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Review Article

## Fermented Herbs: A New Frontier in Phytomedicine

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### Abstract

Medicinal herbs are considered to be environmentally friendly, effective and safe additives for animals. Recently, the application of probiotic fermentation has emerged as a modern biotechnological approach to refine and potentiate herbal therapies. This review aims to provide a comprehensive overview of how probiotic fermentation serves a dual purpose: mitigating the inherent toxicity of certain herbal compounds and simultaneously enhancing the bioactivity and therapeutic efficacy of herbal remedies. The review systematically examines the key methods employed in probiotic herbal fermentation, highlighting the shift from traditional, uncontrolled natural fermentation to modern techniques using defined probiotic strains such as *Lactobacillus*, *Bifidobacterium* and *Bacillus* species. Concurrently, fermentation drives the enhancement of bioactivity. Probiotic enzymes hydrolyze high molecular weight compounds (like glycosides) into more bioavailable and active forms (like aglycones), increasing the content of key functional metabolites such as flavonoids, polyphenols, and saponins.

**Keywords:** Fermentation, probiotic, herbal medicine, *Lactobacillus*.

### INTRODUCTION

Plants are used for health and medical functions since thousands of years. India is a rich source of medicinal plants, and various systems of medicine such as Ayurveda, Siddha, and Unani use several plant extracts against diseases. Ayurveda is the traditional Indian system of medicine from ancient times, mostly using herbal preparations, to prevent or cure various diseases and tumors (Pandey *et al.*, 2013). Active compounds in herbal products have been shown to improve the morphology and functions of the digestive tract, physiological conditions, antioxidant status and immune competences of animals (Sugiharto and Ayasan 2023). In recent years the use of herbal medicine is increased in livestock production due to the side effects of modern drugs, toxic residues in food, microbial resistance and due to the



development of organic livestock production systems. However, the bioactive ingredients of herbal medicines are complex, and some natural products cannot be directly absorbed by animals. Moreover, the contents of most bioactive ingredients in herbal plants are low, and some natural products are toxic to animals. Even the use of herbal products may impair feed palatability and consumption due to their bitter taste and pungent smell.

Biological fermentation technology combines fermentation engineering and enzyme engineering, which effectively reduces anti-nutritional factors in plant-based raw materials, increases active substances and bioactive ingredients in raw materials, improves feed palatability and processing performance, and makes it easy for animals to eat (Olukomaiya et al 2019). With respect to herbal products in particular, fermentation has been confirmed to enhance the active components present in herbal products, increase antioxidant activity, decrease the potential toxicities and improve the effectiveness of herbal products for therapeutic applications (Adli et al., 2024). Depending on the type of microorganisms involved, fermentation will result in the formation of different final products such as lactic acid, ethanol or acetic acid, as different microorganisms may react differently to each substrate (Subramaniyam and Vimala, 2012), e.g. *Lactobacillus* produce lactic acid, mould yield citric acid, whereas yeasts generate ethanol and CO<sub>2</sub>. In this review, we focus on the summary and discussion of current probiotic fermentation of herbs, including the potential mechanisms of herbs fermentation, the fermentation advantages, the probiotics used for fermentation and modern microbial fermentation technologies.

## MECHANISMS OF HERBS FERMENTATION BY PROBIOTICS

Compared with traditional processing methods, fermentation of herbs with probiotics can improve the bioactivity of herbal ingredients under mild processing conditions. *Streptococcus lactis* could efficiently degrade the cellulose, and the fermentation of Astragalus with *S. lactis* increased the contents of crude polysaccharides, total flavonoids, and total saponins in Astragalus roots, stems, and leaves. The enzymes secreted by gut probiotics can hydrolyze and remove glycosyl groups from natural products, which increases their lipophilicity and improves the absorption rate in the gastrointestinal tract. After oral ingestion of liquorice, glycyrrhizin is converted to glycyrrhizic acid, and subsequently converted to glycyrrhetic acid by gut microbiota.

