Insights into Fermentation Technology for Traditional Chinese Medicine: Progress and Applications

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Abstract Traditional Chinese medicine (TCM) has an exemplary role in the treatment and prevention of diseases. However, the advancement of TCM has been constrained by several factors, including its intricate structure, low active ingredient concentration, prolonged growth cycle, and the difficulty in artificial cultivation. In recent years, research on the fermentation technology of TCM has increased. This paper provides an overview of the advantages of TCM fermentation technology, including efficiency enhancement and toxicity reduction, the development of new drugs, and the secondary utilization of dregs. Additionally, it discusses the progress of research on the application of fermented TCM in animal husbandry and disease treatment. The aim is to provide theoretical guidance for TCM fermentation technology research and the development of fermented TCM.
Keywords Fermentation technology; Traditional Chinese medicine; Animal husbandry; Application; Research progress

In China, traditional Chinese medicine (TCM) is held in high esteem, with notable achievements in the prevention and treatment of diseases. Additionally, China boasts a wealth of resources pertaining to TCM, which is regarded as a vital strategic asset[1]. Nevertheless, the advancement of TCM has been constrained by a number of factors, including its intricate structure, low active ingredient concentration, prolonged growth cycle, and the difficulty in artificial cultivation. As a result, it is challenging to meet the needs of the market. As a consequence of the advancement of scientific and technological knowledge, fermented TCM has increasingly captured the attention of the scientific community. The fermentation of TCM represents a specific method of TCM processing. Indeed, China has been utilizing fermentation technology for the processing of TCM for millennia[2]. TCM fermentation technology represents a novel pharmaceutical technology that integrates the processing techniques of TCM with the principles of microbiology and fermentation technology[3]. The fermentation process in modern TCM can employ both single-strain and composite-strain cultures. During the fermentation process, microorganisms produce a variety of new secondary products through the decomposition of TCM or their dregs and extracts (Fig.1). This has the advantages of increasing efficiency and reducing toxicity, generating new active ingredients, and conserving resources[4]. As a result, there is a broader prospect for the development and application of TCM. In recent years, there has been a notable increase in the number of studies conducted on the fermentation technology of TCM. This study aims to provide a comprehensive overview of the advantages of TCM fermentation technology and the progress of research on the application of fermented TCM in animal husbandry and disease treatment. This will serve as a foundation for future research, development and application of TCM fermentation.

1 Advantages of TCM Fermentation

The application of fermentation engineering technology to the pharmaceutical, food, and agricultural industries is a consequence of the development of modern biotechnology. The fermentation technology of TCM can induce the complex chemical components of TCM to react with the enzymes in microorganisms, thereby facilitating biotransformation of the substances in TCM. This process enhances efficacy, reduces toxicity, generates new active substances, and improves the utilization rate of TCM resources (Tab.1). Compared with the traditional production and processing methods of TCM, the modern fermentation technology of TCM exhibits significant superiority.

1.1 Improving utilization and efficacy

TCM materials encompass a multitude of varieties, the majority of which are plant-based (exceeding 90%). Their active ingredients are primarily concentrated within the cytoplasmic matrix, which presents a challenge for human absorption and utilization due to the composition of plant cell walls, comprising cellulose and pectin. The TCM fermentation technology is capable of fully utilizing ligninase, cellulase, and pectinase, along with other extracellular degradation enzymes generated during microbial cultivation, to facilitate the degradation of the plant cell wall, en-

