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The potential of fermentation technology for the process of extracting medicinal plants

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ABSTRACT

Background: Low bioavailability is a standard limitation in medicinal plants. Fermentation has gained attention as a method to enhance the therapeutic potential of active compounds through microbial transformation. Objective: To demonstrate how fermentation improves the efficacy of medicinal plant remedies and their relevance to modern and personalized medicine. Materials and Methods: This review compiles data from studies using microbial strains, such as Lactobacillus, Bacillus, and Aspergillus, with a focus on phytochemical conversions and enhanced bioactivities. This review focused on peer-reviewed research articles, experimental reports, and review papers related to the microbial fermentation of medicinal plants, sourced from scientific databases such as PubMed, ScienceDirect, SpringerLink, and Google Scholar. Selection criteria emphasized studies that examined changes in phytochemical profiles, bioavailability, and biological activities such as antioxidant, anti-inflammatory, and antidiabetic effects after fermentation. Results: Fermentation enhances the antioxidant, anti-inflammatory, and antidiabetic properties of compounds by converting them into more active and bioavailable forms, particularly aglycones. Conclusion: Fermentation presents a promising approach to enhance the efficacy and safety of medicinal plants, thereby supporting the development of personalized therapeutic options.

Keywords: *medicinal plant, fermentation, bioactivity, phytochemical, biotechnology*

1. INTRODUCTION

In recent years, the application of biotechnology, particularly microbial fermentation, in the pre-extraction treatment of medicinal plants has become a crucial strategy to optimize biological efficiency and enhance the utility value of these plants. Fermentation is not only a pre-treatment step but also acts as a "biological factory," helping to transform the compounds in medicinal plants into more easily absorbed forms with enhanced biological activity or reduced toxicity. Fermentation processes can break glycoside bonds, hydrolyze polysaccharides, or alter the structure of phenolic compounds, thereby improving the anti-inflammatory, antioxidant, and other biological activities of medicinal plants [1].

Biological efficiency is altered through fermentation, which opens the door to creating functional food and pharmaceutical products. Microbial strains, such as Lactobacillus sp., Bacillus subtilis, or Saccharomyces cerevisiae, are involved in the transformation process, which enhances the final product's stability, taste, and bioavailability. Some studies have found that polyphenol compounds in ginseng, soybeans, turmeric, green tea, and other herbs significantly increase biological activity and may potentially cure chronic diseases such as diabetes, cancer, and cardiovascular disease after fermentation [2].

The second developing trend is that fermentation makes personalized medicine solutions possible. Through tailoring active ingredients for their benefit, this technology can make medicines "customized" for specific users - such as the elderly, metabolic disease patients, or individuals with an out-of-balance gut microbiota [3].

Fermentation is also considered a sustainable production strategy. This process can utilise agricultural by-products, minimise waste, and does not require toxic chemical solvents like traditional extraction methods. Therefore, it is environmentally friendly and aligns with the trend of green production and sustainable development

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in the modern pharmaceutical and functional food industries [1, 3].

2. MATERIALS AND METHODS

2.1. Materials

This review focused on peer-reviewed research articles, experimental reports, and review papers related to microbial fermentation of medicinal plants. Relevant publications were selected from scientific databases, including PubMed, ScienceDirect, SpringerLink, and Google Scholar. The materials included studies that utilized microbial strains such as Lactobacillus plantarum, Lactobacillus brevis, Bacillus subtilis, Aspergillus oryzae, Rhizopus oryzae, and Saccharomyces cerevisiae for the fermentation of various medicinal herbs, including *Scutellaria baicalensis*, *Panax ginseng*, *Ophiopogon japonicus*, *Polygonum multiflorum*, and *Camellia sinensis*. Selection criteria emphasized studies that examined changes in phytochemical profiles, bioavailability, and biological activities such as antioxidant, anti-inflammatory, and antidiabetic effects after fermentation.

