

REVIEW

[View Article Online](#)
[View Journal](#) | [View Issue](#)Cite this: *Food Funct.*, 2025, **16**, 1656

Recent updates of probiotic dairy-based beverages

Şevval Taşkoparan, Canan Altınay and H. Barbaros Özer *

There is a rapid paradigm shift in the food consumption habits of consumers globally. The interest in healthier, safer, minimally processed and nature-identical foods is the driving force of this paradigm shift. Although the roots of this consumer trend go back further, especially the Covid-19 pandemic has contributed to the acceleration of this process. The effects of probiotics on human health have been known for many years. The commercial success of some probiotic microorganism strains, supported by clinical studies, is also evident. Probiotic microorganisms can be found in commercial products in a wide range of forms including powder, tablets or incorporated into liquid or solid food matrices. Milk and dairy products are suitable vehicles for the delivery of probiotics into the human body. Apart from well-established dairy-based probiotic foods including yogurt and yogurt-type beverages, in recent years some dairy products supplemented or enhanced with postbiotics and paraprobiotics are gaining popularity. The incorporation of next-generation probiotics in probiotic beverage formulations has also attracted the attention of researchers. The current state-of-the art for the utilization of next-generation probiotics, postbiotics and paraprobiotics in dairy-based probiotic beverages is the main focus of this review. Conventional milk-, whey- and buttermilk-based probiotic beverages are also covered.

Received 20th December 2024,

Accepted 5th February 2025

DOI: 10.1039/d4fo06322h

rsc.li/food-function

1. Introduction

The International Scientific Association for Probiotics and Prebiotics (ISAPP) describes probiotics as “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”.^{1,2} According to this definition, for the therapeutic and prophylactic effects of probiotics to occur, they must be present at a certain level in the final product and

this limit is at least 10^6 cfu g^{-1} or mL^{-1} .³ Probiotics have been demonstrated to exert positive health impacts, but there are a number of conditions that must be met before these benefits emerge. For example, preserving the stability of probiotics and maintaining their viability during food production or storage are some of the challenges faced by the industry. Variable interactions with the host, strain-dependent activity, low colonization, and poor dosage control can be listed as limiting factors of probiotic application on food.⁴ In addition to these limiting factors, negative individual responses to the consumption of probiotics may also occur. For instance, uncontrolled or excessive intake of probiotics might possibly cause adverse

Ankara University Faculty of Agriculture Department of Dairy Technology, Diskapi, Ankara, Turkey. E-mail: adabarbaros@gmail.com; Tel: +905368300038



Şevval Taşkoparan

Şevval Taşkoparan is a research assistant at the Department of Dairy Technology, Faculty of Agriculture, Ankara University. She conducts research in the field of dairy technology. She completed her bachelor's degree in Food Engineering at Hacettepe University and is currently pursuing her master's degree at Ankara University. Her research interest focuses on aroma chemistry, fermentation, and cream products.



Canan Altınay

Canan Altınay is a research assistant at the Dairy Technology of Agriculture Faculty at Ankara University. She earned her bachelor's degree from Hacettepe University and her master's degree from Ankara University and is currently pursuing her PhD. Her research focuses on dairy products and technology. She has presented her work at national and international conferences and is involved in various scientific projects.



side effects in immunocompromised individuals and horizontal gene transfer of virulence genes, including antibiotic resistance genes, to bacteria in the gut microbiota has been specified to be a significant issue.⁵

To date, many studies have been done on probiotics and many commercial probiotic foods in various forms have been launched into global markets. Among them, dairy products have a distinct place. Yogurt seems to be the most convenient vehicle for the transfer of probiotic microorganisms into the human body.⁶ Dairy-based beverages are also suitable media for the incorporation of probiotics and many commercial probiotic beverages are available in the markets. The probiotic dairy-based beverages market size was valued at USD 39.74 billion and forecasted to reach USD 95.52 billion by 2033.⁷ Vast majority of these products contain *Lactobacillus* and/or *Bifidobacterium* strains with clinically proven probiotic properties, such as *Lactobacillus acidophilus* La-5, *Bifidobacterium animalis* subsp. *lactis* BB-12, *Lactocaseibacillus paracasei* Shirota and *Lactocaseibacillus rhamnosus* G (LGG).⁸ The dairy-based probiotic beverages market consists of three sub-segments: (a) milk-based beverages (fermented or non-fermented), (b) whey-based beverages and (c) buttermilk- or buttermilk serum-based beverages. Milk and whey-based beverages have been well researched, and many commercial products have been released during the last two decades. In contrast, buttermilk-based probiotic beverages constitute a relatively new category of probiotic beverages.

Although the theory that lactic acid bacteria prolong human life was first developed by Elie Metchnikoff in 1907, Lilly and Stillwell were the first researchers to define probiotics in 1965.⁹ Subsequently, the effects of prebiotics on probiotic microorganisms were identified and synbiotic products started to appear in global markets in the early 2000s.¹⁰ The presence of conventional probiotic/synbiotic milk-based beverages in the global probiotics market remains strong. Although the

functional effects of some probiotic strains on human health have been clinically proven, the incorporation of these strains into food matrices remains a significant challenge for the food industry. In particular, low stability of probiotic microorganisms against food processing and human gastric digestion conditions is an important problem for the food industry. Although many processing strategies have been developed in this regard, few probiotic strains have been able to reach the microbial counts required for the probiotic effect (*i.e.*, 10^6 – 10^8 cfu mL⁻¹ or g⁻¹). The scientific data accumulated during the last 10–15 years have shown that apart from live probiotic microorganisms, metabolites synthesised by these microorganisms and/or dead probiotic cells can also have positive impacts on human health. Based on this, novel functional products containing metabolites and/or inanimate probiotic cells may have strong potential to gradually replace classical probiotic milk-based beverages. Bacterial metabolites with health-promoting effects, also called postbiotics (refer to section 2), are known to be stable against environmental conditions such as temperature, gastric acidity or digestive enzymes.¹⁰ The presence of metabolites derived from probiotic strains in the food matrix instead of live probiotic microorganisms will provide a significant operational advantage for the dairy beverage industry. Microorganisms that have functional characteristics through their metabolites/cell fragments but have low stability against processing technologies and/or GIT conditions will also be utilized in industrial applications.

This review mainly focuses on next-generation probiotic dairy-based beverages and on the state-of-the art of personalised probiotic milk-based beverages. Conventional dairy-based probiotic beverages that have achieved commercial success will be briefly mentioned below.

1.1. Milk-based probiotic beverages

A great number of commercial probiotic milk-based beverages have been enjoying market success for many decades. Among the well-known probiotic milk-based beverages are Yakult (*Lb. casei* Shirota), Actimel (*Lb. casei* strain Danone®), Acidophilus milk (a generic product, *Lb. acidophilus*), Proviva (*Lb. plantarum* strain 299v), GEFILUS (*Lb. rhamnosus* GG), YoPlait (*Bifidobacterium animalis* subsp. *lactis* Bb-12), Bifighurt (*B. longum* CKL 1969 or DSM 2054), Biomild (*Lb. acidophilus* + *Bifidobacterium* spp.), CHAMYTO (*Lb. casei* or *Lb. paracasei*), and Cultura or A/B milk (*Lb. acidophilus* La-5 and *B. animalis* Bb-12). Conventional milk-based probiotic beverages are beyond the scope of this review. A comprehensive evaluation of conventional probiotic milk-based beverages is available in Eminoglu *et al.*, Turkmen *et al.* and Jan *et al.*^{8,11,12}

1.2. Whey-based probiotic beverages

Whey is a byproduct of cheese-making. For a very long time, whey has been considered as a raw material for high value-added products rather than a cheese-making waste. Whey contains high levels of lactose, soluble protein, mineral substances, and small amounts of fat and its composition varies based on factors such as the milk source, cheese type, or



H. Barbaros Özer

H. Barbaros Özer holds BSc and MSc degrees in Dairy Technology. He finished his PhD in Food Science and Technology at The University of Reading (UK). He was appointed as a full professor in 2006. He served as the head of the department of the Ankara University Department of Dairy Technology. He is currently a member of the Scientific Board of Turkish Food Safety Association (GGD) and is an authorized EHEDG trainer.

His major research fields are dairy science and technology, novel product development, food safety, dairy microbiology and dairy-based beverages. Professor Özer has published over 120 scientific papers and proceedings and 5 books.



thermal treatment.^{13–15} Numerous commercial whey-derived or whey-based products have been developed so far and many of them have been in a strong position in global probiotic dairy beverages markets. Apart from the conventional whey products such as whey-based powders (whey powder, whey protein powder, whey protein concentrate powder, whey protein isolate, hydrolysed whey protein powder, etc.), whey ingredients (whey proteins, lactose, minerals, etc.) are also produced from whey with high purity. The latter products are widely utilized by the pharmaceutical industry. There are many clinical studies regarding positive health impacts of whey and whey ingredients, and whey proteins are recognized with high digestibility capacity. Apart from the favourable health impacts of whey sourcing from milk serum proteins (i.e. α -lactalbumin and β -lactoglobulin), it provides a suitable medium for the growth of probiotics. In the last decade, there has been a significant increase in research on whey-based functional beverages including probiotics. Whey is suitably used in probiotic beverage formulations alone or in combination with other dairy (i.e., buttermilk) or non-dairy (i.e., fruit juices) liquids or pulps.^{16–18} The use of prebiotics in probiotic whey beverage formulations is a common practice. However, the selection of the prebiotic agent is of critical importance for the stimulation of probiotic microorganisms. For example, inulin, oligofructose or polydextrose stimulated the growth and viability of *Lb. acidophilus* La-5 and *Str. thermophilus* St-36 in sweet whey beverages, but the growth and viability of *B. animalis* Bb-12 was not influenced by these prebiotics.¹⁹ Similarly, addition of lactulose to sweet probiotic whey beverages was ineffective on the viability and growth of *Lb. acidophilus* La-5, as reported by Matijević *et al.*²⁰ Resistant starch has a positive impact on the viability of *Bifidobacterium pseudocatenulatum* in probiotic whey beverages.

