

Microbes in Action: Powering Sustainable Fermentation for Food, Pharma, and Bioeconomy

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Abstract

Background and Objective: Fermentation, a microbial-driven metabolic process, has been utilized for millennia to produce, preserve, and enhance food and beverages, evolving from traditional practices such as yogurt and wine to modern applications in biofuels and pharmaceuticals. Fermentation has been found to have its earliest evidence more than 7,000 years ago. The principle of fermentation was established in the 19th century, based on the foundational research of Pasteur, who bridged the connection between microbial activity and chemical change, setting the stage for modern microbiology and biotechnology. This review explores microbial roles in fermentation, bridging traditional and biotechnological advancements by comparing bacterial and fungal processes, analyzing key metabolites, and highlighting genetic innovations.

Results and Conclusion: The review comprehensively explores the pivotal role of microbial fermentation, spanning traditional practices to modern innovations, highlighting the extensive diversity of 195 bacterial and 69 fungal species, with lactic acid bacteria (LAB) and *Saccharomyces cerevisiae* being prominent examples. It compares bacterial and fungal fermentation processes, noting that bacterial fermentation often yields higher protein content in products like fermented soybean meal (FSBM), and discusses key metabolites, including primary (amino acids, organic acids, vitamins) and secondary (antibiotics, antitumor agents) compounds, for their industrial and health applications. The review also examines various fermentation methods and their suitability for different products, emphasizing advancements in genetic engineering for strain optimization, while underscoring the health benefits of probiotics and fermented foods and the potential of emerging technologies to address food security and sustainability. In conclusion, microbial fermentation bridges ancient traditions with cutting-edge science, offering transformative potential across industries, where innovations in genetic engineering and process optimization drive efficiency and sustainability, and the expanding microbial repertoire continues to unlock novel applications, integrating fermentation technology with modern biotechnological tools to address global challenges in nutrition, health, and environmental sustainability.

Keywords: Biofuel production, bioeconomy, CRISPR-Cas9, food security, probiotics, solid-state fermentation (SSF), submerged fermentation (SmF), sustainability, synthetic biology.

What is “already known” on this topic:

- The critical role of microbes in fermentation, from traditional foods to advanced bioproducts
- The profiles of 195 bacterial and 69 fungal species driving fermentation across food, pharma, and bioeconomy sectors.

What this article adds:

- It showcases CRISPR and synthetic biology techniques for enhanced fermentation efficiency and novel metabolic production.
- Fermentation's contributions to sustainability, food security, waste valorization, and the circular bioeconomy are highlighted.
- Scalability challenges and future innovations in fermentation technologies are discussed.

1. Introduction

Microorganisms have played a central role in human life, particularly during the food fermentation process. Fermentation has been utilised over the centuries to produce, conserve, and flavour beverages and foods, enhancing their nutritional and sensory qualities. Fermentation is a metabolic process that uses microorganisms to break down carbohydrates into alcohol, organic acids, gases, or other desired by-products [1]. The fermentation processes were induced by naturally occurring populations of bacteria, yeasts, and moulds, whose synergistic activity produced characteristic textures, flavours, and nutritionally beneficial advantages. This has evolved from a mystical art to a science with the discovery of microorganisms by pioneers like Antonie van Leeuwenhoek and Louis Pasteur [2]. Development of microbiology, molecular biology, and bioprocess engineering has made it possible to identify, isolate, and genetically improve microbial strains for large-scale fermentations. Fermentation has numerous applications in the biotechnology industry, including the production of antibiotics, vaccines, enzymes, biofuels, biodegradable plastics, and food products. Considering recent health and sustainability concerns, microbial fermentation offers promising routes for producing plant-based meat alternatives, upcycling agro-industrial waste into high-value products, and generating nutraceuticals and pharmaceuticals.

Probiotic fermentation is another contemporary area of research in food fermentation. It refers to the process where live microorganisms, known as probiotics, are introduced to a food or substrate to undergo fermentation, resulting in a variety of beneficial changes [3]. This process enhances the food's nutritional value, digestibility, and flavour, while also introducing beneficial bacteria that can positively impact the consumer's gut health [4]. Probiotic technology leads the functional food sector based on strain specificity, gut microbiota interaction, and individualised nutrition.

Contamination control issues, regulatory acceptance of genetically modified strains, consumer acceptability, and scaling up of new technology are being addressed more effectively through interdisciplinary and collaborative partnerships at a global level [5]. The function of microbes in fermentation is a balance between tradition and

innovation, promoting an interrelated and symbiotic collaboration between human creativity and microbial activity. Fermentation is a biotechnology that has been utilised for millennia to flavour and preserve food, produce drinks, and create pharmaceuticals. Its roots date back to microbes that transform raw material into staple foods, such as bread, cheese, wine, and beer [2]. Fermentation is coupled with technology to produce a wide variety of products, ranging from traditional fermented foods and specialty beverages on one end and antibiotics, biofuels, and recombinant proteins on the other [6]. The metabolic diversity of microbes has been utilised to produce both submerged and solid-state fermentation systems, each offering distinct advantages for specific applications. The introduction of synthetic biology, genetic engineering, and omics technologies has further transformed microbial fermentation with improved metabolic pathways for precision biomanufacturing.

Technologies such as continuous fermentation, immobilised cell systems, and electro-fermentation have enhanced process efficiency and sustainability. Additionally, their applications in cellular agriculture, biodegradable plastics, and waste valorisation reflect the ability of fermentation to address key challenges in food security, healthcare, and environmental sustainability. Fermentation is alternatively referred to as Zymology or Zymurgy and was practised by humans since the Neolithic era (around 10000 BC). Industrial fermentation involves the use of microorganisms, such as bacteria and fungi, to produce goods beneficial to humans and acidic products with applications in the food industry [7]. Fermentation rate depends on the concentration of microorganisms, cell types, cellular constituents, enzymes, temperature, pH, and the aerobic fermentation factor.

2. Inventory of microbial species used in fermentation

Over the past two decades, the number of microbial species used in fermentation processes has significantly increased. The 2002 International Dairy Federation Inventory, which catalogued 82 bacterial species and 31 yeast and mould species, has been replaced by the current



Inventory of Microbial Food Cultures, which now includes 195 bacterial species and 69 yeast and mould species [8]. This growth is attributed to advanced genomic sequencing techniques, increased demand for a variety of fermented foods, and advancements in microbial biotechnology. The bacterial repository has experienced a meteoric rise in lactic acid bacteria (LAB) genera, with lactobacilli comprising 45 different species used in dairy, meat, vegetable, and cereal fermentations [8]. In 2020, the *Lactobacillus* genus was significantly reorganized, with many species being reclassified into new genera. This included the creation of 23 new genera. For example, *Lactobacillus casei* is now *Lacticaseibacillus casei*, and *Lactobacillus plantarum* is now *Lactiplantibacillus plantarum*. *Lactobacillus rhamnosus* is now *Lacticaseibacillus rhamnosus*, and *Lactobacillus brevis* is now *Levilactobacillus brevis*. *Lactobacillus salivarius* is now *Ligilactobacillus salivarius*, and *Lactobacillus fermentum* is now *Limosilactobacillus fermentum* [9]. The number of *Bifidobacterium* species increased from 4 to 10 due to their importance in probiotic applications. The yeast and mould inventory has grown from traditional *Saccharomyces cerevisiae* and *Aspergillus oryzae* species to include a broad range of non-traditional species such as *Pichia kudriavzevii* for cocoa fermentation and *Neurospora intermedia* for oncom production. The identification and utilisation of extremophiles, such as thermophilic *Geobacillus* species in hot fermentations and halophilic Archaea in high-salt processes, has triggered diversification of microorganisms. It also includes engineered strains developed through the application of both traditional mutagenesis and novel genetic techniques, such as lactose-positive yeast strains for use in dairy applications and bacteriocin-producing LAB variants for enhanced food safety. Regulatory reforms and enhanced safety assessment procedures have enabled the inclusion of previously underutilised species. Concurrently, market demand for flavor, texture, and health-affecting effects has spurred the utilization of microbial diversity from globally dispersed traditional fermented foods [9]. The diversity of microorganisms involved in fermentation processes spans a wide range of taxonomic groups, including bacteria, yeasts, and filamentous fungi. These microbes play pivotal roles in transforming raw substrates into valuable fermented products. As illustrated in Figure 1, the taxonomic distribution highlights the predominance of LAB and *Saccharomyces cerevisiae* in traditional and industrial fermentations, alongside other key genera such as *Aspergillus* sp. and *Bifidobacterium* sp. This microbial richness underscores the versatility of fermentation technology across food, pharmaceutical, and bioeconomic sectors.

The distribution of microbial species used in fermentation was systematically categorised across relevant

taxonomic units, as detailed in Table 1 (bacteria) and Table 2 (fungi/yeasts). Table 1 highlights the predominance of lactobacilli (45 species) and *Bifidobacterium* (10 species) among LAB, alongside *Bacillus* (over 30 species), which are also utilised for industrial enzymes. Table 2 emphasizes *Aspergillus* and *Saccharomyces* as key fungal genera, with *Aspergillus niger* for organic acids and *Saccharomyces cerevisiae* for ethanol. Some taxa, such as *Acetobacter* (vinegar) and *Pichia* (recombinant proteins), reflect diversification. This structured classification shows the microbial richness harnessed in traditional and modern fermentation biotechnologies.

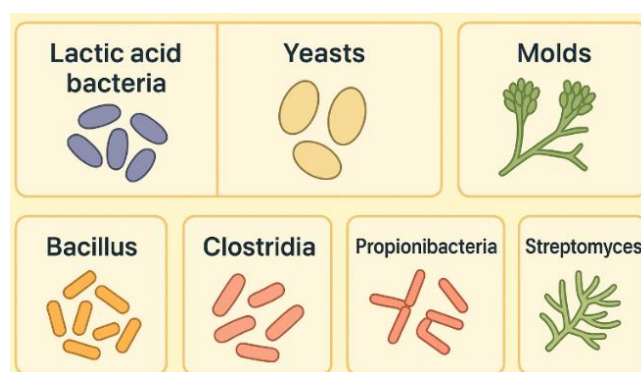


Figure 1. Taxonomic groups of microorganisms involved in fermentation processes.

