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The dried root and rhizome of Alpinia officinarum Hance (A. officinarum) have been widely used in traditional Chinese medicine for thousands of years to alleviate pain, promote digestion, warm the stomach, and disperse cold. This review aims to comprehensively and in-depth summarize the most recent research on the traditional uses, phytochemistry, pharmacokinetics, and pharmacology of A. officinarum. By searching various databases including Web of Science, PubMed, Google Scholar, Elsevier, Springer, ScienceDirect, and China National Knowledge Infrastructure (CNKI) for literature on "A. officinarum Hance," as well as relevant textbooks and digital documents, an overall and critical review of the subject was conducted. The traditional uses of A. officinarum were summarized, and 337 compounds from A. officinarum were summarized, including flavonoids, diarylheptanoids, volatile oils, and other compounds. Studies have found that the crude extract of A. officinarum and its compounds has a wide range of biological activities, such as improving gastrointestinal function, anti-inflammatory properties, anti-tumor activity, antibacterial properties, memory enhancement, and analgesic effects. Modern pharmacological studies have provided strong evidence and explanations for the traditional medicinal uses of A. officinarum, which brings a broad prospect for its medicinal use. However, more research is needed to explore the

Abbreviations: AD, Alzheimer's disease; AUC, area under the curve; AchE, acetylcholinesterase; ALT, alanine aminotransferase; AST, aspartate transaminase; C_{max} peak concentration; COX-2, cyclooxygenase-2; CMA, chaperone-mediated autophagy; DIC, disseminated intravascular coagulation; iNOS, inducible nitric oxide synthase; GG-1, galangin-3-O-β-D-glucuronic acid; GG-2, galangin-7-O-β-D-glucuronic acid; IBS, irritable bowel syndrome; Ka, absorption rate constants; MDA, malondialdehyde; MIC, minimum inhibitory concentration; MOT, motilin; NO, nitric oxide; GAS, gastrin; Papp, apparent absorption coefficients; PGE2, prostaglandin E2; SOD, superoxide dismutase; SP, substance P; SS, serum somatostatin; t_{peak}, peak time; t_{1/2ke}, elimination half-life; t_{1/2ka}, absorption half-life; TC, total cholesterol; TG, triglycerides; VIP, vasoactive intestinal peptide; TLR4, toll-like receptor 4; NGF, nerve growth factor; CGRP, calcitonin gene-related peptide; GU, gastric ulcer.

structure-activity relationship and potential mechanisms of action of its bioactive chemicals. Furthermore, it is essential to conduct more clinical trials in order to accelerate research and development of the drug.

KEYWORDS

Alpinia officinarum Hance, traditional uses, phytochemistry, pharmacology, pharmacokinetic

1 Introduction

With the development of the times, people are increasingly focusing on their wellbeing. The advancement of medical technology has also begun to attract attention. While new drugs for various diseases are constantly being developed, people are actively exploring alternative therapies and natural products due to the toxic side effects of chemical drugs and the uncontrollable risks of biological agents. Alpinia officinarum Hance (A. officinarum), native to China, is one of the most important species of the Zingiberaceae family, which is widely distributed in Fujian, Taiwan, Guangdong, Guangxi, Hainan, and other provinces in China ([Sun et al., 2023](#page-23-0); [Zheng et al., 2024](#page-24-0)). The detailed description of the medical applications of A. officinarum can be traced back to the book "Ming Yi Bie Lu," which was written during the Han Dynasty ([Tao, 1986](#page-23-1)). As a medicinal part, the aromatic rhizome of A. officinarum mainly belongs to the spleen and stomach meridians and was widely used in the treatment of gastrointestinal diseases in ancient China ([Tushar et al., 2010](#page-23-2); [Al Garni et al., 2024](#page-22-0)).