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hance the permeability of the cell membrane, and promote the solubilization of the active ingredients present in TCM. Furthermore, the enzymes secreted by microorganisms can degrade large molecules into small molecules of active substances that can be readily absorbed. This process, known as microbial fermentation, has the potential to enhance the utilization rate and efficacy of TCM. Prior to the fermentation process, Massa Medicata Fermentata does not exhibit the medicinal effects, including the strengthening of the spleen and stomach, the elimination of food, and the regulation of the middle energizer. However, the transformation of chemical components by microorganisms and enzymes during fermentation ultimately produces these effects. Gao *et al.*[34] conducted a comprehensive analysis of the chemical constituents of Massa Medicata Fermentata, both before and after the fermentation process. Their findings revealed that 25 chemical constituents exhibited a notable increase in the fermented Massa Medicata Fermentata, including ferulic acid, protocatechuic acid, and octadecenoic acid. These compounds possess diverse physiological activities, such as anti-inflammatory and antioxidant properties. Additionally, a novel compound, 3, 4, 5-trimethoxybenzoic acid, was identified as a product of the fermentation process. *Ganoderma lucidum*, a highly esteemed edible and medicinal fungus, is renowned for its exceptional medicinal properties. Two-way fermentation technology allows for the fermentation of *G. lucidum* by inoculating it onto a medicinal substrate containing a specific proportion of TCM components[30]. *G. lucidum* is capable of absorbing a plethora of nutrients, including cellulose, starch, protein, lipids, and other nutrients present in TCM, and utilizes for its own growth and product synthesis. This process allows the fungus to produce a multitude of metabolites. Additionally, *G. lucidum* facilitates the dissolution of active ingredients in TCM and the biotransformation of specific active substances, including terpenes, flavonoids, alkaloids, and saponins, within the TCM. This process enhances the biological activity and pharmacological functions of the fermentation products. Son *et al.*[5] employed *G. lucidum* mycelium for the solid state fermentation of *Artemisia capillaris*. Their findings indicated that the resulting product of *A. capillaris*, subjected to solid state fermentation by *G. lucidum*, exhibited enhanced therapeutic efficacy in the treatment of allergic inflammatory injuries. Similarly, Wu *et al.*[6] examined the effects of solid state fermentation by three fungi, namely *G. lucidum*, *Fomes fomentarius*, and *Schizophyllum commune*, on *Pteridium aquilinum*. Their findings revealed that all three fungi were capable of increasing the total flavonoid content of *P. aquilinum*, thereby enhancing its anti-inflammatory effects. Similar medicinal edible fungi include *Phellinus linteus*, *Grifola frondosa*, *Coprinus comatus*, *Pleurotus ostreatus*, *etc.*[35]. In addition to fungi, numerous bacterial species have been employed in the fermentation of TCM. For instance, Wang[36] utilized *Bacillus subtilis* to ferment *Astragalus mongholicus*, resulting in a notable reduction in the total polysaccharide content of *A. mongholicus*, while the levels of total saponins and total flavonoids exhibited a considerable increase. Furthermore, the number and type of glycosides decreased following the fermentation of *A. mongholicus*. However, the content of glycosides and small molecules increased, indicating that the fermentation of *A. mongholicus* by *B. subtilis* was conducive to molecular transformation. Kim *et al.*[11] employed *Bifidobacterium animalis*, a bacterium with high acid-tolerant β-glucosidase activity, to ferment *Panax ginseng*. Following fermentation, the content of ginsenosides Rb1, Re, Rc, and Rb3 decreased, while the content of Rd, Rh1, F2, and Rg3 increased, thereby enhancing the immunomodulatory effects of *P. ginseng*. Similarly, You *et al.*[14] observed that the content of ginsenoside 20 (S)-Rg3, Rh2, and F2 increased by 269.87%, 198.46%, and 153.98%, respectively, following the fermentation of *P. ginseng* by *Lactobacil-*