2.1. Bacteria

2.1.1. Actinobacteriaceae

The microbial richness in the manufacture of fermented foods has undergone extensive taxonomic resolution and growth, indicative of advances in genomic research for the microbial ecology within food substrates. The genus *Brachybacterium* is a component of the surface microbiota of artisanal cheeses, such as Gruyère and Beaufort. It plays a role in proteolysis and flavour enhancement through its enzyme activities. *Microbacterium gubbeenense* is a significant member of the classical red-smear surface cultures employed in surface-ripened cheeses, playing a role in colour development and aroma profile [29]. The genus *Bifidobacterium* has undergone taxonomic revisions, with the redescription of *Bifidobacterium infantis* and the addition of *Bifidobacterium thermophilum* due to its significant roles in functional food applications for probiotic dairy products. *Brevibacterium aurantiacum* is utilised for its essential role in the ripening process, contributing to the flavour complexity and the distinctive orange colour of such cheeses. The *Propionibacterium* genus, including *Propionibacterium freudenreichii* subsp. *globosum* and *Propionibacterium jensenii* (now reclassified as *Acidipropionibacterium jensenii*) [30].



Table 1. Diversity of bacterial isolates involved in fermentation

S. No	Phylum	Family	Genus	No. of species	Role in fermentation	References
1	Actinobacteria	Bifidobacteriaceae	<i>Bifidobacterium</i>	8	Probiotic functions in dairy; gut microbiota modulation	[10]
		Brevibacteriaceae	<i>Brevibacterium</i>	3	Cheese ripening (e.g., Limburger); flavour compound production	[10]
		Corynebacteriaceae	<i>Corynebacterium</i>	4	Glutamate production; fermented meat products	[10]
		Dermabacteraceae	<i>Brachybacterium</i>	2	Cheese maturation; aroma development	[10]
		Microbacteriaceae	<i>Microbacterium</i>	1	Dairy fermentation; enzyme production	[11, 12]
		Micrococcaceae	<i>Arthrobacter</i>	4	Cheese ripening; soil fermentation	[11, 12]
		Micrococcaceae	<i>Kocuria</i>	2	Fermented meat products	[11, 12]
		Micrococcaceae	<i>Micrococcus</i>	2	Meat fermentation; colour stabilisation	[11, 12]
		Propionibacteriaceae	<i>Propionibacterium</i>	5	Swiss cheese (eye formation); vitamin B12 production	[11, 12]
		Streptomycetaceae	<i>Streptomyces</i>	1	Antibiotic production; enzyme synthesis	[13]
Subtotal – 32 Species						
2	Firmicutes	Bacillaceae	<i>Bacillus</i>	3	Natto production: alkaline fermentation	[13]
		Carnobacteriaceae	<i>Carnobacterium</i>	3	Meat/fish preservation	[13]
		Enterococcaceae	<i>Enterococcus</i>	3	Dairy fermentation, probiotic	[14,15]
		Enterococcaceae	<i>Tetragenococcus</i>	2	High-salt fermentations (soy sauce)	[14,15]
		Lactobacillaceae	<i>Lactobacillus</i>	84	Yogurt, sauerkraut, sourdough production	[14,15]
		Lactobacillaceae	<i>Pediococcus</i>	3	Sausage fermentation	[14,15]
		Leuconostocaceae	<i>Leuconostoc</i>	12	Dairy/wine fermentation	[16]
		Leuconostocaceae	<i>Oenococcus</i>	1	Wine malolactic fermentation	[16]
		Leuconostocaceae	<i>Weissella</i>	9	African fermented foods	[16]
		Staphylococcaceae	<i>Staphylococcus</i>	15	Fermented meat products	[16]
		Streptococcaceae	<i>Streptococcus</i>	3	Yoghurt/cheese starter cultures	[16]
		Streptococcaceae	<i>Lactococcus</i>	3	Dairy fermentation	[17]
		Subtotal – 142 Species				
3	Proteobacteria	Acetobacteraceae	<i>Acetobacter</i>	9	Vinegar production	[18]
		Acetobacteraceae	<i>Gluconacetobacter</i>	9	Kombucha production	[18]
		Enterobacteriaceae	<i>Hafnia</i>	9	Cheese flavour development	[19]
		Enterobacteriaceae	<i>Halomonas</i>	1	High-salt fermentations	[19]
		Sphingomonadaceae	<i>Zymomonas</i>	1	Alcohol production (pulque)	[20]
Subtotal – 21 Species						
Total – 195 Species						

2.1.2. Firmicutes

The International Molecular Foods inventory has expanded significantly with advances in microbial taxonomy and the growing industrial demand for specialised starter cultures in a diverse range of food matrices. Some notable additions include three species of *Carnobacterium*, *Tetragenococcus*, *Weissella*, *Enterococcus faecalis*, *Lactobacillus*, *Staphylococcus*, and *Streptococcus*. *Carnobacterium* is essential for meat fermentations, and *Tetragenococcus* comprises species required for high-salt fermentations, such as those used in the production of soy

sauce and fish products. *Weissella* splits species previously classified as part of the *Leuconostoc mesenteroides* complex for their distinctive phylogenetic and metabolic characteristics [31]. *Enterococcus faecalis* is the starter for dairy, meat, and vegetable fermentations, whereas the lactobacilli comprise 82 species. The *Staphylococcus* genus contains 13 species, which prove their critical contribution towards meat fermentation. This also allows for the specific selection of strains to achieve goal-directed fermentation results, such as balanced acidification and aroma formation in sausages or maximum gas formation in sourdough.



Table 2. Diversity of fungal isolates involved in fermentation.

S.No	Phylum	Family	Genus	No. of species	Role in fermentation	References
1	Ascomycota	Cordycipitaceae	<i>Lecanicillium</i>	1	Biocontrol agent in fermented foods	[21]
		Dipodascaceae	<i>Geotrichum</i>	1	Cheese rind formation, vegetable fermentation	[21]
		Dipodascaceae	<i>Yarrowia</i>	1	Lipolytic activity in meat/dairy	[21]
		Dipodascaceae	<i>Galactomyces</i>	1	Dairy fermentation, mycoprotein production	[21]
		Microascaceae	<i>Scopulariopsis</i>	1	Meat fermentation, flavour development	[22]
		Nectriaceae	<i>Fusarium</i>	2	Tempeh production, mycoprotein	[22]
		Saccharomycetaceae	<i>Candida</i>	10	Coffee, cocoa, and dairy fermentations	[23, 24]
		Saccharomycetaceae	<i>Saccharomyces</i>	4	Bread, beer, wine, and sake production	[23, 24]
		Saccharomycetaceae	<i>Pichia</i>	4	Traditional beverage fermentations	[25]
		Trichomaceae	<i>Aspergillus</i>	4	Soy sauce, miso, sake (amylase/protease production)	[26]
Trichomaceae	<i>Penicillium</i>	7	Cheese ripening (Camembert, Roquefort), meat products	[26]		
Subtotal – 58 Species						
2	Basidiomycota	Cystofilobasidiaceae	<i>Cystofilobasidium</i>	1	Pigment production in fermented foods	[27]
		Cystofilobasidiaceae	<i>Guehomyces</i>	1	Dairy fermentation	[27]
Subtotal – 2 Species						
3	Zygomycota	Mucoraceae	<i>Mucor</i>	4	Tempeh, sufu (soybean fermentation)	[28]
		Mucoraceae	<i>Rhizopus</i>	4	Tempeh, alcoholic beverages (amylase production)	[28]
Subtotal – 8 Species						
Total – 68 Species						

2.1.3. Proteobacteriaceae

The International Molecular Foods stock has been supplemented with specialised microbial species, which cover conventional fermentation practices and new biotechnological developments. Acetic acid bacteria, such as *Acetobacter* sp. and *Gluconacetobacter* sp., play a crucial role in the production of vinegar, as well as in the fermentation of cocoa and coffee, and in imparting flavour sensations. *Halomonas elongata* is a halotolerant organism that has been indicated in meat fermentation systems due to its resistance to high sugar levels and acidic environments [32]. This expanded microbiota enables specificity in the fermentation process, as observed in *Acetobacter pasteurianus* strains used to produce artisanal balsamic vinegar. *Zymomonas mobilis*, due to its novel pyruvate decarboxylase and alcohol dehydrogenase II pathway, prefers the irreversible production of ethanol. The industrial application of these microbial resources has demonstrated quantifiable effects, wherein *Gluconacetobacter europaeus* strains reduced vinegar-making times by 30–40 % and specific *Zymomonas mobilis* isolates achieved 15–20 % productivity gains in ethanol production, making fermentation more feasible for tequila production.

2.2. Fungi

2.2.1. Yeast

Fungal taxonomy employed in food production has been extensively utilised, as numerous species formerly associated with the genus *Candida* have been reassigned to more phylogenetically accurate genera. This has significant implications for food science and industry, enabling more accurate strain selection, process optimisation during fermentation, product uniformity, and the prevention of spoilage risk [33]. Examples are *Dekkera bruxellensis*, *Debaryomyces hansenii*, *Hanseniaspora uvarum*, *Kazachstania turicensis*, *Metschnikowia pulcherrima*, *Pichia occidentalis*, *Rhodospiridium* spp., *Saccharomyces pastorianus*, *Saccharomycopsis fibuligera*, *Saturnisporus saitoi*, *Sporobolomyces roseus*, *Torulaspora delbrueckii*, *Trichosporon cutaneum*, *Wickerhamomyces anomalus*, *Yarrowia lipolytica*, *Zygosaccharomyces bailii*, and *Zygosaccharomyces rouxii*. The persistence of some *Candida* species with unknown teleomorphs of fungal life cycles, to explain their sexual phases or validate their taxonomic position using genomic information. The functional properties of these microorganisms are being utilised increasingly, such as *Metschnikowia pulcherrima*'s use in biocontrol to inhibit moulds on vineyards and



Wickerhamomyces anomalus's delivery of killer toxins that inhibit spoilage yeasts in fermented foods [34].

2.2.2. Filamentous fungi

Fungi are well-established in Asian food fermentation traditions, and have been added to the list of microorganisms used in fermented foods in Europe. There is significant potential in adopting well-established fungal starter cultures from Asian food fermentation traditions and incorporating them into European practices. Key fungi include *Aspergillus oryzae*, *Aspergillus sojae*, and *Rhizopus oligosporus*, which are essential to produce Asian fermented foods and beverages such as miso, soy sauce, sake, awamori liquors, and Puerh tea. *Fusarium* species, such as *Fusarium domesticum* and *Fusarium solani*, are utilised in European food applications, including cheese fermentations, Vacherin cheese production, and the development of meat alternatives. *Penicillium* species dominate fungal applications in European dairy traditions, with *Penicillium camemberti* being used in bloomy-rind cheeses such as Camembert and Brie. European charcuterie traditions utilise *Penicillium nalgiovense* and select strains of *Penicillium chrysogenum* for mould-fermented sausages, while *Lecanicillium lecanii* shows promise for cheese ripening applications. Fungal contributions beyond fermentation to include colourant production, with species like *Epicoccum nigrum* and *Penicillium purpurogenum* capable of generating natural pigments [35]. This fungal application highlights the rich diversity of fungal species in global food systems and the significant opportunities for cross-cultural

transfer of fungal technologies in Asian fermentation fungi to European practices for novel product development.