2.2. Methods

A narrative review approach was employed to synthesize findings from selected literature. Articles were analyzed to extract information on fermentation processes, including microbial species, fermentation conditions (e.g., temperature, pH, duration), and biochemical transformations. Special attention was given to converting glycosides to aglycones, releasing free polyphenols, breaking polysaccharides into oligosaccharides, and generating new secondary metabolites. Comparative data were compiled to assess the differences in biological activity between pre- and post-fermentation samples. Furthermore, evidence supporting the application of fermentation in enhancing extractability and supporting personalized therapeutic strategies was prioritized to align with the study objectives.

3. RESULTS AND DISCUSSION

3.1. Advantages and disadvantages of medicinal fermentation technology

3.1.1. Microbial fermentation as a strategy to improve the bioefficacy of medicinal plants

Microbial fermentation helps in the transformation of natural substances through the enzymatic activity of microbes. Microbial enzymes such as β-glucosidase, esterase, α-amylase, cellulase, and protease can hydrolyze complex chemical bonds, producing compounds with simpler structures that are easier to absorb [1, 3].

3.1.2. Hydrolysis of glycosides into aglycone

Many flavonoid, isoflavonoid, and saponin compounds in medicinal herbs exist as glycosides containing sugar molecules. Glycosides are often highly water-soluble but poorly absorbed through the intestine because intestinal enzymes are ineffective in cleaving glycosidic bonds. Fermentation with microorganisms that contain β-glucosidase can convert glycosides into aglycones, facilitating better absorption (Table 1). After fermentation, Baicalin in *Scutellaria baicalensis* is converted to baicalein, which has higher antioxidant and anti-inflammatory activities [1, 3, 4]. In addition to the hydrolysis of glycosides such as baicalin to baicalein, microbial fermentation has shown a broader potential for converting herbal constituents into forms with higher bioactivity and bioavailability. Many herbs contain high levels of flavonoid glycosides, saponins, and polyphenols, which are often poorly absorbed in the intestine. Microbial enzymes, particularly β-glucosidases, play a crucial role in cleaving the sugar moieties from these compounds, resulting in the formation of aglycones that enhance pharmacological activity. For example, in *Scutellaria baicalensis*, the fermentation-induced conversion of baicalin to baicalein not only improves bioavailability but also significantly enhances the antioxidant and anti-inflammatory effects due to the free hydroxyl groups on the aglycone form [5]. Fermentation also plays a vital role in enhancing the antioxidant capacity of various herbal extracts. Lactic acid bacteria (such as *Lactobacillus plantarum*) not only catalyze the hydrolysis of glycosides but are also capable of generating organic acids and short-chain fatty acids on fermentation, which produce favorable effects on gut health and immune regulation. Similar effects were observed in conventional Chinese decoctions, such as Danggui Buxue Tang, where bioactivity against diabetes indicators was enhanced through the use of LAB fermentation. Methods of hot water extraction of medicinal plants, combined with fermentation, not only aid in the conservation and improvement of flavor development but also enhance the therapeutic importance. For example, the fermentation starter "Jiuqu" of Chuanqing people includes *Gluconobacter japonicus* and *Rhizopus oryzae*, which promote the biotransformation of phytochemicals, which can lead to new bioactive molecules [2].

Besides flavonoids, saponins are a group of glycoside compounds commonly found in medicinal herbs, especially in species of the Araliaceae family such as *Panax ginseng* and *Panax notoginseng*. Natural saponins usually exist in the form of glycosides, which have large molecular weights and are difficult to absorb through the digestive tract (Tables 1 and 2). However, microbial fermentation with strains such as *Lactobacillus brevis*, *Phellinus linteus,* or *Aspergillus oryzae* can catalyze the hydrolysis of glycosidic bonds, releasing aglycone forms (e.g., ginsenosides Rg3, Rh1, CK), which are more biologically active and more easily absorbed in the human body [1]. Red ginseng was fermented with *L. brevis*, and the content of rare ginsenosides, such as Rg3, Rg5, and Rk1, increased significantly. These ginsenosides not only have more potent antioxidant and anti-inflammatory activities but also have anti-cancer potential due to their ability to induce cell death (apoptosis) and inhibit cancer cell proliferation [1]. Additionally, ginsenoside CK (compound K), a terminal hydrolysis product of most major saponins such as Rb1, Rd, and Rc, has been proven to possess immunomodulatory, anti-inflammatory, and lipid metabolism activity, which might be helpful in the treatment of chronic diseases such as type 2 diabetes and non-alcoholic fatty liver disease (NAFLD) [5]. The primary process of this conversion occurs through the action of the β-glucosidase enzyme from microorganisms, specifically Lactobacillus (LAB) strains and filamentous fungi such as Aspergillus, during fermentation. The enzymes hydrolyze the sugar units in the saponin molecule slowly, thus enabling the generation of metabolites with increased biological activity. This adjustment not only enhances the pharmacological action of the medicinal herbs but also reduces the toxicity and the side effects of compounds associated with glycosides [1].

