Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

DIALOGUE SOCIAL SCIENCE REVIEW

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Innovative Strategies in Fermented Food Production: Harnessing Genetic and Metabolic Engineering of Lactic Acid Bacteria

Saleem Ahmad (Corresponding Author)
Dr. Ikram-ul-Haq Institute of Industrial Biotechnology (IIIB), Department of Microbiology, Government College University (GCU), Lahore, 54000, Pakistan.
Email: saleemchhimmee@gmail.com
ORCID: https://orcid.org/0009-0000-1148-0087

Tanveer Ahmed
School of Biochemistry and Biotechnology, University of the Punjab, Lahore, Pakistan.
Email: tanveerahmedch756624@gmail.com
ORCID: https://orcid.org/0009-0007-4132-2347

Abdul Samad
School of Biochemistry and Biotechnology, University of the Punjab, Lahore, Pakistan.
Email: abdulsamad.as940@gmail.com
ORCID: https://orcid.org/0009-0001-1887-4852

Sohaib Ur Rehman
School of Biochemistry and Biotechnology, University of the Punjab, Lahore, Pakistan.
Email: sohaiburrahman685@gmail.com
ORCID: https://orcid.org/0009-0001-4471-6815

Muhammad Ghalib
School of Biochemistry and Biotechnology, University of the Punjab, Lahore, Pakistan.
Email: muhammadghalib283@gmail.com
https://orcid.org/0009-0004-9769-6629

Abstract: Fermentation has been a time-honored process used since ancient times to improve the sensory properties and preservation of food. Microorganisms have been used for various types of fermented food because of their outstanding ability to serve as cell factories. Lactic acid bacteria (LAB) play crucial roles in fermentation products ranging from traditional milk products to fruits and vegetables. Recent advances in recombinant DNA technology and genetic engineering via engineered lactic acid bacteria (LAB) have led to significant improvements in the food industry. This review aims to present the ability of engineered LAB to improve and enhance both the quality and the quality of fermented products. We discuss the role of GM-LAB in cheese production and ripening; ethnic fermented foods derived from milk, vegetable and meat; the role of food-derived bioactive compounds such as amino acids, SCFAs and EPS in nutrition and health; the synthesis of flavoring and aroma molecules such as acetaldehyde, diacetyl, and sweeteners such as sorbitol and mannitol;, etc. Finally, we present the ability of GM-LAB as probiotics, in terms of bio preservation, food safety and food waste conversion into biofuel.

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

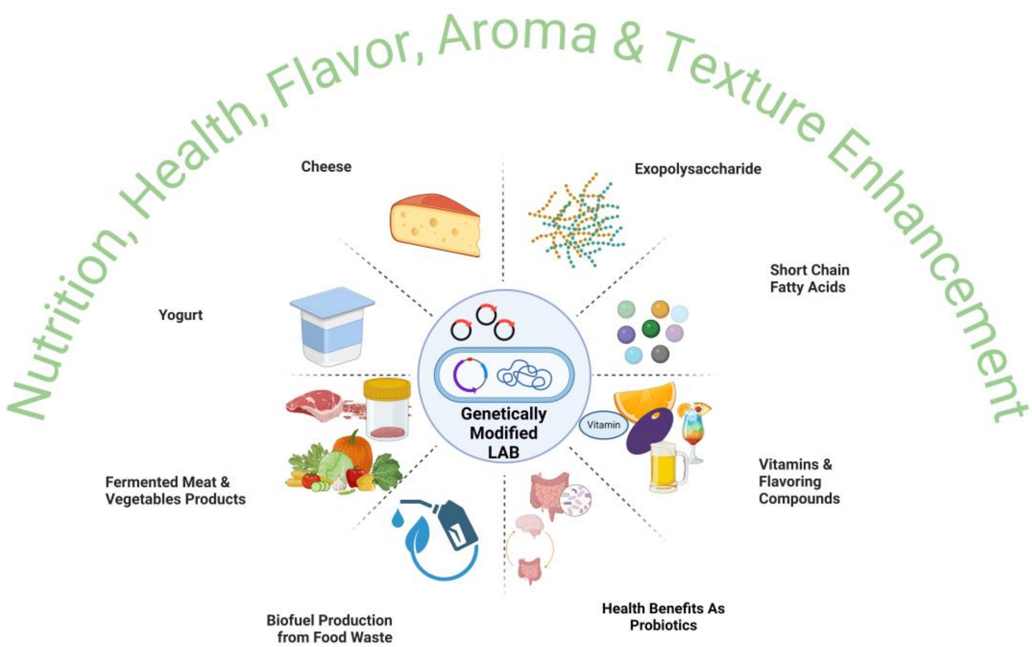

Figure 1: Graphical Abstract

Keywords: Food Microbiology, Lactic Acid Bacteria, Genetic Engineering, Fermentation, Dairy Products, Flavor, Nutrition

1.0. Introduction:

Lactic acid bacteria (LAB) are essential in fermented food products because of their unique flavors, textures, preservation, and nutritional enrichment [1]. LAB are divided into homofermentative and heterofermentative LAB, with homofermentative LAB producing lactic acid and heterofermentative LAB producing lactic acid, ethanol, and carbon dioxide. LAB belong to the phylum Firmicutes, class Bacilli, and order Latobacillales [2]. Homofermentative LAB, such as Lactobacillus and Streptococcus, produce lactic acid as the primary functional product, whereas heterofermentative LAB produce a combination of lactate, ethanol, and CO_2 in varying ratios. LAB are essential for creating and retaining flavor in fermented foods by creating an acidic environment that prevents spoilage microorganisms. Advances in genetic engineering have enabled the use of rDNA techniques to optimize LABs for better flavor profiles, environmental resilience, and increased production efficiency. LAB strains are crucial for the production of distinct foods, such as cheese, yogurt, and pickles[3].

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

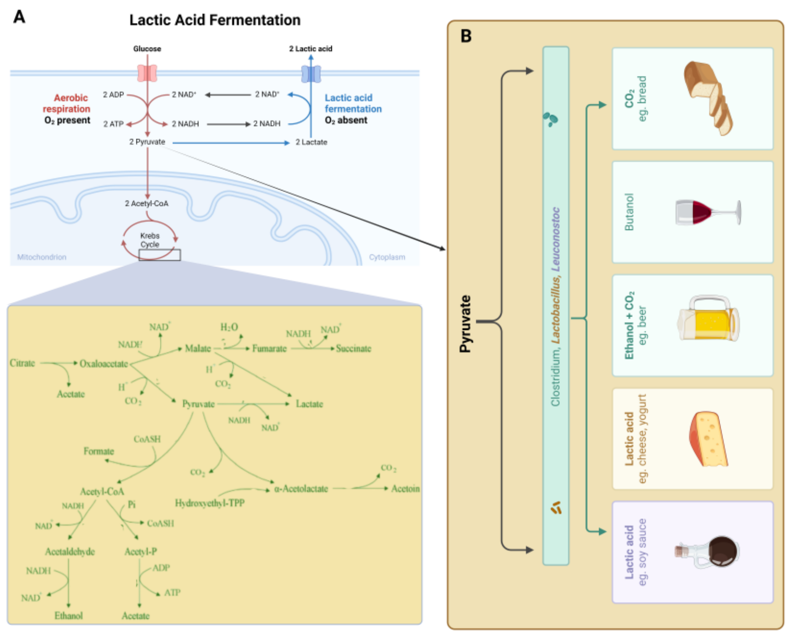

Figure 2: Metabolic Features of Lactic Acid Bacteria and Role in Various Food Products

2.0 *Fermented Food Products Of LAB:*

a) Lab Fermented Dairy Products:

LAB-fermented dairy products, including yogurt, cheeses, cultured cream, and koumiss, are made of lactic acid bacteria, which convert lactose to lactic acid. The process generates CO2, acetate, and other substances, giving the products distinctive freshness. The LAB used in kefir and koumiss also produce ethyl alcohol [4]. The origins of fermented milk can be traced back to the Near East and have gained popularity in Eastern and Central Europe. Nomads produce it accidentally by harmless, acidifying bacteria. Traditional dairy products such as Ergo and Garris are also produced by LAB [5], [6].

Cheese:

The USA and EU produce 70% of the world's cheese, with milk production expected to rise by 9% by 2027. Cheese consumption increased from 17 kg per person in 2010 to 18.44 kg per person in 2020. China and Egypt are expected to triple cheese imports by 2027, whereas the European Union has increased cheese exports. Gulf countries and African regions are projected to import 19% of global cheese by 2027 [7], [8]. Cheese production traditionally relies on calf rennet, an enzyme from the stomach lining of newborn calves. However, researchers have explored alternative, more sustainable sources of rennet, including R. miehei and lactic acid strains. Many microbes, including LAB strains, have been engineered with a heterologous rennet gene to increase cheese quality and product quality [3]. Cheese is a valuable food because of its easily digestible proteins, antioxidant properties, and rich source of fat-soluble vitamins such as riboflavin, niacin, folate, and vitamin B12. Ripened cheeses are high in minerals such as phosphorus and calcium, which can help lower blood pressure and promote fat excretion. Cheing also benefits lactose-intolerant individuals and reduces oxidative stress, contributing to only 5–8% of total sodium intake. For older adults without salt sensitivity, cheese consumption may

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

DIALOGUE SOCIAL SCIENCE REVIEW

Vol. 2 No. 4 (November) (2024)

lower cardiovascular risk [9], [10], [11]. An analysis of the safety features, technological-food traits, and production outcomes of cheese produced from lactic acid bacteria (LAB) strains exhibiting safe properties—such as a lack of gelatinase or hemolytic activities and pathogen inhibition—was published in November 2023 [12]. These isolates demonstrated significant casein breakdown, lipolytic activity, diacetyle concentration, and a high capacity for milk acidification. *L. paracasei CQ1* was the most notable strain in the cheese production test, exhibiting greater sensory attributes. LAB have been utilized for decades in the production of cheese, with LAB playing a pivotal role in determining the unique characteristics of the final product (Table).

Table 1: Various types of cheeses and involvement of different LAB in the production of cheese

Cheese Type	Lactic acid bacteria studied in cheese	Texture	Flavor Profile	Aging Time	Popular Varieties	References
Cheddar	Lacticaseibacillus paracasei,L. casei, L. paracasei, and L. rhamnosus	Firm, Crumbly	Sharp, Nutty	Varies (months)	Mild, Sharp, Extra Sharp	[13]
Brie	*L. paracasei* subsp. *paracasei*, *L. plantarum*, *L. acidophilus*, *L. delbrueckii* subsp. *bulgaricus*, and *L. casei*.	Soft, Creamy	Earthy, Mushroomy	Short (weeks)	Brie de Meaux, Brie de Melun	[14]
Parmesan	*Lactobacillus helveticus, Lactobacillus lactis, and Lactobacillus bulgaricus, Streptococcus thermophiles*	Hard, Granular	Nutty, Salty	Long (years)	Parmigiano-Reggiano, Grana Padano	[15]
Gouda	*Lactococcus and Leuconostoc*	Semi-Hard, Creamy	Mild, Nutty	Varies (months)	Aged Gouda, Smoked Gouda	[16]
Blue Cheese	*Lactobacillus plantarum*, *Lactococcus raffinolactis*, *Leuconostoc mesenteroides* subsp. *dextranicum*, *Enterococcus* spp., *Leuconostoc paramesenteroides*, *Lactobacillus casei*, and *Leuconostoc mesenteroides* subsp. *Mesenteroides*	Soft, Crumbly	Bold, Tangy	Varies (weeks-months)	Roquefort, Stilton, Gorgonzola	[17]
Swiss (Emmental)	*Streptococcus thermophilus*, *Lactobacillus helveticus*, and *Lactobacillus delbrueckii subsp. Bulgaricus*	Firm, Holey	Nutty, Sweet	Varies (months)	Emmental, Gruyère, Raclette	[18]

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Mozzarella	*Lb delbrueckii* ssp. *bulgaricus* (ATCC 11842), *Lactobacillus casei* ssp. *casei* (ATCC 393), *Lactobacillus acidophilus* (ATCC 4356), *Streptococcus salivarius* ssp. *thermophilus* (ATCC 19258), and *Lactobacillus delbrueckii* ssp. *lactis* (ATCC 12315)	Soft, Elastic	Mild, Milky	Fresh (days)	Fresh Mozzarella, Burrata	[19]
Camembert	*Lactococcus lactis* subsp. lactis, *Streptococcus thermophilus*, and *Lactococcus lactis* subsp. Cremoris	Soft, Creamy	Earthy, Buttery	Short (weeks)	Camembert de Normandie	[20]
Feta	*Lactobacillus paraplantarum*, *Lactobacillus delbrueckii*, *Lactobacillus rhamnosus*, *Pediococcus acidilactici*, *Lactobacillus curvatus*, *Lactobacillus paracasei*, *Lactobacillus coryniformis*, *Lactobacillus fermentum*, *Pediococcus parvulus*, and *Lactobacillus pentosus*	Crumbly, Creamy	Tangy, Salty	Fresh (weeks)	Traditional Feta, Bulgarian Feta	[21]
Provolone	*Streptococcus thermophilus,Lactobacillus rhamnosus,Lb. fermentum and Lb. delbrueckii*	Semi-Hard, Smooth	Mild, Smoky	Varies (months)	Mild Provolone, Aged Provolone	[22]

As the 20th century ended and by the start of the 21st century, various technological processes became available to speed up cheese ripening and enable controlled production. These processes include the use of microbial enzymes, genetically modified starter cultures, and 'omics strategies' [23]. For example, heat-treated attenuated *Lactobacillus helveticus* produced an enhanced enzyme called aminopeptidase, which produced bitter flavor characteristics in hard and semihard cheeses [24].

Lactic acid bacterial secondary metabolic compounds play important roles in cheese ripening, flavor, aroma, and texture. These compounds include lactose and lactate residues, citrate and its derivatives, lipolytic compounds, and proteolysis products [25]. These compounds are produced by genetically modified lactic acid bacteria, as discussed later.

The gene encoding glutamate dehydrogenase (gdh) from *Peptoniphilus asaccharolyticus* was expressed in *L. lactis* to produce α-ketoglutarate, as shown by Rijnen *et al.*, 2000. This transformation was found to enhance the process of cheese ripening[26]. Similarly, strains of *Lactobacillus helveticus* with high proteolytic activity, which produces the peptidase genes *Pep*N, *Pep*C, *Pep*X, and *Pep*I, are expressed in *L. lactis* DN209 to accelerate the cheese ripening process [27].

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

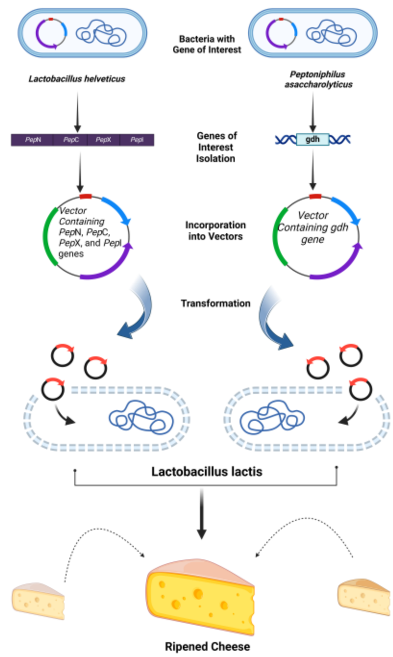

Figure 3:Heterologous gene expression: Recombinant L. lactis carrying peptidase genes from L. helveticus play a significant role in the proteolysis and ripening of cheese

Yogurt:

Yogurt, which has been a dietary staple for centuries, has become a preferred snack for kids globally. The characteristics of yogurt, including its viscosity, smoothness, thickness, and stress resistivity, make it a favorable candidate on the market. These characteristics are crucial not only for palatability but also for proven health benefits. Various methods have been employed to increase yogurt quality, such as the addition of fats, proteins, and sugars such as sucrose and fructose, as well as stabilizers such as pectin and gelatin. However, these approaches fall short of meeting consumer preferences for products with minimal food additives[28], [29], [30].

Exopolysaccharides (EPSs) produced by lactic acid bacteria (LAB) have attracted significant attention in the dairy fermentation industry and serve as agents for viscosity and texture improvement [31], [32]. EPSs derived from yogurt starter cultures can influence yogurt texture and enhance sensory aspects such as mouthfeel, shininess, cleanliness, ropiness, and creaminess. EPS-producing yogurt cultures have shown the potential to reduce syneresis, a prevalent issue in yogurt associated with substantial rearrangements within gel-like networks[30]. In addition to EPS, carbohydrates, lipid catabolic derivatives, pyruvate, amino acids, and proteins are other compounds that contribute to the flavoring texture of yogurt in many ways[33]. These compounds are produced at exponential rates in LAB strains via various rDNA processes. Indeed, *S. thermophilus* and *Lb. delbrueckii subsp. bulgaricus* [32]predominantly play a role in yogurt starter cultures. The finished texture and quality of yogurt are dependent on the ability of these bacteria to produce EPS, as shown by the studies of Han and colleagues[30]. In this study, *S. thermophilus* zlw TM11 and *Lactobacillus delbrueckii subsp. bulgaricus* 3 4.5 were shown to produce the highest EPS compared with the other strains.