3. Comparison of bacterial and fungal Fermentation

Fermented Soybean Meal (FSBM) is a highly nutritious protein source, thanks to the unique metabolic pathways and enzymatic activities of the microorganisms involved. Both fungal and bacterial fermentation processes effectively reduce antinutritional factors and enhance the nutritional quality of the resulting products. However, there are notable differences in specific components that influence the suitability of FSBM for various dietary and health applications [36]. Both the fungal and bacterial fermentations increased crude protein content through microbial biomass accumulation, with fungal-fermented FSBM showing a 19.4% increase in soluble protein, a crucial indicator of digestibility, and a more substantial 63.11% increase in bacterial-fermented FSBM. These fermentations also reduced the immunoreactivity of soybean meal, which is essential for minimising allergic responses and enhancing food safety. Amino acid profiles show that crucial amino acids generally remain stable during fermentation, but specific changes occur depending on the microorganism used. These findings have practical implications for animal feed and human nutrition, where FSBM is increasingly used as a high-quality protein source. A comparative parameter of bacterial and fungal fermentation processes is shown in Table 3.

Table 3. Comparative parameters of bacterial and fungal fermentation processes

S.No	Parameters	Bacterial fermentation	Fungal fermentation	References
1	Microorganisms	Bacteria (lactobacilli, <i>Escherichia coli</i> , <i>Bacillus</i>)	Fungi (<i>Saccharomyces</i> , <i>Aspergillus</i> , <i>Penicillium</i>)	[37]
2	Optimal pH	Neutral to slightly acidic (pH 6-7)	Acidic (pH 4-6)	[38]
3	Optimal Temperature	Mesophilic (20-45°C) or Thermophilic (>45°C)	Mostly mesophilic (25-30°C)	[39]
4	Oxygen Requirement	Aerobic or anaerobic (species-dependent)	Mostly aerobic (some yeasts are facultative anaerobes)	[40]
5	Primary Products	Lactic acid, acetic acid, ethanol, antibiotics, and enzymes	Antibiotics, organic acids, enzymes, ethanol, mycoproteins	[41]
6	Applications	Dairy fermentation (yoghurt, cheese), probiotics, biofuels	Antibiotic production (penicillin), food (tempeh, soy sauce), bioethanol	[42]
7	Growth Rate	Faster (doubling time: 2060 mins)	Slower (doubling time: hours to days)	[43]
8	Substrate Utilization	Prefers simple sugars (glucose, lactose)	Can degrade complex substrates (cellulose, lignin)	[44]
9	Metabolic Pathways	Homolactic, heterolactic, mixed acid fermentation	Ethanol fermentation, citric acid cycle, secondary metabolite production	[45]



4. Metabolites produced by microorganisms

Microorganisms play a crucial role in fermentation processes, generating diverse metabolites that have been utilized for centuries in food preservation and have evolved into high-tech biotechnological applications [46]. Primary metabolites, including amino acids, nucleotides, vitamins, organic acids, and alcohols, are generated during the growing stage of microorganisms and are of industrial importance. Genetically modified strains, such as *Corynebacterium glutamicum* and *Brevibacterium* species, maximise the yield of these metabolites. Secondary metabolites, such as antibiotics, antitumor compounds, and immunosuppressants, are produced during the stationary phase of microbial cultures and have had a profound impact on medicine and agriculture [46]. Downstream processing and fermentation technology enable the effective extraction and purification of these metabolites, facilitating their commercial exploitation. The green advantages of microbial fermentation are being leveraged in global initiatives to achieve a circular bioeconomy.

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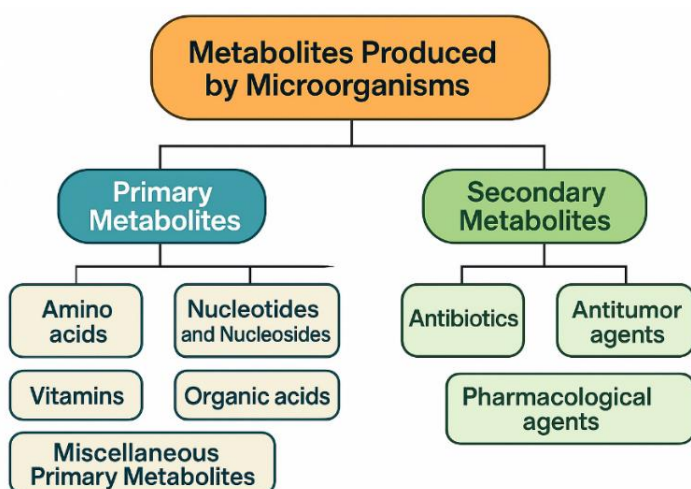


Figure 2. Functional categories of microbial metabolites

4.1. Primary metabolites

Primary metabolites are small, essential molecules found in all living cells that serve as intermediates or end products of metabolic processes. Primary metabolites comprise amino acids, nucleotides, vitamins, solvents, and organic acids, with applications in industry ranging from human and animal nutrition to the production of biofuels and solvents. Innovative applications include the use of monosodium glutamate and nucleotides in food processing, as well as organic acids such as ethylenediaminetetraacetic acid in pharmaceuticals and water treatment. Additionally, bio-based organic acids like succinic acid are utilised in green packaging and textile production [47]. The production of these metabolites at an industrial scale largely depends on microbial fermentation, where microorganisms are genetically and physiologically engineered to overproduce target molecules through sophisticated biotechnological measures. Technological advancements in bioreactor design and downstream processing methods have further enhanced fermentation processes, with the inclusion of systems biology tools providing a systemic view of cellular metabolism and identifying primary genetic targets for manipulation. The transition to a sustainable and circular bioeconomy has raised demand to produce metabolites using low-value, renewable feedstocks, such as lignocellulosic biomass, molasses, and waste glycerol [48]. The output of economically feasible purification processes for high-value metabolites, and the scaling-up of optimised laboratory processes to industrial scale, without decreasing their productivity.

4.1.1. Amino acids

The global amino acid market, valued at over \$6 billion, is a rapidly growing sector in industrial biotechnology. Monosodium glutamate, the most widely produced amino acid, is produced through large-scale fermentation processes using high-performance bacterial strains, primarily *Corynebacterium glutamicum* and its subspecies. Industrial microbiology has successfully achieved inhibition by developing auxotrophic mutants and antimetabolite-resistant mutants to deregulate metabolic pathways and prevent feedback inhibition [49]. Modern strain development often combines both strategies, creating microbial producers with multiple deregulated pathways capable of hyperaccumulating desired compounds. Recombinant DNA technology has revolutionised amino acid production by enabling precise genetic modifications, such as the introduction of plasmid-borne biosynthetic operons, the overexpression of genes encoding rate-limiting enzymes, and the strategic cloning of feedback-resistant enzyme variants. Metabolic engineers have also enhanced production by introducing heterologous genes or amplifying



the first committed step in amino acid biosynthesis to maximise carbon flux toward desired products [50]. Amino acid production may involve synthetic biology to design novel biosynthetic pathways, artificial intelligence (AI) to predict optimal genetic modifications, and the exploration of non-conventional hosts for specialised applications.

4.1.2. Nucleotides and nucleosides

The industrial production of nucleotides through microbial fermentation has gained significant commercial traction due to the growing demand for guanylic acid and inosinic acid, which serve as potent flavour enhancers in the food industry. Three primary biotechnological processes dominate nucleotide manufacturing: (1) the enzymatic hydrolysis of yeast RNA using fungal nucleases to yield adenosine monophosphate (AMP) and guanosine monophosphate (GMP), which are subsequently deaminated to produce inosine monophosphate (IMP); (2) the fermentative production of nucleosides (inosine and guanosine) by metabolically engineered *Bacillus subtilis* mutants, which are later phosphorylated to their respective 5'-nucleotides; and (3) the direct fermentation of sugars to IMP using high-performance *Corynebacterium glutamicum* strains genetically optimized for purine overproduction [51]. A nucleotide biosynthesis is the feedback inhibition exerted by intracellular AMP and GMP, which regulate purine metabolism through the allosteric control of key enzymes, such as phosphoribosyl pyrophosphate synthetase and amidophosphoribosyl transferase. This regulation can be studied using adenine auxotrophic mutants and exploiting antimetabolite resistance strategies, including the deletion of IMP dehydrogenase.

4.1.3. Vitamins

Microbial fermentation is a vital aspect of industrial vitamin production, with over 50 % of commercially manufactured vitamins destined for animal feed supplementation. Seven vital vitamins or vitamin-like compounds are produced through microbial processes: β -carotene (provitamin A), vitamin B12 (cobalamin), vitamin B2 (riboflavin), vitamin B13 (orotic acid), vitamin C (ascorbic acid), γ -linolenic acid (vitamin F), and ergosterol (provitamin D). Riboflavin production has transitioned from chemical synthesis to microbial fermentation, driven by economic and environmental considerations [52]. Vitamin B12 production is another microbial triumph, with *Propionibacterium shermanii* and *Pseudomonas denitrificans* strains engineered to produce approximately 100,000 times more cobalamin than their metabolic needs require. Biotin production has traditionally relied on chemical synthesis through the multi-step Reichstein process; however, this route incorporates a crucial bioconversion step employing *Gluconobacter oxydans* mutants optimised for high sorbitol tolerance. Genetically

modified *Erwinia herbicola* strains incorporating *Corynebacterium* genes enable direct conversion of glucose to 2-keto-L-gulonic acid (2-KLG), the immediate precursor to ascorbic acid.