Hence, by combining traditional fermentation knowledge with cutting-edge biotechnological strategies, a promising solution emerges to enhance the efficacy of herbal drugs. Not only do these approaches enhance pharmacokinetics, but they also offer novel pathways for bioactivity, paving the way for the development of new functional foods and functional pharmaceuticals.

3.1.3. Release of free polyphenols

In many medicinal herbs, polyphenols exist in the form of protein or polysaccharide bonds, which reduces their biological activity. Fermentation helps break these bonds, releasing free polyphenols and thereby increasing antioxidant capacity, which protects cells (Tables 1 and 2). Fermenting green tea (*Camellia sinensis*) with *Lactobacillus plantarum* significantly increased the amount of free EGCG [1, 6, 7]. Studies have shown that fermentation of herbs such as *Curcuma longa*, *Zingiber officinale*, and *Cymbopogon citratus* can enhance their polyphenolic content and free radical scavenging capacity. Turmeric kombucha exhibits higher antioxidant activity after slow fermentation, due to the release of free phenolics that are more effective in neutralizing free radicals, comparable to the activity levels of vitamins C and E [2].

The release of free polyphenols by microbial fermentation activity enhances antioxidant activity and elevates the bioaccessibility and functional activity of herbal preparations overall. Most polyphenols in medicinal plants are, in their natural state, conjugated with sugar groups or proteins, or embedded in polysaccharide matrices, thereby lowering their reactivity and absorption in the gastrointestinal tract. Microbial enzymes such as *β*-glucosidase, tannase, esterase, and cellulase play a key role in hydrolyzing such conjugations in the process of fermentation, making free low-molecular-weight polyphenols with higher antioxidant and anti-inflammatory activities [1]. Fermentation of green tea (*Camellia sinensis*) and *Lactobacillus plantarum* increased epigallocatechin gallate (EGCG) content and its stability and radical-scavenging activity. EGCG, the primary catechin in green tea, is a highly potent antioxidant but unstable under physiological conditions. The catabolic pathways are inhibited through fermentation while the bioactive forms are stabilized, thereby becoming more powerful in biological systems [5].

Therefore, controlled microbial fermentation is a significant biotechnological method to achieve the full antioxidant potential of bound polyphenols in plants. In releasing the compounds from their bound form, fermentation not only increases their activity but also opens up the prospect of having more effective herbal drugs and functional foods.

3.1.4. Breaking down polysaccharides into oligosaccharides

Microbial fermentation significantly enhances the functional properties of herbal polysaccharides by breaking them down into oligosaccharides with lower molecular weights, greater solubility, and improved bioactivity (Tables 1 and 2). These enzymatic transformations-primarily catalyzed by cellulase, xylanase, pectinase, and amylase from lactic acid bacteria and fungi-facilitate the cleavage of *β*-glycosidic bonds in complex plant polysaccharides, leading to the release of bioactive oligosaccharides [8]. A study determined the effects of oligosaccharides from *Radix Ophiopogonis* after fermentation with alcohol and acetic acid (OOV) compared with the unfermented form (OOJ). The results showed that OOV had a lower molecular weight, different sugar composition, and more vigorous *α*-glucosidase inhibitory activity. In diabetic rats, OOV had a higher hypoglycemic effect and better protection of pancreatic islets than OOJ [9].