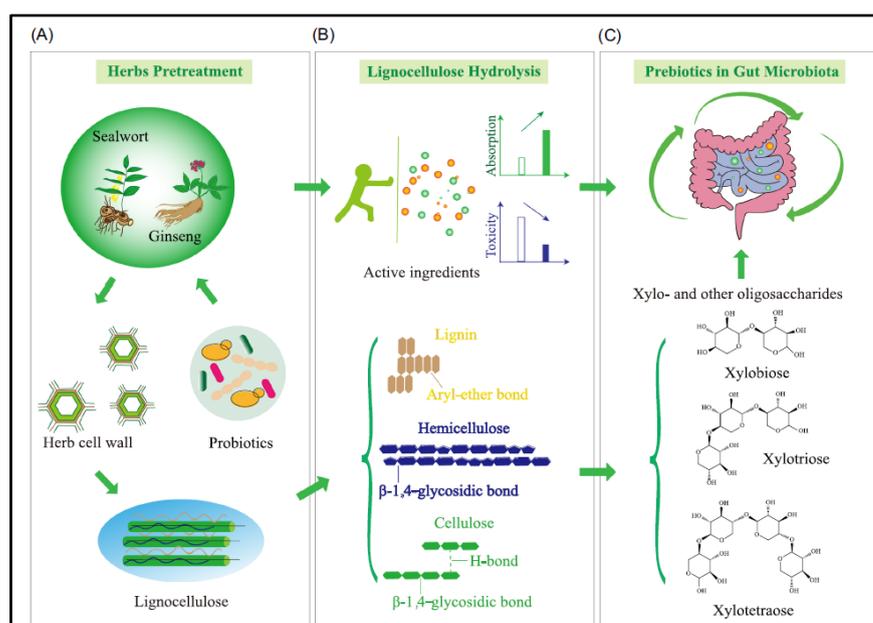
## ADVANTAGES OF PROBIOTIC FERMENTATION OF HERBS

**Promoting the release of effective ingredients and improving the pharmacological activities of herbs**



The effective ingredients of various herbs are mostly distributed in the cytoplasm of root, stem, and leaf cells of plant biomass. The plant cell wall structure is tight, and is mainly composed of cellulose, hemicellulose, and lignin, which hinders the release of bioactive natural products and results in low absorption and utilization of bioactive natural products (Zhao *et al.*, 2014). Probiotics can produce a variety of hydrolytic enzymes, especially lignocellulases, to degrade plant cell wall and promote the release of bioactive natural products (Figure 1 A,B). These released bioactive natural products include flavonoids, glycosides, anthraquinones, terpenoids, alkaloids, and organic acids. Moreover, the lignocellulases can help generate oligosaccharide prebiotics for the gut microbiota of animals (Figure 1C). Therefore, probiotic fermentation can improve the pharmacological activity of herbal products.

After fermentation of herbal medicine with the probiotics, such as *Lactobacillus casei*, *Enterococcus faecalis*, and *Candida utilis*, the contents of soluble total flavonoids, total alkaloids, crude polysaccharides, and total saponins in the fermented Chinese herbs of *Semen vaccariae* and *Leonurus artemisia* increased by 55.14%, 127.28%, 55.42%, and 49.21%, respectively, compared with the natural herbs (Liu *et al.*, 2017). After fermented by *Lactobacillus pentosus*, the contents of quercetin and kaempferol in the extracts of *Lespedeza cuneata* G. Don increased by 242.9% and 266.7%, respectively, which improved potential antioxidative and antiaging functions of the herb (Seong *et al.*, 2017). The microbial fermentation, especially probiotic fermentation, can significantly increase the contents of bioactive natural products and improve the pharmacological effects of herbs.



**FIGURE 1** Lignocellulases and their functions in sealwort, ginseng, and other herbal medicine fermentation. (A) The lignocellulose might prevent the release of bioactive

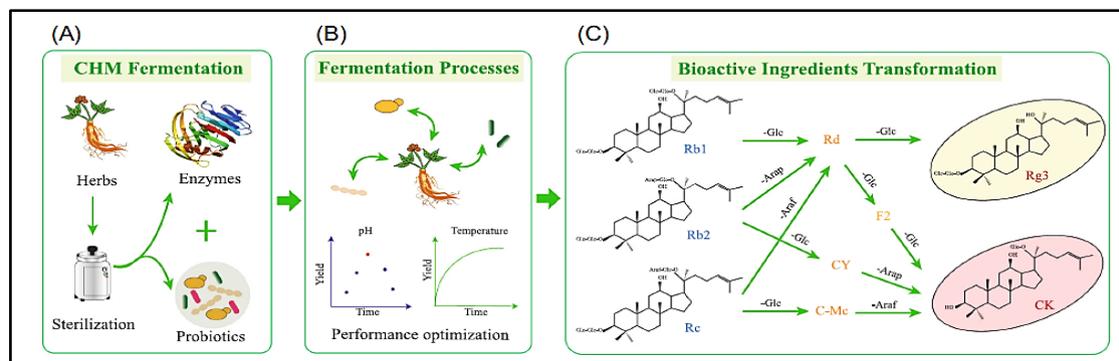
ingredients of herbs, and lignocellulases derived from probiotics or other microbes can be used to degrade herb lignocellulose. (B) Lignocellulose hydrolysis releases bioactive ingredients in herbs, and leads to the generation of oligosaccharides prebiotics. (C) Bioactive ingredients and oligosaccharides are beneficial for the gut microbiota of humans and animals. (Zhang et al., 2023)