Botanical drugs have been widely used to treat many diseases for centuries due to their obvious effectiveness, fewer side effects, and relatively low cost. A. officinarum is known for its extensive clinical applications because it contains a variety of bioactive substances, including flavonoids, diarylheptanoids, volatile oils, phenylpropanoids, and glycosides [\(Pillai et al., 2018](#page-23-3); [Wen et al.,](#page-24-1) [2024\)](#page-24-1). Flavonoids and diarylheptanoids are its main components and have been proven to have a variety of pharmacological effects ([Abubakar et al., 2018\)](#page-22-1). In this paper, the traditional uses, chemical components, and biological activities of A. officinarum were reviewed comprehensively, which provide better guidance for the rational utilization of it.

2 Traditional efficacy and application of
A. officinarum

A. officinarum, which is also known as "Liangjiang" and "Xiaoliangjiang," was first recorded in the "Ming Yi Bie Lu" during the Han Dynasty [\(Tao, 1986](#page-23-1)). As shown in [Table 1,](#page-2-0) the properties of A. officinarum have mainly been described as pungent and warm, while in some ancient books, there have been occasional records of "bitter". It has been recorded in ancient books that A. officinarum mainly enters the two meridians of the spleen and stomach, but rarely enters the heart, liver and Danzhong meridians. The records of A. officinarum in modern works on herbal all belong to the spleen and stomach meridians. Through the analysis of the records of the efficacy of A. officinarum in ancient and modern Chinese botanical drug, it was found that its common features in

terms of efficacy are warming the stomach, dispelling cold, relieving pain, regulating qi, stopping vomiting, and alleviating diarrhea. And, A. officinarum is commonly used to treat epigastric cold pain, vomiting, diarrhea, and food stagnation.

A. officinarum has been widely used in clinics due to its compatibility in many prescriptions, as shown in [Table 2](#page-4-0). A. officinarum is mainly used to warm the spleen and stomach, such as in Er Jiang Pill ([Liu, 2017](#page-23-4)), which can nourish the spleen and stomach, remove cold, and eliminate phlegm, and cure all injuries caused by cold. Such prescriptions also include Wenzhong Liangjiang Pill [\(Liu, 2017\)](#page-23-4) and Qing Zao San [\(Zhu, 2003](#page-24-2)). A. officinarum is a pungent and hot substance that is a pure yang product. It enters the spleen and stomach meridians, which can warm the stomach, reduce reflux and stop vomiting, and strengthen the spleen and stop diarrhea. For example, Ding Qi San ([Zhao, 2018\)](#page-24-3) is suitable for vomiting induced by typhoid. This type of prescription also includes Bi Cheng Qie San [\(Dou,](#page-22-2) [2015\)](#page-22-2). A. officinarum can also enter the heart and Dan zhong, so it can enter the heart and pericardial meridian to warm and circulate qi. The prescriptions suitable for these kinds of conditions are Liang Fu Pill ([Xie, 1990\)](#page-24-4) and Gao Liang Jiang Decoction [\(Sun, 1955\)](#page-23-5). With its fragrant and warm properties, A. officinarum can dissipate the cold, relieve pain, and promote qi. For example, Tian Tai Wu Yao San ([Li, 1959\)](#page-22-3) is applicable to the syndrome of cold coagulation and qi stagnation in the liver meridian. A. officinarum also has the effect of dispelling wind and relieving pain. The Qun Xun San, composed of A. officinarum and scorpion, has significant therapeutic effects on wind-induced toothache and swelling and pain in the cheek ([Wang, 2003\)](#page-23-6). In addition, A. officinarum has certain effects of warming the kidney and enhancing Yang. A. officinarum is compatible with Tetradium ruticarpum (A. Juss.) T. G. Hartley, which can warm the kidneys and dispel cold, and treat kidney deficiencies and waist pain. This type of prescription also includes Baji Pill [\(Liu, 2017\)](#page-23-4).

3 Chemical composition

Up to now, 337 chemical compounds have been extracted from A. officinarum, mainly including flavonoids, diarylheptanoids, phenylpropanes, glycosides, volatile oil, and other compounds.

3.1 Flavonoids

Flavonoid is one of the main components in A. officinarum. A large number of flavonoids were isolated from A. officinarum, which are also the main active components in it. Until now, 21 flavonoids

TABLE 1 Medicinal properties, meridian tropism, and efficacy of A. officinarum.