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

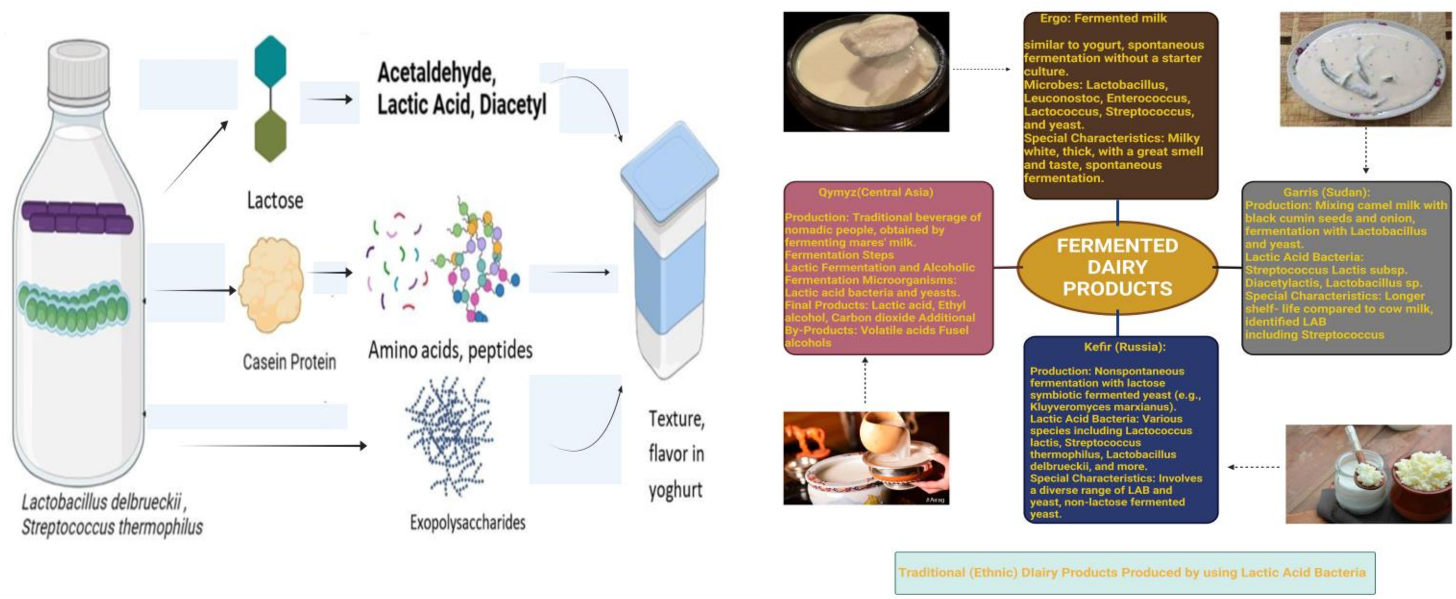

***Figure 4: (Left): Lactobacillus delbrueckii, particularly the subspecies Lactobacillus delbrueckii subsp. bulgaricus, is a crucial contributor to yogurt fermentation and is often the sole fermenting strain in some yogurt. At typical yogurt fermentation temperatures, it rapidly consumes lactose, converting it into lactic acid and producing key compounds that impart distinct flavors and aromas to yogurt. Streptococcus thermophilus, although a minor player on the grand scale, is essential for completing yogurt fermentation. It contributes to acidity and flavor compounds in yogurt, which support L. delbrueckii. Interestingly, genetic evidence suggests that S. thermophilus has evolved over the past 3,000 years, possibly from a previously pathogenic species, indicating its adaptation to the yogurt fermentation process. (Right): Different regional fermented dairy products produced or enhanced by lactic acid bacteria: Garris*[6], *Ergo*[34], *Kefir*[35] *and Qymyz* [36].**

b) Lab Fermented Vegetable and Fruit Products:

Fermented Pickles by Lactic Acid Bacteria

Lactic acid bacteria, such as Lactobacillus plantarum, Lactobacillus, and Lactobacillus, can ferment soluble nutrients in vegetables, resulting in unique flavorful pickles[37], [38]. These bacteria also produce lactobacillin and lactic acid, which contribute to the flavor and antimicrobial properties of pickles. Traditional pickles have been isolated from various bacteria, confirming their different flavoring and metabolic activities. In Chinese pickled mustard [39], these bacteria produce a product with higher lactic acid output, more flavoring compounds, a stronger scent, and superior sensory qualities [40], [41]. Sauerkraut, a popular Chinese cabbage product, is fermented via lactic acid bacteria to create distinct flavors[42]. This process is used to improve the quality and flavor of pickled sauerkraut [43]. Table olives, which are made from subtropical fruits, are fermented via lactic acid bacteria, with essential bacteria such as *Lactobacillus pentosus and Lactobacillus coryniformis* [41], [44]. Potherb mustard, a nutrient-dense crop in China, can be preserved via lactic acid

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

bacterial fermentation [45], [44]. Dry turnip fermentation uses hyperosmotic dehydration to inhibit spoilage germs and enhance flavor. Lactic acid bacteria are added to food to shorten fermentation times, prevent mixed bacterial development, and expedite a decrease in pH [41], [46]. Some strains, such as *Lactobacillus sakei*, have been genetically modified to produce bacteriocin and beta-glucuronidase, which can be useful in fermentation techniques [47]. Various fermented vegetable food products from different regions present unique flavors and health benefits. Khalpi from Nepal is a pickled cucumber snack fermented with lactic acid bacteria, providing a distinct taste. Brem from Bali, Indonesia, is a fermented glutinous rice product with sweet and sour notes that is believed to offer skin health benefits. Rusip from Indonesia involves fish fermentation, in which bacteria are utilized to prevent pathogenic growth and impart a sour taste. Korea's kimchi features Chinese cabbage and lactic acid bacteria, resulting in a diverse mix of flavors. Gochujang, also from Korea, is a fermented paste with chili powder, rice, and lactic acid bacteria, contributing to its unique taste. Gundruk from India is produced through vegetable fermentation, involving various bacteria and sun-drying for preservation [37]. Tempeh and Tofu are well-known examples of fermented soybean products from Indonesia and China, respectively, which are now consumed globally as meat alternative protein sources [48]. LAB produce different polyol and bioactive compounds during the fermentation of vegetable products, which can be enhanced in terms of production and secretion via various genetic modification mechanisms, as described later in this review.

Table 2: Different studies and metabolic engineering processes involved in the production of flavor compounds in LAB.

Metabolic Engineering Target	Genetic Modification Strategy	Improvement in Flavor,Texture	References
Acetaldehyde Production	Inactivation of *glyA* gene in *S. thermophilus* and overexpression in *Lc. Lactis*	80–90% increase in acetaldehyde production	[49], [50]
Acetaldehyde Production	Overexpression of pyruvate decarboxylase (pdc) and NADH oxidase gene (nox) in Lc. Lactis	Almost 50% of consumed glucose converted to acetaldehyde	[49]
Diacetyl Production	Overexpression of als or ilvBN genes and inactivation of ldh or aldB genes in Lc. Lactis	Limited effects due to central position of precursors	[51], [52], [53]
	Combined strategies, such as ldh inactivation with als gene overexpression	Production of high amounts of acetoin rather than diacetyl	[54]
	Random mutagenesis for mutants deficient in α-acetolactate decarboxylase and low lactate dehydrogenase activity in Lc. Lactis	Overproduction of diacetyl (maximum 0.6 mmol/L)	[[55]
	aldB deletion and increased expression of ilvBN in Lc. diacetylactis strain	Increase in diacetyl level to 0.53 mmol/L	[56]
	Overproduction of NADH oxidase	Change from homolactic to	[57]

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

	in Lc. Lactis	highly diacetyl-producing bacterium	
	Promoter engineering for fine-tuning lactate and diacetyl production in Lc. Lactis	NOX activity increased by 58.17-fold, diacetyl production reached 4.16 ± 0.06 mM	[58]
Ester Production	Cloning and overexpression of esterase gene in Lc. lactis with a nisin-controlled expression system	2–5-fold increase in ester yields compared with non-induced cells	[59], [60]

c) Fermented Meat Products:

The history of fermented meat products is vast, and microorganisms play a vital role in their creation. Lactic acid bacteria, especially Lactobacillus species, are crucial in determining the sensory characteristics of these products. *Lactobacillus plantarum, Lactobacillus sakei, Penicillium chrysogenum, Pediococcus lactis, Streptococcus thermophiles*, and other common strains are involved in the fermentation process[61].

Fermentation of meat products results in a vibrant red color due to nitroso-myoglobin development. Recombinant lactic acid bacteria contribute to a unique flavor by producing organic acids, eliminating raw material odors, and creating mild acidity. This process enhances nutritional value by breaking down proteins and producing essential amino acids and vitamins. Additionally, acid production extends shelf-life by inhibiting spoilage microorganisms, and some bacteria release bacteriocin, further preventing spoilage and pathogenic bacterial growth[1], [39], [61], [62].

Table 3: Genera of lactic acid bacteria in the main meat products and their process characteristics

Lactic Acid Bacterial Species	Fermented Meat Product	Particularities	References
L. curvatus 54M16, Pediococcus acidilactici, L. curvatus, Lcp. Plantarum	Various Meat products and Sausages	Antimicrobial effect against L. monocytogenes and B. cereus during sausage fermentation	[63], [64]
Lactic acid bacteria	Dry Fermented Sausages	Contributing to typical dry cured aroma, nitrite and nitrate influence aroma development	[64], [65]
Lactobacillus sake, L. campylobacter, L. plantarum	Fermented Sausage	Dominant LAB in fermented sausages, contribute to preservation, typical fermentation flavor, color, and unique flavor	[66]

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Lactobacillus spp., Enterococcus spp., Leuconostoc spp., Pediococcus spp.	Alheira	Portuguese sausage traditionally made with meats other than pork, such as chicken or game meat. It often includes bread, giving it a unique texture and flavor. The fermentation process in alheira involves the growth of lactic acid bacteria,	[67], [68]
Lactobacillus spp., Macrococcus spp., Enterobacteriaceae	Salchichon	Spanish dry-cured sausage often made from a mixture of pork meat and fat. Seasonings may include garlic, black pepper, and other spices. Fermentation along with subsequent drying and curing, contributes to the development of its flavor, texture, and preservation.	[69]
Lactobacillus spp., Staphylococcus spp.	Fuet	Catalan thin, cured, dry sausage. ,characteristic elongated, Seasoned with garlic and black pepper, giving it a distinctive flavor. It undergoes a drying and curing process, contributing to its firm texture. The sausage is typically fermented and air-dried at a low temperature for a specific duration.	[70]
Lactobacillus spp., Staphylococcus spp.	Chorizo	pork sausage originating from the Iberian Peninsula, seasoned with smoked paprika, garlic, and other spices, imparting a rich and spicy flavor. different varieties, The fermentation of chorizo involves the activity of lactic acid bacteria and coagulase-negative cocci.	[70], [71]
Lactobacillus spp., Staphylococcus spp., Macrococcus spp., Candida spp., Debaryomyces spp.	Salame friulano	meat is mixed with fat and other ingredients, such as salt, spices, nitrate and nitrite	[72], [73]
Latilactobacillus curvatus (formerly Lactobacillus curvatus) MBSa2, L. curvatus, L. sakei	Salami	Bacteriocin MBSa2 added during fermentation reduces Listeria contamination in salami, Main species involved in transformation, coagulase-negative cocci (Staphylococcus xylosus) present during fermentation and ripening	[63]
Pediococcus acidilactici, P. pentosaceus, P. cerevisiae, Lactobacillus	Fermented Ham	Main LAB in fermented ham, play a crucial role in ham fermentation, Pediococcus rapidly ferments glucose to produce lactic acid	[64], [71]

3.0 Metabolism Of Bioactive Compounds by GM-LAB:

a) SCFAs

The human body faces challenges in assimilating complex carbohydrate polymers directly. Polysaccharides, which are abundant in plant-based foods, must be broken down into monosaccharide or disaccharide subunits for absorption and utilization as a source of nutrition and energy [74]. In particular, nonstarch polysaccharides (NSPs) pose difficulties for humans, as they lack enzymes, notably β-glycosidases, which are capable of breaking specific linkages found in NSPs.

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Lactic acid bacteria (LAB) play a crucial role in addressing this limitation by contributing to the fermentation process, either through consuming fermented food products or engaging in catabolism within the gut [75]. NSPs serve as an energy source for LAB, transforming into beneficial derivatives that become valuable nutrition and diet sources for humans. Unlike human enzymes, LAB possess glycosidases, enabling them to target and breakdown NSP-specific bonds. The intricate structures of NSPs, with diverse sugar linkages, pose inefficiencies for human enzymes designed for starch digestion. However, the microbial community in the human gut, particularly lactic acid bacteria, facilitates NSP breakdown through fermentation, leading to the release of beneficial byproducts absorbed by the host. This symbiotic relationship highlights the importance of LAB in enhancing the accessibility of nutrition from complex carbohydrates in the human diet [76].
The fermentation of carbohydrates into short-chain fatty acids (SCFAs) by the gut microbiota, particularly LAB, is projected to provide 2–10% of the overall dietary energy in humans, while it accounts for 16% to over 80% of the overall dietary energy in various other mammals. In humans, SCFAs are expected to account for 60 to 70% of the energy requirements of the cryptic intestinal epithelium and up to 15% of the total energy requirements[77]. Food carbohydrates are utilized in fermentation by LAB into other useful food substances, including lactic acid, ethanol short-chain fatty acids (SCFAs), and exopolysaccharides, via the mechanisms discussed above.

Pyruvate is an essential component of the central carbon metabolism pathway and is necessary for the synthesis of several organic acids, including lactic acid. Increasing the expression of lactate dehydrogenase and controlling the metabolic flux of pyruvate are two methods for producing large amounts of lactic acid [1]. Creating a unique metabolic route in a nonnatural host by expressing numerous genes that produce enzymes relevant to the pathway is another strategy. Integrating a *Corynebacterium* glutamicum short-chain dehydrogenase-encoding gene, CGS9114_RS09725, into *Pediococcus acidilactici*, resulting in a genetically engineered strain with increased D-lactic acid production, illustrates how this method addresses difficulties in obtaining sufficient yields of the required metabolites. Another study by Cano and colleagues revealed that evolutionary engineering of *Lactobacillus pentosus* CECT4023T increased its ability to ferment xylose even at acidic pH values[78].

In 20 g L−1 xylose-containing medium, the strain known as MAX2 presented 1.5- to 2-fold moregreater xylose intake and 1.4-fold greater lactic acid production than did the original strain[79]. Furthermore, as reported by Singh *et al*. in a publication in *Lactobacillus lactis*, a small increase in lactic acid production was observed upon increasing the copy number of the lac operon containing the ldhL gene[80]. The a-Gal structural genes from guar and *Lactobacillus plantarum* ATCC8014 were cloned and expressed in *L. lactis*, which can breakdown nondigestible oligosaccharides (NDOs) and be used to investigate issues related to NDO [80]. Wang and colleagues recently reported the heterologous expression of β-glucosidase from the yak rumen into the *L. lactis* NZ9000 strain to hydrolyze complex carbohydrates. Many other genetic engineering studies in which various engineered LAB convert carbohydrates into lactic acid bacteria with greater efficiencies and rates have been published [81], [82].

