(4) 554–563.
90. İncili Gökhan Kürşad, Pınar Karatepe, Müzeyyen Akgöl, Alper Güngören, Ahmet Koluman, Osman İrfan İlhak, Characterization of lactic acid bacteria postbiotics, evaluation in-vitro antibacterial effect, microbial and chemical quality on chicken drumsticks, Food Microbiology, 2022, 104, 104001.
91. Chaney W.E., Naqvi S.A., Gutierrez M., Gernat A., Johnson T.J., Petry D., Dietary Inclusion of a *Saccharomyces cerevisiae*-Derived Postbiotic Is Associated with Lower *Salmonella enterica* Burden in Broiler Chickens on a Commercial Farm in Honduras, Microorganisms, 2022, 10(3), 544.
92. de Lima Aloizio Lemos, C.A. Guerra, Lucas Marques Costa, V.S. de Oliveira, W.J.F. Lemos, Rosa H. Luchese and A.F. Guerra, A Natural Technology for Vacuum-Packaged Cooked Sausage Preservation with Potentially Postbiotic-Containing Preservative, Fermentation, 2022, 8(3), 106.

93. Hosseini Seyed Ahmad, Amin Abbasi, Sahar Sabahi, Nader Khani, Application of postbiotics produced by lactic acid bacteria in the development of active food packaging, Biointerface Research in Applied Chemistry, 2022, 12(5), 6164-6183.
94. Lee Y.B., Byun E.J., Kim H.S., Potential Role of the Microbiome in Acne: A Comprehensive Review, J Clin Med, 2019, 8(7), 987.