Similarly, the fermentation of Polygonatum cyrtonema using Lactobacillus plantarum increased the yield of oligosaccharides and monosaccharides, while enhancing antioxidant activity and anti-diabetic potential [8]. These improvements were attributed to the microbial degradation of inulin-type polysaccharides and fructooligosaccharides, which are known to function as potent prebiotics that selectively stimulate the growth of Bifidobacterium and Lactobacillus in the gut [5]. In fermented *Scutellaria baicalensis*, although the focus is often on flavonoid aglycones, studies have also demonstrated that oligosaccharides generated during fermentation can synergize with flavonoids to enhance their antioxidant potential and improve intestinal absorption. These oligosaccharides, due to their low degree of polymerization, can resist degradation in the upper GI tract, reaching the colon intact and serving as substrates for beneficial gut microbes [5]. Moreover, the conversion of high-molecular-weight polysaccharides into oligosaccharides contributes to immunomodulatory activity. Specific oligosac-charides produced through fermentation activate macrophages and dendritic cells more effectively than their parent polysaccharides, supporting their use in functional foods that target immunity and metabolic disorders [2].

3.1.5. Generation of new secondary metabolites

Microbial fermentation not only improves the bioavailability of existing compounds but also has the potential to generate new secondary metabolites through biological transformations such as hydrolysis, oxidation-reduction, glycosylation, and cyclization. These compounds often exhibit more substantial or significantly different biological activities than their original precursors, opening up considerable potential for applications in pharmaceuticals and functional foods (Tables 1 and 2).

Table 1. Transformation of bioactive compound groups during fermentation

Compound group	Main biotransformation	Benefits obtained
Flavonoids	Hydrolysis of glycosides to aglycones; hydroxylation/demethylation	Enhanced absorption and antioxidant activity
Saponins	Glycosidic hydrolysis → sapogenins	Lower cholesterol, anticancer, and anti-inflammatory
Glycosides	Enzymatic cleavage of the glycosidic bond (β-glucosidase)	Release of active aglycones, increased bioavailability
Polysaccharides	Hydrolysis by amylase/cellulase → oligosaccharides + SCFAs	Prebiotic effect, gut health improvement, and immune modulation
Alkaloids	Oxidation, hydroxylation, structural transformation (e.g., nicotine → nicotinic acid)	Production of vitamin B3 and other bioactive derivatives

Compound group	Main biotransformation	Benefits obtained
Triterpenoids	Hydroxylation, esterification, methylation	Improved solubility, higher absorption, and more potent anti-inflammatory effects
Polypeptides	Proteolytic hydrolysis → small peptides	Antioxidant, antihypertensive bioactive peptides
Phenolic acids	Oxidation, hydroxylation, decarboxylation (ferulic acid → vanillin)	Increased antioxidant and antimicrobial potential

A typical example is the fermentation of ginsenoside Rb1, a major saponin in ginseng, by *Lactobacillus paralimentarius* LH4. This bacterial strain metabolized Rb1 into intermediates such as ginsenoside Rd and F2. Ultimately, it formed compound K, a saponin with outstanding biological properties, particularly in terms of anti-cancer and anti-inflammatory effects. Compound K does not exist in natural ginseng but is formed through biotransformation, showing the ability to generate new secondary metabolites through fermentation [10]. Fermentation of *Angelica gigantis* radix extract with *Aspergillus oryzae* not only increased the content of decursin and decursinol angelate but also produced a new compound, decursinol, a reduction product of decursin with significantly improved antioxidant and anti-inflammatory activities [1]. In addition, during the fermentation of *Scutellaria baicalensis* with *Lactobacillus brevis*, the researchers also discovered the formation of three new flavonoids that had not been reported before. One had a flavone glycoside structure with a unique methoxy group, suggesting that the bacterial enzyme can promote rare cyclization reactions [5].