4.1.4. Organic acids

Microbial fermentation is the primary method for industrial-scale production of organic acids, utilising microorganisms such as fungi, yeasts, and bacteria to synthesise various acids. Citric acid is the most widely produced organic acid and is crucial in food and beverage applications due to its solubility, taste, and Generally Recognised as Safe (GRAS) status. The pharmaceutical industry allocates approximately 15 % of its production to anticoagulant formulations, effervescent tablets, and drug delivery systems. Citric acid production in *Aspergillus niger* occurs through glycolysis and the tricarboxylic acid cycle. *Candida oleophila* can generate remarkable yields in continuous fed-batch systems through nitrogen-limited cultivation with glucose excess [53]. Acetic acid production through microbial vinegar fermentation is one of the oldest biotechnological processes. The lactic acid industry has undergone a paradigm shift from chemical synthesis to microbial production of lactic acid, which acts as a precursor for biodegradable polylactic acid plastics. Metabolic engineering strategies have revolutionised and enabled the carbon flux through their pathways, including the overexpression of rate-limiting enzymes and the development of novel transport systems. The substrate hydrolysis with acid production allows acid-tolerant organisms to reduce neutralisation costs, and synthetic microbial consortia facilitate mixed acid production from complex feedstocks [53, 54].

4.1.5. Alcohols

Ethyl alcohol (ethanol) is a major metabolite produced through microbial fermentation, with global production exceeding 100 billion litres per year. This is primarily produced from sugar-based or polysaccharide-rich feedstocks using specialised yeast strains adapted to specific carbohydrate substrates. Brazil's Proálcool program is the world's most advanced bioethanol economy, producing 12.5 billion litres annually from sugarcane juice and molasses through highly optimised *Saccharomyces cerevisiae* fermentations, achieving ethanol concentrations of 8 – 12 %. The United States primarily uses corn starch hydrolysates as a substrate, generating over 60 billion litres annually as an oxygenate, which reduces greenhouse gas emissions by 40 – 50 % compared to fossil fuels and serves as a renewable alternative to methyl tert-butyl ether. The transition from first-generation to second-generation ethanol production has spurred intensive research into overcoming biomass recalcitrance through combined physicochemical pretreatment and enzymatic



saccharification using cellulase and hemicellulase cocktails from *Trichoderma reesei* and *Aspergillus* species [55]. Glycerol (glycerin), traditionally synthesised from petrochemical propylene, has seen renewed interest in microbial production, with the osmotolerant yeast *Candida glycerinogenes* yielding 130 g/L at 63 % theoretical efficiency through optimised fed-batch strategies [56].

4.1.6. Miscellaneous Primary Metabolites

Microbial polysaccharides are essential biopolymers utilised in various applications, including food, pharmaceuticals, cosmetics, and industrial processes. The most commercially used microbial exopolysaccharide is xanthan gum, produced by the bacterium *Xanthomonas campestris* through the aerobic fermentation of glucose or sucrose. Dextran, synthesised from sucrose by *Leuconostoc mesenteroides* strains, serves medical purposes as a blood plasma volume expander, an iron-dextran complex for anaemia treatment, and as a chromatographic matrix for protein purification. Pullulan, a fungal exopolysaccharide, exhibits unique film-forming properties, which are utilised in edible packaging, oxygen barrier coatings, and the production of pharmaceutical capsules. Other microbial polysaccharides include scleroglucan for oil recovery, curdlan for use in Japanese foods, bacterial alginate for wound dressings, and succinoglycan for applications in concrete and ceramics [55]. Hyaluronic acid, traditionally extracted from rooster combs, is now predominantly produced through streptococcal fermentation for ophthalmic surgery and cosmetic dermal fillers. The polyhydroxyalkanoate family of biodegradable plastics offers petroleum-free alternatives for packaging, medical implants, and 3D printing filaments [56]. Table 4 summarizes some examples of primary metabolites produced by microorganisms.

4.2. Secondary metabolites

Microbial organisms produce secondary metabolites, which are natural compounds with significant impacts on human health, agriculture, and biotechnology. They include antibiotics such as penicillin and tetracyclines, medicinal compounds, toxins, biopesticides, and bioactive compounds that affect plant and animal growth [57]. These complex molecules are synthesised during the idiophase of microbial growth and are phylogenetically restricted to specific microbial taxa. The secondary metabolites fulfil six important ecological roles: facilitating sexual reproduction, altering membrane permeability, serving as chemical warfare agents, enabling mutualistic interactions, regulating intricate morphological processes, and influencing population-level behaviours. The industrial synthesis of these compounds has revolutionised medicine since the 1940s, with β -lactam antibiotics having saved an estimated 200 million lives annually. Agrochemical uses are similarly revolutionary that managing parasitic nematodes and insect pests, while gibberellic acid increases yields [58].

4.2.1. Antibiotics

Antibiotics are biologically active molecules that target fundamental microbial processes, including DNA replication, RNA synthesis, protein synthesis, cell membrane integrity, cell wall biosynthesis, electron transport, and sporulation and germination pathways. The global antibiotic market comprises approximately 160 antibiotics and their derivatives, dominated by major structural classes, including β -lactams, peptide antibiotics, macrolide polyketides, tetracyclines, aminoglycosides, ansamycins, and glycopeptides. Modern antibiotic development employs three complementary strategies: semisynthetic modification of natural scaffolds, genetic engineering of biosynthetic pathways through recombinant DNA technology, and optimisation of fermentation processes [59].

Table 4: Primary metabolites produced by microorganisms and their applications

S. No	Metabolic category	Examples	Microorganisms Involved	Industrial Applications	References
1	Amino Acids	Monosodium glutamate (MSG), Lysine	<i>Corynebacterium glutamicum</i> , <i>Brevibacterium</i> sp.	Food flavor enhancer, animal feed supplementation	[49, 50]
2	Nucleotides	Inosine monophosphate (IMP), GMP	<i>Bacillus subtilis</i> , <i>Corynebacterium</i> sp.	Flavor enhancers in food, pharmaceutical precursors	[51]
3	Vitamins	Riboflavin (B2), Cobalamin (B12)	<i>Propionibacterium shermanii</i> , <i>Escherichia coli</i>	Nutraceuticals, food fortification	[52]
4	Organic Acids	Citric acid, Lactic acid	<i>Aspergillus niger</i> , <i>Lactobacillus</i> sp.	Food preservatives, biodegradable plastics (PLA), and pharmaceuticals	[53, 54]
5	Alcohols	Ethanol, Glycerol	<i>Saccharomyces cerevisiae</i> , <i>Candida</i> sp.	Biofuels, beverages, cosmetics	[55, 56]
6	Polysaccharides	Xanthan gum, Hyaluronic acid	<i>Xanthomonas campestris</i> , <i>Streptococcus</i> sp.	Food thickeners, medical implants, wound dressings	[55, 56]



Recent antibiotics include daptomycin, a lipopeptide derived from *Streptomyces roseosporus*, due to its unique calcium-dependent membrane disruption mechanism, which is effective against vancomycin-resistant *Enterococci*, methicillin-resistant *Staphylococcus aureus*, and penicillin-resistant *Streptococcus pneumoniae*. The industrial production of these sophisticated fermentation technologies and emerging strategies to address antimicrobial resistance includes genome mining of uncultured microbes and the computational design of synthetic antibiotics.

4.2.2. Antitumor agents

Since the discovery of actinomycins in 1941, microorganisms have become a significant source of potent anticancer agents. Soil-dwelling actinomycetes produce complex compounds like Mitomycin C, Bleomycin, and anthracyclines, as well as epipodophyllotoxins like Etoposide and the enediyne antibiotic Calicheamicin. Taxol, a paclitaxel stabilised by endophytic fungi, has been used in the treatment of breast, ovarian, and lung cancers [60]. This production still relies on plant cell culture due to the challenges is commercially viable fungal fermentation titres. Camptothecin targets topoisomerase I by stabilising the covalent enzyme-DNA intermediate. The limited commercialisation of plant cell culture processes highlights the technical challenges and substantial costs associated with scaling up plant-based production systems.

4.2.3. Pharmacological agents

The discovery of microbial-derived pharmacological agents through targeted enzymatic screening has revolutionised modern medicine, generating over \$1 trillion in pharmaceutical revenue. The natural product drug discovery pipeline faces significant challenges during clinical development due to inadequate target engagement, pharmacokinetic profiles, metabolic instability, formulation difficulties, unexpected immunogenicity, or dose-limiting toxicity. The pharmaceutical industry's use of natural product discovery has a paradoxical effect on drug

exploration funding, particularly for antibiotics and oncology agents, where microbial metabolites have historically played a dominant role. Biotechnology companies have made remarkable advances by applying innovative approaches to microbial drug discovery, including genome mining of uncultured microorganisms through metagenomics, CRISPR-Cas9 activation of silent biosynthetic gene clusters in actinomycetes and fungi, heterologous expression of giant biosynthetic gene clusters in optimised chassis organisms, and high-content screening platforms combining mass spectrometry and bioactivity profiling [61]. Modern techniques are overcoming limitations of natural product discovery, with improved culturing methods enabling the growth of previously "unculturable" microorganisms. As the antimicrobial resistance crisis reevaluates soil actinomycetes as sources of novel antibiotics, pharmaceutical companies are increasingly partnering with biotech firms and academic groups to access innovative microbial platforms, suggesting a renaissance in the discovery of microbial natural products. Table 5 summarizes some examples of secondary metabolites produced by microorganisms.

5. Types of Fermentation Process

Fermentation reactions are driven by microbial processes that fall into three main categories, based on their metabolic pathways and products: lactic acid fermentation, alcoholic fermentation, and acetic acid fermentation (Fig. 3). Lactic acid fermentation, facilitated by LAB, is used to produce yogurt, cheese, sauerkraut, and kimchi. Alcoholic fermentation, driven by yeasts such as *S. cerevisiae*, converts sugars into carbon dioxide and ethanol, forming the basis of beer, wine, and bread making. Acetic acid fermentation, carried out by *Acetobacter* species, oxidizes ethanol to acetic acid, which is essential in vinegar production and condiments [61].