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

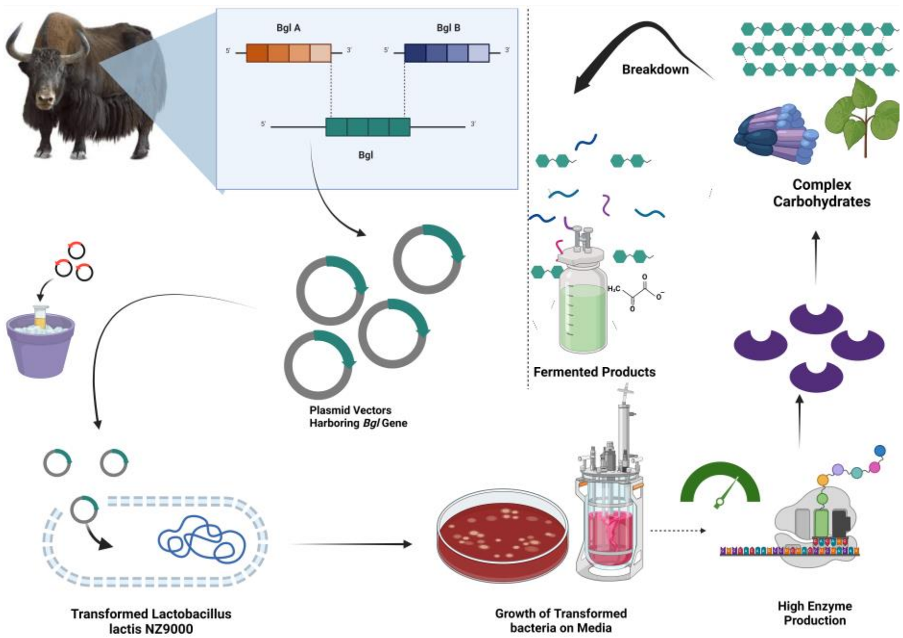

Figure 5: Engineering High-Efficiency β-Glucosidase in Lactic Acid Bacteria: Diagram depicting genetically modifying bacteria for increased β-glucosidase production. Two subunits (bglA and bglB) from the yak rumen are expressed independently and as fused proteins in Lactobacillus lactis NZ9000. The successful construction of engineered strains resulted in the secretory expression of BglA and BglB and the fusion of Bgl, which has distinct molecular weights. Compared with BglA and BglB, Bgl demonstrated significantly greater enzyme activity, particularly on various substrates, emphasizing its potential for efficient cellulose degradation. The optimal conditions for these recombinant enzymes were determined, with 1% salicin identified as the most suitable substrate

LABs produce short-chain fatty acids (SCFAs) from NSPs. Short-chain fatty acids (SCFAs) play crucial roles in promoting human well-being through various positive metabolic effects. These include maintaining gut integrity, lowering the luminal pH, inhibiting harmful bacteria, protecting intestinal epithelial cells, enhancing mineral absorption, providing energy to the intestinal mucosa, stimulating the immune system, reducing the risk of infectious intestinal diseases, and exerting anti-inflammatory and antitumorigenic effects[83]. Overall, SCFAs contribute to a range of health benefits that support overall metabolic health and immune function[84]. A study by Usta-Gorgun & Yilmaz-Ersan using *Bifidobacterium longum* subsp. *Infantis* DSM 20288, *Bifidobacterium animalis* subsp. *lactis* DSM 10140, *Bifidobacterium longum* subsp. *Longum* DSM 20219, and *Bifidobacterium bifidum* DSM 20239 demonstrated that *Bifidobacterium* species effectively utilized salep (glucomannan) and produced lactic, acetic, propionic, and butyric acid during fermentation. The growth of 1% (w/v) salep was comparable to that of 1% (w/v) glucose[84]. A study by Haokok *et al*. (2023) focused on enhancing the conversion of cellulose and xylan (sugarcane bagasse) lactic acid production. Simultaneous saccharification and fermentation (SSF) with newly isolated *Lactiplantibacillus plantarum* TSKKU P-8 (formyl *Lactobacillus plantarum*) and *Levilactobacillus brevis* CHKKU N-6 resulted in a lactic acid yield of 91.9 g/L, with a promising volumetric productivity of 0.85 g/(L·h)[85].

b) Vitamins:

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Vitamins play dual roles in lactic acid bacteria (LAB)-fermented food products, supporting both the microbial fermentation process and the nutritional value of the finished goods. LAB are known to synthesize specific vitamins and increase their bioavailability during fermentation. While most vitamins are produced by non-LAB through rDNA technology, genetic modification can also be used to increase vitamin production in LAB. For example, biotin production can be improved in *E. coli* by overexpressing the bioABFCD operon, and mutations in *S. marcescens* can yield more biotin. Improved riboflavin production can be achieved in *C. ammoniagenes* by cloning and overexpressing its gene, and a vitamin C gene from *Corynebacterium sp*. can be cloned and inserted into E. citreus. Additionally, mutant *Bacillus subtilis* can yield a high ratio of riboflavin. Studies such as [3], [86], [87], [88], [89] have provided successful examples of vitamin production through genetic modification. LAB can produce several B vitamins, including folate (B9), riboflavin (B2), pyridoxine (B6), niacin (B3), and cobalamin (B12), particularly in certain strains of *Bifidobacterium* and *Lactobacillus*. Among LAB, *Lactococcus lactis* has been the subject of most genetic and metabolic engineering research [48], [90].

Sybesma *et al*. discovered the folate-producing gene cluster and overexpressed some of its components in the LAB *Lactococcus lactis*. The overexpression of the extracellular folate gene folKE led to an almost tenfold increase in folate expression and an almost threefold increase in total folate production. Additionally, overexpressing endogenous folKE and folC, which encode FPGS, increased the retention of folate in the cell [91]. This extracellular and intracellular expression has potential for use in large-scale fermented foods. LAB are also important in the sense that many bacteria produce vitamins that the human body cannot naturally synthesize and needs to be acquired via food. LAB play important roles in this process and produce many vitamins that are not produced in the human body [92]. For example, folic acid is a water-soluble vitamin B that contains p-aminobenzoic acid and polyglutamic acid [93]. Coenzymes facilitate the one-carbon transferrin process of nucleotide and protein biosynthesis [94]. Humans do not have genes for precursor synthesis; thus, they rely on absorption from food or intestinal flora synthesis [95]. Strains capable of folic acid synthesis are primarily *Lactococcus, Streptococcus, and Lactobacillus* [96]. LAB follows folic acid synthesis pathways involving Pterin and pABA branches, necessitating their concurrent operation for synthesis. Lactobacillus strains, for example, require the addition of p-aminobenzoic acid (p-aminobenzoic acid (pABA)) to the culture medium to metabolize and produce folic acid. Lactic acid bacteria utilize diverse substrates, such as dairy products and cereals, for vitamin synthesis or conversion. For example, *Streptococcus thermophilus* ST-M6 and TH-4, with the addition of passion fruit byproduct and oligofructose to soy milk, exhibit folic acid production, where passion fruit byproduct acts as a growth factor stimulating folic acid synthesis in lactic acid bacteria [1], [97]. The table below presents examples of important vitamin synthesis through various recombinant techniques by LAB.

Table 4: Vitamin production by lactic acid bacteria via different mechanisms

Vitamin	LAB Bacteria Involved	Synthesis Mechanism	Reference
Folic Acid	*Streptococcus, Lactobacillus, Lactococcus*	Pterin and pABA branches functioning simultaneously	[98]

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Riboflavin	Various LAB, e.g., *Lactiplantibacillus plantarum, Lactococcus lactis* JC017, *L. lactis* subsp. *cremoris* strain NZ9000, *L. fermentum* MTCC8711,*L. mesenteroids*,*L. lactis*	Rib operon, Genetic Engineering for enhanced production, ribG,ribB,ribA,ribH for Riboflavin,engineering/exposure to purine/toxic riboflavin analogue	[99], [100], [101], [102]
Vitamin K2	*Lactococcus lactis* subsp. *cremoris* MG1363	Aerobic fermentation with fructose or trehalose as a carbon source	[103]
Vitamin B2, B3, B6	*Latilactobacillus sakei* UONUMA	Promotion in traditional Japanese beverage (koji amazake)	[104]
Cobalamin	*Limosilactobacillus reuteri* CRL 1098, *Lactobacillus coryniformis* CRL 1001	Well-known cobalamin producing strains	[105]

c) Exopolysaccharides:

Sutherland coined the term "exopolysaccharide (EPS)" to refer to the high-molecular-weight sugars that make up 40–95% of extracellular polymers and are released by bacteria [1]. EPSs can attach strongly to the cell wall to form capsules, or they can attach weakly to be released into the medium. These complex molecules, which can have branches or not, are made up of one or more monosaccharides, usually galactose, glucose, mannose, fucose, rhamnose, and arabinose, with the occasional addition of derivatives such as glucuronic acid and N-acetylgalactosamine. Notably, EPS producers include lactic acid bacteria (LAB), which create polymers with increased biological and physicochemical characteristics[106], [107]. Taste, water-holding capacity, rheological qualities, and microstructural stability are all improved by LAB-derived EPS or LAB-EPS. As a result, EPS work in the food industry as gelling agents, stabilizers, and emulsifiers[108]. Exopolysaccharides (EPSs), which are produced by LAB strains such as *Lactobacillus, Leuconostoc*, *Weissella*, and *Bifidobacterium*, can alter the gut microbiota and increase antioxidant activity. The homopolysaccharides (HoPS) and heteropolysaccharides (HePS) that make up EPS are responsible for the stability and texture of fermented foods[109]. The synthesis of EPS uses up to 70% of microbial energy and acts as a buffer against stress. The food and pharmaceutical sectors find LAB-derived EPS appealing because of its prebiotic, antioxidant, anti-inflammatory, and cholesterol-lowering characteristics. These characteristics are influenced by the molecular weight, glycosidic connections, and composition of EPS. Decreasing cholesterol, relieving inflammation, and improving gut health are some of the possible health advantages of EPSs produced from lactic acid bacteria (LAB) [110], [111], [112], [76].

The genetically manipulated processes reviewed by [113] for *L. lactis* described EPS biosynthesis, which involves a complex process orchestrated by a large operon, epsRXABCDEFGHIJKL, containing 14 genes located on a plasmid when overexpressed on the gene (edsD: responsible for the priming glycosyltransferase), increased EPS production from 113 to 133 mg/L, 343 mg/L enhancement by expressing the eps gene cluster and little to no effect on EPS production by changing the concentration of substrates such as Glu-6P, Glu-1P, UDP-glucose, and UDP-galactose.

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Table 5: Different studies on lactic acid bacterial strains in the production of EPS from various food sources

Bacterial Strain	Source of Presence	EPS Yield (g/L)	References
Leuconostoc mesenteroides/pseudomesenteroides	Fruit and vegetables traditionally fermented in Romania, green tomato, cauliflower, carrot	Evaluated at 15 g/L dextran with 14% α-(1 → 4) linkages	[114], [115]
Leuconostoc lactis	Isolated from Tunisian avocado	2.25g/L	[116]
Weissella cibaria	Isolated from cabbage, spontaneously fermented Malian sour milk, cassava	Up to 36 g/L consecutive α-(1 → 6) linkages and 3.4% of α-(1 → 3) linked branches	[117], [118]
Lactobacillus Species	Various sources including human intestinal microbiota	Less efficient; mainly HePS; varies with strain	[119]
***Lactobacillus plantarum Lb. plantarum* NTU 102 *Lb. plantarum* YO175 and OF101 ,NTMI05 and NTMI20**	isolated from Nigerian fermented food), strains from Turkish sourdough, strains from cow milk	Up to 20 g/L, 1.2 × 106 Da, 1153.8 µg/107 cells, 197 mg/L, 187 mg/L	[120], [121], [122]
***Lactobacillus fermentum* strains 139,263 & 296**	isolated from 'Almagro' eggplants,	47.4 mg/L, 55.1 mg/L, 55.6 mg/L, Up to 1 g/L	[123], [124], [125]
Lactobacillus rhamnosus 9595	fruit juice	2.7 g/L	[126]

d) Amino Acids & Biogenic Amines:

For the growth, reproduction, and maintenance of organisms, amino acids (AAs) are necessary. Although AAs are produced via the use of genetically modified microbes, a safer strain of amino acid producer suitable for food usage is needed. Owing to their ability to hydrolyze extracellular protein molecules into free amino acids (AAs), lactic acid bacteria (LAB) have the potential to produce AAs in a functional manner. A study by Toe and coauthors revealed that *Pediococcus pentosaceus* UP1 has a high ability to produce 15 different amino acids extracellularly [127].

Biogenic amines (B.A.) have gained attention because of their potential for flavoring and taste-producing substances in food, but their excess poses a real risk for many health-related issues [128]. LABs in fermented vegetable products are

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

major producers of amines. Lactic acid fermentation, a traditional technique of sauerkraut preservation, involves bacteria such as yeasts. mesenteroides, Lactobacillus sp., and P. cerevisiae. According to Kalac *et al.*, the mean amounts of putrescine, cadaverine, and tyramine in sauerkraut are 50 mg/kg, 146 mg/kg, and 174 mg/kg, respectively [129]. In addition, German pasteurized and bottled sauerkraut juices presented significant putrescine concentrations—up to 694 mg/dm3. To control B.A. levels in sauerkraut production, certain requirements must be met [130].

Genetic studies have revealed the presence of decarboxylating enzymes or pathways implicated in BA biosynthesis in LAB genera, including *lactobacilli*, *enterococci, lactococci, pediococci, streptococci, and leuconostocs*, which are associated with high levels of BAs [128], [131].

Enterococcus, despite its controversial safety status, is commonly found in various fermented foods, such as cheeses, dry sausages, fish, and wines. Certain strains of Enterococcus, specifically *E. faecium* and *E. faecalis*, have been investigated for their ability to produce BAs, particularly tyramine [132], [133], [134].

[135], [136]and [137] presented another approach for controlling the upregulated and underregulated transcription of tyramine genes in the presence of NaCl. *L. curvatus, Lactobacillus parabuchneri, Lactobacillus plantarum, L. brevis, and L. buchneri* have been studied for their involvement in the production of histamine [138], [139]. Several authors have isolated tyramine-producing strains of *Lactobacillus brevis* from cheeses, indicating that this property is strain-level and may have been acquired horizontally [140], [141]. The strain *S. thermophilus* NCFB2392 has been demonstrated to have decarboxylative ability in lysine decarboxylase broth, resulting in the accumulation of putrescine, cadaverine, and agmatine [142].

Amino acids contribute to the overall flavor of fermented foods and pharmaceutical needs across the globe, from minimum requirements to large-scale production. To meet these requirements, various genetic manipulations have been performed on LAB[143]. Upto 30-fold increased the secretion of essential amino acids due to mutations in genes for polypeptide breakdown and accumulation in *Lactococcus lactis* IPLA838 [144]. Researchers have also produced biosensor systems for controlled production and improved the secretion of amino acids. A study by [127] demonstrated that a specific strain of *Pediococcus pentosaceus* had the greatest ability to produce extracellular amino acids among 15 different LAB, indicating its potential for use in genetic engineering techniques to improve other strains.

e) Flavoring & Aroma Compounds:

To put the urge of taste and flavor in a philosophical concept, taste is a sensory symphony that unfolds within us, weaving together the threads of sweetness, bitterness, sourness, saltiness, and umami. It is a dance of molecules on our taste buds, an orchestra of sensations that transcends mere sustenance. Flavor, the nuanced sibling of taste, introduces itself through aromas, textures, and the lingering echoes of each bite.

The distinct taste, aroma, and sensory qualities of fermented foods are attributed mainly to flavoring chemicals. The metabolic processes of lactic acid bacteria convert raw ingredients into a variety of tasty chemicals during fermentation. The flavors of fermented foods vary greatly, ranging from sour and tangy to savory and umami, depending on the specific fermentation conditions and microorganisms involved [145]. As discussed earlier, LAB produce different compounds that impart special flavors and aromas to fermented food products. There are four commonly described methods (biosynthetic, enzymatic, aerobic degradation, and pyrolysis) for producing flavoring substances, but most flavor substances are metabolic derivatives of citric acid and amino acids produced during fermentation by lactic acid bacteria[1], [146].

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Lactic acid bacteria can produce various compounds by metabolizing citric acid, which is transported to the cell by membrane-associated permeases such as the 2-hydroxycarboxylate transporter. Citric acid is converted to acetate and oxaloacetate, followed by pyruvate and carbon dioxide. Pyruvate metabolism produces lactate, formate, acetate, ethanol, and aromatic molecules such as diacetyl, acetoin, and butanediol. Succinic acid can be produced by certain bacterial strains that use the citrate transporter, but they are unable to convert citric acid to pyruvate [1].

There are various pathways to produce acetaldehyde, including the use of deoxynucleic acid aldolase, the conversion of amino acids into pyruvate, or the process starting with acetaldehyde itself. *Streptococcus thermophilus*, a bacterium used in yogurt-making, has serine hydroxy methyltransferase with threonine aldolase activity that converts threonine into acetaldehyde and glycine [147].

Furthermore, in certain steps of sugar catabolism, LAB can produce sugar alcohols. Polyols, another name for sugar alcohols, are useful as stabilizers, thickeners, and softeners. Leuconostoc and *Levilactobacillus brevis* are LAB that can directly convert fructose to mannitol. Mannitol can be added to meals as a sweetener and has a number of health benefits, as described by [148]. Under specific growth circumstances, several heterofermentative lactic acid bacteria, including *Fructilactobacillus sanfranciscensis, Leuconostoc mesenteroides*, and *Oenococcus oeni*, can produce erythritol, which has a sweetener effect on fermented food [149]. In the production of branched and aromatic amino acids, 2,3-butanedione and 2,3-pentanedione, which are produced via the metabolic activity of Streptococcus thermophilus and *Lactobacillus casei*, are other flavoring additives in fermented food [150], [151].

Recent advancements have focused on reengineering EPS biosynthetic pathways to produce hyaluronic acid, a polysaccharide used in pharmaceuticals and foods. The recombinant expression of the *Streptococcus equi subsp. zooepidemicus* HA synthase gene in *L. lactis* led to 0.08 g/L HA production, and coexpression with UDP-GlcDH significantly increased HA production to 0.65 g/L. Prasad *et al.* achieved 1.8 g/L HA in a bioreactor experiment, highlighting the potential of *L. lactis* as a robust platform for functional polysaccharide production. These results highlight the potential of *L. lactis* as a robust platform for the production of functional polysaccharides[113], [152], [153].