TABLE 1 (Continued) Medicinal properties, meridian tropism, and efficacy of A. officinarum.

have been isolated, including 18 flavones, 2 flavanones, and 1 flavanol, as shown in [Figure 1](#page-5-0) and [Table 3.](#page-5-1)

3.2 Diarylheptanoids

Diarylheptanoid is a group of compounds that contain a 1,7 disubstituted aromatic ring and a heptane skeleton and is an important chemical component of A. officinarum. At present, 49 diarylheptanoid compounds have been isolated from A. officinarum, including 42 chain diarylheptanoids, six cyclic diarylheptanoids, and one polymer of diarylheptanoid and flavonoid, as shown in [Figure 2](#page-6-0) and [Table 4.](#page-7-0)

3.3 Volatile oil

A. officinarum is a type of pungent and warm botanical drugs with a high content of volatile oil. Its spicy scent is one of the indicators used to judge the quality of this herbal medicine. At present, 241 volatile oils have been separated from A. officinarum, mainly including terpenoids (monoterpenes, sesquiterpenoids), aldehydes, ketones, ethers, alcohols, phenols, and other compounds, as shown in [Table 5.](#page-8-0)

3.4 Other compounds

In addition, A. officinarum contains 7 phenylpropanoids, 11 glycosides, 5 organic acids, 2 sterols and their glycosides, and 1 lactone, as shown in [Figure 3](#page-12-0) and [Table 6](#page-13-0).

4 Pharmacokinetic study of the active compounds of A. officinarum

As one of the main active compounds of A. officinarum, galangin (3,5,7-trihydroxyflavone) has a variety of biological activities. Once galangin is consumed, it is metabolized in the intestine and liver, where it undergoes glucuronidation, methylation, and sulfation reactions. The pharmacokinetics of galangin-3-O-β-D-glucuronic acid (GG-1) and galangin-7-O-β-D-glucuronic acid (GG-2), two metabolites of A. officinarum, were studied in vivo. It was found [\(Liu et al., 2021\)](#page-23-14) that, after oral administration of A. officinarum extract (0.3 g/kg) in rats, the peak concentrations (C_{max}) of GG-1 and GG-2 were 6069.6 \pm 1140.6 and 10596.0 \pm 2395.7 ng/mL, respectively, reaching their peak concentrations at 0.2 ± 0.1 h. Area under curve (0-t) (AUC_{0-t}), mean residence time (0-t) (MRT_{0-t}), and t_{1/2} of GG-1 were 2390.9 ± 678.0 h μ g/L, 1.4 \pm 0.8 h, and 2.2 \pm 0.7 h, respectively, while the corresponding values of GG-2 were 4554.9 ± 884.9 h·µg/L, 1.6 ± 0.7 h,