Table 5: Secondary metabolites produced by microorganisms and their applications

S. No	Metabolic category	Examples	Microorganisms involved	Industrial applications	References
1	Antibiotics	Penicillin, Daptomycin	<i>Penicillium chrysogenum</i> , <i>Streptomyces</i> sp.	Treat bacterial infections, combat antimicrobial resistance	[57, 59]
2	Antitumor Agents	Taxol (Paclitaxel), Mitomycin C	<i>Fusarium solani</i> , <i>Streptomyces</i> sp.	Cancer chemotherapy	[60]
3	Immunosuppressants	Cyclosporin A	<i>Tolypocladium inflatum</i>	Organ transplantation, autoimmune disease management	[58]
4	Toxins	Aflatoxin	<i>Aspergillus flavus</i>	Research on toxicity and biocontrol	[35]
5	Pigments	β -Carotene, Monascorubrin	<i>Blakeslea trispora</i> , <i>Monascus purpureus</i>	Natural food colorants, nutraceuticals	[30]
6	Bioactive Peptides	Nisin, Surfactin	<i>Lactococcus lactis</i> , <i>Bacillus subtilis</i>	Food preservatives, antimicrobial agents	[34]



Further, there are two methods of fermentation processes: solid-state fermentation (SSF) and submerged fermentation (SmF). SSF is mainly used in enzyme production and the production of fermented foods such as cheese, tofu, etc, while SmF is more prevalent in industrial antibiotic and organic acid production due to its better process control [61]. Technologies like mixed-culture fermentation improve the production of complex products, and anaerobic digestion by methanogenic archaea converts organic waste into biogas to fulfill renewable energy requirements. Advanced genetic engineering devices, like CRISPR-Cas9 and synthetic biology, streamline the microbial engineering process with optimised metabolic routes [62]. Recombinant microbes are utilised in precision fermentation for the production of animal-free proteins and therapeutics, ensuring sustainability in biotechnology.

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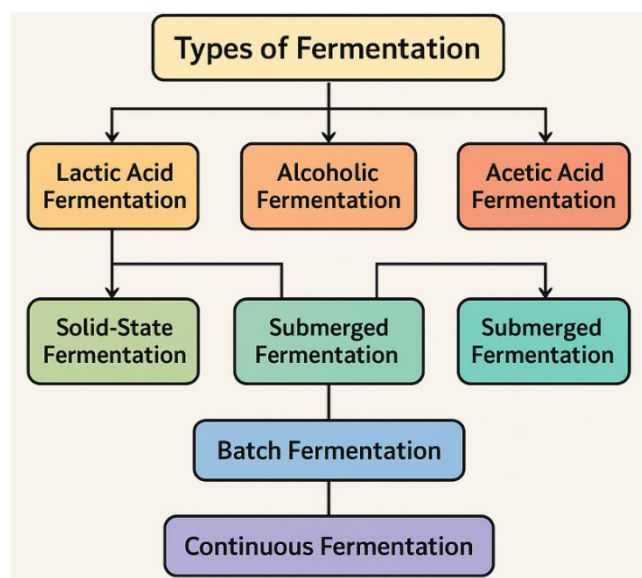


Figure 3. Classification of fermentation types and processes

5.1. Lactic acid fermentation

Lactic Acid (LA) is the main metabolic byproduct that LAB generates. LA finds numerous uses in food, cosmetics, textiles, and pharmaceutical industries [62]. LA can be used

to produce packaging materials, fibres, and foams by transforming into polylactic acid (PLA), which is a green, biodegradable, and biocompatible polymer. In addition, LA is applied in the food and beverage industry to manufacture soft drinks, sweets, milk products, and bakery products, as it has an acidulant characteristic. In the cosmetic industry, LA is utilised as a moisturiser because it can retain water, as a skin lightener, and as a rejuvenator, as it can prevent tyrosinase formation [63]. The medical sector also employs LA because it is utilised in the production of topical creams, lotions, surgical dressings, and prostheses. Lactic acid fermentation improves protein solubility as well as the availability of certain micronutrients and limiting amino acids. This process significantly reduces the levels of tannins (50 %), phytates, and oligosaccharides (90 %). Raw materials containing starch undergo LA fermentation to form the amino acid lysine, vitamins such as vitamin B and K, folate, and micronutrients in the fermented products. Agricultural substrates can be utilised for LA production. Substrates mainly consist of carbon and nitrogen compounds. A lignocellulosic agricultural residue has three main polymers: cellulose, hemicellulose, and lignin. Pretreatments are a crucial factor in the conversion of biomass into LA [64].

Alkali pretreatments enhance the enzymatic digestibility of the fibres. However, lignocellulosic materials are mostly pretreated with acids. The primary issue with acid pretreatment is the production of small amounts of cell growth inhibitors, which can further deactivate enzymes and affect the efficiency of LA bacteria during fermentation. LA is commonly made through biotechnological methods involving LA fermentation and biochemical alterations [65]. The production yield of LA depends on the pH (3.5 – 9.6), temperature (5 – 45 °C), and LAB strain producers, and the presence of nutrients (such as amino acids, peptides, nucleotides, and vitamins). Various strains from the genera *Leuconostoc*, *Lactococcus*, *Lactobacillus*, *Pediococcus*, *Enterococcus*, *Streptococcus*, *Vagococcus*, *Aerococcus*, *Carnobacterium*, *Tetragenococcus*, *Oenococcus*, and *Weissella* have been identified as LA producers. These industrial food fermentations primarily utilise *Lactobacillus*, *Lactococcus*, *Leuconostoc*, and *Pediococcus* as starter cultures

5.2. Alcoholic Fermentation

Alcoholic fermentation (AF) is a process used for thousands of years to produce wine. At the industrial level, microbial fermentation is used to convert cellulose and hemicellulose into fermentable sugars, which are then used to produce ethanol [61]. During AF, yeast generally ferments raw materials in the presence of oxygen, but it can also perform fermentation in the absence of oxygen. When oxygen is lacking, the fermentation process occurs in the



cytoplasm of the yeast. Under anaerobic conditions, Pyruvic acid ($C_3H_3O_3$) is first converted into acetaldehyde, an intermediate molecule that releases carbon dioxide before being transformed into ethanol. During AF, NAD^+ is reduced to NADH, which facilitates an electron exchange necessary for ATP production. Thiamine is an essential vitamin for the metabolism of yeasts, and its deficiency can even lead to yeast death [66]. Additionally, thiamine acts as a cofactor for various enzymes involved in the production of wine-related flavour compounds. It also plays a role in yeast survival *via* thiamine-dependent stress protection functions. Nitrogen is another essential factor for the growth and metabolism of yeast. A deficiency of nitrogen is considered a general reason for sluggish or stuck fermentation. Nitrogen is supplied externally by ammonium salts to prevent fermentative problems [67]. AF includes the fermentation of wine, beer, and cider. Non-*Saccharomyces* yeasts were considered contaminants in wine and beer production. Procedures such as pasteurisation, sulfite addition, and equipment cleaning were used to eliminate these microbes and their role in the spontaneous fermentation of wine, thereby enhancing the final product's sensory quality.

5.3. Acetic acid Fermentation

Acetic acid bacteria (AAB) are aerobic, Gram-negative bacteria that possess a strong ability to oxidize ethanol and synthesize acetic acid, in addition to their resistance to acid. They are generally utilized in industrial vinegar fermentation to produce vinegar, fruit vinegar, gluconic acid products, and to facilitate the formation of biofuel cells. AAB has played a notable role in the manufacturing of fermented foods and beverages, including lambic beer, kombucha, vinegar, and kefir [61]. AAB is also called 'oxidative bacteria' that oxidize carbohydrates, ethanol, and sugar alcohols into various products like aldehydes, ketones, and organic acids. Fruits and vegetables rich in nutritional components, such as amino acids, organic acids, phenols, vitamins, and minerals, are primarily used to produce fermented vinegar [68]. These components can aid in digestion, facilitate fatigue recovery, and support diabetes management, while also possessing anti-obesity and anticancer properties. Acetic acid is primarily derived from natural gas or mineral oil and serves as a crucial industrial feedstock. In the industrial sector, acetic acid is generally utilised in the production of vinegar. It is also used to form vinyl acetate, which is used in vinyl plastics, adhesives, textile finishes, and latex paints, an industry that is expanding rapidly due to increased demand for synthetic fibres. At the industrial level, acid stress arises from low biomass and a low production rate, which has been proven to be a significant constraint in the process [69].

6. Methods of fermentation

Fermentation technology has evolved from traditional practices to current technologies, utilizing microbial physiology in various industries. SSF utilizes moist solid substrates to produce concentrated enzymes and flavors [70, 71]. In contrast, SmF employs liquid media in aerated bioreactors for the large-scale production of pharmaceuticals, such as penicillin and streptomycin. Surface fermentation techniques have been enhanced in bed reactors to increase oxygenation and productivity. Batch fermentation remains essential for traditional foods such as yoghurt and wine, as well as for contemporary biopharmaceuticals that require strict aseptic conditions [70]. Continuous fermentation systems support cultures in exponential growth by continuously feeding nutrients and harvesting product, allowing for high yields in the production of bioethanol and single-cell protein. Recent innovations have provided immobilised cell fermentation, enhanced stability, and recycling in high-fructose corn syrup processing and wastewater treatment. Extremophile fermentation methods employ thermophiles or acidophiles under extreme conditions for niche applications such as biomining [71].

6.1. Submerged Fermentation

Submerged fermentation (SmF) is a method in which microorganisms grow in an aqueous nutrient broth with a high free water content, transforming microbial cultivation from an art to a science. It is typically carried out in stirred-tank or airlift bioreactors, offering control over key parameters such as dissolved oxygen, pH, temperature, and nutrient concentration, thereby enabling optimal conditions for microbial growth. The transition from traditional surface culture methods to submerged systems represented a significant leap in productivity, enabling *Aspergillus niger* to produce citric acid levels ranging from 5 g/L to over 200 g/L through more efficient oxygen transfer and metabolic control in deep-tank fermenters. Current SmF applications span various industries, including pharmaceuticals, food technology, and biofuel production, for their industrial enzymes [72]. High-density culture methods and sophisticated fed-batch operations have achieved record product titres, with industrial enzymes reaching 50 g/L and monoclonal antibodies at 510 g/L. Advances in bioreactor design, including disposable single-use systems and wave-mixed bags, have enhanced sterility and flexibility for vaccine manufacturing with mammalian cell cultures [73]. SmF is irreplaceable due to its scalability and reproducibility, presently supporting the commercial manufacture of more than 60 % of biopharmaceuticals and 80 % of industrial enzymes.



6.2. Solid State Fermentation

Solid-state fermentation (SSF) is a method that combines traditional food production with biotechnological processes. It involves cultivating microorganisms on humid solid substrates without the use of free-flowing water, thereby simulating their natural environments while conserving energy and maximising benefits [70, 71, 74]. This ancient method, long used for Asian food fermentations such as tempeh and koji, has been revitalised as an advanced biomanufacturing platform by contemporary process engineering and the improvement of microbial strains. Modern SSF applications span various industries, including food, enzyme production, and biocontrol. Recent innovations have overcome conventional SSF limitations by utilising automated tray bioreactors, rotating drum systems for heat removal, and packed-bed reactors with real-time CO₂ monitoring, thereby enhancing the process [75]. Despite scale-up and process control issues, SSF's low water demands and capacity to use 80 % lower-cost substrates make it an essential technology for sustainable production [76, 77]. The technology's scalability is demonstrated by its industrial applications, including the production of fungal enzymes, organic acids, and bioactive compounds, which feature reduced purification complexity [78]. SSF faces

challenges, including heat accumulation in dense substrates and non-uniform microbial growth resulting from substrate heterogeneity. A comparative analysis of SSF and SmF is given in Table 6.