Sorbitol produced by genetically modified LAB via various mechanisms has been reported. By taking advantage of the reversibility of sorbitol 6-P dehydrogenase (S6PDH), we were able to reverse the sorbitol catabolic pathway in *L. casei and L. plantarum*. This enzyme increases the synthesis of sorbitol by converting it from sorbitol 6-P to fructose 6-P. The gutF gene has been inserted into the chromosomal lactose operon of the *L. casei* BL232 strain by genetic modification to produce lactose-inducible S6PDH activity, resulting in a 4.3% conversion rate. Other mechanisms, such as LDH and mtlD gene inactivation and plasmid-mediated S6PDH overexpression in LDH-deficient LAB, have been described in the literature for sorbitol production [149], [154].

Table 6: Fermented food substances and specific flavor-imparting compounds produced by lactic acid bacteria.

LAB Strain	Fermented Food	Flavor and Aroma Compounds	References
Lacticaseibacillus paracasei 4341	Italian long ripened cheeses	Aroma and sour substances	[155]
Limosilactobacillus reuteri INIA P572	Cheese	Enhanced formation of 12 volatile compounds, reduction of 5 other volatile compounds	[156]
Lactobacillus	Stilton cheese	High concentrations of alcohol,	[157]

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

		organic acids, and acetone	
Lacticaseibacillus paracasei strains	Cheese	Sulfuric flavor from cysteine and methionine metabolism	[158]
Lactiplantibacillus plantarum, Lactiplantibacillus plantarum, Furfurilactobacillus rossiae, Lacticaseibacillus casei	Sourdough	Compounds related to sour aromas of bread	[159]
Lactiplantibacillus plantarum	Sourdough	Promotion of C4-C6 alcohol production	[160]
Oenococcus oeni and Lactobacillus	Wine	Malic acid-lactic acid fermentation, impact on ester production	[161]
Lentilactobacillus buchneri, Limosilactobacillus reuteri, Limosilactobacillus fermentum, Levilactobacillus brevis	Zhenjiang aromatic vinegar	Conversion of 2-acetolactate into acetoin, formation of flavor substances	[162]

f) Food Safety & Shelf Life:

A report by the CAST (Council for Agricultural Science and Technology) indicated that the number of foodborne/food-associated disease cases in humans is between 6.5 and 33 M, which is almost twice the number of cancer diagnoses annually reported by the CDC [163]. Animal-based foods are particularly perishable because of their neutral pH, high nutritional content, and moisture content. To maintain food safety and quality, proper processing is necessary [164]. As consumers prefer chemical preservatives less, the use of biological preservatives is increasing. LAB have been suggested as an alternative to traditional chemical preservatives since lactic acid bacteria are considered safe and healthy, and their use results in a clean label [165].

Lactic acid bacteria (LAB) and significant metabolites produced by LAB, such as reuterin, bacteriocins, diacetyl, reutericyclin, organic acids, acetoin, and hydrogen peroxide, are found naturally in many fermented foods, making LAB essential and natural bio preservative [166]. LAB prevent the growth of some foodborne pathogens and spoilage germs. Bacteriocins, a broad range of ribosomal synthesized antimicrobial peptides, are capable of eliminating closely related bacterial strains and help suppress harmful bacteria in various food matrices, such as cheese, meat, and vegetables [167], [168].

Even the most notorious and persistent foodborne pathogens, such as *L. monocytogenes*, *M. luteus*, and S. typhimurium, have been proven to be inhibited by the novel bacteriocin *Lacticaseibacillus paracasei* ZFM54, which exhibits wide-spectrum inhibitory action by forming pores in the cell wall [168].

Table 7: Different antimicrobial compounds useful in biopreservation and food safety

Antimicrobial compounds	LAB Strains	References
Reuterin	*Limosilactobacillus reuteri*	[169]
Gassericin	*Lactobacillus gasseri*	[170]
Enterocin	*Enteroccocus spp.*	[171]
Succinic acid	*Lactococcus lactis subsp. Lactis*	[172], [173]
Butyric Acid	*Lactobacillusacidophilus*	[174]

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

Hydrogen Peroxide	*Lactobacillus johnsonii*	[175]

Biofilms produced by LAB play a role in food safety by inhibiting notorious pathogenic microbes. For example, [176] transformed *Lactobacillus plantarum* PA21 with the *gfp* gene via a plasmid vector called pMG36e, which contains the same gene, resulting in the formation of strong biofilms. Biofilms have been demonstrated to have inhibitory effects on pathogenic and food spoilage bacteria. The *gfp* gene has been expressed in *Bacillus subtilis* via recombinant engineering, making it a biosensor for detecting increased quantities of arsenic pollution. Lactic acid bacteria also have the ability to express green fluorescent protein (GFP), so they can act as potential biosensors for determining pollution and toxins in the food industry[177].

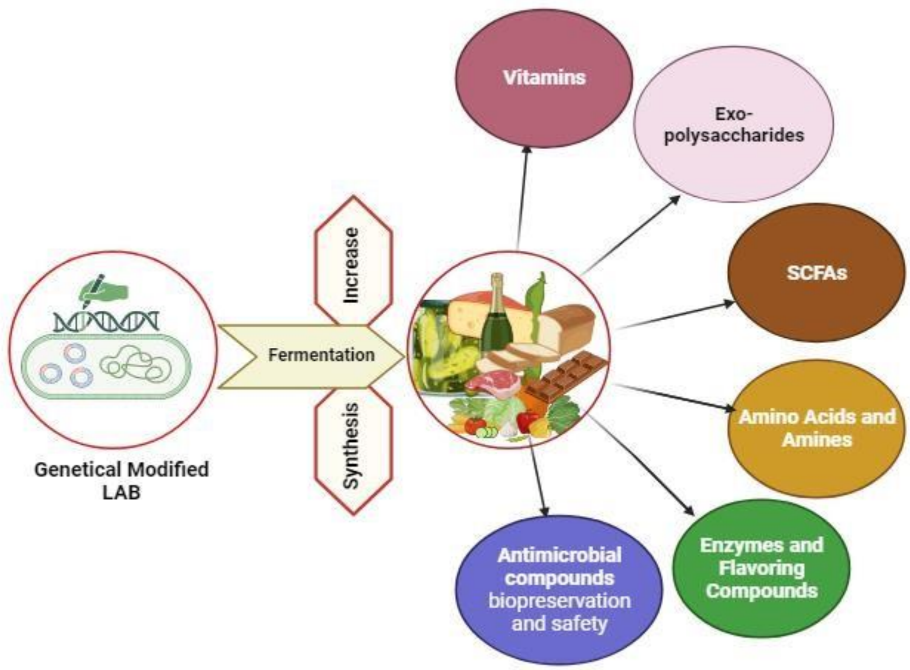

Figure 6: Nutritional enhancing compounds

4.0 Tackling Food Waste; Turning Food Waste into Biofuel:

According to weforum.org, approximately 931 M tons of food waste are produced each year globally, of which 61% comes from households, 26% from food services and 13% from industries and retail. These millions of tons of wasted food, if not

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

swiftly and properly treated, can cause health issues and pollute the air, water, and land. Total solid waste includes protein, fat, carbohydrate and other products in scale-able ranges[178].

a) Lactate Production

The study by L. Song, Liu, *et al*., 2022 aimed to investigate the direct production of lactic acid (LA) from household food waste (HFW) in Shanghai via lactic acid bacteria (LAB) without the need for saccharification. Researchers have evaluated several LAB strains, including *Lactobacillus rhamnosus* ATCC 7469, *Lactobacillus delbrueckii subsp. bulgaricus*, and *Streptococcus thermophilus*, to determine their ability to produce LA. The ideal conditions for achieving a concentration of LA (30.25 g/L) were 37 °C and pH 6.8, and sterile HFW and *Lactobacillus rhamnosus* ATCC 7469 were used. The study revealed a positive correlation between the substrate concentration and LA generation, and a high inoculum size and concentration resulted in a relatively high LA concentration. After 32 days of repeated batch fermentation, the average LA concentration was 26.8 g/L, and the LA output was 0.20 g/g TCOD[179].

The primary product produced by *L. lactis* is L-lactate, which can reach up to 100 g/L in a medium that contains whole wheat flour hydrolysate. Research indicates that certain *L. lactis* strains, which can metabolize both pentoses and hexoses, have the potential to use less expensive substrates, such as lignocellulose hydrolysates, as feedstocks[180].

b) Ethanol Production

Ethanol is produced from food waste with *Lb. plantarum* at room temperature, with a concentration of ethanol of up to 45 grams per liter, as reported previously [181]. To reduce pathogenic development and stop compositional changes, storing or processing the food waste that has been collected in an energy-intensive manner may be necessary. Knocking out genes for LDH enzymes and inserting Adh or PDC in lactic acid homofermentative bacteria is a simple way to efficiently produce ethanol from various food waste substances[113]. *L. lactis* has also been engineered for ethanol production as a biofuel using renewable feedstocks [182].

Recent genetic engineering efforts have led to the successful construction of a recombinant *L. lactis* capable of producing ethanol as the sole fermentation product, despite limited success. This involved removing several genes encoding lactate dehydrogenase (LDH) homologs and heterologously expressing codon-optimized pyruvate decarboxylase/alcohol dehydrogenase (PDC/AdhB) from *Z. mobilis*. The engineered strain was cultivated in a cost-effective medium containing whey waste, resulting in efficient and inexpensive ethanol production [183].

c) Butanol Isomers

Efforts to engineer *L. lactis* for butanol production involved the introduction of key enzymes from *Clostridium beijerinckii* through insertion. However, the low titer achieved suggested challenges in commercial production, possibly due to insufficient availability of acetyl-CoA, a precursor for butanol. This problem can be overcome by increasing the supply of acetyl-CoA via the introduction of a robust pyruvate dehydrogenase complex, which appears crucial for improving butanol production in *L. lactis*[197]. *Lactobacillus brevis* has been engineered with the *crt, bcd-etf and hbd* genes to express the clostridial CoA-driven pathway to produce 1-butanol [184].

d) 2,3-Butanediol Isomers

L. lactis and other strains have been studied for their ability to produce 2,3-butanediol (2,3-BDO), which is a biofuel and platform chemical. Studies have shown that glucose flux can be redirected to 2,3-BDO production by overexpressing native α-acetolactate synthase (Als) and acetoin reductase (ButA) in an LDH-deficient strain. Various genetic engineering and optimization strategies and fermentation conditions have been used to achieve high-titer and high-yield production of different 2,3-BDO isomers (meso-2,3-BDO, (R, R)-2,3-BDO, and (S, S)-2,3-BDO) in recombinant *L. lactis* strains. These findings highlight the potential of *L. lactis* as an efficient cell factory for synthesizing biochemicals and biofuels [185], [186].

5.0 LAB Do More Than Just Lactic Acid Production:

Lactic acid bacteria have been used for the production of alternative plant-based proteins. *L. lactis* has been successfully engineered as a cell factory for the production of plant proteins and bioactive compounds. For example, the expression of coumarate CoA ligase (4CL) and a sweet-tasting protein from *Arabidopsis thaliana* and *Pentadiplandra brazzeana*, respectively, marked the first successful expression of a functional plant protein in *L. lactis*. This breakthrough in plant protein expression paved the way for metabolic engineering, leading to the production of industrially applicable secondary metabolites[187]. A study by Hernández *et al*. (2007) reported the successful expression of alcohol acyltransferase (SAAT) and linalool/nerolidol synthase (FaNES) in strawberry by *L. lactis*, resulting in the production of linalool, a flavoring and scent compound used in various essential oils containing cosmetics and fragrances. The research group also successfully expressed two plant terpene synthases from orchid and kesum (Persicaria minor) in *L. lactis*, producing the natural antimicrobial substances germacrene D and β-sesquiphellandrene, respectively [188]. In addition, several studies have investigated the production of plant-based dairy and meat products with high nutritional and protein values via lactic acid bacteria [78], [189], [190], [191], [192].

Extensive research on genetically modified lactic acid bacteria and their metabolic engineering has been carried out to improve their probiotic characteristics for various conditions, such as treating diseases, including cancers, vaccine delivery and therapeutics, nutritional benefits, antioxidant properties, and immunity [193], [194], [195], [196], [197], [198], [199], [200], [201], [202]. The probiotic LAB in the gut can modulate the human brain and play an emerging role in behavior and mental health [203], [204], [205], [206]. Additionally, lactic acid bacteria have been engineered for the production of sweeteners such as mannitol, xylitol and sorbitol, which are also important in cheese flavoring and nonfood flavoring metabolites[207].

Strategies such as the use of LDH-deficient strains to increase the production of α-acetolactate and other fermentation products have been employed. The manipulation of the NADH:NAD+ co-factor ratio also influences fermentation patterns, which can shift from homolactic fermentation to mixed-acid fermentation. By adjusting the conditions, a significant portion of fermentation products can be rerouted through the LDH pathway [188], [188], [207]. Metabolic engineering in *L. lactis* has focused on customizing fermentation products by redirecting lactate–pyruvate metabolism, resulting in the production of flavor compounds[208], such as diacetyl and acetoin, which are mentioned somewhere in this article. Additionally, NSP-based edible films and coatings have gained commercial attention as green alternatives for storing, shipping, and packaging food products because of their compatibility with various food products. These compounds and substances are produced by lactic acid bacteria during various fermentative processes and are synthesized for this purpose [209], [210]. These edible coatings also act as carriers of probiotics in food products[211], [212].

6.0 Outlook and Future Perspectives:

Owing to the development of genetic tools such as CRISPR-Cas9 and the discovery of new recombinase and CRISPR systems in LAB species, recombinant lactic acid bacteria (LAB) have a bright future. These developments are anticipated to expand the potential uses of LAB in probiotics, food additives, and therapeutics. Greater regulatory approval and the

Dialogue Social Science Review (DSSR)
www.journalforeducationalresearch.online

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

search for new LAB species will support the expansion of the application of LAB across a range of industries, guaranteeing that the advantages of LAB will be sustained in the creation of cutting-edge goods for the health and welfare of people[213]. Genetic engineering (GE) has demonstrated that altered microbes are more resistant to fermentation conditions. This is accomplished by giving the microbial genome a thermoresistant gene, which makes it resistant to the high temperatures observed in fermenters. This makes it possible to produce stable, swiftly proliferating clones of particular microorganisms, lactic acid bacteria in particular. GM LAB have been utilized extensively in fermentation applications and are preferred over native microflora[3], [213].

To increase productivity, metabolic engineering modifies enzymatic cell functions, concentrating on chemical transformation, supramolecular assembly, and energy transfer. Owing to the use of recombinant DNA technology, cells can contain additional or different genes[3]. The main goals of fermentation are to increase yield, expedite processes, save energy, prevent byproducts, and develop resistant strains. In fermenters, microbes are essential for the production of desired foods or chemicals under carefully regulated circumstances. The final products are purified through downstream procedures after fermentation[214], [215]. Owing to legislative limitations and low consumer acceptance, the safety of genetically modified lactic acid bacteria (GM-LAB) poses a serious challenge, especially in the European Union. Prioritizing biocontainment techniques can help achieve regulatory acceptability and overcome these challenges. By reducing the possible hazards connected to GM-LAB, these tactics seek to guarantee their safe and controlled use. One potential answer to these problems is the implementation of efficient biocontainment methods, which will open the door for the responsible and sustainable application of GM-LAB. Thus, resolving these issues is essential for gaining broad acceptance and guaranteeing the safety of GM-LAB[216].

7.0 Conclusion:

The use of lactic acid bacteria (LAB) as cell factories for the synthesis of different food products, nutritive-health-promoting values, bioactive substances, biopreservatives, and even for the management of food waste for the creation of biofuel has been widespread. LAB have shown novel functions through genetic engineering, metabolic engineering, and other technologies, resulting in more productive processes and increased yields. LAB have the potential to be a flexible and sustainable platform for the synthesis of a large variety of useful compounds, which makes them viable substitutes for a number of industrial uses. It is anticipated that ongoing developments in metabolic and genetic engineering will further improve LAB capabilities and open the door to a wider range of applications in the synthesis of useful compounds and other biologically active substances.

References:

[1] Y. Wang *et al.*, “Metabolism Characteristics of Lactic Acid Bacteria and the Expanding Applications in Food Industry,” *Front. Bioeng. Biotechnol.*, vol. 9, p. 612285, May 2021, doi: 10.3389/fbioe.2021.612285.

[2] E. J. Quinto, P. Jiménez, I. Caro, J. Tejero, J. Mateo, and T. Girbés, “Probiotic Lactic Acid Bacteria: A Review,” *FNS*, vol. 05, no. 18, pp. 1765–1775, 2014, doi: 10.4236/fns.2014.518190.

[3] N. Mallikarjuna and K. Yellamma, “Genetic and Metabolic Engineering of Microorganisms for the Production of Various Food Products,” in *Recent Developments in Applied Microbiology and Biochemistry*, Elsevier, 2019, pp. 167–182. doi: 10.1016/B978-0-12-816328-3.00013-1.

[4] V. Castellone, E. Bancalari, J. Rubert, M. Gatti, E. Neviani, and B. Bottari, “Eating Fermented: Health Benefits of LAB-Fermented Foods,” *Foods*, vol. 10, no. 11, p. 2639, Oct. 2021, doi: 10.3390/foods10112639.

[5] K. J. Heller, “Probiotic bacteria in fermented foods: product characteristics and starter organisms,” *The American Journal of Clinical Nutrition*, vol. 73, no. 2, pp. 374s–379s, Feb. 2001, doi: 10.1093/ajcn/73.2.374s.