### Reducing toxicities and side effects of herbs

Some herbs have certain toxicities to animals, and direct oral intake of them would generate serious toxic effects. Probiotics can degrade or modify the toxic components, thus, reduce the toxicities or side effects of herbal plants (Li et al., 2017). Conjugated anthraquinones are the main components leading to severe diarrhea of rhubarb. Fermentation of rhubarb with *Kluyveromyces marxianus* KM12 could convert conjugated anthraquinone to free anthraquinone, and the side effects of severe diarrhea generated by rhubarb were alleviated (Ma et al., 2013). Compared with the original crude *Croton tiglium*, fermentation of *C. tiglium* with *Ganoderma lucidum* and *Beauveria bassiana* could decrease acute oral toxicity by about four times, and have no inflammation effect and hemocytolysis (Liu et al., 2011).

### Generating new bioactive substances and enhancing the bioavailability of herbal products

Probiotic fermentation transforms Chinese herbal medicines (CHM) ingredients to new bioactive compounds, and this might bring new pharmacological characteristics to CHM (Figure 2). Ginsenosides are the main physiologically bioactive natural products of ginseng, and ginsenosides Rb1, Rb2, Rc, Re, and Rg1 constitute more than 80% of the total ginsenosides in *Panax ginseng* (Zhao et al., 2021). The probiotic, *Bifidobacterium animalis* subsp. *lactis* LT 19-2, can effectively convert main ginsenosides Rb2 and Rb3 in red ginseng extracts to rare ginsenosides of Rd, Rh1, F2, and Rg3 (Figure 2C) (Kim et al., 2019).