7. Probiotic bacteria in fermentation technology

Probiotics are beneficial microorganisms that can modulate gut microbiota, enhance intestinal barrier function, and stimulate immune responses. They have shown clinical efficacy in managing gastrointestinal disorders, metabolic conditions, and immune-mediated diseases [91]. Probiotics are being used in non-dairy carriers, such as fruit juices, cereal-based substrates, chocolate, and freeze-dried pharmaceutical formulations [91]. The physiological robustness of probiotic strains is crucial, as it requires acid tolerance, bile resistance, and the ability to adhere to mucosa. They exert beneficial effects through mechanisms such as competitive exclusion of pathogens, production of antimicrobial compounds, modulation of intestinal epithelial tight junctions, and immunomodulation.

Table 6. Comparative analysis of solid-state fermentation (SSF) and submerged fermentation (SmF)

S. No	Parameters	Solid State Fermentation (SSF)	Submerged Fermentation (SmF)	References
1	Water activity	Low water activity (~0.6–0.9)	High water activity (~1.0)	[79]
2	Oxygen supply	Aerobic (depends on substrate porosity)	Aerobic/Anaerobic (controlled by aeration)	[80]
3	Microorganisms Used	Fungi (e.g., <i>Aspergillus</i> , <i>Rhizopus</i>), some bacteria, and yeasts.	Bacteria, yeasts, and some fungi (e.g., <i>Saccharomyces</i>).	[81]
4	Substrates	Agricultural residues (wheat bran, rice husk, sugarcane bagasse), agro-industrial wastes.	Soluble carbon sources (glucose, sucrose, molasses), synthetic media.	[82]
5	Process control	Difficult (limited mixing, heat, and mass transfer).	Easier (pH, temperature, aeration, and agitation can be controlled).	[83]
6	Energy Requirement	Low (no agitation, less sterilisation needed).	High (agitation, aeration, sterilisation).	[84]
7	Scaleup difficulty	Challenging (heterogeneous conditions).	Easier (homogeneous conditions, well-established bioreactors).	[85]
8	Product concentration	High (low water content concentrates products).	Lower (diluted in liquid medium).	[86]
9	Downstream Processing	Simpler (fewer impurities, easier recovery).	Complex (requires filtration, centrifugation, and extraction).	[87]
10	Applications	Enzyme production (cellulases, amylases). Biofuels (ethanol, biogas). Food fermentation (tempeh, koji). Bioremediation.	Antibiotics (penicillin, streptomycin). Organic acids (citric, lactic acid). Recombinant proteins (insulin, vaccines). Ethanol production.	[88]
11	Advantages	Low cost. High product yield. Natural habitat for fungi. Less wastewater generation.	Better process control. Uniform nutrient distribution. Suitable for high-growth microbes.	[89]
12	Disadvantages	Poor heat dissipation. Limited to slow-growing microbes. Heterogeneous conditions.	High energy costs. Expensive media. Complex downstream processing.	[90]



The LAB are the backbone of probiotic formulations due to their GRAS status and multifunctional metabolism. Modern probiotic development employs advanced screening techniques, omics analyses, and stabilisation technologies. The concept of "next-generation probiotics" encompasses engineered strains with targeted functionalities and consortium formulations that combine traditional probiotics with prebiotic fibres [92]. The probiotics lie in precision formulations tailored to individual microbiomes, engineered live biotherapeutics for non-gut indications, and integration with faecal microbiota transplantation protocols.

Probiotics are beneficial microorganisms that can modulate gut microbiota, enhance intestinal barrier function, and stimulate immune responses (Figure 4). They have shown clinical efficacy in managing gastrointestinal disorders, metabolic conditions, and immune-mediated diseases [91]. Probiotics are being used in non-dairy carriers, such as fruit juices, cereal-based substrates, chocolate, and freeze-dried pharmaceutical formulations [91]. The physiological robustness of probiotic strains is crucial, as it requires acid tolerance, bile resistance, and the ability to adhere to mucosa. They exert beneficial effects through mechanisms such as competitive exclusion of pathogens, production of antimicrobial compounds, modulation of intestinal epithelial tight junctions, and immunomodulation. The LAB are the backbone of probiotic formulations due to their GRAS status and multifunctional metabolism. Modern probiotic development employs advanced screening techniques, omics analyses, and stabilisation technologies. The concept of "next-generation probiotics" encompasses engineered strains with targeted functionalities and consortium formulations that combine traditional probiotics with prebiotic fibres [92].

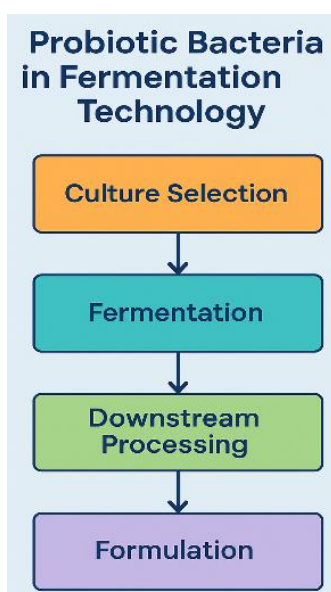


Figure 4. Probiotic bacteria production in fermentation technology

8. Microbial fermentation of food products

Microbial fermentation is a biotechnological process that uses bacteria, yeasts, and moulds to transform raw agricultural materials into nutritious, palatable, and shelf-stable foods. It is used in cereal, legume, vegetable, meat, fish, and dairy fermentations, sourdough bread production, and the conversion of sugars to ethanol and CO₂. Filamentous fungi undergo proteolytic and amylolytic transformations in traditional Asian staples, including soy sauce, miso, and tempeh. Modern applications combine traditional knowledge with precision fermentation, using defined starter cultures to standardise artisanal products [93]. Emerging technologies use omics tools and synthetic biology to control pathogens and ensure process consistency. The global fermented food market, valued at \$700 billion, spans dairy (40%), alcoholic beverages (30%), and plant-based products (20%). Innovations include probiotic-enriched non-dairy alternatives, low-alcohol wines, and mycoprotein-based meat analogues. Challenges persist in scaling artisanal processes, such as maintaining microbial viability in low-moisture fermented meats and controlling phage infections. These also include CRISPR-engineered starters for reducing allergens, substrate fermentations, and personalised fermented foods tailored to their microbiomes [94]. Microbial fermentation plays a transformative role in converting raw vegetables and soybeans into nutrient-rich fermented products. This process enhances bioavailability, reduces antinutritional factors, and introduces beneficial bioactive compounds (Figure 5). Traditional practices like kimchi and tempeh production exemplify how microbial activity improves sensory and functional properties, while modern applications leverage precision starter cultures for consistency and scalability

8.1. Fermented vegetable products

Microbes play a central role in vegetable fermentation, connecting traditional food preservation methods to novel biotechnological developments. Spontaneous vegetable fermentations with *Leuconostoc*, *Lactobacillus*, and *Pediococcus* species have resulted in their relevant products, such as sauerkraut, Korean kimchi, and fermented olives [94]. Major innovations utilise this microbial richness to convert vegetable matrices into functional foods, including sauerkraut-like beetroot kvass, fermented using *Lactocaseibacillus casei* A4, and soybeans fermented with *Bacillus subtilis*. Primary methods such as high-pressure processing and SSF of okara enhance protein content and decrease oligosaccharides. The microbial vegetable fermentation utilises precision ecology strategies, including AI-based predictive models and sophisticated bioreactor designs, with real-time metabolomics capabilities [95].



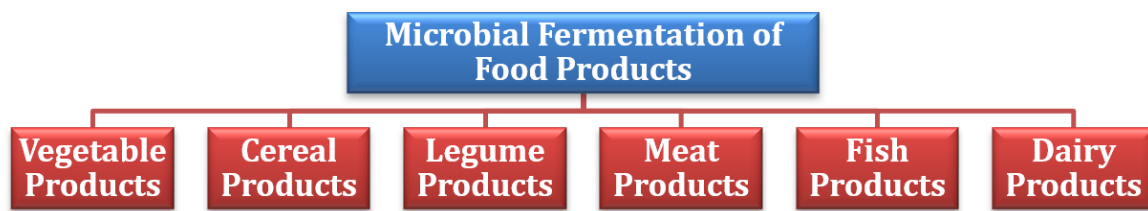


Figure 5. Microbial fermentation of various types of food products.

Pharmaceutical uses are unfolding, e.g., oral vaccines developed in fermented lettuce that produce cholera toxin B sub-units, and the vegetable waste upcycling circular bioeconomy through *Aspergillus oryzae* fermentation for glucoamylases production in starch processing. This shift from traditional craft to industrialised biotechnology illustrates that microbiological innovation persists in elevating simple vegetables into potent tools for nutritional security, sustainable agriculture, and preventive medicine [96].

8.2. Fermented cereal products

Cereals are a multifaceted substrate for microbial fermentation, providing a rich matrix of carbohydrates, proteins, and bioactive compounds that serve as both microbial growth media and prebiotic materials. Nevertheless, their nutritional composition must be strategically fortified through fermentation to compensate for internal constraints, such as the low bioavailability of proteins and antinutrients. Conventional cereal-based fermentations worldwide demonstrate the ecological microbial capacity to enhance free amino acids, reduce phytate levels, and produce bioactive peptides. Oat is a viable cereal matrix because it contains a high proportion of β -glucans, which promote *Bifidobacterium* activity and constitute protective colloidal systems. Maize fermentation presents special challenges due to its high starch content and poor protein quality [97]. Common fermented cereal-based foods include bread, dosa, idli, ingera, etc [98].

Sourdough is a type of bread that uses the fermentation of wheat flour by naturally occurring yeast and lactobacilli to raise the dough. Sourdough bread, at its most basic, is made from three ingredients: flour, water, and salt. Sourdough bread is often considered healthier than regular bread due to its fermentation process, which can improve nutrient absorption and potentially benefit gut health [99]. While both types of bread can be part of a healthy diet, sourdough's unique characteristics offer some advantages.