Since sensory problems are often encountered with whey-based beverages, the combinations of whey with fruit juice and/or skimmed milk may offer a solution for this problem. Overall, if the whey ratio exceeds 50% in the formulation of probiotic beverages, the possibility of sensory problems is likely to increase.²¹ De-proteinized whey,²² UF-whey permeates and retentates,²³ and UF-permeate enriched with whey retentate (10%)²⁴ are also suitable matrices for the development of probiotic whey-based beverages. Microencapsulation of probiotic microorganisms is a well-known technology to protect probiotics from harsh environmental conditions. In the selection of the microencapsulation agent, care should be taken to protect the probiotic microorganism as well as not to cause sensory and physical problems in the product. Obradović *et al.* reported that chitosan did not affect the viability of probiotic cells during fermentation but the physical properties of the final beverage was improved.²⁵ It was shown that the use of Ca-alginate as a coating material increased the physical stability of the probiotic Doogh beverage (a traditional Iranian dairy-based beverage) and triggered the development of off-flavours during cold storage.²⁶

There are a limited number of *in vitro* and *in vivo* studies targeting the health impacts of probiotic whey beverages.

Increased body weight and body mass index,²⁷ decreased acetate concentration and increased butyrate levels,²⁸ decreased allergenicity,²⁹ increased bioactive peptide levels,³⁰ and decreased colitis symptoms³¹ are among the health effects associated with probiotic whey beverages. Rosa *et al.* demonstrated that probiotic whey-milk beverages fermented by *Lb. casei* 01, *Lb. acidophilus* La-5, *B. animalis* Bb-12 or *Lb. acidophilus* La-3 positively affected the production of bioactive peptides and phenolic compounds.³² While *Lb. casei* 01 produced anti-hypertensive peptides at higher concentrations, *Lb. acidophilus* La-3 promoted the formation of phenolic compounds more than the other probiotic strains. Some of the outputs of the scientific studies carried out on whey-based probiotic beverages are summarized in Table 1.

1.3. Buttermilk-based probiotic beverages

Buttermilk is a by-product of butter-making and contains mainly milk fat globule membrane (MFGM) materials and water-soluble milk components (lactose, minerals and proteins).⁵⁰ MFGM materials contain polar lipids such as phospho- and sphingolipids as well as neutral lipid fractions such as triglycerides, diglycerides, monoglycerides, cholesterol and their esters.⁵¹ In addition to lipid fractions, MFGM also contains proteins integral, peripheral or weakly bound to the MFGM surface such as mucin, xanthine oxidase/dehydrogenase, CD36, PAS 6/7, adipophilin and butyrophilin.^{52–54} Due to its rich chemical composition, it can be used as an emulsifier and a stabiliser in food systems and also shows positive health effects.⁵⁵ However, compared to whey, both scientific studies dedicated to the development of buttermilk-based probiotic beverages and the commercial examples of functional buttermilk beverages are limited. Antunes *et al.* formulated a probiotic buttermilk beverage enriched with sucrose or sucralose. The end product had a probiotic bacteria count high enough for a therapeutic effect (>107 cfu mL⁻¹) after four weeks of cold storage.⁵⁶ The stimulated growth of *B. animalis* subsp. *lactis* in buttermilk was demonstrated by Antunes *et al.*⁵⁷ A symbiotic buttermilk beverage developed by Hashem contained red beetroot puree, carboxymethyl cellulose and *Lb. acidophilus* as probiotic species.⁵⁸ The formulated product had high sensory scores as well as high probiotic counts at the end of a 3-week storage period under cold conditions. MilkyMist – an Indian dairy innovator – has launched the world's first UHT probiotic buttermilk beverage recently. Akshayakalpa – an Indian dairy company – produces organic probiotic buttermilk commercially.

2. Postbiotics and paraprobiotics in dairy-based beverages

Recent studies have demonstrated the health benefits beyond the inherent viability of probiotics.^{59–61} Therefore, the viability of microorganisms for a probiotic effect may no longer be necessary since clinical benefits are not directly linked to viable bacteria.⁶⁰ The view that some of the health benefits attributed



Table 1 Main outputs of some recent studies on whey-based probiotic beverages

Strain	Additives/combinations	Main outputs	Ref.
Technological outputs			
<i>Lb. acidophilus</i> La-5, <i>Lb. casei</i> LBC-81	Soy isoflavones and phytosterols	• Beverage supplemented with phytosterols received higher sensory scores.	33
Kefir starter culture	Prebiotic fructo-oligosaccharides (FOS) and refined sugar	• Antimicrobial and antioxidant activities were evident.	34
Kefir starter culture		• Antagonistic effect against <i>Salmonella</i> spp. <i>enteritidis</i> was demonstrated.	35
<i>B. animalis</i> subsp. <i>lactis</i> Bb-12	Carbonated whey beverage	• A slight time-dependent sedimentation was observed.	36
<i>Lb. acidophilus</i> La-5	Channa whey and pineapple juice mixture (0 : 100, 15 : 85, 25 : 75 and 35 : 65%)	• The survivability rate of the probiotic strain used was >80% during 56 days of storage.	37
<i>Lb. rhamnosus</i> ATCC 7469	Milk + whey	• The probiotic counts were above $>10^7$ cfu mL ⁻¹ after three weeks of cold storage.	38
<i>Lb. acidophilus</i> , <i>B. animalis</i> subsp. <i>lactis</i> and <i>Streptococcus thermophilus</i>	Milk + whey	• At higher whey concentrations in the formula (>50%), sensory acceptance of the beverage decreased.	21
<i>Lb. rhamnosus</i> and <i>Lb. acidophilus</i>	Fermented milk (40.2), sucrose (5.6%) and fruit preparation (5.2%)	• The counts of probiotic microorganisms were $>10^6$ cfu mL ⁻¹ at the time of consumption.	39
<i>Lb. acidophilus</i> , <i>Lb. bulgaricus</i> and <i>Str. thermophilus</i>		• The growth of probiotic strain was stimulated by yogurt starter bacteria.	40 and 41
<i>Lb. rhamnosus</i> NCDO 243, <i>B. bifidum</i> NCDO 2715 and <i>Propionibacterium freudenreichii</i> subsp. <i>shermanii</i>	De-proteinized whey	• Both organoleptical properties and the probiotic counts of the final product were acceptable.	22
<i>Lb. acidophilus</i> , <i>Lb. casei</i> and <i>Lb. rhamnosus</i>	UF-whey retentate and UF-whey permeate	• Overall physical and sensory properties of the formulated beverage were satisfactory after 14 days of cold storage.	23
<i>Lb. acidophilus</i> M92, <i>Lb. plantarum</i> L4 and <i>Enterococcus faecium</i> L3	UF-permeate enriched with whey retentate (10%)	• Probiotic strains successfully acidified the milk and colony counts of the probiotics were <i>ca.</i> 8 log ₁₀ .	24
<i>B. animalis</i> Bb-12, <i>Lb. acidophilus</i> La-5 and <i>Str. thermophilus</i> St-36	Prebiotics (inulin, oligofructose and polydextrose)	• Prebiotics stimulated the growth of probiotics other than <i>B. animalis</i> Bb-12.	19
<i>B. animalis</i> subsp. <i>lactis</i>	UHT-goat milk plus cheese whey	• Mixed beverage containing 45% goat cheese whey and 6% oligofructose yielded the highest probiotic colony count after 28 days of cold storage.	42
<i>Str. thermophilus</i> and <i>B. animalis</i> subsp. <i>lactis</i>	Kiwi powder (1%)	• Antioxidant capacities of the beverages made from reconstituted cow, sheep and goat WPC were superior.	43
<i>Bifidobacterium</i> spp.	Inulin or resistant starch	• Resistant starch positively affected the growth and viability of <i>Bifidobacterium pseudocatenulatum</i> .	44
Probiotic strains	Microencapsulated probiotics	• Chitosan was ineffective on the viability of probiotic microorganisms.	25
Microencapsulated <i>Lb. acidophilus</i> La-5 and <i>B. animalis</i> subsp. <i>lactis</i> Bb-12	Peppermint essence nanoliposomes (1–2%)	• Beverage supplemented with 2% nanoliposome received the highest sensory scores.	45
<i>Lb. acidophilus</i>	Pineapple juice	• Combination of cheese whey (65%) and pineapple juice (35%) yielded a better product.	46
Xylooligosaccharide (prebiotic)	Cold-plasma-treated whey beverage	• Cold plasma treated beverage had higher levels of bioactive compounds.	47
Health effects			
<i>Str. thermophilus</i> and <i>Lb. bulgaricus</i>	Umbu (<i>Spondias tuberosa</i>) fruit pulp (10%)	• Increased body weight and albumin level and decreased cholesterol level in malnourished animals.	27
<i>Lb. rhamnosus</i> RC007		• Increased body weight and body mass index in malnourished children.	48
<i>Str. thermophilus</i> 2 K, <i>Lb. bulgaricus</i> BK, <i>Lb. bulgaricus</i> K, <i>Lb. plantarum</i> W42 and <i>B. lactis</i> Bi30		• Increased anti- and pro-inflammatory cytokines IL-10 and TNF- α , goblet cells, and intraepithelial lymphocytes in intestinal fluids in mice.	29
		• Reduction in the levels of allergy markers interleukin-4 (IL-4), immunoglobulin E, and specific immunoglobulin G1.	
		• Secretion of major regulators of IL-10 and TGF- β enhanced.	
Spontaneous fermentation or natural whey starter		• 49 bioactive and 21 ACE-inhibitor peptides were released during fermentation.	30
		• Spontaneous fermentation resulted in a higher ACE-inhibitory and DPP-IV-inhibitory activities.	



Table 1 (Contd.)