The above examples demonstrate the significant potential of microbial fermentation in enhancing pharmacological properties and paving new directions in the discovery of natural active substances. Identifying and optimizing fermentation conditions to produce new secondary metabolites is a promising research direction in modern pharmaceutical technology.

3.2. Increasing the use of low-value medicinal resources

Fermentation has now been developed as a biotechnological tool to maximize the medicinal value of herbs, although it was previously hindered by low activity or inherent toxicity. Many medicinal herbs contain valuable constituents in inactive biological forms, which have poor bioavailability or are shielded by toxic materials. Fermentation using microbes enables such constituents to be transformed into active and safer forms, thereby unlocking their therapeutic value (Tables 1 and 2). The majority of medicinal plants have potential activities but are not commonly used due to disagreeable taste, low active ingredient content, or natural toxicity. Fermentation is used to remove or reduce natural toxins (such as alkaloids, tannins, and oxalates), transform insoluble materials into water-soluble substances, improve sensory attributes, and reduce strong smells, bitterness, or aftertastes. This allows for the use of cheap, easily cultivated raw materials, even farm waste, to generate worth while also assisting in alleviating pressure on wild resource exploitation [1, 11].

For example, *Polygonum multiflorum*, a commonly used traditional herb, is known for its hepato-protective and anti-aging properties; however, its application is limited due to the presence of hepatotoxic anthraquinones, such as emodin. Fermentation with *Aspergillus oryzae* has been reported to significantly reduce the content of toxic anthraquinones while simultaneously enhancing antioxidant activity through the release of phenolic compounds and the transformation of stilbene glycosides into their more active aglycone forms [2]. *Cassia obtusifolia*, rich in anthraquinones and flavonoid glycosides, shows limited bioactivity in its raw form. However, microbial fermentation by lactic acid bacteria improves its taste, increases total phenolic and flavonoid content, and enhances activities such as α-glucosidase inhibition and antioxidant capacity, thus transforming it into a promising antidiabetic and functional food candidate [5]. In another case, agricultural by-products such as rice bran, often discarded or underutilized, have been fermented with *Bacillus subtilis* and *Lactobacillus plantarum*, resulting in enhanced levels of γ-oryzanol and ferulic acid - compounds with well-known anti-inflammatory and neuroprotective properties. Fermentation also reduces phytic acid, a known anti-nutritional factor, increasing the bio-availability of minerals such as iron and zinc [4].

These conversions enhance the drug's action in the end product and improve organoleptic properties, such as flavor and texture, making them more acceptable for human use. Furthermore, fermentation reduces the reliance on wild plants by making feasible the utilization of extensive, inexpensive, or wasteful material resources from agriculture and forestry, thus maintaining biodiversity conservation and sustainable resource use [1, 8].

Overall, microbial fermentation represents a sustainable, cost-effective approach to valorize low-value medicinal resources, transforming them into high-value therapeutic agents with reduced toxicity and improved bioavailability.

3.3. Fermented medicinal herbs will help extract more effectively

The fermentation process of medicinal herbs by microorganisms can break down the cell walls of plants, facilitating the extraction of substances more quickly and efficiently, while also increasing the solubility of these substances in water, a particularly favorable solvent (Tables 1 and 2). In addition, some strains of microorganisms can also produce selective hydrolytic enzymes, thereby supporting the extraction of target molecules without extracting additional impurities, which is suitable for producing active essences [1, 12].

Microbial fermentation enhances biological activity and improves the efficiency of extracting beneficial compounds from medicinal herbs. One of the primary mechanisms is the decomposition of plant cell walls by hydrolytic enzymes produced by microorganisms such as cellulase, hemi-cellulase, pectinase, or *β*-glucosidase. As a result, the structure of plant tissue is broken down, allowing the active ingredients inside to escape and dissolve more readily in friendly solvents such as water, thereby reducing the need to use toxic organic solvents. For example, during the fermentation of *Scutellaria baicalensis* with *Lactobacillus brevis*, the content of baicalein (aglycone) increased significantly because the enzyme *β*-glucuronidase broke the glycosidic bond, making the compound more soluble and more active [4]. Most flavonoids exist in the form of glycosides that are insoluble and difficult to absorb. Fermentation helps to remove the sugar part and release the highly active aglycone. Fermentation of *Scutellaria baicalensis* increases the extraction capacity of baicalein, and at the same time, the extraction is more selective and has fewer impurities than that from unfermented medicinal herbs [4].