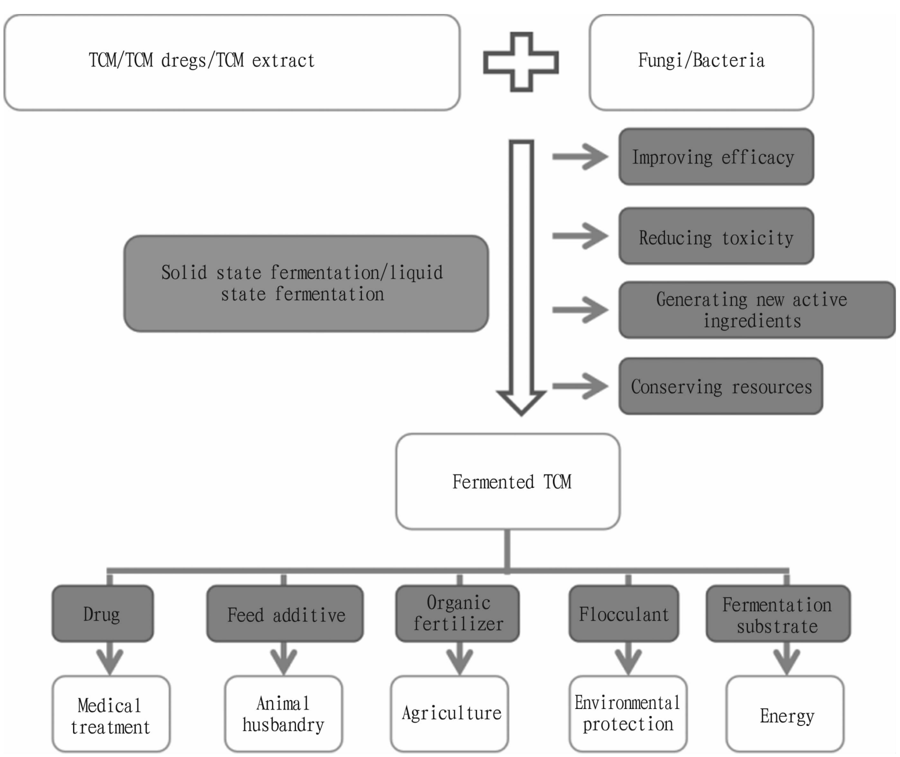

Fig.1 Advantages of TCM fermentation and application of fermented TCM

Tab.1 Advantages and specific effects of TCM fermentation technology

Advantage	Strain	TCM	Specific efficacy	Reference
Enhancing efficacy	*Ganoderma lucidum*	*Artemisia capillaris*	Enhancing anti-inflammatory effect	[5]
	G. lucidum, Fomes fomentarius, Schizophyllum commune	*Pteridium aquilinum*	Increasing total flavonoid content and significantly improving anti-inflammatory effects	[6]
	Aspergillus oryzae	*Trichosanthes kirilowii, Houpoea officinalis, Salvia miltiorrhiza, Glycyrrhiza uralensis*	Promoting the release of active substances and enhancing antioxidant and antibacterial activities	[7]
	Rhizopus oligosporus	*Astragalus mongholicus, Atractylodes macrocephala, Saposhnikovia divaricata*	Enhancing the proliferation of lymphocytes to increase immune activity	[8]
	Eurotium cristatum	*A. mongholicus*	Enhancing hypoglycemic and antioxidant activity	[9]
	Yeast	*Codonopsis pilosula*	Increasing the content of active ingredients and antioxidant activity	[10]
	Bifidobacterium animalis	Red ginseng *(Panax ginseng)*	Enhancing immunomodulatory functions	[11]
	Lactobacillus plantarum	*Aloe vera*	Accelerating burn healing and reducing inflammatory response	[12]
	L. plantarum	*Epimedium brevicornu*	Significantly improving antioxidant activity	[13]
	Lactobacillus fermentum	*Panax ginseng*	Increasing ginsenoside content, reducing hepatic inflammation, decreasing alcohol-induced oxidative damage in the liver, and increasing levels of antioxidant enzymes	[14]
	Aspergillus niger, Bacillus subtilis, Candida utilis	*Moringa oleifera*	Improving protein nutritional quality, reducing anti-nutritional factors and increasing antioxidant activity	[15]
Reducing toxicity	*G. lucidum*	Radix Aconiti	Significantly reducing ester alkaloid content and thus toxicity	[16]
	G. lucidum	*Aconitum carmichaeli*	Reducing toxicity and enhancing the efficacy of warming yang and strengthening the body resistance	[17]
	Cunninghamella blakesleeana	*Strychnos nux-vomica*	Reducing the toxicity of *S. nux-vomica*	[18]
	Sphingobium sp.	Radix Aristolochiae	Degrading aristolochic acid I, aristolochic acid I in the aqueous decoction of Radix Aristolochiae to reduce the acute nephrotoxicity of aqueous decoction of Radix Aristolochiae	[19]
	Pichia kudriavzevii, Weissella confusa	Rubber seed	Effectively removing cyanide and reduce rubber seed toxicity	[20]
Producing new active ingredients	*C. blakesleeana*	Glycyrrhetinic acid	Producing a novel substance 3-keto-15β-hydroxy-18β-glycyrrhetinic acid	[21]
	Grifola frondosa	*Gastrodia elata*	Converting gastrodin to parishin	[22]
	Monascus purpureus	*P. ginseng*	Producing the rare ginsenoside Rg3	[23]
	B. subtilis	*Panax notoginseng*	Producing new active substances ginsenosides	[24]
	Lactobacillus acidophilus	*Prunus mume, Rhus chinensis, Taraxacum mongolicum*	The transformation of the TCM ingredients produces a more beneficial effect on mice with diarrhea, which is more conducive to promoting the development of immune organs and enhancing the beneficial intestinal flora of mice	[25]
	Yeast, lactobacillus, acetic acid bacteria	Rosa, jujube kernel	Producing a new substance, jujuboside B, which enhances the calming and tranquilizing effect	[26]
Conserving resources	Angel yeast	*Hypericum perforatum dregs, Salviae miltiorrhiza dregs*	Being used in ethanol fermentation production	[27]
	Coriolus hirsutus	*Rheum palmatum* dregs	Being used as a substrate for the fermentation of laccase by *C. hirsutus* to increase laccase production	[28]
	Cordyceps militaris	*Schisandra chinensis* dregs	Improving intestinal digestion and absorption ability and disease resistance of weaned piglets	[29]
	M. purpureus	*P. notoginseng* dregs	Being used as fermentation substrate to produce red pigment	[30]
	L. plantarum	Jianwei Xiaoshi tablets dregs	Being used as drug to treat *Helicobacter pylori* infection	[31]
	Pig fecal bacteria	Korean ginseng dregs	Changing the structure of pig intestinal flora and improving pig intestinal health	[32]
	Chicken-derived mixed bacteria	*Scutellaria baicalensis* stems and leaves	Being used as feed additive to improve digestion and immune function of yellow feather broilers	[33]