Strain	Additives/combinations	Main outputs	Ref.
<i>Lb. rhamnosus</i> (MTCC-5897)		<ul style="list-style-type: none"> • Severity of colitis and emergence of clinical symptoms reduced. • Improved immune homeostasis and barrier integrity were observed. 	31
<i>Lb. casei</i> , <i>Lb. paracasei</i> and <i>Lb. brevis</i>	Inulin (5%), vitamin A (0.5 mg L ⁻¹), vitamin C (50 mg L ⁻¹) and potassium iodide (0.5%)	<ul style="list-style-type: none"> • The acute score toxicity and <i>in vivo</i> evaluation of allergenic properties proved the safety of the whey-based probiotic beverage. 	49

to probiotic microorganisms are provided by the non-viable probiotic cells or metabolites synthesized by or released after inactivation of probiotic microorganisms has triggered the development of concepts of postbiotics and paraprobiotics. Today, potential health benefits of postbiotics and paraprobiotics are being studied widely in comparison with probiotics.⁶²

Postbiotics are described as “preparation of inanimate microorganisms and/or their components that confers a health benefit on the host” by ISAAP.⁶³ According to this definition, a postbiotic must contain inactivated cells or cell components. However, the presence of cell metabolites is not a prerequisite for postbiotic identification. Paraprobiotics are defined as “non-viable probiotic or non-probiotic cells with intact structure or crude cell fragments, which, when administered in adequate amounts, confer a benefit on human or animal consumers”.⁶⁴ Both definitions need to be clarified by international scientific and regulatory bodies in order to harmonise the terminologies and to eliminate uncertainties in the global functional food trade.

ISAAP claims that metabolites purified from inactive cells such that no cell biomass and/or components remain are not postbiotics, regardless of their possible health benefits.⁶⁵ Therefore, it is stated that when metabolites are purified, each will be considered as a separate component and may have a synergistic effect with cell cytoplasm substances, rather than these health-promoting components being purified separately. However, this definition does not fully satisfy some part of the scientific community and regulatory bodies. For example, the methodology employed to distinguish defined molecular markers from undefined matrices released from microbial cells is unclear. Additionally, the lack of well-defined markers of efficacy in products containing inanimate microorganisms is another point that needs to be focused on. On the other hand, no risk of translocation from the gut lumen to the blood, targeting the oral cavity, skin, genitourinary tract and nasopharynx as well as the intestine, easier standardization, higher stability under a wide range of pH and temperature conditions and little or no interaction with food matrix components are among the advantages of postbiotics and paraprobiotic over probiotics. The health effects attributed to postbiotics are explained by four dissimilar underlying mechanisms that can affect independently or in combination, and these mechanisms are as follows: enhancing the gut microbiota, modulating systemic metabolism and immune response, improving the epithelial barrier function and signalling through the nervous system.^{63–66}

The production of postbiotics and paraprobiotics essentially consists of three stages: choosing the appropriate microbial strain, producing biomass and separating (for postbiotics) or not separating (for paraprobiotics) the resultant biomass using an appropriate method such as sonication, high pressure application, heat treatment or radiation treatments. Postbiotics generally cover exopolysaccharides, cell-wall fragments such as teichoic acids and lipoteichoic acids, supernatants, bacterial lysates, short-chain fatty acids (SCFAs), enzymes, vitamins and phenols.⁶⁷ In most cases, separation of soluble fractions and intact cells by an appropriate technique such as membrane filtration or centrifugation is necessary to produce postbiotics.

Readers are recommended to refer to Cuevas-González *et al.* and Monteiro *et al.* for more details on health-promoting mechanisms of postbiotics and paraprobiotics.^{60,68}

There are a number of commercial products containing postbiotics and paraprobiotics available in the markets. Majority of these products are designed for pharmaceutical purposes (*i.e.*, Hylak®Forte, CytoFlora®, Zakofalk®, Bactistatin, Pro-Symbioflor®, Postbiotix, Totipro PE0401, EpiCor®, Lacteol Fort® and Del-ImmuneV®).⁶⁰ Fermented foods such as yogurt, kefir, kombucha and pickled vegetables naturally contain postbiotics.⁶⁹ The incorporation of postbiotics into functional dairy beverages is also an exciting new development in the beverage industry. *In situ* production of postbiotics or their subsequent addition to the product are thought to be two different strategies.⁷⁰ It has been reported that *in situ* production of postbiotics by lactic acid bacteria rather than their subsequent addition to the product resulted in significant anti-listerial activity in milk stored under cold conditions.⁷¹ In a recent study, the laxative effects of milk fermented with *Lactocaseibacillus paracasei* and its postbiotics in BALB/c mice in a loperamide hydrochloride-induced constipation model were examined.⁷² The mice were fed with fermented milk at concentrations of 4.86, 9.71, 14.58, and 48.60 mL kg⁻¹ day⁻¹. Constipation symptoms were relieved in mice consuming fermented milk at 14.58 mL kg⁻¹ and 48.60 mL kg⁻¹ concentrations. An alleviation in colon inflammation, decreasing defecation time, and increasing levels of *Firmicutes* and *Actinobacteriota* species in the intestinal flora were also reported.

Postbiotics and paraprobiotics are more resistant to processing conditions compared to probiotics. Additionally, paraprobiotics and postbiotics facilitate minimization of the risk of bacteraemia because they contain inanimate microorganisms



or cell metabolites.^{60,73,74} It was reported that consumption of fermented milk containing non-viable intact *Lactobacillus gasseri* (CP2305) reduced intestinal disorders⁷⁵ such as irritable bowel syndrome, regulated the gut environment and function,⁷⁶ reduced stress-related symptoms, and improved intestinal patterns and quality of sleep during stressful situations.^{61,77,78} Canani *et al.* reported that consumption of fermented milk containing *Lactobacillus paracasei* CBAL74 as a paraprobiotic resulted in modulation of the intestinal microbiota in children.⁷⁹ Some of the potential health benefits of postbiotics and paraprobiotics in dairy-based beverage matrices are presented in Table 2. Despite the promising scientific findings on the positive health impacts of postbiotics and paraprobiotics, their inclusion in dairy-based beverage formulations requires a more concrete scientific background. To date, majority of the research on postbiotics and paraprobiotics has focused on the characterization and isolation/purifi-

cation of bioactive compounds. There is a need to have a deeper knowledge on the characteristics of newer postbiotic compounds and set the ideal blend of these postbiotics in the selected food matrices for the expected health benefits. Also, the method of preparation, lack of *in vivo* and clinical trials, dose-response status and mode of administration are the major restrictions of postbiotics and paraprobiotics for commercial applications. From the regulatory point of view, there is a complexity as postbiotics can fit within various regulatory categories. Currently, the Food and Drug Administration (FDA) is yet to establish specific regulation regarding postbiotics. In the EU, postbiotics are subject to novel food regulation and health claim regulation as with probiotics and prebiotics.⁶⁵ Therefore, a comprehensive safety and toxicological evaluation is required. In this context, safety evaluation of inanimate microorganisms (postbiotics or paraprobiotics) is expected to be simpler than that of live microorganisms (probiotics). The

Table 2 Some recent studies on *in vitro* and *in vivo* health and anti-bacterial effects of postbiotics and paraprobiotics

Postbiotics/paraprobiotics	Food matrices	Bioactivity	Main outputs	Ref.
<i>In vitro</i> studies				
Intracellular and extracellular contents of <i>Lactobacillus satsumensis</i> LPBF1, <i>Leuconostoc mesenteroides</i> LPBF2 and <i>S. cerevisiae</i> LPBF3	Honey-based kefir	Antioxidant activity ranging from 20 to 28% of (DPPH) inhibition	• Preventive effect on oxidative DNA damage and cellular oxidation	100
Cell-free supernatant and paraprobiotics of <i>Lb. reuteri</i> PTCC 1655		Anti-proliferative and anti-metastatic effects	• Inhibitory effects on colon cancer stem-like cells (HT29-ShE cells)	101
Postbiotics of <i>Lb. rhamnosus</i> : surface layer protein, genomic DNA, and unmethylated cytosine-phosphate-guanine containing oligodeoxynucleotides		Immunomodulatory effect	• Inhibitory effect of most postbiotic fractions on the activity of toll-like receptor, mitogen-activated protein kinases, extracellular regulated protein kinases, and nuclear factor-kappa B signalling pathways	102
Exopolysaccharide (R-5-EPS) isolated from fermented milk of <i>Lb. helveticus</i> LZ-R-5	Tibetan kefir	Immunomodulatory effect	• Significant immunomodulatory effect by R-5-EPS	103
Fraction with Mw <6000 in the supernatant produced from <i>Lb. paracasei</i> FX-6	Kefir	Anti-microbial effect	• A remarkable inhibitory effect on the growth of <i>Pseudomonas putida</i>	104
Supernatant of kefir and kefir-like products	Kefir-like beverages	Antibacterial, antioxidant and cytotoxic effects on Caco-2 cells	• Radical scavenging activities of skim milk kefir and buttermilk kefir-like supernatants were found to be higher than the Trolox standard	105
Exopolysaccharides from <i>Lb. paracasei</i> VL8	Viili (Nordig fermented dairy beverage)	Immunoregulatory effect	• EPS derived from <i>Lb. paracasei</i> VL8 exerted an immunomodulatory effect	106
<i>Lb. acidophilus</i> supernatant	Fermented milk	Antimicrobial effect	• <i>Lb. acidophilus</i> supernatant showed an anti-microbial effect on <i>S. enteritidis</i>	107
<i>In vivo</i> studies				
Intracellular content of <i>Lb. casei</i> CRL 431		Antioxidant effect	• Aflatoxin-induced lipid peroxidation decreased with increased antioxidant capacity	108
100H DSF commercial culture	Fermented milk	Protecting mice against <i>Salmonella</i> infection	• High survivability of mice fed with the cell-free supernatant of skim milk fermented by 100H DSF culture	109
Heat-killed <i>Lb. helveticus</i> strain MCC1848		Anxiolytic- or antidepressant-like effects	• MCC1848 may alleviate anxiety or depression in mice subjected to social defeat stress	110
Paraprobiotic of <i>Lb. paracasei</i> PS23 (inactivated at 95 °C)	Fermented milk	Anti-collitis effect	• Reduced intestinal epithelial permeability, and enhanced resistance to pathogens in mice with colitis	111
Postbiotic <i>Lactocaseibacillus paracasei</i>	Fermented milk	Reduction of constipation and modulation of the intestinal flora structure in mice	• Relieved constipation symptoms in mice consuming fermented milk	72



EFSA Panel published its opinions on the safety of three model heat-killed postbiotics namely *Bacteroides xylanisolvens*,⁸⁰ *Akkermansia muciniphila*⁸¹ and *Mycobacterium setense manresensis*⁸² under the proposed conditions of usage. Heat-killed *Bacteroides xylanisolvens* and *Akkermansia muciniphila* were authorised by the EFSA in 2015 and 2022 as a novel food, respectively.^{83,84} It should be noted that there is still no specific regulation covering postbiotics in the EU but they are subject to novel food regulation and health claim regulation.⁶⁵ It is clear that health claims associated with postbiotics must be approved by the EFSA before being commercialized.