Book title	Prescription name	Composition	Therapeutic application	Reference
Tai Ping Hui Min He Ji Ju Fang	Er Jiang Pill	A. officinarum, Zingiber oj-jicinale Rosc	Nourish the spleen and warming the stomach, removing cold and eliminating phlegm, treating the pain of heart and spleen, and all injuries caused by cold	Liu (2017)
	Wen Zhong Liang Jiang Pill	A. officinarum, Rhizoma Zingiberis Preparata, Atractylodes macrocephala Koidz., Cinnamomum cassia (L.) D. Don, Glycyrrhizae Praeparata cum Melle Radix et Rhizoma	Cold phlegm gathering, Qi stagnation, vomiting after eating, vomiting, cold diarrhea, colic and tingling lateral thorax	
	Ba Ji Pill	A. officinarum, Kadsura longipedunculata Finet and Gagnep., Morinda officinalis F. C. How, Cinnamomum cassia (L.) D. Don, Tetradium ruticarpum (A. Juss.) T. G. Hartley	Deficiency of Yuan Qi, heavy waist and crotch, night sweat, chronic uterine coldness, irregular menses, leucorrhea, leukorrhea with bloody discharge	
Zhu Shi Ji Yan Fang	Qing Zao San	A. officinarum, Zingiber oj-jicinale Rosc, Citrus reticulata Blanco, Glycyrrhiza uralensis Fisch	Diarrhea, swelling and pain in the chest and abdomen	Zhu (2003)
Sheng Ji Zong Lu	Ding Qi San	A. officinarum, Alpinia katsumadai Hayata, Aucklandia lappa Decne., Glycyrrhiza uralensis Fisch	Vomiting during typhoid fever	Zhao (2018)
Bian Que Xin Shu	Bi Cheng Qie San	A. officinarum, Piper cubeba L.f., Cinnamomum cassia (L.) D. Don, Syringa oblata Lindl., Magnolia officinalis Rehd.et Wils., Platycodon grandiflorus (Jacq.) A.DC, Citrus reticulata Blanco, Sparganium stoloni erum, Buch. -Ham., Glycyrrhiza uralensis Fisch., Cyperus rotundus L	Deficiency of spleen and stomach, stabbing pain of chest and abdomen, dilatation of both sides of the chest, dizziness, fatigued cumbersome limbs, fever, diarrhea	Dou (2015)
Liang Fang Ji Ye	Liang Fu Pill	A. officinarum, Cyperus rotundus L	liver depression and Qi stagnation, stomach cold coagulation, epigastric pain	Xie (1990)
Bei Ji Qian Jin Yao Fang	Gao Liang Jiang Decoction	A. officinarum, Magnolia officinalis Rehd.et Wils., Angelica sinensis (Oliv.) Diels, Guixin	A sudden cramp in the chest and abdomen, the unbearable boredom of both costal branches	Sun (1955)
Yi Xue Fa Ming	Tian Tai Wu Yao San	A. officinarum, Lindera aggregata (Sims) Kosterm., Aucklandia costus Falc., Foeniculum vuLgare Mill., Citrus reticulata Blanco, Areca catechu L., MeLia toosendanSieb.et Zucc., Croton tiglium L	Cold coagulation and Qi stagnation of liver meridian	Li (1959)
Shi Zhai Bai Yi Xuan Fang	Qun Xun San	A. officinarum, Buthus martensii Karsch	Wind-toothache, swelling and pain of cheek	Wang (2003)
Sheng Ji Zong Lu	Wa Na Qi San	A. officinarum, Callorhimus ursinus Linnaeus, Tetradium ruticarpum (A. Juss.) T. G. Hartley, Nardostachys jatamansi (D. Don) DC., Citrus reticulata Blanco	Deficiency of the kidney, Qi deficiency of heart and spleen, intolerable cold pain of small intestine	Zhao (2018)

TABLE 2 Prescription name, composition and therapeutic application of A. officinarum.

and 3.3 ± 0.2 h, respectively. Obviously, the most significant difference between GG-1 and GG-2 is the AUC0-t and Cmax, where the parameter values of GG-2 are almost twice those of GG-1.

In addition, a previous study [\(Xin Zhang et al., 2021](#page-24-11)) found that microemulsion can promote the absorption of galangin and improve its bioavailability. The blood concentration of galangin in Liangfu Pill could not be detected after the rabbits were given Liangfu Pill by gavage once. For Liangfu micromilk, the absorption half-life $(t_{1/2ka})$ of galangin was 0.29 h, the peak time (t_{peak}) was 0.75 h, the elimination half-life (t_{1/2ke}) was 1.47 h, C_{max} was 38.46 μg/L, and the AUC was 129.42 (μg·h)/L. In another study [\(Xianhua Du et al.,](#page-24-12) [2008\)](#page-24-12), it was found that a self-microemulsion of galangin was absorbed throughout the entire intestinal tract of rats. The absorption rate constants (K_a) in the duodenum, jejunum, ileum, and colon were 2.37, 1.70, 2.29, and 3.98 times higher than those of the galangin suspension, respectively. Additionally, the apparent absorption coefficients (Papp) were 3.58, 2.56, 3.57, and 5.16 times higher than those of the galangin suspension, respectively. The relative bioavailability of the self-microemulsion of galangin was 220%, compared to the galangin suspension.