lus fermentum. This resulted in a notable enhancement in antioxidant activity. Additionally, mouse experiments demonstrated that fermented *P. ginseng* mitigated liver lipid accumulation and inflammation, thereby reducing alcohol-induced oxidative damage in the liver. *L. fermentum* has also been employed for the fermentation of *Epimedium brevicornu*. The content of multilevel polyglycosides and secondary glycosides of the fermented *E. brevicornu* flavone was diminished, whereas the content of polyphenols, polysaccharides, and total flavonoids was markedly augmented, thereby demonstrating enhanced antioxidant efficacy [13]. The use of mixed strains for the fermentation of TCM has also been documented, with the objective of enhancing their efficacy. For example, Shi *et al.* [15] employed three mixed strains of *Aspergillus niger*, *B. subtilis* and *Candida utilis* for solid state fermentation of *Moringa oleifera* stem and leaf powder, which resulted in a significant increase in the *in vitro* protein digestibility of the fermented *M. oleifera*. Additionally, the antinutritional factors, including hydrolysable tannin, saponin, and phytic acid, were reduced, and antioxidant activity was significantly improved. These findings suggest that fermentation can enhance the nutritional quality and efficacy of TCM.

1.2 Reducing drug toxicity The majority of TCM possess inherent toxicity, and their improper utilization may result in adverse effects on the liver and kidneys[37]. In the event that the toxicity of TCM is not adequately addressed, it becomes impractical to employ them in clinical settings. The process of fermentation enables the microorganisms present in TCM to metabolize the compounds they encounter. The enzymes secreted by these microorganisms can then modify or decompose the toxic components present in TCM, thereby reducing the toxicity of the drug. To illustrate, *Pinellia ternata* is characterized by a pungent and toxic quality, predominantly attributed to the presence of specialized crystals comprising calcium oxalate needle crystals and protein. Additionally, the lectin protein in *P. ternata* has the potential to intensify the irritation caused by the aforementioned needle crystals. The fermentation of *P. ternata* with other auxiliary materials has been demonstrated to significantly reduce the irritation to the conjunctiva of rabbits. Furthermore, the content of calcium oxalate needle crystals is relatively reduced, indicating that the fermentation of *P. ternata* can reduce its toxicity[38]. The fermentation of the Wuyao Shunqi San, a composite herbal medicine comprising a variety of herbs with toxic side effects, by *Lactobacillus* spp. did not result in the detection of acute toxicity or genotoxicity[39]. This finding suggests that fermentation may reduce the toxicity of the original formulation. Huanfengdan Yaomu is a TCM that contains a variety of toxic ingredients, including Aconiti Radix, *P. ternata*, *Arisaema erubescens*, *etc.* It has been demonstrated that the natural fermentation process, which is dominated by *Bacillus*, *Enterobacter*, *Pediococcus*, *Saccharomycopsis*, and *Incertae sedis*, results in a notable reduction in the concentration of highly toxic alkaloids, including aconitine and benzoylaconine[40]. Xiang[19] screened and isolated a strain of *Sphingobium* sp. that was capable of effectively degrading aristolochic acid I, a toxic compound with adverse effects, from the root system of *Aristolochia debilis*. The strain was employed for the fermentation of an aqueous decoction of Radix Aristolochiae, and it was determined that the degradation of aristolochic acid I reached over 90%, thereby reducing the toxicity of Radix Aristolochiae. Deng *et al.* [20] employed a mixed fermentation of rubber seeds with *Pichia kudriavzevii* and *Weissella confusa* to achieve a cyanide removal rate of over 88.9%. This process not only reduced the toxicity of cyanide but also enhanced the aroma through yeast fermentation. In conclusion, the application of herbal fermentation technology represents an efficacious approach to the reduction of the toxicity and toxic side effects associated with TCM.