3. Next generation probiotics and dairy-based beverages

The concept of next-generation probiotics (NGPs), also called designer probiotics and smart probiotics, is emerging in order to enhance the function of traditional probiotics and develop personalized treatment by increasing the expression of specific therapeutic components.^{85,86} *Akkermansia muciniphila*, *Eubacterium hallii*, *Roseburia intestinalis*, *Faecalibacterium prausnitzii* and *Ruminococcus bromii* are given as examples of NGPs and are stated to have positive health-promoting effects on various diseases such as improvement of metabolic functions, diabetes, atherosclerosis, colorectal cancer and inflammatory bowel diseases, respectively.⁸⁷ Numerous clinical studies have been conducted to reveal the health effects of novel NGPs and their metabolites. For example, *Akkermansia muciniphila* (ATCC BAA-835 T) isolated from the human gut was reported to activate T cells by increasing acetate levels, thereby reducing the risk of ovarian cancer in mice.^{88,89} It was suggested that specific metabolites or membrane proteins of the same microorganism may be effective in the prevention of obesity, diabetes, metabolic syndrome and neurodegenerative diseases.^{90,91} Fengycin – a postbiotic secreted by *Bacillus subtilis* ZK3814 – effectively mitigates infections by *Staphylococcus aureus* by specifically targeting the quorum sensing mechanism in *S. aureus*.⁹² Deconjugation of taurocholate into cholate by EcN-CbH – an engineered probiotic – suppresses the growth of spore-forming *Clostridioides difficile*, leading to inhibition of infections caused by *C. difficile* in mouse models.⁹³

The FDA defines live biotherapeutic products (LBPs) as “a biological product that: contains live organisms, such as bacteria; is applicable to the prevention, treatment, or cure of a disease or condition of human beings; and is not a vaccine”.⁹⁴ According to this definition, non-genetically modified NGPs are classified as live biotherapeutics, while recombinant probiotics represent a different group.⁹⁵ Therefore, NGPs differ from traditional probiotics because they are subject to different legal regulations and have the potential to contain genetically modified microorganisms.^{95,96} In this context, it is important to design special recombinant probiotics developed through genetic engineering applications such as the CRISPR/Cas9 gene editing tool or plasmid-mediated recombination to

eliminate various limiting factors such as the production of non-specific antimicrobials, the presence of mobile antimicrobial resistance genes, and the different levels of effectiveness in different hosts of traditional probiotics.^{96–98} Effective colonization on the gastrointestinal tract, the production of specific therapeutic compounds, and the optimization of metabolic processes are made feasible by the development of genetically modified probiotics.^{96,98,99}

On the other hand, the utilization of bioengineering solutions in the creation of NGPs capable of using prebiotics in order to increase the viability of NGPs is noteworthy.¹¹² Despite the technical advantages of NGPs, there are some constraints on the utilization of these organisms in foods including insufficient risk assessment on their safe use, limited isolation sources, difficulty in culturing conditions and, more importantly, legal restriction of the use of genetically modified organisms in many countries.⁹⁵

4. Personalized nutrition and dairy-based probiotic beverages

Rapidly changing and fast lifestyle brings about various health problems. Metabolic syndrome, heart diseases, type 2 diabetes, irritable bowel syndrome, gastroesophageal reflux disease, and psychological disorders such as depression and anxiety are examples of health problems that have targeted many people in recent years.^{113–118} This fact has directed consumers toward more nutritious foods, and countless diet options have been proposed to the consumers. The food industry has put more effort to meet this demand.¹¹⁹ However, each diet applied causes different responses in individuals.^{119–122} Since each person has a unique microbiota and metabolism, the idea of personalized nutrition becomes more popular today. Personalized nutrition describes a nutritional routine in which the nutritional order is recreated in accordance with the individual by examining complex diet–host microbiota interactions, considering that each individual's requirements are different.^{123–125} At this point, due to the regulation of host-derived factors and their high diversity, shaping the microbiota with environmental factors such as dietary exposure is important in the control and prevention of diseases.¹²⁶ It has been suggested that probiotic supplementation in personalized diets can bring about modifications by influencing an individual's microbiota and, consequently, their metabolism. Phenotypic screening and a target-oriented bottom-up strategy have replaced the conventional, top-down approach in recent years, which involved assessing observational data and the findings of clinical trials involving humans and/or animals.¹²⁷ One of the topics that has gained interest recently is the development of tailored probiotics based on the needs of the individual by assessing the individual data and the parameters it influences collectively.¹²⁸ It is critical to modify foods and drinks that include probiotics to suit individual dietary needs and assess the results.



At this point, many dairy companies are developing specific fermented beverages and foods to meet individual needs.⁷⁴ The yogurt developed by Hori Nyugyo Dairy for women suffering from cold fingers that is claimed to regulate the temperature of the hands and feet of consumers and the triple yogurt offered by Morinaga Milk for consumption by individuals suffering from hypertension, containing the company's patented Met-Lys-Pro hydrolysed casein peptide, are listed as commercial examples of probiotic-based foods and beverages in personalized nutrition.^{74,129,130}

Fermented milks supplemented with probiotics contribute to the regulation of intestinal flora by promoting the growth of beneficial bacteria in the host's microbiota and decreasing the generation of excess metabolites by harmful microorganisms.^{131,132} Diet programs were tailored to meet the needs of individuals using a web-based program called RISTOMED. Consumers were presented diets supplemented with VSL#3 containing probiotic strains (*Bifidobacterium infantis* DSM 24737, *Bifidobacterium longum* DSM 24736, *Bifidobacterium breve* DSM 24732, *Lactobacillus acidophilus* DSM 24735, *Lactobacillus delbrueckii* ssp. *bulgaricus* DSM 24734, *Lacticaseibacillus paracasei* DSM 24733, *Lacticaseibacillus plantarum* DSM 24730, and *Streptococcus thermophilus* DSM 24731) for 8 weeks. Results showed that supplementation of VSL#3 increased the folate and vitamin B₁₂ concentrations in individuals with reduced inflammation. Furthermore, supplementing with VSL#3 resulted in a decrease in homocysteine levels in individuals and an increase in colony counts of *Bifidobacterium* in the gut microbiome, suggesting that it may be protective against neurological and cardiovascular disorders.

Healey *et al.* demonstrated that healthy people who regularly consume fiber had a relatively stronger gut microbiota response to inulin-type fructan prebiotics than individuals whom consume fewer fiber-rich foods.¹³³ In this context, it is predicted that the consumption of probiotic-based dairy beverages containing inulin may cause a positive microbiota response in individuals. Modulation of faecal microbiota by probiotic species/strains such as *Lactobacillus* spp. is seen in some individuals,^{134,135} but not in others.^{125,136} The conflicting results are attributed to the unique microbiota of individuals, as well as the individual effect of personalized diets on host metabolism and the complexity of diet–host microbiota interactions.^{125,137}

5. Future perspectives

The strain-dependent effects of probiotics, the metabolic and physiological factors of the host, and the balance of an individual's gut microbiota make probiotic beverage formulations complex. At this point, it is predicted that if individual-specific needs are taken into account in the development of probiotic-based dairy beverages, they can play an active role in the treatment and prevention of diseases, and thus a positive outcome

can be obtained from the increasing interest in probiotic-based dairy beverages.

As discussed above, keeping probiotic microorganisms in sufficient numbers in milk-based beverages seems to be the most important challenge. This difficulty also limits the probiotic microorganism options that may be suitable for industrial applications. Although probiotic microorganisms are accepted in the GRAS status, they also carry the risk of weakening resistance to infections in individuals with weak immune systems. However, the risks of high consumption of postbiotics have not yet been clarified. It is essential to clarify a dose–response relationship for postbiotics. The accumulation of clinical data on the health effects of next-generation probiotic microorganisms and postbiotic/paraprobiotics and achieving a certain scientific satisfaction level will accelerate the adaptation of these functional components to industrial applications. In addition, the development of risk analysis methodologies for these products and understanding their behaviour against novel food processes (high hydrostatic pressure, pulsed electric field, ultrasonication, *etc.*) will be advantageous for industrial applications.

The difficulties in optimization of probiotic dairy-based beverages can be overcome with the adaptation of artificial intelligence and 3D printing technologies into personalized nutrition formulations.^{124,138,139} Daily meals and physical activity are collected in a database through mobile applications designed to increase individual access to personalized nutrition. The data collected are stated to be very useful for developing a personalized diet plan that takes into account each person's needs and dietary goals.¹⁴⁰

Author contributions

ŞT, CA and HBÖ: conceptualization. ŞT and CA: writing – original draft. HBÖ: writing – reviewing and editing of the final draft and handling of the revisions. All authors read and approved the final manuscript.

Visualization

All the tables used in the text have been prepared by HBÖ, ŞT and CA.

Data availability

There is no data availability in this review article.

Conflicts of interest

We have no competing interests to declare in this review.