5 Pharmacological effects of A. officinarum

A. officinarum is an important traditional Chinese medicine, and its main chemical components are flavonoids, volatile oils, and diarylheptanoids. Modern pharmacological studies have shown that A. officinarum has various pharmacological effects, including anti-ulcer, inhibition of gastrointestinal motility, anti-inflammatory and analgesic, antioxidant, anti-tumor, antibacterial, and hypoglycemic properties, as shown in [Table 7.](#page-14-0)

5.1 Effects on gastrointestinal function

A. officinarum is an essential medicine for treating deficiencycold of the spleen and stomach, as well as epigastric cold pain in traditional Chinese medicine. It is mainly used in the treatment of digestive tract diseases such as dyspepsia, acid reflux, and gastric ulcers. [Wei \(2019\)](#page-24-13) used anhydrous ethanol and aspirin to induce two types of gastric ulcers models to study the effects of

different extracts of A. officinarum on mice with gastric ulcers. The results showed that the aqueous extract of A. officinarum had a good anti-ulcer effect and decreased the ulcer index. It was inferred that the mechanism of the anti-ulcer effect of A. officinarum may be through inhibiting inflammatory factors, reducing gastrin (GAS), increasing cyclooxygenase-2 (COX-2), and prostaglandin E2 (PGE2), thereby enhancing the protective effect of the gastric mucosa and reducing gastric injury. [Wang](#page-23-18) [et al. \(2011\)](#page-23-18) studied the therapeutic effect of the volatile oil of A. officinarum on gastric ulcers. The results showed that the volatile oil of A. officinarum could reduce the gastric ulcer index and increase the ulcer inhibition rate in mice. A. officinarum reduces the levels of serum motilin (MOT) and substance P (SP), while increasing the levels of serum somatostatin (SS) and vasoactive intestinal peptide (VIP) in order to exert its anti-ulcer effect. In addition, the study found that the volatile oil of A. officinarum can increase the levels of serum nitric oxide (NO), expand the blood vessel walls, improve the microcirculation of the gastric mucosa, strengthen the mucosal barrier, scavenge oxygen free radicals, and protect the normal function of the gastric mucosa.

A. officinarum has an obvious gastrointestinal spasmolytic effect, and its decoction can inhibit gastrointestinal propulsive movement. [Gui et al. \(2021\)](#page-22-15) observed the effect of the total flavonoids of A. officinarum on the propulsive movement of the small intestine in normal rats using the charcoal powder method. The results showed that the total flavonoids of A. officinarum not only significantly inhibited the intestinal motility of normal rats, but also antagonized the hyperfunction of the small intestine induced by neostigmine. The mechanism may be that it affects the secretion and release of gastrointestinal hormones, such as somatostatin and vasoactive intestinal peptide, thus relaxing the smooth muscle. Cheng Yuan et al. [\(Cheng et al., 2015](#page-22-16)) studied the effects of

various active components of A. officinarum on intestinal spasms induced by acetylcholine and on normal intestinal muscles in isolated rabbits. The results showed that the active components of A. officinarum extract could inhibit the spontaneous movement of intestinal muscles in a dose-dependent manner. Among these components, flavonoids and diphenylheptanes were the most prominent, and they were stronger than anisodamine. The mechanism of A. officinarum in improving gastrointestinal function is shown in [Figure 4](#page-20-0).

5.2 Analgesic and anti-inflammatory effect

A. officinarum is hot and pungent, which has the effect of dispelling cold and relieving pain. As the use of non-steroidal anti-inflammatory drugs for long-term treatment of inflammation can cause obvious side effects, plants are constantly being developed as potential anti-inflammatory agents. [Chen et al. \(2009\)](#page-22-22) used the carrageenan rat foot swelling model, the xylene mouse ear swelling model, and a capillary permeability experiment to study the antiinflammatory effect of the total flavonoids extracted from A. officinarum. The mouse hot plate method and torsion test were used to observe the analgesic effect of the total flavonoids extracted from A. officinarum. The results showed that the total flavonoids