Table 2. Microbial strains and fermentation conditions

Microbial strain	Conditions/ Enzymes produced	Compounds transformed
Lactobacillus plantarum	Produces β-glucosidase; gut fermentation	Flavonoid glycosides → aglycones
Bifidobacterium bifidum	Secretes enzymes for flavonoid metabolism	Flavonoids → aglycones, phenolic acids
Enterococcus spp.	Hydrolyzes phenolic compounds	Complex phenolics → simple phenolic acids
Aspergillus niger	Produces amylase, cellulase, β-glucosidase	Glycosides, polysaccharides → aglycones, oligosaccharides
Saccharomyces cerevisiae	Alcoholic fermentation; glycoside hydrolysis	Release of aglycones, organic acids
Bacillus subtilis/ B. pumilus	Produces protease, amylase	Proteins → peptides; starch → maltose, glucose
Pseudomonas spp.	Catechol dioxygenase	Phenolic acids → catechol, pyruvate
Rhizopus spp.	Esterase, hydroxylase activity	Triterpenoids → hydroxylated/esterified derivatives
Streptomyces spp.	β-glucosidase, cellulase, protease	Glycosides → aglycones; proteins → peptides

Microbial strain	Conditions/ Enzymes produced	Compounds transformed
Cunninghamella spp.	Hydroxylase	Ursolic acid → 3β-hydroxy-ursolic acid
Phanerochaete chrysosporium	Produces laccase, peroxidase	Phenolic acids → vanillin, quinones, other aromatic compounds

Tannins and alkaloids are also active groups that are often poorly soluble in water, causing a strong astringent and bitter taste. Fermentation can partially hydrolyze the polymer structure of tannins, helping to release easily soluble derivatives while reducing astringency, making extraction more manageable, and increasing sensory value. Fermentation of *Radix Ophiopogonis* with acetic acid helps to produce oligosaccharides with higher biological activity and better solubility [8].

In summary, fermentation is an effective biological tool for enhancing the extraction efficiency of medicinal herbs and improving the solubility and selectivity of target compounds during the extraction process, while reducing solvent usage and aligning with the current trend of "green" extraction.

3.4. Basis for developing new generation pharmaceutical products

In addition to creating traditional products, such as previous extraction technologies, fermentation can also produce synbiotic products, which combine probiotics (beneficial microorganisms) with prebiotics (fermented medicinal substrates). Fermented products can exhibit vigorous activity, have fast-acting effects, and are generally low in toxicity. They are suitable for individuals with poor health and those who are easily irritated, such as older adults and children. The combination of medicinal fermentation technology and pharmaceutical extraction has opened up a new direction in developing new-generation medicinal preparations, especially products that are both probiotic (beneficial microorganisms) and prebiotic (fermented biological substrates advantageous to the intestinal microflora). The fermentation process chemically transforms the ingredients in medicinal herbs, accumulating beneficial organisms, especially strains of *Lactobacillus*, *Bifidobacterium*, and *Bacillus subtilis*. These microorganisms support digestion and contribute to immune regulation, drug metabolism in the intestine, and increased absorption of active ingredients [3, 4, 7, 13].

A typical example is the product from the fermentation process of *Ophiopogon japonicus* roots - a traditional medicinal herb; when fermented with acetic acid, it creates oligosaccharides with apparent biological activity and is also an ideal substrate for probiotics to grow in the intestine [8]. These products function as prebiotics, regulate blood sugar levels, and enhance pancreatic function in experimental animals. Red ginseng fermentation with *Lactobacillus paralimentarius* has shown the ability to produce compound K, a saponin derivative with more vigorous activity and easier absorption, and this enzyme-rich fermentation medium can be used as a “living biological platform” for combined probiotic preparations [10].