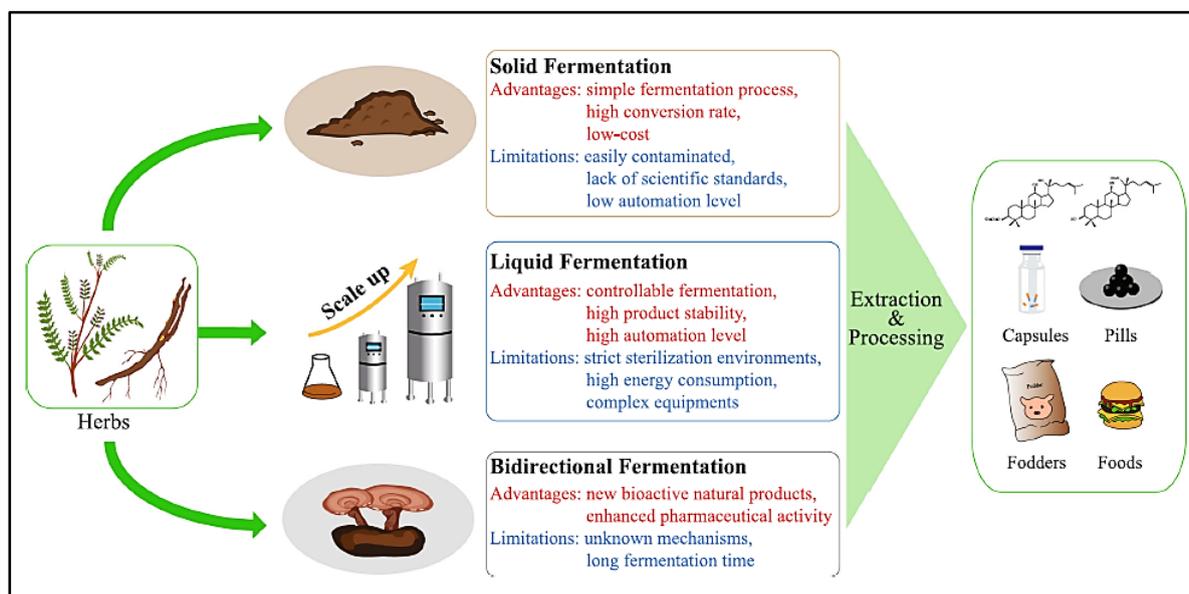


**FIGURE 2** Biotransformation of ginsenosides to active rare ginsenosides using efficient enzymes or probiotics. (A) The herbs of *Panax ginseng* are sterilized for probiotic

fermentation, and the enzymes and probiotics are the main driving forces for CHM fermentation. (B) Probiotic performance during ginseng fermentation can be optimized to improve bioactive ingredient yield. (C) Ginsenosides can be transformed to the bioactive rare ginsenosides during CHM fermentation.; (CHM, Chinese herbal medicines). (Zhang *et al.*, 2023)

### Reducing production costs and protecting environments

Probiotic fermentation of herbal compounds can increase the contents of effective ingredients and decrease the consumption of main herbal product. Rare ginsenosides have been used to produce anticancer drugs, foods, and health care products and probiotic fermentation could reduce the consumption of *P. ginseng* and the production costs of rare ginsenosides (Zhang *et al.*, 2023). Huazhenghuisheng oral liquid (HOL), a clinical anti-lung and liver cancer drug, is produced with 35 kinds of CHM. Fermentation of HOL residues with *Aspergillus cristatus* CB10002 could produce valuable compounds of anthraquinones (Kong *et al.*, 2019). Probiotic fermentation can help reduce herbs consumption and provide a green recycling strategy of herb residues, which would save natural herbal sources, reduce production costs, and protect environments.



**FIGURE 3** Different probiotic herbal fermentation strategies and their characterization. The liquid, solid, and bidirectional fermentation were used for herbs fermentation. After extraction and purification, the final products of herbal fermentation could be used as drugs, fodders, and foods.

### PROBIOTIC FERMENTATION TECHNIQUES FOR HERBS

Traditional herbal fermentation technique is solid-state fermentation, which uses wild type microorganisms in the environments to complete the fermentation process without



accurate control of ambient temperature and humidity. The fermentation endpoint of solid-state fermentation is often determined by individual experience. Therefore, the efficacy, safety, and stability of traditional fermented herbs are not stable, and this might be due to insufficient strain purity, uncontrollable fermentation conditions, and lack of standardized fermentation process and appropriate monitoring indicators. Compared with traditional fermentation technique, modern fermentation technology integrates microbial ecology, fermentation engineering, and bioengineering, leading to new herbal fermentation techniques (Li et al., 2020). On the basis of fermentation forms, modern fermentation techniques can be divided into solid fermentation, liquid fermentation, and bidirectional fermentation with medicinal fungi (Figure 3).

## CONCLUSION

In conclusion, probiotic fermentation represents a transformative biotechnological approach in the processing of medicinal herbs, offering a sophisticated upgrade over traditional methods. By employing defined probiotic strains such as *Lactobacillus*, *Bifidobacterium*, and *Bacillus* species, this technique achieves a dual purpose: it effectively mitigates the inherent toxicity of certain herbal compounds while simultaneously enhancing the bioactivity and therapeutic efficacy of the remedies. Probiotic fermentation increases the content of key active ingredients like flavonoids, polyphenols, and saponins, reduces production costs and supports environmental sustainability through the recycling of herbal residues. With the advancement of modern fermentation technologies—solid, liquid and bidirectional—the process has become more controlled, standardized, and efficient.

## FUTURE PERSPECTIVES

Probiotic fermentation of herbs can generate easily absorbed bioactive compounds and reduce toxicities. Therefore, discovering efficient and safe probiotic strains and developing novel fermentation strategies for herbal fermentation are of great interest. Optimization of fermentation equipments and parameters are necessary to obtain high titer, rate, and yield of herbal bioactive products. Although probiotics are safe for the human body, the products of probiotic fermentation should accept a comprehensive and scientific safety evaluation. Looking forward, continued research into novel probiotic strains, optimized fermentation parameters, and rigorous safety evaluations will be essential to fully harness the potential of fermented herbs in medicine and livestock production.

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