extracted from A. officinarum had a significant inhibitory effect on acute inflammation models, such as toe swelling induced by carrageenan, auricle swelling induced by xylene, and an increase in celiac capillary permeability induced by acetic acid in mice. The total flavonoids of A. officinarum can inhibit pain induced by acetic acid and heat stimulation in mice. [Liang et al. \(2013\)](#page-22-23) studied the therapeutic and analgesic effects of total flavonoids from A. officinarum (GLJ) on acetic acid-induced visceral hypersensitivity in rats with irritable bowel syndrome (IBS). The results showed that GLJ had a certain inhibitory effect on pain induced by heat stimulation, acetic acid, and formaldehyde in mice. Zha Wangjian et al. ([Cha, 2015](#page-22-24)) found that galangin can inhibit airway inflammation and airway hyperresponsiveness to some extent in a mouse model of asthma. In addition, A. officinarum and its main compounds have anti-inflammatory effects on LPSinduced inflammation in RAW264.7 cells. This may be related to the inhibition of NF-κB activation. The anti-inflammatory mechanism of the total flavonoids of A. officinarum is shown in [Figure 5A.](#page-21-0)

5.3 Antioxidant effect

An antioxidant is a type of active substance that can eliminate the inhibition of lipid peroxidation by free radicals. It can prevent

TABLE 4 The structure of diarylheptanoids in A. officinarum.

TABLE 5 Volatile oil from A. officinarum.

TABLE 5 (Continued) Volatile oil from A. officinarum.