Engineered consortia of lactobacilli can be used to convert nixtamalized maize into nutritionally fortified products by enhancing free folate levels and minimising aflatoxin contamination. Rice fermentation undergoes a metabolic renaissance during germination, yielding a nutrient-rich substrate that supports exceptional probiotic

growth. Next-generation fermentation technologies are surpassing cereal limitations, including extrusion pretreatment, pulsed electric field treatment, and microencapsulation strategies [100]. The emerging field of cereal-based probiotic foods involves precision-fermented designer synbiotics, such as CRISPR-engineered *Lp. plantarum* strains that produce cereal phytases, and AI-based bioreactor systems for maximising fermentation conditions in real-time.

8.3. Fermented legume products

In traditional fermented food processing, legumes such as soybeans, lentils, chickpeas, and mung beans are subjected to fermentation by autochthonous microorganisms. The fermentation process involves the breakdown of complex macromolecules like proteins and carbohydrates into simpler, more bioavailable forms. Microorganisms such as *Bacillus* species, LAB, and yeast play key roles in these transformations, producing enzymes that degrade anti-nutritional factors and enhance nutrient bioavailability [101]. The resulting fermented products range from Asian soy-based condiments like nato, miso, and tempeh [102] to African condiments that include dawadawa and ugba [103].

8.4. Fermented meat products

Meat serves as a protective substrate for probiotic bacteria, providing an ideal environment for LAB to thrive. Modern probiotic meat fermentations use facultative heterofermentative LAB strains that convert carbohydrates into lactic acid and switch to heterofermentative pathways when sugars are limited [104]. Advanced strain selection focuses on meat-adapted probiotics with bile salt hydrolase activity and acid tolerance. *Lactobacillus amylovorus* and *Lactobacillus gallinarum* are effective in fermented meats due to their proteolytic activity and resistance to meat-derived stressors. Process optimisation involves controlled fermentation at 20 - 26 °C with 85 - 95 % relative humidity for 48 - 72 h, followed by drying at 12 - 15 °C. Technological challenges include preventing probiotic inhibition by traditional curing agents, optimising aw reduction, and managing lipid oxidation [105]. These also include CRISPR-engineered *Lactobacillus sakei* strains, AI-optimised fermentation protocols, and hybrid products



combining plant proteins with probiotic-fermented meat for sustainable functional foods.

8.5 Fermented fish products

Fermented fish products are a vital part of traditional diets in many coastal and Southeast Asian cultures, where they serve as a source of protein, probiotics, and unique flavors. These products are typically produced through spontaneous fermentation, relying on indigenous microbes, such as LAB and halophilic *Tetragenococcus* species, to break down proteins and lipids, thereby enhancing digestibility and shelf life. Examples include fish sauces (e.g., Thai *nam pla*), pastes (e.g., Korean *jeotgal*), and dried fermented fish (e.g., African *lanhouin*), each with distinct regional variations in preparation and microbial consortia [106]. The fermentation process involves salting, aging, and enzymatic hydrolysis, which reduce the pH and inhibit pathogenic bacteria while generating bioactive peptides, free amino acids, and umami compounds, such as glutamate. LAB strains such as *Lactobacillus plantarum* and *Pediococcus pentosaceus* dominate these fermentations, contributing to preservation and health benefits, including antioxidant and antihypertensive properties [106]. However, improper fermentation can lead to the accumulation of biogenic amines (e.g., histamine), necessitating the use of strict hygiene and starter cultures for safety [107].

8.5 Fermented dairy products

Fermented dairy products have been consumed for millennia, initially as a method of food preservation before their health benefits became widely recognized [2]. These products are created by fermenting milk or other raw ingredients with the help of microorganisms, predominantly LAB, which contribute to the fermentation process. LABs are responsible for the development of bioactive compounds that offer a range of health advantages, such as immunomodulatory, antimicrobial, and antioxidant effects. Popular fermented dairy products, including yogurt, kefir,

and cheese, are consumed globally and contribute to improved gastrointestinal health, enhanced digestion, and potentially lower risks of conditions like osteoporosis, diabetes, and inflammatory bowel diseases [108]. Additionally, fermented dairy products support the gut microbiome, which has a significant influence on overall health, making them a valuable component of a balanced diet [109].

Modern advancements focus on optimizing fermentation conditions (e.g., temperature, salt concentration) and introducing defined starter cultures to standardize quality and accelerate production. Emerging techniques, such as bacteriophage therapy to control spoilage bacteria and omics tools to profile microbial dynamics, are further refining these traditional processes [110]. Despite their cultural significance, fermented fish products face challenges in global acceptance due to strong odors and sensory preferences. Innovations like deodorization techniques and hybrid products (e.g., fish-vegetable blends) aim to broaden appeal while retaining nutritional benefits. Research continues to explore their potential as functional foods, particularly for gut health and mineral bioavailability [111].

The role of microorganisms such as *Leuconostoc*, *Lactobacillus*, and *Pediococcus* in vegetable fermentations like sauerkraut and kimchi highlights the significance of lactic acid bacteria (LAB)-driven acidification in spontaneous fermentation processes (Table 7). Similarly, *Bifidobacterium*, *Lactobacillus*, and *Aspergillus oryzae* are crucial in the solid-state fermentation of cereals and soy products, resulting in traditional foods like tempeh and miso. Controlled fermentation of meat products utilizing species like *Lactobacillus amylovorus* enhances preservation and probiotic content. In fermented fish products, microbial action by *Lactobacillus plantarum* and *Tetragenococcus* is key in flavor development and preservation strategies (Table 7).

Table 7. Overview of fermented food products, microbial agents, and their applications

S. No	Fermented Food Products	Microorganisms Involved	Fermentation process	Applications	References
1	Vegetable Products	<i>Leuconostoc</i> , <i>Lactobacillus</i> , <i>Pediococcus</i>	Spontaneous fermentation; LAB-driven acidification	Sauerkraut, kimchi, fermented olives, beetroot kvass	[92, 93, 94]
2	Cereal and Soya Products	<i>Bifidobacterium</i> , <i>Lactobacillus</i> , <i>Aspergillus oryzae</i>	Solid-state fermentation (SSF); Enzymatic hydrolysis of starch/proteins	Tempeh, miso, soy sauce, probiotic-enriched cereals	[95, 96]
3	Meat Products	<i>Lactobacillus amylovorus</i> , <i>Lactobacillus gallinarum</i>	Controlled fermentation (20 – 26 °C, 85 – 95 % humidity); LAB-driven preservation	Fermented sausages, probiotic meat products	[97, 98]
4	Fermented Fish Products	<i>Lactobacillus plantarum</i> , <i>Tetragenococcus</i>	Salting, aging, enzymatic hydrolysis; LAB and halophilic bacteria	Biogenic amine accumulation, deodorization techniques, and bacteriophage therapy	[99, 100, 101, 102]



9. Genetic recombination in microbial fermentation

Genetic recombination has revolutionised microbial fermentation, allowing targeted genetic modifications that optimise fermentation efficiency, expand substrate utilisation, and unlock new bioactive compound synthesis. This approach bridges the ancient fermentation practices with their industrial applications, enabling the engineering of strains with enhanced metabolic capabilities, improved yield, and novel functionalities. In industrial applications, recombination has limitations like those of random mutagenesis; however, it enables the strategic stacking of beneficial traits [112]. For example, it facilitates the amplification of Biosynthetic Gene Clusters (BGCs) in *Streptomyces* spp. for antibiotic overproduction, the insertion of heterologous pathways into *Saccharomyces cerevisiae* for enhancing bioethanol production, and in *Lactobacillus* spp. for increasing lactic acid yield. Synthetic biology tools, such as CRISPR interference (CRISPRi), multiplex automated genome engineering, and recombinase-assisted genome rewriting, enable precise pathway optimisation. The engineering of *Escherichia coli* strains exemplifies this to enhance shikimate pathway activity to produce aromatic compounds, and the modification of *Aspergillus oryzae* for increased protease secretion in soy fermentation. Recombination also facilitates the activation of silent gene clusters, uncovering cryptic metabolites with pharmaceutical potential, such as the discovery of novel polyketides in *Penicillium* through promoter swapping or the heterologous expression of fungal BGCs in *S. cerevisiae* for scalable drug precursor synthesis [113]. In food fermentation, genetically stabilised *Lactobacillus* hybrids exhibit robust acid tolerance and phage resistance. At the same time, recombinant *Acetobacter* strains with enhanced cellulose synthase activity revolutionise kombucha production for the synthesis of biodegradable materials. The environmental and economic benefits of recombinant fermentation with engineered *Clostridium* spp. Converting lignocellulosic waste into butanol at 90 % theoretical yield and *Yarrowia lipolytica* recombinants producing omega-3 fatty acids from agro-industrial byproducts [114].

10. Novel genetic technologies for microbial fermentation

The evolution of microbial fermentation has been significantly transformed by the advent of novel genetic technologies, including precision genome editing, synthetic biology, and computational bioengineering. These technologies have enabled unprecedented control over microbial metabolism, unlocking new possibilities in

industrial biotechnology, food production, and pharmaceutical development [115]. CRISPR-Cas9 systems have emerged as the cornerstone of modern genetic manipulation in fermentation science, allowing for targeted gene knockouts, precise promoter engineering, multiplexed genome editing, base editors, and prime editors. Synthetic biology platforms, such as Gibson Assembly and Golden Gate cloning, facilitate the construction of entire biosynthetic pathways. Meanwhile, cell-free transcription-translation systems accelerate the prototyping of metabolic circuits before their integration into the chromosomal genome. Machine learning (ML) algorithms predict the optimal genetic modifications by analysing multi-omics datasets, as demonstrated by AI-designed lactobacilli strains with 300 % increased lactic acid productivity through optimised redox balancing. Advanced Genome-scale models (GEMs), such as iJO1366 for *Escherichia coli* and iMM904 for *Saccharomyces cerevisiae*, simulate metabolic fluxes to identify knockout targets [116]. Novel DNA synthesis technologies enable the construction of entire synthetic chromosomes, while *in vivo* genome rewriting systems allow megabase-scale deletions in *Streptomyces* spp. to eliminate competitive routes. Phage-assisted continuous evolution enables the generation of hyperactive enzymes in real-time, while directed evolution platforms produce stable microbial mutants. Epigenetic engineering tools are employed to silence unwanted genes without introducing permanent mutations, while RNA interference dynamically regulates metabolic fluxes. Microbial consortia engineering employs quorum-sensing circuits for population management, allowing division-of-labour fermentations [117]. New technologies, such as DNA data storage within microbial genomes and biological cryptography, are pushing the frontiers of fermentation beyond its conventional uses. A quantum biology understanding of electron transport chain manipulation yields *Rhodobacter* strains that produce 200 % more hydrogen. Connecting these technologies with traditional fermentation techniques ensures the responsible application, most notably in food-grade microbes [118]. These encompass neuromorphic biocomputing within fermenters, completely autonomous AI-based strain evolution, and nanotechnology-supportive microbial hybrids [119, 120].