References

- 1 ISAAP, International Scientific Association for Probiotics and Prebiotics Expert Panel, <https://isappscience.org/scientists/resources/%20probiotics/>, (accessed 01/12/2024).
- 2 C. Hill, F. Guarner, G. Reid, G. R. Gibson, D. J. Merenstein, B. Pot, L. Morelli, R. B. Canani, H. J. Flint, S. Salminen, P. C. Calder and M. E. Sanders, The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic, *Nat. Rev. Gastroenterol. Hepatol.*, 2014, **11**, 506–514.
- 3 C. P. Champagne, R. P. Ross, M. Saarela, K. F. Hansen and D. Charalampopoulos, Recommendations for the viability assessment of probiotics as concentrated cultures and in food matrices, *Int. J. Food Microbiol.*, 2011, **149**, 185–193.
- 4 J. Suez, N. Zmora, E. Segal and E. Elinav, The pros, cons, and many unknowns of probiotics, *Nat. Med.*, 2019, **25**, 716–729.
- 5 T. Zhang, W. Zhang, C. Feng, L.-Y. Kwok, Q. He and Z. Sun, Stronger gut microbiome modulatory effects by postbiotics than probiotics in a mouse colitis model, *npj Sci. Food*, 2022, **6**, 53.
- 6 B. Ozer and G. Akdemir-Evrendilek, Dairy Foods Quality, and Analytical Techniques, ed. A. G. Cruz, S. Ranadheera, F. Nazzaro and A. Mortazaviani, Elsevier Publ., UK, 2022, ch. 6, pp. 117–137.
- 7 Spherical Insights, Global Probiotic Drinks Market Insights Forecasts to 2033, <https://www.sphericalinsights.com/reports/probiotic-drinks-market> (accessed 20/10/2024).
- 8 G. Eminoglu, H. C. Akal and H. B. Ozer, Microbes in the Food Industry, ed. N. Chhikara, A. Panghal and G. Chaudhary, Scrivener Publ., 2023, ch. 3, pp. 87–138.
- 9 D. M. Lilly and R. H. Stillwell, Probiotics: growth-promoting factors produced by microorganisms, *Science*, 1965, **147**, 747–748.
- 10 J. Ji, W. Jin, S.-J. Liu, Z. Jiao and X. Li, Probiotics, prebiotics, and postbiotics in health and disease, *MedComm*, 2023, **4**, e420.
- 11 T. Jan, R. Negi, B. Sharma, S. Kumar, S. Singh, A. K. Rai, S. Shreaz, S. Rustagi, N. Chaudhary, T. Kaur, D. Kour, M. A. Sheikh, K. Kumar, A. N. Yadav and N. Ahmed, Next generation probiotics for human health: An emerging perspective, *Heliyon*, 2024, **10**, e35980.
- 12 N. Turkmen, C. Akal and B. Özer, Probiotic dairy-based beverages: A review, *J. Funct. Foods*, 2019, **53**, 62–75.
- 13 M. Pescuma, G. F. de Valdez and F. Mozzi, Whey-derived valuable products obtained by microbial fermentation, *Appl. Microbiol. Biotechnol.*, 2015, **99**, 6183–6196.
- 14 O. Kareb and M. Aider, Whey and its derivatives for probiotics, prebiotics, synbiotics, and functional foods: a critical review, *Probiotics Antimicrob. Proteins*, 2019, **11**, 348–369.
- 15 A. Pires, N. G. Marnotes, O. Díaz, A. Cobos and C. Pereira, Dairy by-products: a review on the valorization of whey and second cheese whey, *Foods*, 2021, **10**, 1067.
- 16 K. Skryplonek, I. Dmytrów and A. Mituniewicz-Malek, Probiotic fermented beverages based on acid whey, *J. Dairy Sci.*, 2019, **102**, 7773–7780.
- 17 V. Tripathi and Y. K. Jha, Development of whey beverage with antagonistic characteristics and probiotics, *Int. J. Food Prop.*, 2004, **7**, 261–272.
- 18 W. F. Castro, A. G. Cruz, D. Rodrigues, G. Ghiselli, C. A. F. Oliveira, J. A. F. Faria and H. T. Godoy, Short communication: Effects of different whey concentrations on physicochemical characteristics and viable counts of starter bacteria in dairy beverage supplemented with probiotics, *J. Dairy Sci.*, 2013, **96**, 96–100.
- 19 O. Yerlikaya, A. Akpinar, F. Torunoglu, Ö. Kınık, N. Akbulut and H. Uysal, Effect of some prebiotic combination on viability of probiotic bacteria in reconstituted whey and milk beverages, *Agro Food Ind. Hi-Tech*, 2012, **23**, 27–29.
- 20 B. Matijević, R. Božanić and T. Ljubica, The influence of lactulose on growth and survival of probiotic bacteria *Lactobacillus acidophilus* La-5 and *Bifidobacterium animalis* subsp. *lactis* BB-12 in reconstituted sweet whey, *Mljekarstvo*, 2009, **59**, 20–27.
- 21 A. Akpinar, F. Torunoglu, O. Yerlikaya, O. Kınık, N. Akbulut and H. Uysal, Fermented probiotic beverages produced with reconstituted whey and cow milk: Sensorial and rheological properties, *Agro Food Ind. Hi-Tech*, 2015, **26**, 24–27.
- 22 T. Maity, K. Rakesh and A. K. Misra, Development of healthy whey drink with *Lactobacillus rhamnosus*, *Bifidobacterium bifidum* and *Propionibacterium freudenreichii* subsp. *shermanii*, *Mljekarstvo*, 2008, **58**, 315–325.
- 23 C. Pereira, M. Henriques, D. Gomes, A. Gómez-Zavaglia and G. De Antoni, Novel functional whey-based drinks with great potential to the dairy industry, *Food Technol. Biotechnol.*, 2015, **53**, 307–314.
- 24 A. Pavunc, T. Josip, J. Novak, J. Frece, M. Stjepan, K. Slavko and Š. Jagoda, Production of fermented probiotic beverages from milk permeate enriched with whey retentate and identification of present lactic acid bacteria, *Mljekarstvo*, 2009, **59**, 11–19.
- 25 N. Obradović, T. Krunić, K. Trifković, M. Bulatović, M. Rakin, M. Rakin and B. Bugarski, Influence of chitosan coating on mechanical stability of biopolymer carriers with probiotic starter culture in fermented whey beverages, *Int. J. Polym. Sci.*, 2015, **2015**, 1–8.
- 26 A. Mortazavian, Effects probiotic-containing microcapsules on viscosity, phase separation and sensory attributes of drink based on fermented milk, *Milchwissenschaft*, 2010, **65**, 177–179.
- 27 G. d. R. L. Mendes, H. F. d. Souza, J. P. A. Lopes, A. C. S. Rocha, R. B. Faria, F. R. d. Santos, B. M. A. C. de Mesquita, S. H. S. Santos, C. A. F. Durães, S. R. Ferreira, S. C. O. S. Boitrago, J. S. Leal, E. S. Kamimura and I. V. Brandi, A fermented milk drink with Umbu (*Spondias tuberosa*) pulp and whey is effective for weight



- gain and re-nutrition in malnourished: An in vivo study in mice and children, *Food Res. Int.*, 2024, **181**, 114083.
- 28 N. Smith, N. Maloney, S. Shaw, G. Horgan, C. Fyfe, J. Martin, K. Scott and A. Johnstone, Daily fermented whey consumption alters the fecal short-chain fatty acid profile in healthy adults, *Front. Nutr.*, 2020, **7**, 165.
 - 29 B. Wróblewska, A. Kaliszewska-Suchodola, L. H. Markiewicz, A. Szyc and E. Wasilewska, Whey fermented with beneficial microbes modulates immune response and lowers responsiveness to milk allergens in mouse model, *J. Funct. Foods*, 2019, **54**, 41–52.
 - 30 A. Helal, C. Nasuti, L. Sola, G. Sassi, D. Tagliazucchi and L. Solieri, Impact of spontaneous fermentation and inoculum with natural whey starter on peptidomic profile and biological activities of cheese whey: a comparative study, *Fermentation*, 2023, **9**, 270.
 - 31 H. Kaur, T. Gupta, S. Kapila and R. Kapila, Protective effects of potential probiotic *Lactobacillus rhamnosus* (MTCC-5897) fermented whey on reinforcement of intestinal epithelial barrier function in colitis induced murine model, *Food Funct.*, 2021, **12**, 6102–6116.
 - 32 L. S. Rosa, M. L. Santos, J. P. Abreu, R. S. Rocha, E. A. Esmerino, M. Q. Freitas, E. T. Mársico, P. H. Campelo, T. C. Pimentel, M. C. Silva, A. A. Souza, F. C. S. Nogueira, A. G. Cruz and A. J. Teodoro, Probiotic fermented whey-milk beverages: Effect of different probiotic strains on the physicochemical characteristics, biological activity, and bioactive peptides, *Food Res. Int.*, 2023, **164**, 112396.
 - 33 E. Seyhan, H. Yaman and B. Özer, Production of a whey-based functional beverage supplemented with soy isoflavones and phytosterols, *Int. J. Dairy Technol.*, 2016, **69**, 114–121.
 - 34 H. Devi, T. P. Singh, R. Siwach and V. Chaudhary, Development of nutri-functional paneer whey-based kefir drink, *J. Food Sci. Technol.*, 2025, **62**, 254–263.
 - 35 A. Londero, C. Iraporda, G. L. Garrote and A. G. Abraham, Cheese whey fermented with kefir micro-organisms: Antagonism against *Salmonella* and immunomodulatory capacity, *Int. J. Dairy Technol.*, 2015, **68**, 118–126.
 - 36 A. Alves, L. Spadoti, P. B. Zacarchenco and F. K. H. S. Trento, Probiotic functional carbonated whey beverages: development and quality evaluation, *Beverages*, 2018, **4**, 49.
 - 37 M. Z. Islam, S. Tabassum, M. Harun-ur-Rashid, G. E. Vegarud, M. S. Alam and M. A. Islam, Development of probiotic beverage using whey and pineapple (*Ananas comosus*) juice: Sensory and physico-chemical properties and probiotic survivability during *in vitro* gastrointestinal digestion, *J. Agric. Food Res.*, 2021, **4**, 100144.
 - 38 M. Bulatovic, T. Krunić, M. Vukasinovic-Sekulic, D. Zarić and M. Rakin, Quality attributes of fermented whey-based beverage enriched with milk and probiotic strain, *RSC Adv.*, 2014, **4**, 55503–55510.
 - 39 M. N. Oliveira, I. Sodini, R. Remeuf, J. P. Tissier and G. Corrieu, Manufacture of fermented lactic beverages containing probiotic cultures, *J. Food Sci.*, 2002, **67**, 2336–2341.
 - 40 M. Molero-Méndez, G. Castro-Albornoz and W. Briñez-Zambrano, Formulation of a probiotic fermented beverage based on whey, *Rev. Cient. Fac. Cienc. Vet. Univ. Zulia*, 2017, **27**, 142–147.
 - 41 M. Molero-Méndez, C. Aiello-Mazzarri, J. Araujo-Morillo and W. Briñez-Zambrano, Physicochemical and microbiological quality and lifetime of probiotic fermented beverages based on whey, *Rev. Cient. Fac. Cienc. Vet. Univ. Zulia*, 2017, **27**, 265–269.
 - 42 E. O. d. Silveira, J. H. L. Neto, L. A. d. Silva, A. E. S. Raposo, M. Magnani and H. R. Cardarelli, The effects of inulin combined with oligofructose and goat cheese whey on the physicochemical properties and sensory acceptance of a probiotic chocolate goat dairy beverage, *LWT – Food Sci. Technol.*, 2015, **62**, 445–451.
 - 43 N. Dinkci, V. Akdeniz and A. Akalin, Probiotic whey-based beverages from cow, sheep and goat milk: antioxidant activity, culture viability, amino acid contents, *Foods*, 2023, **12**, 610.
 - 44 F. Baruzzi, S. Candia, L. Quintieri, L. Caputo and F. De Leo, Development of a synbiotic beverage enriched with *Bifidobacteria* strains and fortified with whey proteins, *Front. Microbiol.*, 2017, **8**, 640.
 - 45 K. Naemeh, M. S. Ali, M. Elham and A. Akram, Production of the whey protein-based probiotic beverages incorporated with *Bifidobacterium bifidum*, *Lactobacillus acidophilus*, and peppermint essence nanoliposomes, *J. Food Meas. Charact.*, 2023, **17**, 2708–2717.
 - 46 M. Shukla, Y. Jha and S. Emire, Development of probiotic beverage from whey and pineapple juice, *J. Food Process. Technol.*, 2013, **4**, 1–4.
 - 47 K. C. S. Ribeiro, N. M. Coutinho, M. R. Silveira, R. S. Rocha, H. S. Arruda, G. M. Pastore, R. P. C. Neto, M. I. B. Tavares, T. C. Pimentel, P. H. F. Silva, M. Q. Freitas, E. A. Esmerino, M. C. Silva, M. C. K. H. Duarte and A. G. Cruz, Impact of cold plasma on the techno-functional and sensory properties of whey dairy beverage added with xylooligosaccharide, *Food Res. Int.*, 2021, **142**, 110232.
 - 48 G. García, M. E. Agosto, L. Cavaglieri and C. Dogi, Effect of fermented whey with a probiotic bacterium on gut immune system, *J. Dairy Res.*, 2020, **87**, 134–137.
 - 49 G. Abitayeva, G. Bissenova, B. Mussabayeva, Y. Naimanov, T. Tultabayeva and S. Serikovna, Development, quality and safety evaluation of a probiotic whey beverage, *Funct. Foods Health Dis.*, 2023, **13**, 347.
 - 50 R. Rombaut, J. V. Camp and K. Dewettinck, Phospho- and sphingolipid distribution during processing of milk, butter and whey, *Int. J. Food Sci. Technol.*, 2006, **41**, 435–443.
 - 51 R. E. Ward, J. B. German and M. Corredig, in *Advanced Dairy Chemistry – Volume 2 Lipids*, ed. P. F. Fox and P. L. H. McSweeney, Springer, Boston, MA, 2006, ch. 6, pp. 213–244.