In addition, the development of “bioconversion platform” technology - a bioconversion platform that combines extraction and fermentation - enables the creation of highly effective, fast-acting preparations that can be produced in various forms, including powders, soluble granules, or fermented drinks. These products are especially suitable for the elderly, children, people with weak digestive systems, or those undergoing treatment for chronic diseases because of their safety and tolerability [5].

3.5. Potential in personalised medicine

With the development of precision medicine and gut microbiology, fermented medicinal products can play a key role in personalised treatment, such as selecting the right probiotic strain for the patient's body, creating products compatible with the specific gut microbiota for each individual, and supporting the recovery of disturbed microbiota (due to antibiotics, stress, diet) [1, 14]. For example, patients with metabolic disorders can use soybean products fermented with *Bacillus subtilis* to increase endogenous insulin and improve glycemic response [15].

In addition to selecting the right strain of microorganisms for the patient's body, medicinal fermentation technology also lays the groundwork for the development of personalized medical products through its ability to interact with the intestinal microflora characteristic of each individual. Many studies have demonstrated that the composition of the intestinal microflora significantly influences the pharmacological effects of natural compounds, particularly polyphenols, saponins, and alkaloid groups found in traditional medicinal herbs, which often exhibit low bioavailability. The fermentation process with probiotic bacteria such as *Lactobacillus*, *Bacillus subtilis*, or *Bifidobacterium* not only helps to convert these compounds into a more easily absorbed form but also creates new metabolites with more vigorous activity, suitable for the absorption and metabolism characteristics of each user's body [10].

Fermenting soybeans with *Bacillus subtilis* can help convert isoflavone glycosides into aglycone forms (such as daidzein and genistein), which significantly improves glycemic response in people with metabolic syndrome or type 2 diabetes, thanks to its ability to affect both endogenous insulin secretion and peripheral insulin sensitivity. This opens the way for the development of personalized probiotics - where treatment regimens are based not only on pathology but also on gut microbiota patterns and individual metabolic responses [15]. Furthermore, products combining fermented medicinal herbs and probiotics can also be designed as synbiotics (containing both live probiotics and a prebiotic base of fermented medicinal herbs). They provide both active compounds and help restructure the intestinal microflora, which is especially beneficial for individuals with sensitive digestive systems or disorders resulting from antibiotic use, stress, or unhealthy diets [14]. From this foundation, scientists anticipate that in the future, fermented medicinal products will be designed specifically based on individual microbiome profiling and genetic data, thereby contributing significantly to the development of personalized therapy for each patient [14].

In addition, the extraction of compounds after fermentation is also more effective because this process helps break down the plant cell wall, increasing the solubility of active ingredients in friendly solvents such as water while reducing toxicity and impurities, which is very important for products for the elderly, children, or people with chronic diseases. From there, fermentation technology not only helps optimize treatment effectiveness but also personalizes the method of use, making it suitable for each patient, thereby contributing to the development of precision medicine based on individual microorganisms and specific body physiology.

3.6. Challenges and prospects of medicinal fermentation technology before extraction

Although fermentation technology shows significant potential in enhancing the therapeutic efficacy of medicinal plants, several challenges remain that limit its broader application. One major challenge is biosafety control. While beneficial microbial strains such as *Lactobacillus* and *Bifidobacterium* are widely used, certain fungi, particularly *Aspergillus* species, may produce secondary metabolites, including mycotoxins, if fermentation conditions such as pH, temperature, and aeration are not strictly controlled [1, 14]. This highlights the necessity of rigorous quality assurance protocols to prevent contamination and ensure the safety of fermented medicinal products.

Another critical challenge is batch-to-batch consistency. The phytochemical composition of medicinal plants is highly variable, depending on factors such as geographical origin, harvest season, and storage conditions. This variability can be further amplified during fermentation, leading to inconsistencies in the concentration of active metabolites and final biological activities [5, 15]. Ensuring reproducible phytochemical profiles requires careful strain selection, standardized processing of raw materials, and strict monitoring of fermentation parameters.