[6] Y. B. Soemarie, T. Milanda, and M. I. Barliana, “Fermented Foods as Probiotics: A Review,” *J Adv Pharm Technol Res*, vol. 12, no. 4, pp. 335–339, 2021, doi: 10.4103/japtr.japtr_116_21.

[7] F. Canellada, A. Laca, A. Laca, and M. Díaz, “Environmental impact of cheese production: A case study of a small-scale factory in southern Europe and global overview of carbon footprint,” *Science of The Total Environment*, vol. 635, pp. 167–177, Sep. 2018, doi: 10.1016/j.scitotenv.2018.04.045.

[8] A. I. Nájera, S. Nieto, L. J. R. Barron, and M. Albisu, “A Review of the Preservation of Hard and Semi-Hard Cheeses: Quality and Safety,” *Int J Environ Res Public Health*, vol. 18, no. 18, p. 9789, Sep. 2021, doi: 10.3390/ijerph18189789.

[9] B. K. Alba, A. E. Stanhewicz, P. Dey, R. S. Bruno, W. L. Kenney, and L. M. Alexander, “Controlled Feeding of an 8-d, High-Dairy Cheese Diet Prevents Sodium-Induced Endothelial Dysfunction in the Cutaneous Microcirculation of Healthy, Older Adults through Reductions in Superoxide,” *The Journal of Nutrition*, vol. 150, no. 1, pp. 55–63, Jan. 2020, doi: 10.1093/jn/nxz205.

[10] H. Zheng *et al.*, “Metabolomics Investigation To Shed Light on Cheese as a Possible Piece in the French Paradox Puzzle,” *J. Agric. Food Chem.*, vol. 63, no. 10, pp. 2830–2839, Mar. 2015, doi: 10.1021/jf505878a.

[11] I. López-Expósito, L. Amigo, and I. Recio, “A mini-review on health and nutritional aspects of cheese with a focus on bioactive peptides,” *Dairy Sci. & Technol.*, vol. 92, no. 5, pp. 419–438, Sep. 2012, doi: 10.1007/s13594-012-0066-5.

[12] J. Valdiviezo-Marcelo *et al.*, “Technological potential of native lactic acid bacteria isolated from Swiss-type artisanal cheese (Ancash, Peru) for their application in food,” *Front. Sustain. Food Syst.*, vol. 7, p. 1212229, Nov. 2023, doi: 10.3389/fsufs.2023.1212229.

[13] S. S. Shah *et al.*, “Properties of an acid-tolerant, persistent Cheddar cheese isolate, Lacticaseibacillus paracasei GCRL163,” *J Ind Microbiol Biotechnol*, vol. 48, no. 9–10, p. kuab070, Dec. 2021, doi: 10.1093/jimb/kuab070.

[14] R. Unno *et al.*, “Lactic acid bacterial diversity in Brie cheese focusing on salt concentration and pH of isolation medium and characterisation of halophilic and alkaliphilic lactic acid bacterial isolates,” *International Dairy Journal*, vol. 109, p. 104757, Oct. 2020, doi: 10.1016/j.idairyj.2020.104757.

[15] J. M. Kongo and F. X. Malcata, “Cheese: Types of Cheeses – Hard,” in *Encyclopedia of Food and Health*, Elsevier, 2016, pp. 763–767. doi: 10.1016/B978-0-12-384947-2.00134-3.

[16] W. Park, J. Yoo, S. Oh, J.-S. Ham, S.-G. Jeong, and Y. Kim, “Microbiological Characteristics of Gouda Cheese Manufactured with Pasteurized and Raw Milk during Ripening Using Next Generation Sequencing,” *Food Sci Anim Resour*, vol. 39, no. 4, pp. 585–600, Aug. 2019, doi: 10.5851/kosfa.2019.e49.

[17] T. M. López-Dı´az, C. Alonso, C. Román, M. L. Garcı´a-López, and B. Moreno, “Lactic acid bacteria isolated from a hand-made blue cheese,” *Food Microbiology*, vol. 17, no. 1, pp. 23–32, Feb. 2000, doi: 10.1006/fmic.1999.0289.

[18] M. C. Coelho, F. X. Malcata, and C. C. G. Silva, “Lactic Acid Bacteria in Raw-Milk Cheeses: From Starter Cultures to Probiotic Functions,” *Foods*, vol. 11, no. 15, p. 2276, Jul. 2022, doi: 10.3390/foods11152276.

[19] F. Losito, A. Arienzo, G. Bottini, F. R. Priolisi, A. Mari, and G. Antonini, “Microbiological safety and quality of Mozzarella cheese assessed by the microbiological survey method,” *Journal of Dairy Science*, vol. 97, no. 1, pp. 46–55, Jan. 2014, doi: 10.3168/jds.2013-7026.

[20] J. Mei, Q. Guo, Y. Wu, and Y. Li, “Microbial diversity of a Camembert-type cheese using freeze-dried Tibetan kefir coculture as starter culture by culture-dependent and culture-independent methods,” *PLoS One*, vol. 9, no. 10, p. e111648, 2014, doi: 10.1371/journal.pone.0111648.

[21] A. Tzora *et al.*, “Microbiota ‘Fingerprint’ of Greek Feta Cheese through Ripening,” *Applied Sciences*, vol. 11, no. 12, p. 5631, Jun. 2021, doi: 10.3390/app11125631.

[22] M. Aponte, V. Fusco, R. Andolfi, and S. Coppola, “Lactic acid bacteria occurring during manufacture and ripening of Provolone del Monaco cheese: Detection by different analytical approaches,” *International Dairy Journal*, vol. 18, no. 4, pp. 403–413, Apr. 2008, doi: 10.1016/j.idairyj.2007.10.011.

[23] B. A. Law, “Controlled and accelerated cheese ripening: the research base for new technology,” *International Dairy Journal*, vol. 11, no. 4–7, pp. 383–398, Jul. 2001, doi: 10.1016/S0958-6946(01)00067-X.

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

[24] J. A. Centeno and J. Carballo, “Current Advances in Cheese Microbiology,” *Foods*, vol. 12, no. 13, p. 2577, Jul. 2023, doi: 10.3390/foods12132577.
[25] X. Zheng, X. Shi, and B. Wang, “A Review on the General Cheese Processing Technology, Flavor Biochemical Pathways and the Influence of Yeasts in Cheese,” *Front Microbiol*, vol. 12, p. 703284, 2021, doi: 10.3389/fmicb.2021.703284.
[26] L. Rijnen, P. Courtin, J. C. Gripon, and M. Yvon, “Expression of a heterologous glutamate dehydrogenase gene in Lactococcus lactis highly improves the conversion of amino acids to aroma compounds,” *Appl Environ Microbiol*, vol. 66, no. 4, pp. 1354–1359, Apr. 2000, doi: 10.1128/AEM.66.4.1354-1359.2000.
[27] V. Joutsjoki, S. Luoma, M. Tamminen, M. Kilpi, E. Johansen, and A. Palva, “Recombinant Lactococcus starters as a potential source of additional peptidolytic activity in cheese ripening,” *J Appl Microbiol*, vol. 92, no. 6, pp. 1159–1166, Jun. 2002, doi: 10.1046/j.1365-2672.2002.01652.x.
[28] P. V. Behare, R. Singh, S. K. Tomar, R. Nagpal, M. Kumar, and D. Mohania, “Effect of exopolysaccharide-producing strains of Streptococcus thermophilus on technological attributes of fat-free lassi,” *Journal of Dairy Science*, vol. 93, no. 7, pp. 2874–2879, Jul. 2010, doi: 10.3168/jds.2009-2300.
[29] B. Ismail and K. M. Nampoothiri, “Production, purification and structural characterization of an exopolysaccharide produced by a probiotic Lactobacillus plantarum MTCC 9510,” *Arch Microbiol*, vol. 192, no. 12, pp. 1049–1057, Dec. 2010, doi: 10.1007/s00203-010-0636-y.
[30] X. Han *et al.*, “Improvement of the Texture of Yogurt by Use of Exopolysaccharide Producing Lactic Acid Bacteria,” *BioMed Research International*, vol. 2016, pp. 1–6, 2016, doi: 10.1155/2016/7945675.
[31] W. J. Lee and J. A. Lucey, “Formation and Physical Properties of Yogurt,” *Asian Australas. J. Anim. Sci*, vol. 23, no. 9, pp. 1127–1136, Aug. 2010, doi: 10.5713/ajas.2010.r.05.
[32] D. A. Savaiano and R. W. Hutkins, “Yogurt, cultured fermented milk, and health: a systematic review,” *Nutr Rev*, vol. 79, no. 5, pp. 599–614, Apr. 2021, doi: 10.1093/nutrit/nuaa013.
[33] C. Chen, S. Zhao, G. Hao, H. Yu, H. Tian, and G. Zhao, “Role of lactic acid bacteria on the yogurt flavour: A review,” *International Journal of Food Properties*, vol. 20, no. sup1, pp. S316–S330, Dec. 2017, doi: 10.1080/10942912.2017.1295988.
[34] G. Mulaw, T. Sisay Tessema, D. Muleta, and A. Tesfaye, “In Vitro Evaluation of Probiotic Properties of Lactic Acid Bacteria Isolated from Some Traditionally Fermented Ethiopian Food Products,” *Int J Microbiol*, vol. 2019, p. 7179514, 2019, doi: 10.1155/2019/7179514.
[35] M. R. Prado *et al.*, “Milk kefir: composition, microbial cultures, biological activities, and related products,” *Front. Microbiol.*, vol. 6, Oct. 2015, doi: 10.3389/fmicb.2015.01177.
[36] A. Kondybayev, G. Loiseau, N. Achir, C. Mestres, and G. Konuspayeva, “Fermented mare milk product (Qymyz, Koumiss),” *International Dairy Journal*, vol. 119, p. 105065, Aug. 2021, doi: 10.1016/j.idairyj.2021.105065.
[37] S. S. Behera, A. F. El Sheikha, R. Hammami, and A. Kumar, “Traditionally fermented pickles: How the microbial diversity associated with their nutritional and health benefits?,” *Journal of Functional Foods*, vol. 70, p. 103971, Jul. 2020, doi: 10.1016/j.jff.2020.103971.
[38] null Monika, null Savitri, V. Kumar, A. Kumari, K. Angmo, and T. C. Bhalla, “Isolation and characterization of lactic acid bacteria from traditional pickles of Himachal Pradesh, India,” *J Food Sci Technol*, vol. 54, no. 7, pp. 1945–1952, Jun. 2017, doi: 10.1007/s13197-017-2629-1.
[39] M. Yang *et al.*, “Characterizing the impact of species/strain-specific Lactiplantibacillus plantarum with community assembly and metabolic regulation in pickled Suancai,” *Food Research International*, vol. 174, p. 113650, Dec. 2023, doi: 10.1016/j.foodres.2023.113650.
[40] G. D. Sáez, Flomenbaum L, and Zárate G, “Lactic Acid Bacteria from Argentinean Fermented Foods: Isolation and Characterization for their Potential Use as Vegetable Starters,” *Food Technol. Biotechnol.*, vol. 56, no. 3, 2018, doi: 10.17113/ftb.56.03.18.5631.
[41] B. Mao and S. Yan, “Lactic Acid Bacteria and Fermented Fruits and Vegetables,” in *Lactic Acid Bacteria*, W. Chen, Ed., Singapore: Springer Singapore, 2019, pp. 181–209. doi: 10.1007/978-981-13-7283-4_7.

[42] M. A. Zabat, W. H. Sano, J. I. Wurster, D. J. Cabral, and P. Belenky, "Microbial Community Analysis of Sauerkraut Fermentation Reveals a Stable and Rapidly Established Community," *Foods*, vol. 7, no. 5, p. 77, May 2018, doi: 10.3390/foods7050077.

[43] M. Lee, J. H. Song, M. Y. Jung, S. H. Lee, and J. Y. Chang, "Large-scale targeted metagenomics analysis of bacterial ecological changes in 88 kimchi samples during fermentation," *Food Microbiology*, vol. 66, pp. 173–183, Sep. 2017, doi: 10.1016/j.fm.2017.05.002.

[44] G. Perpetuini, R. Prete, N. Garcia-Gonzalez, M. Khairul Alam, and A. Corsetti, "Table Olives More than a Fermented Food," *Foods*, vol. 9, no. 2, p. 178, Feb. 2020, doi: 10.3390/foods9020178.

[45] D. Liu, C. Zhang, J. Zhang, X. Xin, and X. Liao, "Metagenomics reveals the formation mechanism of flavor metabolites during the spontaneous fermentation of potherb mustard (Brassica juncea var. multiceps)," *Food Research International*, vol. 148, p. 110622, Oct. 2021, doi: 10.1016/j.foodres.2021.110622.

[46] H. Mathur, T. P. Beresford, and P. D. Cotter, "Health Benefits of Lactic Acid Bacteria (LAB) Fermentates," *Nutrients*, vol. 12, no. 6, p. 1679, Jun. 2020, doi: 10.3390/nu12061679.

[47] E. Elisabeth Sørvig 1, Sonja Grönqvist, Kristine Naterstad, Geir Mathiesen, Vincent G H Eijsink, Lars Axelsson, S. GrÃ¶nqvist, K. Naterstad, G. Mathiesen, V. G. H. Eijsink, and L. Axelsson, "Construction of vectors for inducible gene expression in Lactobacillus sakei and L plantarum," *FEMS Microbiology Letters*, vol. 229, no. 1, pp. 119–126, Dec. 2003, doi: 10.1016/S0378-1097(03)00798-5.

[48] A. E. Graham and R. Ledesma-Amaro, "The microbial food revolution," *Nat Commun*, vol. 14, no. 1, p. 2231, Apr. 2023, doi: 10.1038/s41467-023-37891-1.

[49] R. S. Bongers, M. H. N. Hoefnagel, and M. Kleerebezem, "High-Level Acetaldehyde Production in *Lactococcus lactis* by Metabolic Engineering," *Appl Environ Microbiol*, vol. 71, no. 2, pp. 1109–1113, Feb. 2005, doi: 10.1128/AEM.71.2.1109-1113.2005.

[50] A. C. S. D. Chaves, M. Fernandez, A. L. S. Lerayer, I. Mierau, M. Kleerebezem, and J. Hugenholtz, "Metabolic engineering of acetaldehyde production by Streptococcus thermophilus," *Appl Environ Microbiol*, vol. 68, no. 11, pp. 5656–5662, Nov. 2002, doi: 10.1128/AEM.68.11.5656-5662.2002.

[51] F. Aymes, C. Monnet, and G. Corrieu, "Effect of α-acetolactate decarboxylase inactivation on α-acetolactate and diacetyl production by Lactococcus lactis subsp. lactis biovar diacetylactis," *Journal of Bioscience and Bioengineering*, vol. 87, no. 1, pp. 87–92, Jan. 1999, doi: 10.1016/S1389-1723(99)80013-9.

[52] M. Curic, B. Stuer-Lauridsen, P. Renault, and D. Nilsson, "A general method for selection of alpha-acetolactate decarboxylase-deficient Lactococcus lactis mutants to improve diacetyl formation," *Appl Environ Microbiol*, vol. 65, no. 3, pp. 1202–1206, Mar. 1999, doi: 10.1128/AEM.65.3.1202-1206.1999.

[53] N. Goupil, G. Corthier, S. D. Ehrlich, and P. Renault, "Imbalance of leucine flux in Lactococcus lactis and its use for the isolation of diacetyl-overproducing strains," *Appl Environ Microbiol*, vol. 62, no. 7, pp. 2636–2640, Jul. 1996, doi: 10.1128/aem.62.7.2636-2640.1996.

[54] C. Platteeuw, J. Hugenholtz, M. Starrenburg, I. Van Alen-Boerrigter, and W. M. De Vos, "Metabolic engineering of Lactococcus lactis: influence of the overproduction of alpha-acetolactate synthase in strains deficient in lactate dehydrogenase as a function of culture conditions," *Appl Environ Microbiol*, vol. 61, no. 11, pp. 3967–3971, Nov. 1995, doi: 10.1128/aem.61.11.3967-3971.1995.

[55] C. Monnet, F. Aymes, and G. Corrieu, "Diacetyl and alpha-acetolactate overproduction by Lactococcus lactis subsp. lactis biovar diacetylactis mutants that are deficient in alpha-acetolactate decarboxylase and have a low lactate dehydrogenase activity," *Appl Environ Microbiol*, vol. 66, no. 12, pp. 5518–5520, Dec. 2000, doi: 10.1128/AEM.66.12.5518-5520.2000.

[56] A. R. Neves, A. Ramos, C. Shearman, M. J. Gasson, J. S. Almeida, and H. Santos, "Metabolic characterization of *Lactococcus lactis* deficient in lactate dehydrogenase using *in vivo* ^{13} C-NMR," *European Journal of Biochemistry*, vol. 267, no. 12, pp. 3859–3868, Jun. 2000, doi: 10.1046/j.1432-1327.2000.01424.x.