1.3 Generating new active ingredients

The structure of the natural active ingredients of TCM is complex and varied. Microorganisms produce various secondary metabolites and enzymes through fermentation and metabolism. These secondary metabolites may serve as the active ingredients of drugs or their precursors. Meanwhile, the various enzyme systems can be used to synthesize new compounds by structural modification and biotransformation of the natural active ingredients of TCM through various catalytic reactions, including hydroxylation, hydrolysis of glycosidic bonds, glycosidylation, isomerization, and other catalytic reactions. Following pharmacological screening, the potential for developing new drugs suitable for clinical use is established[41]. For instance, the fermentation of glycyrrhetinic acid by the fungus *Cunninghamella blakesleeana* results in the formation of a novel compound, 3-keto-15β-hydroxy-18β-glycyrrhetinic acid[21]; the fermentation of *P. ginseng* by *Monascus purpureus* results in the synthesis of the rare ginsenoside Rg3 [23]; the fermentation of *Panax notoginseng* by *B. subtilis* has been demonstrated to result in the production of a novel active substance, ginsenoside Rh4[24]. In a previous study, Na *et al.* [22] employed the fungus *Grifola frondosa* to conduct liquid state fermentation on an extract derived from *Gastrodia elata*. Following fermentation, the gastrodin in *G. elata* was transformed into parishin, which had been demonstrated to enhance memory function. Zhang *et al.*[26] employed Kombucha, a mixture of yeast, lactobacillus, and acetic acid bacteria, as the raw material for the fermentation of rose and jujube kernels. This process enhanced the sedative-hypnotic function of rose and jujube kernels and improved their flavor. Additionally, a new substance, jujuboside B, was detected in the fermentation product. Consequently, the fermentation technology of TCM has the potential to yield novel active ingredients and represents an efficacious strategy for the development of new drugs. However, the fermentation of TCM will inevitably result in the production of numerous unidentified secondary metabolites. Therefore, the development of new drugs through the fermentation technology of TCM is a promising avenue of research, albeit one that is still in its infancy.

1.4 Conserving resources It is reported that China's annual output of TCM is as high as 70 million t. During the production and processing of TCM, more than 35 million t of waste, including TCM dregs, are directly discarded. This excessive waste of TCM resources represents a significant issue that requires appropriate attention[42]. The residual components of TCM contain a plethora of nutrients, including plant fiber, polysaccharides, proteins, lipids, flavonoids, alkaloids, terpenes, and trace elements. These can be utilized as substrates for microbial fermentation, facilitating the production of other substances. The application of fermentation technology can effectively reduce the wastage of resources inherent to TCM, thereby achieving the objective of resource conservation. The sustainable development of TCM dregs may be facilitated by anaerobic and aerobic fermentation. The potential applications of anaerobic fermentation in solving the fuel shortage include the conversion of organic matter in TCM dregs into simple inorganic matter, with the resulting inorganic matter mainly comprising energy substances such as biogas and ethanol. The residual material of *Hypericum perforatum* contains a considerable quantity of cellulose, which has the potential to be fermented for ethanol production. Ma *et al.*[27] attempted to produce ethanol by anaerobic fermentation of the medicinal dregs of *Hypericum perforatum* using Angel yeast and discovered that the addition of *Salvia miltiorrhiza* medicinal dregs enhanced ethanol production, achieving ethanol yields of up to 6.0 g/L. The residual materials from TCM can be transformed into a variety of valuable products, including fermented culture substrates, livestock feed, and feed additives, through aerobic fermentation. This process not only creates valuable products but also effectively converts waste into resources. In a study conducted by Yue *et al.*[28], the impact of diverse TCM dregs on laccase production by *Coriolus hirsutus* was examined. The findings revealed that the rhapontin present in *Rheum palmatum* dregs could stimulate laccase secretion, consequently enhancing laccase production and enzyme activity. He[29] employed the use of *Cordyceps militaris* in a two-way solid state fermentation process of *Schisandra chinensis* dregs with medicinal fungi, resulting in the production of 5.1 mg/g of cordycepin following 15 d of fermentation. The fermented dregs were then used as a feed additive for weaned piglets, and it was found that the fermented dregs of *S. chinensis* could improve the intestinal digestion and absorption ability and disease resistance of weaned piglets, thereby greatly improving the utilization value of *S. chinensis* dregs. In a study conducted by Han *et al.*[32], the *in vitro* fermentation of Korean ginseng dregs using pig fecal flora was investigated. The findings revealed that the pig fecal flora could utilize Korean ginseng dregs as a carbon source and alter the fecal flora structure. This suggests that the utilization of Korean ginseng dregs could enhance the intestinal health of pigs. Consequently, the possibility of reutilizing Korean ginseng dregs was established. In addition to the residual materials from TCM that can be repurposed in a resourceful manner, some of the byproducts generated during the harvesting and processing of TCM can also be fully utilized. For example, a considerable quantity of *Scutellaria baicalensis* stems and leaves is generated during the harvesting of *S. baicalensis* roots, with the overwhelming majority of them being discarded as waste. In order to enhance the resource utilization of *S. baicalensis* stems and leaves, Hu *et al.*[33] employed a fermentation process utilizing chicken-derived β-glucosidase-producing mixed bacteria. The resulting fermentation products were then utilized as feed additives for broilers. The findings indicated that the fermented stems and leaves of *S. baicalensis* exhibited the potential to enhance the apparent digestibility and improve the immune function of yellow feather broilers. Consequently, the recycling of TCM resources in a manner that is both environmentally friendly and economically beneficial can be achieved through the use of microbial fermentation technology.