- 52 S. Danthine, C. Blecker, M. Paquot, N. Innocente and C. Deroanne, Évolution des connaissances sur la membrane du globule gras du lait : synthèse bibliographique, *Lait*, 2000, **80**, 209–222.
- 53 K. Dewettinck, R. Rombaut, N. Thienpont, T. T. Le, K. Messens and J. Van Camp, Nutritional and technological aspects of milk fat globule membrane material, *Int. Dairy J.*, 2008, **18**, 436–457.
- 54 R. Jiménez-Flores and G. Brisson, The milk fat globule membrane as an ingredient: why, how, when?, *Dairy Sci. Technol.*, 2008, **88**, 5–18.
- 55 C. Vanderghem, P. Bodson, S. Danthine, M. Paquot, C. Deroanne and C. Blecker, Milk fat globule membrane and buttermilks: From composition to valorization, *Biotechnol., Agron., Soc. Environ.*, 2010, **14**, 485–500.
- 56 A. Antunes, É. Silva, A. Van Dender, E. Marasca, I. Moreno, E. Faria, M. Padula and A. Lerayer, Probiotic buttermilk-like fermented milk product development in a semiindustrial scale: Physicochemical, microbiological and sensory acceptability, *Int. J. Dairy Technol.*, 2009, **62**, 556–563.
- 57 A. Antunes, E. Marasca, I. Moreno, F. Dourado, L. Rodrigues and A. Lerayer, Development of a probiotic buttermilk, *Food Sci. Technol.*, 2007, **27**, 83–90.
- 58 M. Hashem, Supplementation of buttermilk with red beet root for producing fermented milk beverage, *Egypt. J. Agric. Res.*, 2018, **96**, 1111–1125.
- 59 J. E. Aguilar-Toalá, R. Garcia-Varela, H. S. Garcia, V. Mata-Haro, A. F. González-Córdova, B. Vallejo-Cordoba and A. Hernández-Mendoza, Postbiotics: An evolving term within the functional foods field, *Trends Food Sci. Technol.*, 2018, **75**, 105–114.
- 60 P. F. Cuevas-González, A. M. Liceaga and J. E. Aguilar-Toalá, Postbiotics and paraprobiotics: From concepts to applications, *Food Res. Int.*, 2020, **136**, 109502.
- 61 C. P. Barros, J. T. Guimarães, E. A. Esmerino, M. C. K. H. Duarte, M. C. Silva, R. Silva, B. M. Ferreira, A. S. Sant'Ana, M. Q. Freitas and A. G. Cruz, Paraprobiotics and postbiotics: concepts and potential applications in dairy products, *Curr. Opin. Food Sci.*, 2020, **32**, 1–8.
- 62 S. Sadighbathi, P. Saris, S. Amiri and A. Yousefvand, Development and properties of functional yoghurt enriched with postbiotic produced by yoghurt cultures using cheese whey and skim milk, *Front. Microbiol.*, 2023, 1276268.
- 63 S. Salminen, M. C. Collado, A. Endo, C. Hill, S. Lebeer, E. M. M. Quigley, M. E. Sanders, R. Shamir, J. R. Swann, H. Szajewska and G. Vinderola, The International Scientific Association of Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics, *Nat. Rev. Gastroenterol. Hepatol.*, 2021, **18**, 649–667.
- 64 R. Siciliano, A. Reale, M. Mazzeo, S. Morandi, T. Silveti and M. Brasca, Paraprobiotics: a new perspective for functional foods and nutraceuticals, *Nutrients*, 2021, **13**, 1225.
- 65 G. Vinderola, M. E. Sanders, M. Cunningham and C. Hill, Frequently asked questions about the ISAPP postbiotic definition, *Front. Microbiol.*, 2024, **14**, 1324565.
- 66 R. Yan, X. Zeng, J. Shen, Z. Wu, Y. Guo, Q. Du, M. Tu and D. Pan, New clues for postbiotics to improve host health: a review from the perspective of function and mechanisms, *J. Sci. Food Agric.*, 2024, **104**, 6376–6387.
- 67 J. Żółkiewicz, A. Marzec, M. Ruszczyński and W. Feleszko, Postbiotics—a step beyond pre-and probiotics, *Nutrients*, 2020, **12**, 2189.
- 68 S. Monteiro, C. Schnorr and M. Pasquali, Paraprobiotics and postbiotics—current state of scientific research and future trends toward the development of functional foods, *Foods*, 2023, **12**, 2394.
- 69 S. Chaluvadi, A. Hotchkiss and K. Yam, Probiotics, Prebiotics, and Synbiotics, ed. R. R. Watson and V. R. Preedy, Elsevier Publ., Amsterdam, 2016, ch. 36, pp. 515–523.
- 70 K. Viswanathan and S. Muthusamy, Review on the current trends and future perspectives of postbiotics for developing healthier foods, *eFood*, 2022, **3**, e47.
- 71 S. A. Pujato, A. d. L. Quiberoni, M. C. Candioti, J. A. Reinheimer and D. M. Guglielmotti, *Leuconostoc citreum* MB1 as biocontrol agent of *Listeria monocytogenes* in milk, *J. Dairy Res.*, 2014, **81**, 137–145.
- 72 C. Xue, M. Li, M. Luo, B. Zhang and Y. Wang, Efficacy of *Lactocaseibacillus paracasei* fermented milk on a model of constipation induced by loperamide hydrochloride in BALB/c mice, *J. Food Sci.*, 2024, **89**, 6733–6744.
- 73 M. K. Salminen, H. Rautelin, S. Tynkkynen, T. Poussa, M. Saxelin, V. Valtonen and A. Järvinen, Lactobacillus bacteremia clinical significance, and patient outcome, with special focus on probiotic *L. rhamnosus* GG, *Clin. Infect. Dis.*, 2004, **38**, 62–69.
- 74 T. Zhang, S. Geng, T. Cheng, K. Mao, B. Chitrakar, J. Gao and Y. Sang, From the past to the future: Fermented milks and their health effects against human diseases, *Food Front.*, 2023, **4**, 1747–1777.
- 75 D. Sawada, T. Sugawara, Y. Ishida, K. Aihara, Y. Aoki, I. Takehara, K. Takano and S. Fujiwara, Effect of continuous ingestion of a beverage prepared with *Lactobacillus gasseri* CP2305 inactivated by heat treatment on the regulation of intestinal function, *Food Res. Int.*, 2016, **79**, 33–39.
- 76 T. Sugawara, D. Sawada, Y. Ishida, K. Aihara, Y. Aoki, I. Takehara, K. Takano and S. Fujiwara, Regulatory effect of paraprobiotic *Lactobacillus gasseri* CP2305 on gut environment and function, *Microb. Ecol. Health Dis.*, 2016, **27**, 30259.
- 77 K. Nishida, D. Sawada, Y. Kuwano, H. Tanaka, T. Sugawara, Y. Aoki, S. Fujiwara and K. Rokutan, Daily administration of paraprobiotic *Lactobacillus gasseri* CP2305 ameliorates chronic stress-associated symptoms in Japanese medical students, *J. Funct. Foods*, 2017, **36**, 112–121.