[57] J. Hugenholtz, M. Kleerebezem, M. Starrenburg, J. Delcour, W. De Vos, and P. Hols, "*Lactococcus lactis* as a Cell Factory for High-Level Diacetyl Production," *Appl Environ Microbiol*, vol. 66, no. 9, pp. 4112–4114, Sep. 2000, doi: 10.1128/AEM.66.9.4112-4114.2000.

ISSN Online: 3007-3154
ISSN Print: 3007-3146

DIALOGUE SOCIAL SCIENCE REVIEW

Vol. 2 No. 4 (November) (2024)

[58] T. Guo, J. Kong, L. Zhang, C. Zhang, and S. Hu, "Fine Tuning of the Lactate and Diacetyl Production through Promoter Engineering in Lactococcus lactis," *PLoS ONE*, vol. 7, no. 4, p. e36296, Apr. 2012, doi: 10.1371/journal.pone.0036296.

[59] L. Fernández *et al.*, "Cloning, Characterization, Controlled Overexpression, and Inactivation of the Major Tributyrin Esterase Gene of *Lactococcus lactis*," *Appl Environ Microbiol*, vol. 66, no. 4, pp. 1360–1368, Apr. 2000, doi: 10.1128/AEM.66.4.1360-1368.2000.

[60] R. Holland *et al.*, "Esterases of lactic acid bacteria and cheese flavour: Milk fat hydrolysis, alcoholysis and esterification," *International Dairy Journal*, vol. 15, no. 6–9, pp. 711–718, Jun. 2005, doi: 10.1016/j.idairyj.2004.09.012.

[61] S. Cui and Z. Fan, "Lactic Acid Bacteria and Fermented Meat Products," in *Lactic Acid Bacteria*, W. Chen, Ed., Singapore: Springer Singapore, 2019, pp. 211–225. doi: 10.1007/978-981-13-7283-4_8.

[62] H. Luo, P. Li, H. Zhang, X. Diao, and B. Kong, "Nitrosylmyoglobin formation in meat by Lactobacillus fermentum AS1.1880 is due to its nitric oxide synthase activity," *Meat Science*, vol. 166, p. 108122, Aug. 2020, doi: 10.1016/j.meatsci.2020.108122.

[63] M. Govari *et al.*, "Antimicrobial Proteins and Peptides as a Promising Weapon to Promote Food Safety Under the One Health Approach," in *Encyclopedia of Food Safety*, Elsevier, 2023, pp. 510–530. doi: 10.1016/B978-0-12-822521-9.00160-X.

[64] D. Wang *et al.*, "The Changes Occurring in Proteins during Processing and Storage of Fermented Meat Products and Their Regulation by Lactic Acid Bacteria," *Foods*, vol. 11, no. 16, p. 2427, Aug. 2022, doi: 10.3390/foods11162427.

[65] M. Flores, L. Perea-Sanz, and C. Belloch, "Nitrite reduction in fermented meat products and its impact on aroma," in *Advances in Food and Nutrition Research*, vol. 95, Elsevier, 2021, pp. 131–181. doi: 10.1016/bs.afnr.2020.10.002.

[66] F. Leroy and L. De Vuyst, "Fermented Foods: Fermented Meat Products," in *Encyclopedia of Food and Health*, Elsevier, 2016, pp. 656–660. doi: 10.1016/B978-0-12-384947-2.00283-X.

[67] H. Albano *et al.*, "Phenotypic and genetic heterogeneity of lactic acid bacteria isolated from 'Alheira', a traditional fermented sausage produced in Portugal," *Meat Science*, vol. 82, no. 3, pp. 389–398, Jul. 2009, doi: 10.1016/j.meatsci.2009.02.009.

[68] D. A. Anagnostopoulos and D. Tsaltas, "Fermented Foods and Beverages," in *Innovations in Traditional Foods*, Elsevier, 2019, pp. 257–291. doi: 10.1016/B978-0-12-814887-7.00010-1.

[69] J. Fernández-López, E. Sendra, E. Sayas-Barberá, C. Navarro, and J. A. Pérez-Alvarez, "Physico-chemical and microbiological profiles of 'salchichón' (Spanish dry-fermented sausage) enriched with orange fiber," *Meat Science*, vol. 80, no. 2, pp. 410–417, Oct. 2008, doi: 10.1016/j.meatsci.2008.01.010.

[70] T. Aymerich, B. Martín, M. Garriga, and M. Hugas, "Microbial Quality and Direct PCR Identification of Lactic Acid Bacteria and Nonpathogenic Staphylococci from Artisanal Low-Acid Sausages," *Appl Environ Microbiol*, vol. 69, no. 8, pp. 4583–4594, Aug. 2003, doi: 10.1128/AEM.69.8.4583-4594.2003.

[71] S. Cui and Z. Fan, "Lactic Acid Bacteria and Fermented Meat Products," in *Lactic Acid Bacteria*, W. Chen, Ed., Singapore: Springer Singapore, 2019, pp. 211–225. doi: 10.1007/978-981-13-7283-4_8.

[72] N. Francesca, C. Sannino, G. Moschetti, and L. Settanni, "Microbial characterisation of fermented meat products from the Sicilian swine breed 'Suino Nero Dei Nebrodi,'" *Ann Microbiol*, vol. 63, no. 1, pp. 53–62, Mar. 2013, doi: 10.1007/s13213-012-0444-5.

[73] K. Rantsiou and L. Cocolin, "New developments in the study of the microbiota of naturally fermented sausages as determined by molecular methods: A review," *International Journal of Food Microbiology*, vol. 108, no. 2, pp. 255–267, Apr. 2006, doi: 10.1016/j.ijfoodmicro.2005.11.013.

[74] A. Lovegrove *et al.*, "Role of polysaccharides in food, digestion, and health," *Critical Reviews in Food Science and Nutrition*, vol. 57, no. 2, pp. 237–253, Jan. 2017, doi: 10.1080/10408398.2014.939263.

[75] Q. Song *et al.*, "Review of the relationships among polysaccharides, gut microbiota, and human health," *Food Research International*, vol. 140, p. 109858, Feb. 2021, doi: 10.1016/j.foodres.2020.109858.

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

[76] E. Zannini, D. M. Waters, A. Coffey, and E. K. Arendt, “Production, properties, and industrial food application of lactic acid bacteria-derived exopolysaccharides,” *Appl Microbiol Biotechnol*, vol. 100, no. 3, pp. 1121–1135, Feb. 2016, doi: 10.1007/s00253-015-7172-2.

[77] L. K. Brahe, A. Astrup, and L. H. Larsen, “Is butyrate the link between diet, intestinal microbiota and obesity-related metabolic diseases?,” *Obesity Reviews*, vol. 14, no. 12, pp. 950–959, Dec. 2013, doi: 10.1111/obr.12068.

[78] F. Canon, M.-B. Maillard, M.-H. Famelart, A. Thierry, and V. Gagnaire, “Mixed dairy and plant-based yogurt alternatives: Improving their physical and sensorial properties through formulation and lactic acid bacteria cocultures,” *Current Research in Food Science*, vol. 5, pp. 665–676, 2022, doi: 10.1016/j.crfs.2022.03.011.

[79] E. Cubas-Cano, C. González-Fernández, and E. Tomás-Pejó, “Evolutionary engineering of Lactobacillus pentosus improves lactic acid productivity from xylose-rich media at low pH,” *Bioresource Technology*, vol. 288, p. 121540, Sep. 2019, doi: 10.1016/j.biortech.2019.121540.

[80] S. K. Singh, S. U. Ahmed, and A. Pandey, “Metabolic engineering approaches for lactic acid production,” *Process Biochemistry*, vol. 41, no. 5, pp. 991–1000, May 2006, doi: 10.1016/j.procbio.2005.12.004.

[81] J. Y. Tak, W. J. Jang, J. M. Lee, S. Suraiya, and I.-S. Kong, “Expression in Lactococcus lactis of a β-1,3-1,4-glucanase gene from Bacillus sp. SJ-10 isolated from fermented fish,” *Protein Expression and Purification*, vol. 162, pp. 18–23, Oct. 2019, doi: 10.1016/j.pep.2019.05.006.

[82] S. D. Kurniasih, A. Alfi, D. Natalia, O. K. Radjasa, and Z. Nurachman, “Construction of individual, fused, and co-expressed proteins of endoglucanase and β-glucosidase for hydrolyzing sugarcane bagasse,” *Microbiological Research*, vol. 169, no. 9–10, pp. 725–732, Sep. 2014, doi: 10.1016/j.micres.2014.02.002.

[83] C.-H. Kang, J.-S. Kim, H. M. Park, S. Kim, and N.-S. Paek, “Antioxidant activity and short-chain fatty acid production of lactic acid bacteria isolated from Korean individuals and fermented foods,” *3 Biotech*, vol. 11, no. 5, p. 217, May 2021, doi: 10.1007/s13205-021-02767-y.

[84] B. Usta-Gorgun and L. Yilmaz-Ersan, “Short-chain fatty acids production by Bifidobacterium species in the presence of salep,” *Electronic Journal of Biotechnology*, vol. 47, pp. 29–35, Sep. 2020, doi: 10.1016/j.ejbt.2020.06.004.

[85] C. Haokok, S. Lunprom, A. Reungsang, and A. Salakkam, “Efficient production of lactic acid from cellulose and xylan in sugarcane bagasse by newly isolated Lactiplantibacillus plantarum and Levilactobacillus brevis through simultaneous saccharification and co-fermentation process,” *Heliyon*, vol. 9, no. 7, p. e17935, Jul. 2023, doi: 10.1016/j.heliyon.2023.e17935.

[86] H. Fang, J. Kang, and D. Zhang, “Microbial production of vitamin B12: a review and future perspectives,” *Microb Cell Fact*, vol. 16, no. 1, p. 15, Dec. 2017, doi: 10.1186/s12934-017-0631-y.

[87] J. L. Revuelta, R. Ledesma-Amaro, P. Lozano-Martinez, D. Díaz-Fernández, R. M. Buey, and A. Jiménez, “Bioproduction of riboflavin: a bright yellow history,” *Journal of Industrial Microbiology and Biotechnology*, vol. 44, no. 4–5, pp. 659–665, May 2017, doi: 10.1007/s10295-016-1842-7.

[88] J. C. C. Rosa, L. T. Colombo, M. C. T. Alvim, N. Avonce, P. Van Dijck, and F. M. L. Passos, “Metabolic engineering of Kluyveromyces lactis for L-ascorbic acid (vitamin C) biosynthesis,” *Microb Cell Fact*, vol. 12, no. 1, p. 59, Dec. 2013, doi: 10.1186/1475-2859-12-59.

[89] M. Sauer, P. Branduardi, M. Valli, and D. Porro, “Production of l-ascorbic acid by metabolically engineered Saccharomyces cerevisiae and Zygosaccharomyces bailii.,” *Appl Environ Microbiol*, vol. 70, no. 10, pp. 6086–6091, Oct. 2004, doi: 10.1128/AEM.70.10.6086-6091.2004.

[90] J. L. Revuelta, C. Serrano-Amatriain, R. Ledesma-Amaro, and A. Jiménez, “Formation of folates by microorganisms: towards the biotechnological production of this vitamin,” *Appl Microbiol Biotechnol*, vol. 102, no. 20, pp. 8613–8620, Oct. 2018, doi: 10.1007/s00253-018-9266-0.

[91] W. Sybesma, M. Starrenburg, M. Kleerebezem, I. Mierau, W. M. De Vos, and J. Hugenholtz, “Increased Production of Folate by Metabolic Engineering of Lactococcus lactis,” *Appl Environ Microbiol*, vol. 69, no. 6, pp. 3069–3076, Jun. 2003, doi: 10.1128/AEM.69.6.3069-3076.2003.

[92] B. Thöny, G. Auerbach, and N. Blau, “Tetrahydrobiopterin biosynthesis, regeneration and functions,” *Biochemical Journal*, vol. 347, no. 1, pp. 1–16, Apr. 2000, doi: 10.1042/bj3470001.

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

[93] H. Pertiwi, M. Y. Nur Mahendra, and J. Kamaludeen, “Folic Acid: Sources, Chemistry, Absorption, Metabolism, Beneficial Effects on Poultry Performance and Health,” *Veterinary Medicine International*, vol. 2022, pp. 1–9, Aug. 2022, doi: 10.1155/2022/2163756.
[94] J. W. Locasale, “Serine, glycine and one-carbon units: cancer metabolism in full circle,” *Nat Rev Cancer*, vol. 13, no. 8, pp. 572–583, Aug. 2013, doi: 10.1038/nrc3557.
[95] Y. Shulpekova *et al.*, “The Concept of Folic Acid in Health and Disease,” *Molecules*, vol. 26, no. 12, p. 3731, Jun. 2021, doi: 10.3390/molecules26123731.
[96] M. Khalili, A. H. Rad, A. Y. Khosroushahi, H. Khosravi, and S. Jafarzadeh, “Application of Probiotics in Folate Bio-Fortification of Yoghurt,” *Probiotics Antimicrob Proteins*, vol. 12, no. 2, pp. 756–763, Jun. 2020, doi: 10.1007/s12602-019-09560-7.
[97] B. N. Abdul Hakim, N. J. Xuan, and S. N. H. Oslan, “A Comprehensive Review of Bioactive Compounds from Lactic Acid Bacteria: Potential Functions as Functional Food in Dietetics and the Food Industry,” *Foods*, vol. 12, no. 15, p. 2850, Jul. 2023, doi: 10.3390/foods12152850.
[98] M. Khalili, A. H. Rad, A. Y. Khosroushahi, H. Khosravi, and S. Jafarzadeh, “Application of Probiotics in Folate Bio-Fortification of Yoghurt,” *Probiotics Antimicrob Proteins*, vol. 12, no. 2, pp. 756–763, Jun. 2020, doi: 10.1007/s12602-019-09560-7.
[99] C. Burgess, M. O’connell-Motherway, W. Sybesma, J. Hugenholtz, and D. van Sinderen, “Riboflavin production in Lactococcus lactis: potential for in situ production of vitamin-enriched foods,” *Appl Environ Microbiol*, vol. 70, no. 10, pp. 5769–5777, Oct. 2004, doi: 10.1128/AEM.70.10.5769-5777.2004.
[100] C. M. Burgess, E. J. Smid, G. Rutten, and D. Van Sinderen, “A general method for selection of riboflavin-overproducing food grade micro-organisms,” *Microb Cell Fact*, vol. 5, no. 1, p. 24, Dec. 2006, doi: 10.1186/1475-2859-5-24.
[101] X. Y. Chen, C. Levy, and M. G. Gänzle, “Structure-function relationships of bacterial and enzymatically produced reuterans and dextran in sourdough bread baking application,” *International Journal of Food Microbiology*, vol. 239, pp. 95–102, Dec. 2016, doi: 10.1016/j.ijfoodmicro.2016.06.010.
[102] Y.-Y. Ge, J.-R. Zhang, H. Corke, and R.-Y. Gan, “Screening and Spontaneous Mutation of Pickle-Derived Lactobacillus plantarum with Overproduction of Riboflavin, Related Mechanism, and Food Application,” *Foods*, vol. 9, no. 1, p. 88, Jan. 2020, doi: 10.3390/foods9010088.
[103] Y. Liu, E. O. Van Bennekom, Y. Zhang, T. Abee, and E. J. Smid, “Long-chain vitamin K2 production in Lactococcus lactis is influenced by temperature, carbon source, aeration and mode of energy metabolism,” *Microb Cell Fact*, vol. 18, no. 1, p. 129, Dec. 2019, doi: 10.1186/s12934-019-1179-9.
[104] Y. Oguro, T. Nishiwaki, R. Shinada, K. Kobayashi, and A. Kurahashi, “Metabolite profile of koji amazake and its lactic acid fermentation product by Lactobacillus sakei UONUMA,” *Journal of Bioscience and Bioengineering*, vol. 124, no. 2, pp. 178–183, Aug. 2017, doi: 10.1016/j.jbiosc.2017.03.011.
[105] A. C. Torres, V. Vannini, G. Font, L. Saavedra, and M. P. Taranto, “Novel Pathway for Corrinoid Compounds Production in Lactobacillus,” *Front. Microbiol.*, vol. 9, p. 2256, Sep. 2018, doi: 10.3389/fmicb.2018.02256.
[106] G. M. Daba, M. O. Elnahas, and W. A. Elkhateeb, “Contributions of exopolysaccharides from lactic acid bacteria as biotechnological tools in food, pharmaceutical, and medical applications,” *International Journal of Biological Macromolecules*, vol. 173, pp. 79–89, Mar. 2021, doi: 10.1016/j.ijbiomac.2021.01.110.
[107] J. Zhang, Y. Xiao, H. Wang, H. Zhang, W. Chen, and W. Lu, “Lactic acid bacteria-derived exopolysaccharide: Formation, immunomodulatory ability, health effects, and structure-function relationship,” *Microbiological Research*, vol. 274, p. 127432, Sep. 2023, doi: 10.1016/j.micres.2023.127432.
[108] F. Li, X. Jiao, J. Zhao, X. Liao, Y. Wei, and Q. Li, “Antitumor mechanisms of an exopolysaccharide from Lactobacillus fermentum on HT-29 cells and HT-29 tumor-bearing mice,” *International Journal of Biological Macromolecules*, vol. 209, pp. 552–562, Jun. 2022, doi: 10.1016/j.ijbiomac.2022.04.023.
[109] K. M. Lynch, E. Zannini, A. Coffey, and E. K. Arendt, “Lactic Acid Bacteria Exopolysaccharides in Foods and Beverages: Isolation, Properties, Characterization, and Health Benefits,” *Annu. Rev. Food Sci. Technol.*, vol. 9, no. 1, pp. 155–176, Mar. 2018, doi: 10.1146/annurev-food-030117-012537.