2 Application of Fermented TCM

2.1 Application of fermented TCM in animal husbandry The practice of livestock farming has been the subject of criticism due to concerns surrounding the presence of antibiotic dregs in the meat produced. The misuse of antibiotics in animal feed has the potential to cause significant adverse effects, including the risk of antibiotic resistance, the emergence of superbugs, and environmental contamination. These concerns have been recognized as a matter of serious concern. The Ministry of Agriculture and Rural Development has formally declared that as of July 1, 2020, Chinese feed manufacturers have ceased production of commercial feed containing growth-promoting drugs or feed additives (with the exception of those derived from TCM), marking the advent of a comprehensive "ban on antibiotics" in China's livestock and poultry feed. This also signifies that the growth and production cycle of animals will be prolonged, thereby increasing the infection rate. This presents a significant challenge for livestock farmers. However, green and safe fermented TCM can be utilized as feed additives to substitute the use of antibiotics[43]. In recent years, research on the development of fermented TCM into feed and feed additives is currently experiencing a period of growth and expansion (Tab.2). As evidenced by Tab.2, fermented TCM has been demonstrated to promote the growth and development of animals, regulate the intestinal flora of animals, prevent and control pathogenic bacterial infections, and improve the immunity of animals. These effects contribute to the reduction of aquaculture costs, improvement of food quality and economic benefits, and reduction of environmental pollution. Furthermore, the majority of fermented TCM in China are popularized and utilized in the form of solid feed additives, which are predominantly employed to enhance animal growth performance[58]. In addition to solid state preparations, fermented TCM also includes liquid state preparations, which are predominantly utilized in the prevention and treatment of intestinal diseases.

2.2 Application of fermented TCM in the treatment of diseases In the treatment of diseases with pharmaceuticals, some conditions require an increase in dosage to achieve control. However, this approach may result in complications over time. TCM offers a gentler, longer-lasting alternative with minimal side effects. Additionally, it can assist in managing complications associated with various diseases, offering a unique advantage over Western medicine. The benefits of fermented TCM are further exemplified in the production of novel secondary metabolites. These metabolites can enhance the efficacy or eliminate the toxicity of TCM without affecting its efficacy, thus offering a promising avenue for the application of fermented TCM in medicinal therapy. A study conducted by Yin *et al.*[59] substantiated the efficacy of the biofermented warm moxibustion ointment in treating shoulder periarthritis. A substantial body of evidence from numerous studies indicates that secondary metabolites derived from fermented TCM, including alkaloids and phenylpropanoids, possess efficacy in reducing blood glucose levels and have been extensively utilized in the management of diabetes [60]. Furthermore, other researchers selected distinct probiotics for fermentation of Jianwei Xiaoshi tablet dregs. The resulting fermentation supernatants exhibited functional efficacy in the treatment of *Helicobacter pylori* infection [31], antibiotic-induced diarrhea [61], and spleen deficiency [62], respectively. These findings indicate that fermented TCM may offer significant promise for the prevention and treatment of various diseases. Nevertheless, the current state of fermentation of TCM remains in its nascent stages of development. There are numerous secondary metabolites that have yet to be discovered and identified, and the mechanisms underlying the therapeutic effects of many fermented TCMs remain to be elucidated. Consequently, there is a significant scope for further advancement in the field of fermentation technology as it pertains to the treatment of medicine.