- 78 K. Nishida, D. Sawada, T. Kawai, Y. Kuwano, S. Fujiwara and K. Rokutan, Para-psycho-biotic *Lactobacillus gasseri* CP2305 ameliorates stress-related symptoms and sleep quality, *J. Appl. Microbiol.*, 2017, **123**, 1561–1570.
- 79 R. B. Canani, F. De Filippis, R. Nocerino, M. Laiola, L. Paparo, A. Calignano, C. De Caro, L. Coretti, L. Chiariotti, G. Jack and D. Ercolini, Specific signatures of the gut microbiota and increased levels of butyrate in children treated with fermented cow's milk containing heat-killed *Lactobacillus paracasei* CBA L74, *Appl. Environ. Microbiol.*, 2017, **83**, e01206–17.
- 80 EFSA Panel on Dietetic Products, Nutrition and Allergies, Scientific Opinion on the safety of 'heat-treated milk products fermented with *Bacteroides xylanisolvens* DSM 23964' as a novel food, *EFSA J.*, 2015, **13**, 3956.
- 81 EFSA Panel on Nutrition, Novel Foods and Food Allergens, D. Turck, T. Bohn, J. Castenmiller, S. De Henauw, K. I. Hirsch-Ernst, A. Maciuk, I. Mangelsdorf, H. J. McArdle, A. Naska, C. Pelaez, K. Pentieva, A. Siani, F. Thies, S. Tsabouri, M. Vinceti, F. Cubadda, T. Frenzel, M. Heinonen, R. Marchelli, M. Neuhäuser-Berthold, M. Poulsen, M. P. Maradona, J. R. Schlatter, H. van Loveren, R. Ackerl and H. K. Knutsen, Safety of pasteurised *Akkermansia muciniphila* as a novel food pursuant to Regulation (EU) 2015/2283, *EFSA J.*, 2021, **19**, e06780.
- 82 EFSA Panel on Nutrition, Novel Foods and Food Allergens, D. Turck, J. Castenmiller, S. De Henauw, K. I. Hirsch-Ernst, J. Kearney, A. Maciuk, I. Mangelsdorf, H. J. McArdle, A. Naska, C. Pelaez, K. Pentieva, A. Siani, F. Thies, S. Tsabouri, M. Vinceti, F. Cubadda, K. H. Engel, T. Frenzel, M. Heinonen, R. Marchelli, M. Neuhäuser-Berthold, M. Poulsen, Y. Sanz, J. R. Schlatter, H. van Loveren, Q. Sun, W. Gelbmann and H. K. Knutsen, Safety of heat-killed *Mycobacterium setense* manresensis as a novel food pursuant to Regulation (EU) 2015/2283, *EFSA J.*, 2019, **17**, e05824.
- 83 EFSA, Authorising the placing on the market of heat-treated milk products fermented with *Bacteroides xylanisolvens* (DSM 23964) as a novel food under Regulation (EC) No 258/97 of the European Parliament and of the Council, https://eur-lex.europa.eu/eli/dec_impl/2015/1291/oj/eng.
- 84 EFSA, Authorising the placing on the market of pasteurised *Akkermansia muciniphila* as a novel food under Regulation (EU) 2015/2283 of the European Parliament and of the Council and amending Commission Implementing Regulation (EU) 2017/2470, https://eur-lex.europa.eu/eli/reg_impl/2022/168/oj/eng.
- 85 R. Martín, S. Miquel, L. Benevides, C. Bridonneau, V. Robert, S. Hudault, F. Chain, O. Berteau, V. Azevedo, J. M. Chatel, H. Sokol, L. G. Bermúdez-Humarán, M. Thomas and P. Langella, Functional characterization of novel *Faecalibacterium prausnitzii* strains Isolated from healthy volunteers: a step forward in the use of *F. prausnitzii* as a next-generation probiotic, *Front. Microbiol.*, 2017, **8**, 1226.
- 86 Z. J. S. Mays, T. C. Chappell and N. U. Nair, Quantifying and engineering mucus adhesion of probiotics, *ACS Synth. Biol.*, 2020, **9**, 356–367.
- 87 M. Kumari, P. Singh, B. H. Nataraj, A. Kokkiligadda, H. Naithani, S. A. Ali, P. V. Behare and R. Nagpal, Fostering next-generation probiotics in human gut by targeted dietary modulation: An emerging perspective, *Food Res. Int.*, 2021, **150**, 110716.
- 88 M. W. J. van Passel, R. Kant, E. G. Zoetendal, C. M. Plugge, M. Derrien, S. A. Malfatti, P. S. G. Chain, T. Woyke, A. Palva, W. M. de Vos and H. Smidt, The genome of *Akkermansia muciniphila*, a dedicated intestinal mucin degrader, and its use in exploring intestinal metagenomes, *PLoS One*, 2011, **6**, e16876.
- 89 Z. Wang, X. Qin, D. Hu, J. Huang, E. Guo, R. Xiao, W. Li, C. Sun and G. Chen, *Akkermansia* supplementation reverses the tumor-promoting effect of the fecal microbiota transplantation in ovarian cancer, *Cell Rep.*, 2022, **41**, 111890.
- 90 P. D. Cani, C. Depommier, M. Derrien, A. Everard and W. M. de Vos, *Akkermansia muciniphila*: paradigm for next-generation beneficial microorganisms, *Nat. Rev. Gastroenterol. Hepatol.*, 2022, **19**, 625–637.
- 91 P. D. Cani and W. M. de Vos, Next-generation beneficial microbes: the case of *Akkermansia muciniphila*, *Front. Microbiol.*, 2017, **8**, 1765.
- 92 P. Piewngam, Y. Zheng, T. H. Nguyen, S. W. Dickey, H.-S. Joo, A. E. Villaruz, K. A. Glose, E. L. Fisher, R. L. Hunt, B. Li, J. Chiou, S. Pharkjaksu, S. Khongthong, G. Y. C. Cheung, P. Kiratisin and M. Otto, Pathogen elimination by probiotic *Bacillus* via signalling interference, *Nature*, 2018, **562**, 532–537.
- 93 E. Koh, I. Y. Hwang, H. L. Lee, R. De Sotto, J. W. J. Lee, Y. S. Lee, J. C. March and M. W. Chang, Engineering probiotics to inhibit *Clostridioides difficile* infection by dynamic regulation of intestinal metabolism, *Nat. Commun.*, 2022, **13**, 3834.
- 94 Food and Drug Administration, Early clinical trials with live biotherapeutic products: Chemistry, manufacturing, and control information, <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/early-clinical-trials-live-biotherapeutic-products-chemistry-manufacturing-and-control-information>, (accessed 10/10/2024).
- 95 B. H. Nataraj, S. K. Shivanna, P. Rao, R. Nagpal and P. V. Behare, Evolutionary concepts in the functional biotics arena: a mini-review, *Food Sci. Biotechnol.*, 2021, **30**, 487–496.
- 96 M. A. Hasnain, D. K. Kang and G.-S. Moon, Research trends of next generation probiotics, *Food Sci. Biotechnol.*, 2024, **33**, 2111–2121.
- 97 N. Aggarwal, A. M. E. Breedon, C. M. Davis, I. Y. Hwang and M. W. Chang, Engineering probiotics for therapeutic applications: recent examples and translational outlook, *Curr. Opin. Biotechnol.*, 2020, **65**, 171–179.
- 98 H. E. Romero-Luna, A. Hernández-Mendoza, A. F. González-Córdova and A. Peredo-Lovillo, Bioactive