[110] J. Angelin and M. Kavitha, “Exopolysaccharides from probiotic bacteria and their health potential,” *International Journal of Biological Macromolecules*, vol. 162, pp. 853–865, Nov. 2020, doi: 10.1016/j.ijbiomac.2020.06.190.
[111] M. Guérin, C. R.-D. Silva, C. Garcia, and F. Remize, “Lactic Acid Bacterial Production of Exopolysaccharides from Fruit and Vegetables and Associated Benefits,” *Fermentation*, vol. 6, no. 4, p. 115, Nov. 2020, doi: 10.3390/fermentation6040115.
[112] V. Ripari, “Techno-Functional Role of Exopolysaccharides in Cereal-Based, Yogurt-Like Beverages,” *Beverages*, vol. 5, no. 1, p. 16, Feb. 2019, doi: 10.3390/beverages5010016.
[113] J. Liu, S. H. J. Chan, J. Chen, C. Solem, and P. R. Jensen, “Systems Biology – A Guide for Understanding and Developing Improved Strains of Lactic Acid Bacteria,” *Front. Microbiol.*, vol. 10, p. 876, Apr. 2019, doi: 10.3389/fmicb.2019.00876.
[114] Grosu-Tudor, Silvia-Simona, and Medana Zamfir., “Exopolysaccharide production by selected lactic acid bacteria isolated from fermented vegetables.,” *Scientific Bulletin Series F. Biotechnologies 18: 2285-1364.*, 2014.
[115] R. Juvonen *et al.*, “The impact of fermentation with exopolysaccharide producing lactic acid bacteria on rheological, chemical and sensory properties of pureed carrots (Daucus carota L.),” *International Journal of Food Microbiology*, vol. 207, pp. 109–118, Aug. 2015, doi: 10.1016/j.ijfoodmicro.2015.04.031.
[116] N. Besrour-Aouam *et al.*, “Different Modes of Regulation of the Expression of Dextransucrase in Leuconostoc lactis AV1n and Lactobacillus sakei MN1,” *Front. Microbiol.*, vol. 10, p. 959, May 2019, doi: 10.3389/fmicb.2019.00959.
[117] R. Z. Ahmed, K. Siddiqui, M. Arman, and N. Ahmed, “Characterization of high molecular weight dextran produced by Weissella cibaria CMGDEX3,” *Carbohydrate Polymers*, vol. 90, no. 1, pp. 441–446, Sep. 2012, doi: 10.1016/j.carbpol.2012.05.063.
[118] K. M. Lynch, E. Zannini, A. Coffey, and E. K. Arendt, “Lactic Acid Bacteria Exopolysaccharides in Foods and Beverages: Isolation, Properties, Characterization, and Health Benefits,” *Annu. Rev. Food Sci. Technol.*, vol. 9, no. 1, pp. 155–176, Mar. 2018, doi: 10.1146/annurev-food-030117-012537.
[119] N. Salazar *et al.*, “Production of exopolysaccharides by Lactobacillus and Bifidobacterium strains of human origin, and metabolic activity of the producing bacteria in milk,” *Journal of Dairy Science*, vol. 92, no. 9, pp. 4158–4168, Sep. 2009, doi: 10.3168/jds.2009-2126.
[120] M. Y. M. Imran *et al.*, “Statistical optimization of exopolysaccharide production by Lactobacillus plantarum NTMI05 and NTMI20,” *International Journal of Biological Macromolecules*, vol. 93, pp. 731–745, Dec. 2016, doi: 10.1016/j.ijbiomac.2016.09.007.
[121] C.-F. Liu, K.-C. Tseng, S.-S. Chiang, B.-H. Lee, W.-H. Hsu, and T.-M. Pan, “Immunomodulatory and antioxidant potential of Lactobacillus exopolysaccharides,” *J. Sci. Food Agric.*, p. n/a-n/a, 2011, doi: 10.1002/jsfa.4456.
[122] L. A. Silva, J. H. P. Lopes Neto, and H. R. Cardarelli, “Exopolysaccharides produced by Lactobacillus plantarum: technological properties, biological activity, and potential application in the food industry,” *Ann Microbiol*, vol. 69, no. 4, pp. 321–328, Apr. 2019, doi: 10.1007/s13213-019-01456-9.
[123] E. C. Ale, M. F. Rojas, J. A. Reinheimer, and A. G. Binetti, “Lactobacillus fermentum: Could EPS production ability be responsible for functional properties?,” *Food Microbiology*, vol. 90, p. 103465, Sep. 2020, doi: 10.1016/j.fm.2020.103465.
[124] I. Sánchez, L. Palop, and C. Ballesteros, “Biochemical characterization of lactic acid bacteria isolated from spontaneous fermentation of ‘Almagro’ eggplants,” *International Journal of Food Microbiology*, vol. 59, no. 1–2, pp. 9–17, Jul. 2000, doi: 10.1016/S0168-1605(00)00256-7.
[125] I. Sánchez, S. Seseña, and L. Palop, “Identification of lactic acid bacteria from spontaneous fermentation of ‘Almagro’ eggplants by SDS-PAGE whole cell protein fingerprinting,” *International Journal of Food Microbiology*, vol. 82, no. 2, pp. 181–189, Apr. 2003, doi: 10.1016/S0168-1605(02)00260-X.
[126] S. Badel, T. Bernardi, and P. Michaud, “New perspectives for Lactobacilli exopolysaccharides,” *Biotechnology Advances*, vol. 29, no. 1, pp. 54–66, Jan. 2011, doi: 10.1016/j.biotechadv.2010.08.011.
[127] C. J. Toe, H. L. Foo, T. C. Loh, R. Mohamad, R. Abdul Rahim, and Z. Idrus, “Extracellular Proteolytic Activity and Amino Acid Production by Lactic Acid Bacteria Isolated from Malaysian Foods,” *IJMS*, vol. 20, no. 7, p. 1777, Apr. 2019, doi: 10.3390/ijms20071777.

[128] F. Barbieri, C. Montanari, F. Gardini, and G. Tabanelli, "Biogenic Amine Production by Lactic Acid Bacteria: A Review," *Foods*, vol. 8, no. 1, p. 17, Jan. 2019, doi: 10.3390/foods8010017.

[129] P. Kalac, "The effects of lactic acid bacteria inoculants on biogenic amines formation in sauerkraut," *Food Chemistry*, vol. 70, no. 3, pp. 355–359, Aug. 2000, doi: 10.1016/S0308-8146(00)00103-5.

[130] R. Sharma, P. Garg, P. Kumar, S. K. Bhatia, and S. Kulshrestha, "Microbial Fermentation and Its Role in Quality Improvement of Fermented Foods," *Fermentation*, vol. 6, no. 4, p. 106, Nov. 2020, doi: 10.3390/fermentation6040106.

[131] I. K. Lappa, A. Terpou, L. A. Bosnea, and A. Papadaki, "Lactic acid bacteria and biogenic amines in food: Biological importance and human health," in *Lactic Acid Bacteria in Food Biotechnology*, Elsevier, 2022, pp. 181–194. doi: 10.1016/B978-0-323-89875-1.00010-9.

[132] E. Bargossi *et al.*, "Tyrosine decarboxylase activity of enterococci grown in media with different nutritional potential: tyramine and 2-phenylethylamine accumulation and tyrDC gene expression," *Front. Microbiol.*, vol. 6, Apr. 2015, doi: 10.3389/fmicb.2015.00259.

[133] S. Bonetta, S. Bonetta, E. Carraro, J. D. Coïsson, F. Travaglia, and M. Arlorio, "Detection of Biogenic Amine Producer Bacteria in a Typical Italian Goat Cheese," *Journal of Food Protection*, vol. 71, no. 1, pp. 205–209, Jan. 2008, doi: 10.4315/0362-028X-71.1.205.

[134] V. Ladero *et al.*, "Is the production of the biogenic amines tyramine and putrescine a species-level trait in enterococci?," *Food Microbiology*, vol. 30, no. 1, pp. 132–138, May 2012, doi: 10.1016/j.fm.2011.12.016.

[135] F. Liu *et al.*, "Effect of NaCI Treatments on Tyramine Biosynthesis of Enterococcus faecalis," *Journal of Food Protection*, vol. 78, no. 5, pp. 940–945, May 2015, doi: 10.4315/0362-028X.JFP-14-443.

[136] M. Solheim, S. L. La Rosa, T. Mathisen, L. G. Snipen, I. F. Nes, and D. A. Brede, "Transcriptomic and Functional Analysis of NaCl-Induced Stress in Enterococcus faecalis," *PLoS ONE*, vol. 9, no. 4, p. e94571, Apr. 2014, doi: 10.1371/journal.pone.0094571.

[137] E. Bargossi, F. Gardini, V. Gatto, C. Montanari, S. Torriani, and G. Tabanelli, "The Capability of Tyramine Production and Correlation between Phenotypic and Genetic Characteristics of Enterococcus faecium and Enterococcus faecalis Strains," *Front. Microbiol.*, vol. 6, Dec. 2015, doi: 10.3389/fmicb.2015.01371.

[138] M. L. Latorre-Moratalla *et al.*, "Distribution of Aminogenic Activity among Potential Autochthonous Starter Cultures for Dry Fermented Sausages," *Journal of Food Protection*, vol. 73, no. 3, pp. 524–528, Mar. 2010, doi: 10.4315/0362-028x-73.3.524.

[139] D. Wüthrich, H. Berthoud, D. Wechsler, E. Eugster, S. Irmler, and R. Bruggmann, "The Histidine Decarboxylase Gene Cluster of Lactobacillus parabuchneri Was Gained by Horizontal Gene Transfer and Is Mobile within the Species," *Front. Microbiol.*, vol. 8, Feb. 2017, doi: 10.3389/fmicb.2017.00218.

[140] L. Buňková *et al.*, "The effect of ripening and storage conditions on the distribution of tyramine, putrescine and cadaverine in Edam-cheese," *Food Microbiology*, vol. 27, no. 7, pp. 880–888, Oct. 2010, doi: 10.1016/j.fm.2010.04.014.

[141] T. Komprda, R. Burdychová, V. Dohnal, O. Cwiková, P. Sládková, and H. Dvořáčková, "Tyramine production in Dutch-type semi-hard cheese from two different producers," *Food Microbiology*, vol. 25, no. 2, pp. 219–227, Feb. 2008, doi: 10.1016/j.fm.2007.11.006.

[142] E. Kuley, E. Balıkcı, İ. Özoğul, S. Gökdogan, and F. Özoğul, "Stimulation of cadaverine production by foodborne pathogens in the presence of Lactobacillus, Lactococcus, and Streptococcus," *Journal of Food Science*, vol. 77, no. 12, Dec. 2012, doi: 10.1111/j.1750-3841.2012.02825.x.

[143] K. R. Choi and S. Y. Lee, "Systems metabolic engineering of microorganisms for food and cosmetics production," *Nat Rev Bioeng*, vol. 1, no. 11, pp. 832–857, Jun. 2023, doi: 10.1038/s44222-023-00076-y.

[144] J. A. Hernandez-Valdes *et al.*, "Enhancement of amino acid production and secretion by Lactococcus lactis using a droplet-based biosensing and selection system," *Metabolic Engineering Communications*, vol. 11, p. e00133, Dec. 2020, doi: 10.1016/j.mec.2020.e00133.

[145] A. Krastanov, P. J. Yeboah, N. Dulari Wijemanna, A. S. Eddin, R. D. Ayivi, and S. A. Ibrahim, "Volatile Aromatic Flavor Compounds in Yogurt: A Review," in *Food Science and Nutrition*, vol. 1, S. A. Ibrahim, Ed., IntechOpen, 2023. doi: 10.5772/intechopen.109034.

[146] G. Smit, B. A. Smit, and W. J. M. Engels, "Flavour formation by lactic acid bacteria and biochemical flavour profiling of cheese products," *FEMS Microbiol Rev*, vol. 29, no. 3, pp. 591–610, Aug. 2005, doi: 10.1016/j.fmrre.2005.04.002.
[147] Y. Wang *et al.*, "Metabolism Characteristics of Lactic Acid Bacteria and the Expanding Applications in Food Industry," *Front Bioeng Biotechnol*, vol. 9, p. 612285, 2021, doi: 10.3389/fbioe.2021.612285.
[148] S. Jeske, E. Zannini, K. M. Lynch, A. Coffey, and E. K. Arendt, "Polyol-producing lactic acid bacteria isolated from sourdough and their application to reduce sugar in a quinoa-based milk substitute," *International Journal of Food Microbiology*, vol. 286, pp. 31–36, Dec. 2018, doi: 10.1016/j.ijfoodmicro.2018.07.013.
[149] M. E. Ortiz, J. Bleckwedel, R. R. Raya, and F. Mozzi, "Biotechnological and in situ food production of polyols by lactic acid bacteria," *Appl Microbiol Biotechnol*, vol. 97, no. 11, pp. 4713–4726, Jun. 2013, doi: 10.1007/s00253-013-4884-z.
[150] E. Bancalari *et al.*, "An integrated strategy to discover Lactobacillus casei group strains for their potential use as aromatic starters," *Food Research International*, vol. 100, pp. 682–690, Oct. 2017, doi: 10.1016/j.foodres.2017.07.066.
[151] G. Chammas, R. Saliba, G. Corrieu, and C. Beal, "Characterisation of lactic acid bacteria isolated from fermented milk 'laban,'" *International Journal of Food Microbiology*, vol. 110, no. 1, pp. 52–61, Jul. 2006, doi: 10.1016/j.ijfoodmicro.2006.01.043.
[152] S. B. Prasad, G. Jayaraman, and K. B. Ramachandran, "Hyaluronic acid production is enhanced by the additional co-expression of UDP-glucose pyrophosphorylase in Lactococcus lactis," *Appl Microbiol Biotechnol*, vol. 86, no. 1, pp. 273–283, Mar. 2010, doi: 10.1007/s00253-009-2293-0.
[153] M. V. Shah, S. S. Badle, and K. B. Ramachandran, "Hyaluronic acid production and molecular weight improvement by redirection of carbon flux towards its biosynthesis pathway," *Biochemical Engineering Journal*, vol. 80, pp. 53–60, Nov. 2013, doi: 10.1016/j.bej.2013.09.013.
[154] V. Monedero, G. Pérez-Martínez, and M. J. Yebra, "Perspectives of engineering lactic acid bacteria for biotechnological polyol production," *Appl Microbiol Biotechnol*, vol. 86, no. 4, pp. 1003–1015, Apr. 2010, doi: 10.1007/s00253-010-2494-6.
[155] E. Bancalari *et al.*, "An integrated strategy to discover Lactobacillus casei group strains for their potential use as aromatic starters," *Food Research International*, vol. 100, pp. 682–690, Oct. 2017, doi: 10.1016/j.foodres.2017.07.066.
[156] N. Gómez-Torres, M. Ávila, D. Delgado, and S. Garde, "Effect of reuterin-producing Lactobacillus reuteri coupled with glycerol on the volatile fraction, odour and aroma of semi-hard ewe milk cheese," *International Journal of Food Microbiology*, vol. 232, pp. 103–110, Sep. 2016, doi: 10.1016/j.ijfoodmicro.2016.05.031.
[157] D. Mugampoza, K. Gkatzionis, R. S. T. Linforth, and C. E. R. Dodd, "Acid production, growth kinetics and aroma profiles of Lactobacillus flora from Stilton cheese," *Food Chemistry*, vol. 287, pp. 222–231, Jul. 2019, doi: 10.1016/j.foodchem.2019.02.082.
[158] D. Wüthrich, C. Wenzel, T. Bavan, R. Bruggmann, H. Berthoud, and S. Irmler, "Transcriptional Regulation of Cysteine and Methionine Metabolism in Lactobacillus paracasei FAM18149," *Front. Microbiol.*, vol. 9, p. 1261, Jun. 2018, doi: 10.3389/fmicb.2018.01261.
[159] M. Winters *et al.*, "Defined co-cultures of yeast and bacteria modify the aroma, crumb and sensory properties of bread," *J Appl Microbiol*, vol. 127, no. 3, pp. 778–793, Sep. 2019, doi: 10.1111/jam.14349.
[160] T. Liu, Y. Li, Y. Yang, H. Yi, L. Zhang, and G. He, "The influence of different lactic acid bacteria on sourdough flavor and a deep insight into sourdough fermentation through RNA sequencing," *Food Chemistry*, vol. 307, p. 125529, Mar. 2020, doi: 10.1016/j.foodchem.2019.125529.
[161] M. S. Cappello, G. Zapparoli, A. Logrieco, and E. J. Bartowsky, "Linking wine lactic acid bacteria diversity with wine aroma and flavour," *International Journal of Food Microbiology*, vol. 243, pp. 16–27, Feb. 2017, doi: 10.1016/j.ijfoodmicro.2016.11.025.
[162] Z.-M. Lu *et al.*, "Elucidating and Regulating the Acetoin Production Role of Microbial Functional Groups in Multispecies Acetic Acid Fermentation," *Appl Environ Microbiol*, vol. 82, no. 19, pp. 5860–5868, Oct. 2016, doi: 10.1128/AEM.01331-16.