2.3 Application of fermented TCM in other aspects The utilization of fermented TCM is not limited to the domains of animal husbandry and disease treatment. Its applications extend to the domains of ecological organic fertilizer, flocculant, and fermentation culture substrate in agriculture, food, the environment, and energy industries. The dregs of TCM contain essential components for soil health, including nitrogen, phosphorus, potassium, and organic matter. These dregs are a kind of lightweight, permeable, and light substrate raw material, making them a promising source for the development of ecological organic fertilizers. The use of TCM dregs as a replacement for common chemical fertilizers following fermentation has been demonstrated to enhance soil physicochemical properties, thereby increasing crop yield and quality. For example, Li *et al.*[63] employed probiotic bacteria, including *B. megaterium*, *B. mucilaginosus*, and *Azotobacter chroo-coccum*, in addition to EM bacterium, to conduct solid state fermentation of yellow ginger dregs. The resulting ecological organic fertilizers were prepared in accordance with the standard after the conditions were optimized. In a study conducted by Tan *et al.*[30], *P. notoginseng* dregs were employed as a fermentation substrate for a solid state fermentation culture of *Monascus purpureus*, resulting in the production of melanin. The bacterial biomass reached a concentration of 0.241 6 g/g of fermentation cultures, while the color value of the red pigment reached 14.63 U/g of fermentation cultures. The red pigment obtained from this process has potential applications in the food additive industry. Wang[64] obtained *Pseudomonas trivialis* and *Neurospora tetrasperma* from the screening of TCM dregs, utilizing these two strains of bacteria to ferment the TCM dregs. The resulting microbial flocculants were observed to play the role of flocculation and precipitation in kaolin suspension, and were subsequently employed in water treatment and environmental protection, thus achieving the objective of "treating waste with waste". In a study conducted by Zhang *et al.* [65], *Astragalus membranaceus* dregs were utilized as the primary raw material. Through the addition of *Pichia stipitis* and *Saccharomyces cerevisiae*, a fusion strain was obtained, resulting in the production of 20.4 g/L bioethanol after optimization of the fermentation process technology. This study demonstrated the potential of microbial fermentation of TCM dregs for the development of biofuel.

3 Summary and Prospect

TCM is a high-quality resource that is unique to China. The application of modern fermentation technology has significantly facilitated the advancement and utilization of TCM resources, thereby pro-

Tab.2 Example of microbial fermentation of TCM dregs developed into feed and feed additives