Process optimization is also a limiting factor. Slight variations in fermentation time, microbial inoculum, or substrate preparation may significantly alter enzymatic activity and the yield of active compounds. For instance, the fermentation of green tea with *Lactobacillus plantarum* demonstrated enhanced antioxidant activity only under precise pH and temperature conditions [15]. Scaling up such tightly controlled laboratory conditions to industrial-level production while maintaining product quality remains a significant challenge.

Despite these obstacles, the prospects of medicinal fermentation technology remain highly promising. Fermentation aligns with sustainable development goals by reducing reliance on organic solvents and allowing the valorization of low-value plant materials [2, 11]. Moreover, its role in generating novel secondary metabolites such as compound K from ginsenosides or decursinol from *Angelica* highlights its potential in the discovery of new therapeutic agents [1, 10]. In addition, the integration of fermentation into personalized medicine, through tailoring probiotics and biotransformation pathways to individual microbiome profiles, opens new opportunities for precision healthcare [14].

In summary, while biosafety risks, consistency issues, and process optimization represent ongoing challenges, advances in microbial biotechnology and quality control strategies are likely to overcome these barriers. This will facilitate the development of safe, effective, and standardized fermented medicinal products, thereby ensuring their future role as a cornerstone in modern phytopharmaceuticals.

4. CONCLUSION

Before extraction, fermentation is considered a sophisticated and hopeful biotechnological method for medicinal material research. Instead of conducting extraction directly, as is commonly practiced, the initial step is fermentation, which allows the microorganisms, particularly bacteria and yeasts, to transform the natural components available in the plant materials into more absorbable or bioactive forms. This method not only improves the utility of active constituents to a considerable degree but also can generate novel derivatives with higher potential. Inducing the fermentation process before extraction enables the reconstruction of the medicinal compound's chemical makeup in a differential manner, which enhances therapeutic action and reduces the risk of side effects or toxicity. These products also possess superior biocompatibility and are less harmful when applied by human beings. This strategy represents a significant step forward in integrating traditional medical wisdom, based on centuries of medicinal plant use, with modern scientific techniques, including microbiology, analytical biochemistry, and pharmacokinetics. Integrating fermentation technology into phytopharmaceutical research and development (R&D) opens new avenues for evidence-based, individualized therapies and facilitates the development of sustainable, eco-friendly medical solutions.

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Tiềm năng của công nghệ lên men cho quá trình chiết xuất dược liệu

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TÓM TẮT

Tổng quan: Một số thuốc thảo dược truyền thống có hoạt tính thấp. Quá trình lên men như một giải pháp nhằm tăng hiệu quả điều trị thông qua sự chuyển hóa các chất có hoạt tính mạnh bởi vi sinh vật. Mục tiêu: Làm rõ cách thức mà quá trình lên men giúp cải thiện hiệu lực điều trị của dược liệu và vai trò của nó trong y học hiện đại và cá thể hóa. Phương pháp: Tổng hợp các nghiên cứu về lên men vi sinh sử dụng các chủng như Lactobacillus, Bacillus và Aspergillus, tập trung vào quá trình chuyển hóa các hợp chất thực vật và tăng hoạt tính sinh học. Bài nghiên cứu này tập trung vào các bài báo nghiên cứu và các bài báo đánh giá liên quan đến quá trình lên men vi sinh của cây thuốc từ các cơ sở dữ liệu khoa học như PubMed, ScienceDirect, SpringerLink và Google Scholar. Kết quả: Lên men giúp tăng các hoạt tính như chống oxy hóa, kháng viêm và chống tiểu đường nhờ biến đổi các hợp chất thành dạng dễ hấp thu và có hoạt tính mạnh hơn, đặc biệt là aglycone. Kết luận: Lên men là hướng đi tiềm năng để nâng cao giá trị dược liệu, mang lại lựa chọn điều trị hiệu quả và an toàn hơn, phù hợp với từng cá nhân.

Từ khóa: *dược liệu, lên men, hoạt tính sinh học, hóa thực vật, công nghệ sinh học*

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