The integration of advanced genetic technologies has revolutionized microbial fermentation, enabling precise control over metabolic pathways and unlocking novel applications in biotechnology. Techniques such as CRISPR-Cas9, synthetic biology platforms, and machine learning algorithms have been instrumental in optimizing microbial strains for enhanced productivity and functionality (Figure 6). These innovations facilitate targeted gene editing, pathway engineering, and real-time metabolic flux analysis, bridging the gap between traditional fermentation practices



and modern industrial demands. For instance, AI-designed microbial strains have demonstrated significant improvements in yield, while synthetic consortia engineering allows for division-of-labour fermentations, further expanding the scope of microbial applications in sustainable biomanufacturing.

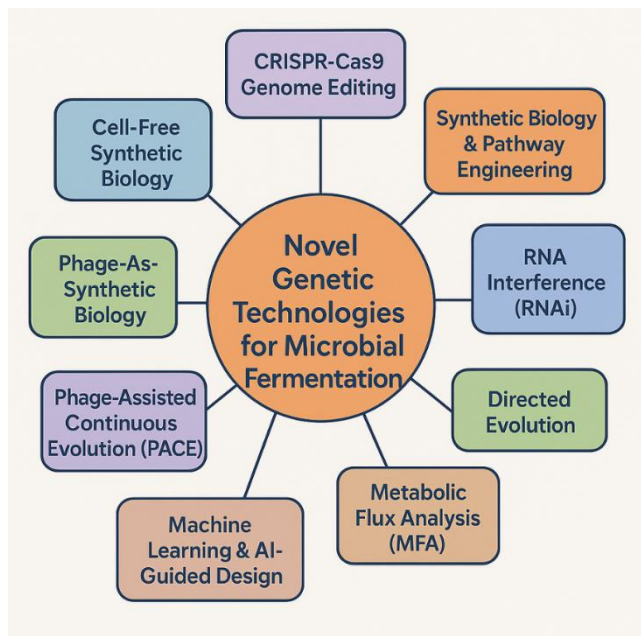


Figure 6. Innovative tools in synthetic biology and fermentation optimization.

11. Challenges and Future Directions

Despite the significant advancements in microbial fermentation, several challenges remain that hinder its full potential. Major challenges in the scalability of fermentation processes, particularly in SSF, are issues like mass transfer, heat accumulation, and heterogeneity of microbial growth [74, 75, 80]. In SmF, the high costs associated with downstream processing limit the economic feasibility of large-scale production [121]. Another critical issue is the regulatory and consumer acceptance of genetically modified microorganisms, which, despite their potential to enhance yield and efficiency, often face scepticism due to safety and ethical concerns [122]. Furthermore, contamination control and maintaining consistent product quality across batches remain persistent hurdles in industrial fermentation [121].

Looking ahead, the integration of emerging technologies such as AI and ML offers promising solutions to optimize fermentation processes. These tools can predict optimal conditions, monitor real-time fermentation dynamics, and identify genetic modifications to enhance microbial performance [123]. Another future direction is the development of more robust and versatile microbial strains through advanced genetic engineering techniques like CRISPR-Cas9 and synthetic biology. These innovations

could enable microbes to utilize a broader range of substrates, including agricultural and industrial waste, thereby promoting sustainability and reducing production costs [124].

Sustainability will also play a pivotal role in the future of fermentation. The shift toward circular bioeconomy models emphasizes the need to valorize waste streams and reduce the environmental footprint of fermentation processes. For instance, leveraging lignocellulosic biomass and other low-cost substrates can make fermentation more eco-friendly and economically viable. Additionally, the exploration of extremophiles - microorganisms thriving in extreme conditions could unlock novel applications in harsh industrial environments, further expanding the scope of fermentation technology [125]. Finally, interdisciplinary collaboration will be essential to address these challenges and drive innovation. Partnerships between academia, industry, and regulatory bodies can accelerate the development of safe, efficient, and scalable fermentation processes. By combining traditional knowledge with cutting-edge science, the field can overcome current limitations and unlock new opportunities in food security, healthcare, and environmental sustainability. The future of microbial fermentation lies in its ability to adapt, innovate, and integrate diverse technologies to meet global demands.

12. Conclusion

Microbial fermentation is an intricate process that combines human ingenuity and microbial metabolism, blending ancient techniques with cutting-edge biotechnology. It has progressed from being an empirical process to a sophisticated science, stimulated by discoveries in microbiology, molecular biology, and genetic engineering. The discovery and description of numerous microbial species have broadened the platform of fermentation, enabling the production of a vast array of metabolites, including primary compounds such as amino acids, organic acids, vitamins, and alcohols, as well as secondary metabolites like antibiotics and pharmacologically active metabolites. These transformation processes have revolutionised various industries, including food, beverage, pharmaceutical, biofuel, and biodegradable. The application of new genetic technologies, including CRISPR-Cas9, synthetic biology, and computational bioengineering, has improved the efficiency and precision of microbial fermentation. Techniques like SSF and SmF have been optimised to suit sustainable waste valorisation, enzyme production, and the synthesis of high-value compounds. Probiotic technology synergises fermentation and human well-being, providing value-specific benefits in gut microbiota modulation, immune system enhancement, and disease prevention. Conventional food product



fermentation has been optimised with the application of precision starter cultures, omics technologies, and AI-based process optimisation. The future of microbial fermentation is bright, with transdisciplinary innovation integrating synthetic biology, nanotechnology, and AI, presenting multiple opportunities in cellular agriculture, personalised nutrition, and a circular bioeconomy.

13. Declaration of competing interest

The authors report no conflict of interest.

14. Authors' Contributions

P. Saranraj conceptualized the manuscript, supervised the research, and contributed to the writing and editing of the original draft. Ramesh C. Ray provided critical insights into the review's structure and content, focusing on microbial diversity and fermentation processes. Ashish Kumar Nayak contributed to the sections on genetic engineering and modern biotechnological applications. B. Lokeshwari and K. Gayathri assisted in compiling data on microbial species and metabolites, as well as reviewing the literature. P. Sivasakthivelan contributed to the sections on fermentation methods and comparative analyses. Kianoush Khosravi-Darani provided expertise on industrial applications and the health benefits of fermented products. All authors reviewed and approved the final manuscript.

15. Using Artificial Intelligent Chatbots

No artificial intelligence chatbots have been used in any section of work.

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میکروپها در عمل: تقویت تخمیر پایدار برای غذا، داروسازی و اقتصاد زیستی

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چاپ ۳۰ اوت ۲۰۲۵

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چکیده

سابقه و هدف: تخمیر، یک فرآیند متابولیکی مبتنی بر میکروبی، برای هزاران سال برای تولید، نگهداری و بهبود کیفیت غذا و نوشیدنی‌ها مورد استفاده قرار گرفته است و از شیوه‌های سنتی مانند ماست و شراب به کاربردهای مدرن در سوخت‌های زیستی و داروسازی تکامل یافته است. اولین شواهد تخمیر بیش از ۷۰۰۰ سال پیش یافت شده است. اصل تخمیر در قرن نوزدهم و بر اساس تحقیقات بنیادی پاستور، که ارتباط بین فعالیت میکروبی و تغییر شیمیایی را برقرار کرد، پایه گذاری شد و زمینه را برای میکروبیولوژی و بیوتکنولوژی مدرن فراهم کرد. این بررسی، نقش‌های میکروبی در تخمیر را بررسی می‌کند و با مقایسه فرآیندهای باکتریایی و قارچی، تجزیه و تحلیل متابولیت‌های کلیدی و برجسته کردن نوآوری‌های ژنتیکی، پیشرفت‌های سنتی و بیوتکنولوژیکی را به هم پیوند می‌دهد.

بحث و نتیجه‌گیری: این بررسی به طور جامع نقش محوری تخمیر میکروبی را بررسی می‌کند و شیوه‌های سنتی را تا نوآوری‌های مدرن در بر می‌گیرد و تنوع گسترده ۱۹۵ گونه باکتریایی و ۶۹ گونه قارچی را برجسته می‌کند که باکتری‌های اسید لاکتیک (LAB) و ساکارومایسس سرویزیه نمونه‌های برجسته آن هستند. این مقاله فرآیندهای تخمیر باکتریایی و قارچی را مقایسه می‌کند و خاطر نشان می‌کند که تخمیر باکتریایی اغلب محتوای پروتئین بالاتری را در محصولاتی مانند کنجاله سویای تخمیر شده (FSBM) تولید می‌کند و متابولیت‌های کلیدی، از جمله ترکیبات اولیه (اسیدهای آمینه، اسیدهای آلی، ویتامین‌ها) و ثانویه (آنتی‌بیوتیک‌ها، عوامل ضد تومور) را برای کاربردهای صنعتی و بهداشتی آنها مورد بحث قرار می‌دهد. این بررسی همچنین روش‌های مختلف تخمیر و مناسب بودن آنها برای محصولات مختلف را بررسی می‌کند و بر پیشرفت‌های مهندسی ژنتیک برای بهینه‌سازی سویه تأکید می‌کند، در حالی که بر مزایای سلامتی پروبیوتیک‌ها و غذاهای تخمیر شده و پتانسیل فناوری‌های نوظهور برای پرداختن به امنیت غذایی و پایداری تأکید می‌کند. در نتیجه، تخمیر میکروبی، سنت‌های باستانی را با علم پیشرفته پیوند می‌دهد و پتانسیل تحول‌آفرینی را در صنایع ارائه می‌دهد، جایی که نوآوری‌ها در مهندسی ژنتیک و بهینه‌سازی فرآیند، کارایی و پایداری را هدایت می‌کنند و گسترش گنجینه میکروبی همچنان به گشودن کاربردهای جدید ادامه می‌دهد و فناوری تخمیر را با ابزارهای بیوتکنولوژیکی مدرن ادغام می‌کند تا به چالش‌های جهانی در تغذیه، سلامت و پایداری محیط زیست بپردازد.

واژگان کلیدی: تولید سوخت زیستی، اقتصاد زیستی، CRISPR-Cas9، امنیت غذایی، پروبیوتیک‌ها، تخمیر حالت جامد (SSF)، تخمیر غوطه‌ور (SmF)، پایداری، زیست‌شناسی مصنوعی