Types of TCM	Fermented strain	Fermentation type	Main effect	Reference
Fuzheng Jiedu powder extract	*Lactobacillus*	Liquid state fermentation	Improving the growth performance of broilers and promoting the development of immune organs	[44]
Andrographis paniculata, *Pulsatilla chinensis*, Herba Patriniae, *Coptis chinensis*, *Phellodendron amurense*, Radix Aucklandiae, *Glycyrrhiza uralensis*	*Bacillus subtilis*, *Lactobacillus plantarum*, *Candida utilis*	Liquid state fermentation	Performing better than antibiotics against *Escherichia coli* disease in broilers, improving broiler immunity	[45]
Astragalus membranaceus, *G. uralensis*	*Lactobacillus*	Liquid state fermentation	Improving growth performance, immune function and meat quality of broilers	[46]
A. paniculata, *P. chinensis*, *Herba Patriniae*, *C. chinensis*, *P. amurense*, Radix Aucklandiae, *G. uralensis*	*B. subtilis*, *L. plantarum*, *C. utilis*	Liquid state fermentation	Improving the efficacy and immunity against *E. coli* disease in broilers	[45]
A. membranaceus, *Angelica sinensis*	*B. subtilis*	Liquid state fermentation	Improving the growth performance, immunity, antioxidant capacity and duodenal villus morphology in white feather broilers	[47]
Areca catechu, *A. membranaceus*, *Codonopsis pilosula*, *Crataegus pinnatifida*, *Poria cocos*, *G. uralensis*, Fructus Hordei Germinatus	*B. subtilis*, *Zygosaccharomyces rouxii*	Solid state fermentation	Improving broiler growth performance and increasing diversity of foregut microbial communities	[48]
A. membranaceus, Radix Isatidis, *Epimedium brevicorn, etc.*	*Lactobacillus*, *B. subtilis*, *yeast*	Solid state fermentation	Improving the growth performance, immunity and antioxidant function in heat-stressed broilers, and increasing muscle amino acid content	[49]
Folium Isatidis, *A. membranaceus*, *Echinacea purpurea*	*B. subtilis*, *Citrobacter*	Solid state fermentation	Improving the growth performance and slaughter performance of meat ducks	[50]
Pericarpium Granati, Folium Ginkgo, *G. uralensis*	*L. plantarum*, *Saccharomyces cerevisiae*	Solid state fermentation	Improving the meat quality and immunity of pigs	[51]
Qizha Koufuye dregs	*B. subtilis*, *Clostridium butyricum*, lactobacillus, yeast	Solid state fermentation	Improving the intestinal morphology and structure of weaned pigs and immunity of weaned piglets	[52]
A. membranaceus, *Atractylodes macrocephala*, Cortex Fraxini, Atractylodes Lancea, *C. chinensis*, *Pleuropterus multiflorus*, Pericarpium Citri Reticulatae, Charred Triplet, Pine needle, *Cyrtomium fortunei*	*Lactobacillus*, *B. subtilis*, yeast	Solid state fermentation	Improving the piglet growth and antioxidant capacity, reducing diarrhea, and improving intestinal microflora	[53]
Cowherb seed, *Leonurus japonicus*	*C. utilis*, *Lactobacillus casei*, *Enterococcus faecalis*	Solid state fermentation	Improving the performance and immunity of lactating sows and the survival rate of weaned piglets	[54]
C. pilosula, *A. membranaceus*, *A. macrocephala*, *Cistanche deserticola*, *Gardenia jasminoides*, Radix Glycyrrhizae Preparata	Yeast, *Aspergillus niger*	Solid state fermentation	Improving the ability of cows to resist heat stress, reducing the number of milk somatic cells and the incidence of occult mastitis in cows, and improving the performance of cows	[55]
Pericarpium Citri Reticulatae, *C. pinnatifida*, *Ziziphus zizyphus*, *Taraxacum mongolicum*, GeO_2, rice bran	*S. cerevisiae*	Solid state fermentation	Improving the dietary nutrient digestibility, weight and slaughter rate in fattening pigs	[56]
A. membranaceus, *G. uralensis*, Radix Isatidis, *Lycium chinense*	*C. utilis*, *B. subtilis*, *Lactobacillus rhamnosus*	Liquid state fermentation	Enhancing the growth and antioxidant capacity of carp, and improving the structure of intestinal flora	[57]

pelling the growth of China's pharmaceutical industry and the production of Chinese-made goods. At present, the majority of research on fermented TCM remains at the laboratory stage, with a primary focus on the selection and breeding of fermentation strains, optimization of fermentation conditions, research on new active ingredients and feed additives, and other related areas. Nevertheless, the medium and enlarged cultivation of the fermentation process and the isolation and purification of the products have not yet reached the stage of industrialization. Significant challenges remain, including the lack of clarity regarding the mechanism of fermented TCM and the absence of safety evaluation standards for fermented TCM.

Firstly, quality control and safety evaluation standards for TCM should be established without delay, and standardized research methods for fermented TCM must be implemented to ensure the modernization and advancement of TCM. Secondly, the utilization of a range of histological techniques and bioinformatics is essential to reinforce the research on the fermentation mechanism of fermented TCM and to establish the criteria for selecting different fermentation strains for different active ingredients of TCM. Ultimately, the optimization of the TCM fermentation process, the advancement of microprocessor computers, and the development of novel probe fermenters and ancillary equipment should be prioritized to enhance the degree of automation and production efficiency, reduce energy consumption and environmental pollution, and align the characteristics of the target products with the objective of achieving low-cost and high-efficiency separation. Furthermore, ongoing research is focused on elucidating the alterations in microbial communities during mixed-bacteria fermentation, the interrelationship between fermented TCMs and the intestinal microbiota, and the pharmacodynamic evaluation and efficacy localization of fermented TCMs. In conclusion, further research is required into the pharmacology, nutriology, immunology, microbiology, bioinformatics, engineering technology and other related disciplines of fermented TCM. This research will provide scientific theoretical guidance and evaluation criteria for the screening and pairing of TCM and probiotics, as well as for the optimization and amplification of fermentation engineering.

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