ISSN Online: 3007-3154
ISSN Print: 3007-3146

Vol. 2 No. 4 (November) (2024)

[163] N. Wiernasz, J. Cornet, M. Cardinal, M.-F. Pilet, D. Passerini, and F. Leroi, "Lactic Acid Bacteria Selection for Biopreservation as a Part of Hurdle Technology Approach Applied on Seafood," *Front. Mar. Sci.*, vol. 4, p. 119, May 2017, doi: 10.3389/fmars.2017.00119.
[164] A. Zapaśnik, B. Sokołowska, and M. Bryła, "Role of Lactic Acid Bacteria in Food Preservation and Safety," *Foods*, vol. 11, no. 9, p. 1283, Apr. 2022, doi: 10.3390/foods11091283.
[165] S. Sieuwerts, P. A. Bron, and E. J. Smid, "Mutually stimulating interactions between lactic acid bacteria and Saccharomyces cerevisiae in sourdough fermentation," *LWT*, vol. 90, pp. 201–206, Apr. 2018, doi: 10.1016/j.lwt.2017.12.022.
[166] M. L. Chikindas, R. Weeks, D. Drider, V. A. Chistyakov, and L. M. Dicks, "Functions and emerging applications of bacteriocins," *Current Opinion in Biotechnology*, vol. 49, pp. 23–28, Feb. 2018, doi: 10.1016/j.copbio.2017.07.011.
[167] S. A. Ibrahim *et al.*, "Lactic Acid Bacteria as Antimicrobial Agents: Food Safety and Microbial Food Spoilage Prevention," *Foods*, vol. 10, no. 12, p. 3131, Dec. 2021, doi: 10.3390/foods10123131.
[168] T. Zimmerman, S. A. Siddiqui, W. Bischoff, and S. A. Ibrahim, "Tackling Airborne Virus Threats in the Food Industry: A Proactive Approach," *IJERPH*, vol. 18, no. 8, p. 4335, Apr. 2021, doi: 10.3390/ijerph18084335.
[169] J. L. Arqués, E. Rodríguez, M. Nuñez, and M. Medina, "Combined effect of reuterin and lactic acid bacteria bacteriocins on the inactivation of food-borne pathogens in milk," *Food Control*, vol. 22, no. 3–4, pp. 457–461, Mar. 2011, doi: 10.1016/j.foodcont.2010.09.027.
[170] K. Arakawa *et al.*, "Effects of gassericins A and T, bacteriocins produced by Lactobacillus gasseri, with glycine on custard cream preservation," *Journal of Dairy Science*, vol. 92, no. 6, pp. 2365–2372, Jun. 2009, doi: 10.3168/jds.2008-1240.
[171] K. Arakawa *et al.*, "Effects of gassericins A and T, bacteriocins produced by Lactobacillus gasseri, with glycine on custard cream preservation," *Journal of Dairy Science*, vol. 92, no. 6, pp. 2365–2372, Jun. 2009, doi: 10.3168/jds.2008-1240.
[172] S. A. Ibrahim *et al.*, "Lactic Acid Bacteria as Antimicrobial Agents: Food Safety and Microbial Food Spoilage Prevention," *Foods*, vol. 10, no. 12, p. 3131, Dec. 2021, doi: 10.3390/foods10123131.
[173] S. Özcelik, E. Kuley, and F. Özogul, "Formation of lactic, acetic, succinic, propionic, formic and butyric acid by lactic acid bacteria," *LWT*, vol. 73, pp. 536–542, Nov. 2016, doi: 10.1016/j.lwt.2016.06.066.
[174] S. Özcelik, E. Kuley, and F. Özogul, "Formation of lactic, acetic, succinic, propionic, formic and butyric acid by lactic acid bacteria," *LWT*, vol. 73, pp. 536–542, Nov. 2016, doi: 10.1016/j.lwt.2016.06.066.
[175] C.-M. Lin, S. S. Moon, M. P. Doyle, and K. H. Mcwatters, "Inactivation of Escherichia coli O157:H7, Salmonella enterica Serotype Enteritidis, and Listeria monocytogenes on Lettuce by Hydrogen Peroxide and Lactic Acid and by Hydrogen Peroxide with Mild Heat," *Journal of Food Protection*, vol. 65, no. 8, pp. 1215–1220, Aug. 2002, doi: 10.4315/0362-028X-65.8.1215.
[176] T. Jalilsood *et al.*, "Inhibition of pathogenic and spoilage bacteria by a novel biofilm-forming Lactobacillus isolate: a potential host for the expression of heterologous proteins," *Microb Cell Fact*, vol. 14, no. 1, p. 96, Dec. 2015, doi: 10.1186/s12934-015-0283-8.
[177] L. I. Valenzuela-García *et al.*, "Design of a Whole-Cell Biosensor Based on Bacillus subtilis Spores and the Green Fluorescent Protein To Monitor Arsenic," *Microbiol Spectr*, vol. 11, no. 4, pp. e00432-23, Aug. 2023, doi: 10.1128/spectrum.00432-23.
[178] L. Song, D. Yang, R. Liu, S. Liu, L. Dai, and X. Dai, "Microbial production of lactic acid from food waste: Latest advances, limits, and perspectives," *Bioresource Technology*, vol. 345, p. 126052, Feb. 2022, doi: 10.1016/j.biortech.2021.126052.
[179] L. Song, S. Liu, R. Liu, D. Yang, and X. Dai, "Direct lactic acid production from household food waste by lactic acid bacteria," *Science of The Total Environment*, vol. 840, p. 156479, Sep. 2022, doi: 10.1016/j.scitotenv.2022.156479.
[180] Abdullah-Al-Mahin, S. Sugimoto, C. Higashi, S. Matsumoto, and K. Sonomoto, "Improvement of Multiple-Stress Tolerance and Lactic Acid Production in *Lactococcus lactis* NZ9000 under Conditions of Thermal Stress by Heterologous Expression of *Escherichia coli dnaK*," *Appl Environ Microbiol*, vol. 76, no. 13, pp. 4277–4285, Jul. 2010, doi: 10.1128/AEM.02878-09.

[181] M. Bibra, D. Samanta, N. K. Sharma, G. Singh, G. R. Johnson, and R. K. Sani, "Food Waste to Bioethanol: Opportunities and Challenges," *Fermentation*, vol. 9, no. 1, p. 8, Dec. 2022, doi: 10.3390/fermentation9010008.

[182] J. Liu, S. H. Dantoft, A. Würtz, P. R. Jensen, and C. Solem, "A novel cell factory for efficient production of ethanol from dairy waste," *Biotechnol Biofuels*, vol. 9, no. 1, p. 33, Dec. 2016, doi: 10.1186/s13068-016-0448-7.

[183] J. Liu, S. H. Dantoft, A. Würtz, P. R. Jensen, and C. Solem, "A novel cell factory for efficient production of ethanol from dairy waste," *Biotechnol Biofuels*, vol. 9, no. 1, p. 33, Dec. 2016, doi: 10.1186/s13068-016-0448-7.

[184] S. Nawab, N. Wang, X. Ma, and Y.-X. Huo, "Genetic engineering of non-native hosts for 1-butanol production and its challenges: a review," *Microb Cell Fact*, vol. 19, no. 1, p. 79, Dec. 2020, doi: 10.1186/s12934-020-01337-w.

[185] V. Kandasamy, J. Liu, S. H. Dantoft, C. Solem, and P. R. Jensen, "Synthesis of (3R)-acetoin and 2,3-butanediol isomers by metabolically engineered Lactococcus lactis," *Sci Rep*, vol. 6, no. 1, p. 36769, Nov. 2016, doi: 10.1038/srep36769.

[186] J. Liu, Z. Wang, V. Kandasamy, S. Y. Lee, C. Solem, and P. R. Jensen, "Harnessing the respiration machinery for high-yield production of chemicals in metabolically engineered Lactococcus lactis," *Metabolic Engineering*, vol. 44, pp. 22–29, Nov. 2017, doi: 10.1016/j.ymben.2017.09.001.

[187] I. Hernández, D. Molenaar, J. Beekwilder, H. Bouwmeester, and J. E. T. Van Hylckama Vlieg, "Expression of Plant Flavor Genes in *Lactococcus lactis*," *Appl Environ Microbiol*, vol. 73, no. 5, pp. 1544–1552, Mar. 2007, doi: 10.1128/AEM.01870-06.

[188] A. A.-L. Song, L. L. A. In, S. H. E. Lim, and R. A. Rahim, "A review on Lactococcus lactis: from food to factory," *Microb Cell Fact*, vol. 16, no. 1, p. 55, Dec. 2017, doi: 10.1186/s12934-017-0669-x.

[189] F. Boukid *et al.*, "Fermentation for Designing Innovative Plant-Based Meat and Dairy Alternatives," *Foods*, vol. 12, no. 5, p. 1005, Feb. 2023, doi: 10.3390/foods12051005.

[190] H. Elhalis, X. Y. See, R. Osen, X. H. Chin, and Y. Chow, "Significance of Fermentation in Plant-Based Meat Analogs: A Critical Review of Nutrition, and Safety-Related Aspects," *Foods*, vol. 12, no. 17, p. 3222, Aug. 2023, doi: 10.3390/foods12173222.

[191] G. Goksen *et al.*, "A glimpse into plant-based fermented products alternative to animal based products: Formulation, processing, health benefits," *Food Research International*, vol. 173, p. 113344, Nov. 2023, doi: 10.1016/j.foodres.2023.113344.

[192] A. R. Harper, R. C. J. Dobson, V. K. Morris, and G. Moggré, "Fermentation of plant-based dairy alternatives by lactic acid bacteria," *Microbial Biotechnology*, vol. 15, no. 5, pp. 1404–1421, May 2022, doi: 10.1111/1751-7915.14008.

[193] 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," *Current Opinion in Biotechnology*, vol. 65, pp. 171–179, Oct. 2020, doi: 10.1016/j.copbio.2020.02.016.

[194] K. C. P. Cruz, L. O. Enekegho, and D. T. Stuart, "Bioengineered Probiotics: Synthetic Biology Can Provide Live Cell Therapeutics for the Treatment of Foodborne Diseases," *Front Bioeng Biotechnol*, vol. 10, p. 890479, 2022, doi: 10.3389/fbioe.2022.890479.

[195] R. Drolia *et al.*, "Receptor-targeted engineered probiotics mitigate lethal Listeria infection," *Nat Commun*, vol. 11, no. 1, p. 6344, Dec. 2020, doi: 10.1038/s41467-020-20200-5.

[196] F. F. Duan, J. H. Liu, and J. C. March, "Engineered Commensal Bacteria Reprogram Intestinal Cells Into Glucose-Responsive Insulin-Secreting Cells for the Treatment of Diabetes," *Diabetes*, vol. 64, no. 5, pp. 1794–1803, May 2015, doi: 10.2337/db14-0635.

[197] Y. J. Goh and R. Barrangou, "Portable CRISPR-Cas9 ^{N} System for Flexible Genome Engineering in Lactobacillus acidophilus, Lactobacillus gasseri, and Lactobacillus paracasei," *Appl Environ Microbiol*, vol. 87, no. 6, pp. e02669-20, Feb. 2021, doi: 10.1128/AEM.02669-20.

[198] D. Lubkowicz, C. L. Ho, I. Y. Hwang, W. S. Yew, Y. S. Lee, and M. W. Chang, "Reprogramming Probiotic *Lactobacillus reuteri* as a Biosensor for *Staphylococcus aureus* Derived AIP-I Detection," *ACS Synth. Biol.*, vol. 7, no. 5, pp. 1229–1237, May 2018, doi: 10.1021/acssynbio.8b00063.

[199] J. Ma *et al.*, "Engineered probiotics," *Microb Cell Fact*, vol. 21, no. 1, p. 72, Apr. 2022, doi: 10.1186/s12934-022-01799-0.

[200] N. Mao, A. Cubillos-Ruiz, D. E. Cameron, and J. J. Collins, "Probiotic strains detect and suppress cholera in mice," *Sci. Transl. Med.*, vol. 10, no. 445, p. eaao2586, Jun. 2018, doi: 10.1126/scitranslmed.aao2586.

[201] K. Mugwanda *et al.*, "Recent advances in genetic tools for engineering probiotic lactic acid bacteria," *Biosci Rep*, vol. 43, no. 1, p. BSR20211299, Jan. 2023, doi: 10.1042/BSR20211299.

[202] S. Taghinezhad-S *et al.*, "Probiotic-Based Vaccines May Provide Effective Protection against COVID-19 Acute Respiratory Disease," *Vaccines (Basel)*, vol. 9, no. 5, p. 466, May 2021, doi: 10.3390/vaccines9050466.

[203] H. Sharma and J. Bajwa, "Approach of probiotics in mental health as a psychobiotics," *Arch Microbiol*, vol. 204, no. 1, p. 30, Jan. 2022, doi: 10.1007/s00203-021-02622-x.

[204] T. Jan *et al.*, "Diversity, distribution and role of probiotics for human health: Current research and future challenges," *Biocatalysis and Agricultural Biotechnology*, vol. 53, p. 102889, Oct. 2023, doi: 10.1016/j.bcab.2023.102889.

[205] F. Ansari, M. Neshat, H. Pourjafar, S. M. Jafari, S. A. Samakkhah, and E. Mirzakhani, "The role of probiotics and prebiotics in modulating of the gut-brain axis," *Front. Nutr.*, vol. 10, p. 1173660, Jul. 2023, doi: 10.3389/fnut.2023.1173660.

[206] L. G. Bermúdez-Humarán, E. Salinas, G. G. Ortiz, L. J. Ramirez-Jirano, J. A. Morales, and O. K. Bitzer-Quintero, "From Probiotics to Psychobiotics: Live Beneficial Bacteria Which Act on the Brain-Gut Axis," *Nutrients*, vol. 11, no. 4, p. 890, Apr. 2019, doi: 10.3390/nu11040890.

[207] I. S. P. Savizi, T. Soudi, and S. A. Shojaosadati, "Systems biology approach in the formulation of chemically defined media for recombinant protein overproduction," *Appl Microbiol Biotechnol*, vol. 103, no. 20, pp. 8315–8326, Oct. 2019, doi: 10.1007/s00253-019-10048-1.

[208] M. Papagianni, "METABOLIC ENGINEERING OF LACTIC ACID BACTERIA FOR THE PRODUCTION OF INDUSTRIALLY IMPORTANT COMPOUNDS," *Computational and Structural Biotechnology Journal*, vol. 3, no. 4, p. e201210003, Oct. 2012, doi: 10.5936/csbj.201210003.

[209] E. Díaz-Montes and R. Castro-Muñoz, "Edible Films and Coatings as Food-Quality Preservers: An Overview," *Foods*, vol. 10, no. 2, p. 249, Jan. 2021, doi: 10.3390/foods10020249.

[210] Y. Koide, H. Ikake, Y. Muroga, and S. Shimizu, "Effect of the cast-solvent on the morphology of cast films formed with a mixture of stereoisomeric poly(lactic acids)," *Polym J*, vol. 45, no. 6, pp. 645–650, Jun. 2013, doi: 10.1038/pj.2012.192.

[211] L. Kumar, D. Ramakanth, K. Akhila, and K. K. Gaikwad, "Edible films and coatings for food packaging applications: a review," *Environ Chem Lett*, vol. 20, no. 1, pp. 875–900, Feb. 2022, doi: 10.1007/s10311-021-01339-z.

[212] S. P. M. Silva, J. A. Teixeira, and C. C. G. Silva, "Recent advances in the use of edible films and coatings with probiotic and bacteriocin-producing lactic acid bacteria," *Food Bioscience*, vol. 56, p. 103196, Dec. 2023, doi: 10.1016/j.fbio.2023.103196.

[213] J. Wu, Y. Xin, J. Kong, and T. Guo, "Genetic tools for the development of recombinant lactic acid bacteria," *Microb Cell Fact*, vol. 20, no. 1, p. 118, Jun. 2021, doi: 10.1186/s12934-021-01607-1.

[214] N. Anesiadis, W. R. Cluett, and R. Mahadevan, "Dynamic metabolic engineering for increasing bioprocess productivity," *Metabolic Engineering*, vol. 10, no. 5, pp. 255–266, Sep. 2008, doi: 10.1016/j.ymben.2008.06.004.

[215] R. R. Kumar and S. Prasad, "Metabolic engineering of bacteria," *Indian J Microbiol*, vol. 51, no. 3, pp. 403–409, Jul. 2011, doi: 10.1007/s12088-011-0172-8.

[216] T. V. Plavec and A. Berlec, "Safety Aspects of Genetically Modified Lactic Acid Bacteria," *Microorganisms*, vol. 8, no. 2, p. 297, Feb. 2020, doi: 10.3390/microorganisms8020297.