- peptides produced by engineered probiotics and other food-grade bacteria: A review, *Food Chem.: X*, 2022, **13**, 100196.
- 99 J. Bober, C. Beisel and N. Nair, Synthetic biology approaches to engineer probiotics and members of the human microbiota for biomedical applications, *Annu. Rev. Biomed. Eng.*, 2018, **20**, 277–300.
 - 100 B. de Oliveira Coelho, F. Fiorda-Mello, G. V. de Melo Pereira, V. Thomaz-Soccol, S. K. Rakshit, J. C. de Carvalho and C. R. Soccol, In vitro probiotic properties and DNA protection activity of yeast and lactic acid bacteria isolated from a honey-based kefir beverage, *Foods*, 2019, **8**, 485.
 - 101 F. Maghsood, B. Johari, M. Rohani, H. Madanchi, Z. Saltanatpour and M. Kadivar, Anti-proliferative and anti-metastatic potential of high molecular weight secretory molecules from probiotic *Lactobacillus reuteri* cell-free supernatant against human colon cancer stem-like cells (HT29-ShE), *Int. J. Pept. Res. Ther.*, 2020, **26**, 2619–2631.
 - 102 S. R. Qi, Y. J. Cui, J. X. Liu, X. Luo and H. F. Wang, *Lactobacillus rhamnosus* GG components, SLP, gDNA and CpG, exert protective effects on mouse macrophages upon lipopolysaccharide challenge, *Lett. Appl. Microbiol.*, 2020, **70**, 118–127.
 - 103 X. You, Z. Li, K. Ma, C. Zhang, X. Chen, G. Wang, L. Yang, M. Dong, X. Rui, Q. Zhang and W. Li, Structural characterization and immunomodulatory activity of an exopolysaccharide produced by *Lactobacillus helveticus* LZ-R-5, *Carbohydr. Polym.*, 2020, **235**, 115977.
 - 104 X. Duan, S. Chen, S. Duan, C. Lan, Z. Yang, Y. Cao and J. Miao, Antibiotic activities of the natural antimicrobial substance produced by *Lactobacillus paracasei* FX-6 against *Pseudomonas putida*, *LWT*, 2020, **123**, 109096.
 - 105 C. J. McGovern, B. D. González-Orozco and R. Jiménez-Flores, Evaluation of kefir grain microbiota, grain viability, and bioactivity from fermenting dairy processing by-products, *J. Dairy Sci.*, 2024, **107**, 4259–4276.
 - 106 J. Gao, Q. Li, Y. Liu, B. Yang, F. A. Sadiq, X. Li, S. Mi and Y. Sang, Immunoregulatory effect of *Lactobacillus paracasei* VL8 exopolysaccharide on RAW264.7 cells by NF- κ B and MAPK pathways, *J. Funct. Foods*, 2022, **95**, 105166.
 - 107 A. Kamali, H. Hosseini, R. Mahmoudi, B. Pakbin, N. Gheibi, A. M. Mortazavian and S. Shojaei, The sensory evaluation and antimicrobial efficacy of *Lactobacillus acidophilus* supernatant on *Salmonella enteritidis* in milk, *Food Sci. Nutr.*, 2024, **12**, 1902–1910.
 - 108 J. E. Aguilar-Toalá, H. Astiazarán-García, M. C. Estrada-Montoya, H. S. García, B. Vallejo-Cordoba, A. F. González-Córdova and A. Hernández-Mendoza, Modulatory effect of the intracellular content of *Lactobacillus casei* CRL 431 against the Aflatoxin B1-induced oxidative stress in rats, *Probiotics Antimicrob. Proteins*, 2018, **11**, 470–477.
 - 109 E. Dunand, P. Burns, A. Binetti, C. Bergamini, G. H. Peralta, L. Forzani, J. Reinheimer and G. Vinderola, Postbiotics produced at laboratory and industrial level as potential functional food ingredients with the capacity to protect mice against *Salmonella* infection, *J. Appl. Microbiol.*, 2019, **127**, 219–229.
 - 110 H. Maehata, Y. Kobayashi, E. Mitsuyama, T. Kawase, T. Kuhara, J. Z. Xiao, T. Tsukahara and A. Toyoda, Heat-killed *Lactobacillus helveticus* strain MCC1848 confers resilience to anxiety or depression-like symptoms caused by subchronic social defeat stress in mice, *Biosci., Biotechnol., Biochem.*, 2019, **83**, 1239–1247.
 - 111 K. Y. Lee, Y. C. Tsai, S. Y. Wang, Y. P. Chen and M. J. Chen, Coculture strategy for developing *Lactobacillus paracasei* PS23 fermented milk with anti-colitis effect, *Foods*, 2021, **10**, 2337.
 - 112 S. K. Murali and T. J. Mansell, Next generation probiotics: Engineering live biotherapeutics, *Biotechnol. Adv.*, 2024, **72**, 108336.
 - 113 M. Mazidi, P. Rezaie, A. P. Kengne, M. G. Mobarhan and G. A. Ferns, Gut microbiome and metabolic syndrome, *Diabetes Metab. Syndr.*, 2016, **10**, S150–S157.
 - 114 P. W. Franks and M. I. McCarthy, Exposing the exposures responsible for type 2 diabetes and obesity, *Science*, 2016, **354**, 69–73.
 - 115 C. Christensen, A. Knudsen, E. K. Arnesen, J. G. Hatlebakk, I. S. Sletten and L. T. Fadnes, Diet, food, and nutritional exposures and inflammatory bowel disease or progression of disease: an umbrella review, *Adv. Nutr.*, 2024, **15**, 100219.
 - 116 M. Zhang, Z. K. Hou, Z. B. Huang, X. L. Chen and F. B. Liu, Dietary and lifestyle factors related to gastroesophageal reflux disease: a systematic review, *Ther. Clin. Risk Manage.*, 2021, **17**, 305–323.
 - 117 T. Monique, Diet and depression, *Harvard Health Publishing*, 2020 <https://www.health.harvard.edu/blog/diet-and-depression-2018022213309> (accessed on 2.8.2024).
 - 118 D. Gibson-Smith, M. Bot, I. Brouwer, M. Visser, E. Giltay and B. Penninx, Association of food groups with depression and anxiety disorders, *Eur. J. Nutr.*, 2020, **59**, 767–778.
 - 119 M. Lombardo, E. Guseva, M. A. Perrone, A. Müller, G. Rizzo and M. A. Storz, Changes in eating habits and physical activity after COVID-19 pandemic lockdowns in Italy, *Nutrients*, 2021, **13**, 4522.
 - 120 S. E. Berry, A. M. Valdes, D. A. Drew, F. Asnicar, M. Mazidi, J. Wolf, J. Capdevila, G. Hadjigeorgiou, R. Davies, H. Al Khatib, C. Bonnett, S. Ganesh, E. Bakker, D. Hart, M. Mangino, J. Merino, I. Linenberg, P. Wyatt, J. M. Ordovas, C. D. Gardner, L. M. Delahanty, A. T. Chan, N. Segata, P. W. Franks and T. D. Spector, Human postprandial responses to food and potential for precision nutrition, *Nat. Med.*, 2020, **26**, 964–973.
 - 121 S. S. Heinzmann, C. A. Merrifield, S. Rezzi, S. Kochhar, J. C. Lindon, E. Holmes and J. K. Nicholson, Stability and robustness of human metabolic phenotypes in response to sequential food challenges, *J. Proteome Res.*, 2012, **11**, 643–655.



- 122 K. S. Vimalaswaran, C. I. Le Roy and S. P. Claus, Foodomics for personalized nutrition: how far are we?, *Curr. Opin. Food Sci.*, 2015, **4**, 129–135.
- 123 C. Celis-Morales, J. Lara and J. Mathers, Personalising nutritional guidance for more effective behaviour change, *Proc. Nutr. Soc.*, 2014, **73**, 130–138.
- 124 M. J. Reinders, A. D. Starke, A. R. H. Fischer, M. C. D. Verain, E. L. Doets and E. J. Van Loo, Determinants of consumer acceptance and use of personalized dietary advice: A systematic review, *Trends Food Sci. Technol.*, 2023, **131**, 277–294.
- 125 A. A. Kolodziejczyk, D. Zheng and E. Elinav, Diet-microbiota interactions and personalized nutrition, *Nat. Rev. Microbiol.*, 2019, **17**, 742–753.
- 126 G. Rodgers and F. Collins, Precision nutrition—the answer to “what to eat to stay healthy”, *J. Am. Med. Assoc.*, 2020, **324**, 735–736.
- 127 P. Veiga, J. Suez, M. Derrien and E. Elinav, Moving from probiotics to precision probiotics, *Nat. Microbiol.*, 2020, **5**, 878–880.
- 128 D. E. Kiousi, M. Rathosi, M. Tsifintaris, P. Chondrou and A. Galanis, Pro-biomics: Omics technologies to unravel the role of probiotics in health and disease, *Adv. Nutr.*, 2021, **12**, 1802–1820.
- 129 Morinaga Triple Yogurt, <https://triple-yogurt.jp/>, (accessed 13/10/2024).
- 130 Horimilk-Warming Yogurt for Adults, <https://horimilk.co.jp/topics/2824/>, (accessed 11/10/2024).
- 131 H. Aslam, W. Marx, T. Rocks, A. Loughman, V. Chandrasekaran, A. Ruusunen, S. L. Dawson, M. West, E. Mullarkey, J. A. Pasco and F. N. Jacka, The effects of dairy and dairy derivatives on the gut microbiota: a systematic literature review, *Gut Microbes*, 2020, **12**, 1799533.
- 132 L. Valentini, A. Pinto, I. Bourdel-Marchasson, R. Ostan, P. Brigidi, S. Turroni, S. Hrelia, P. Hrelia, S. Bereswill, A. Fischer, E. Leoncini, M. Malaguti, C. Blanc-Bisson, J. Durrieu, L. Spazzafumo, F. Buccolini, F. Pryen, L. M. Donini, C. Franceschi and H. Lochs, Impact of personalized diet and probiotic supplementation on inflammation, nutritional parameters and intestinal microbiota – The “RISTOMED project”: Randomized controlled trial in healthy older people, *Clin. Nutr.*, 2015, **34**, 593–602.
- 133 G. Healey, R. Murphy, C. Butts, L. Brough, K. Whelan and J. Coad, Habitual dietary fibre intake influences gut microbiota response to an inulin-type fructan prebiotic: a randomised, double-blind, placebo-controlled, cross-over, human intervention study, *Br. J. Nutr.*, 2018, **119**, 176–189.
- 134 D. A. Goossens, D. M. Jonkers, M. G. Russel, E. E. Stobberingh and R. W. Stockbrügger, The effect of a probiotic drink with *Lactobacillus plantarum* 299v on the bacterial composition in faeces and mucosal biopsies of rectum and ascending colon, *Aliment. Pharmacol. Ther.*, 2006, **23**, 255–263.
- 135 C. Ferrario, V. Taverniti, C. Milani, W. Fiore, M. Laureati, I. De Noni, M. Stuknyte, B. Chouaia, P. Riso and S. Guglielmetti, Modulation of fecal clostridiales bacteria and butyrate by probiotic intervention with *Lactobacillus paracasei* DG varies among healthy adults, *J. Nutr.*, 2014, **144**, 1787–1796.
- 136 N. B. Kristensen, T. Bryrup, K. H. Allin, T. Nielsen, T. H. Hansen and O. Pedersen, Alterations in fecal microbiota composition by probiotic supplementation in healthy adults: a systematic review of randomized controlled trials, *Genome Med.*, 2016, **8**, 52.
- 137 D. Zeevi, T. Korem, N. Zmora, D. Israeli, D. Rothschild, A. Weinberger, O. Ben-Yacov, D. Lador, T. Avnit-Sagi, M. Lotan-Pompan, J. Suez, J. A. Mahdi, E. Matot, G. Malka, N. Kosower, M. Rein, G. Zilberman-Schapira, L. Dohnalová, M. Pevsner-Fischer, R. Bikovsky, Z. Halpern, E. Elinav and E. Segal, Personalized nutrition by prediction of glycemic responses, *Cell*, 2015, **163**, 1079–1094.
- 138 M. Boland, F. Alam and J. Bronlund, Trends in Personalized Nutrition, ed. C. M. Galanakis, Academic Press, Amsterdam, 2019, ch. 8, pp. 195–222.
- 139 A. Sadeghi, A. C. Karaca, M. Ebrahimi, E. Assadpour and S. M. Jafari, The 3D printed probiotic products; an emerging category of the functional foods for the next-generations, *Trends Food Sci. Technol.*, 2024, **148**, 104526.
- 140 T. Ma, H. Wang, M. Wei, T. Lan, J. Wang, S. Bao, Q. Ge, Y. Fang and X. Sun, Application of smart-phone use in rapid food detection, food traceability systems, and personalized diet guidance, making our diet more health, *Food Res. Int.*, 2022, **152**, 110918.