NO. Compound name Reference NO. Compound name Reference 124 α-guaiene [Gao et al. \(2012\)](#page-22-28) 245 eicosan [Zou et al. \(2018\)](#page-24-18) 125 γ-gurenene $\sqrt{3}$ Cao et al. (2012) 246 hecosane [Zou et al. \(2018\)](#page-24-18) 126 beta-juniperene [Gao et al. \(2012\)](#page-22-28) 247 docosane [Zou et al. \(2018\)](#page-24-18) 127 aristolochene [Gao et al. \(2012\)](#page-22-28) 248 pentacosane [Zou et al. \(2018\)](#page-24-18) 128 (+)-hornene [Gao et al. \(2012\)](#page-22-28) 249 trisane [Zou et al. \(2018\)](#page-24-18) 129 epizonarene [Gao et al. \(2012\)](#page-22-28) 250 tetracosane [Zou et al. \(2018\)](#page-24-18) 130 β-cedrene β Cao et al. (2012) 251 hexadecane [Zou et al. \(2018\)](#page-24-18) 131 delta-juniperene [Gao et al. \(2012\),](#page-22-28) [Yuan](#page-24-20) [et al. \(2016\)](#page-24-20) 252 1-docosene [Zou et al. \(2018\)](#page-24-18) 132 calamene [Gao et al. \(2012\)](#page-22-28) 253 cholesta-3,5-diene [Zou et al. \(2018\)](#page-24-18) 133 alpha-elemene [Gao et al. \(2012\)](#page-22-28) 254 2,3-dihydrobenzofuran [Tang et al. \(2021\)](#page-23-28) 134 (−)-isoprene [Gao et al. \(2012\)](#page-22-28) 255 2,4-cyclohexadien-1-one,3,5-bis(1,1 dimethylethyl)-4-hydroxy-[Zou et al. \(2018\)](#page-24-18) 135 neosyringatricyclone [Gao et al. \(2012\)](#page-22-28) 256 2,4-dimethylbenzo[h]quinoline [Zou et al. \(2018\)](#page-24-18) 136 ylangene 2018 2001 vuan et al. (2016) 257 toluene 2018 2018 2018 2018 2018 137 α-copaene [Zhai et al. \(2014a\)](#page-24-19), [Yuan](#page-24-20) [et al. \(2016\)](#page-24-20) 258 2,4-dimethylstyrene [Dong and Cai \(2015\)](#page-22-29) 138 β-elemene [Yuan et al. \(2016\)](#page-24-20) 259 (1R,2S,3S)-1,2-dimethyl-3 isopropenylcyclopentanol [Zou et al. \(2018\)](#page-24-18) 139 santalene [Yuan et al. \(2016\)](#page-24-20) 260 t-cadinol [Zou et al. \(2018\)](#page-24-18) 140 trans-bergamotene [Yuan et al. \(2016\)](#page-24-20) 261 β-santalol [Gao et al. \(2012\)](#page-22-28) 141 fragranene [Yuan et al. \(2016\)](#page-24-20) 262 pentanoic acid,2-ethylhexyl ester [Zou et al. \(2018\)](#page-24-18) 142 geranene D [Yuan et al. \(2016\)](#page-24-20) 263 decane, 3,3,6-trimethyl- [Zou et al. \(2018\)](#page-24-18) 143 cyclic isofolene [Yuan et al. \(2016\)](#page-24-20) 264 2-dodecen-1-yl succinic anhydride [Zou et al. \(2018\)](#page-24-18) 144 beta-selinene [Yuan et al. \(2016\)](#page-24-20) 265 2-octylcyclopropaneoctanal [Zou et al. \(2018\)](#page-24-18) 145 β-bisabolene [Yuan et al. \(2016\)](#page-24-20) 266 3-methyloctadecane [Zou et al. \(2018\)](#page-24-18) 146 β-panasinsene [Yuan et al. \(2016\)](#page-24-20) 267 1H-pyrrole, 1-butyl- [Zou et al. \(2018\)](#page-24-18) 147 γ-cadinene [Yuan et al. \(2016\)](#page-24-20) 268 bergamotenol [Zou et al. \(2018\)](#page-24-18) 148 selina-3,7 (11)-diene [Yuan et al. \(2016\)](#page-24-20) 269 methyl eugenol [Zou et al. \(2018\)](#page-24-18) 149 germacrene B [Yuan et al. \(2016\)](#page-24-20) 270 2-hydroxy-1,8-cineole [Yuan et al. \(2016\)](#page-24-20) 150 allomanerene [Zhai et al. \(2014a\)](#page-24-19) 271 (E)-linalool oxide (furanoid) [Zhai et al. \(2014a\)](#page-24-19) 151 α-amorphene [Zhai et al. \(2014a\)](#page-24-19) 272 (cis)-2-methyl-2-vinyl-5-isopropyltetrahydrofuran [Zhai et al. \(2014a\)](#page-24-19) 152 caryophyllene oxide [Dong and Cai \(2015\),](#page-22-29) [Yuan et al. \(2016\)](#page-24-20) 273 juniper camphor [Zou et al. \(2018\)](#page-24-18) 153 2-methyl-1-propanol butyrate [Dong and Cai \(2015\)](#page-22-29) 274 α-bergamotol [Yuan et al. \(2016\)](#page-24-20) 154 bornyl L-acetate [Zhai et al. \(2014a\),](#page-24-19) [Dong](#page-22-29) [and Cai \(2015\)](#page-22-29) 275 5-hydroxy-1,7-diphenyl-3-heptanone [Yuan et al. \(2016\)](#page-24-20) 155 acetate-(4-phenyl)-2-butyl ester [Dong and Cai \(2015\)](#page-22-29) 276 (E,E)-2,6-dimethyl-2,6-octadienedial [Zhai et al. \(2014a\)](#page-24-19) 156 methyl cinnamate [Dong and Cai \(2015\)](#page-22-29) 277 3-methylene-6-hepten-2-one [Zhai et al. \(2014a\)](#page-24-19) 157 methyl isovalerate [Dong and Cai \(2015\)](#page-22-29) 278 1-cmethylene-6-hepten-2-one [Zhai et al. \(2014a\)](#page-24-19) 158 isobutyl isobutyrate [Zhai et al. \(2014a\),](#page-24-19) [Zou](#page-24-18) [et al. \(2018\)](#page-24-18) 279 1-nonyne [Zhai et al. \(2014a\)](#page-24-19)

TABLE 5 (Continued) Volatile oil from A. officinarum.

TABLE 5 (Continued) Volatile oil from A. officinarum.

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the damage caused by lipid peroxidation to organisms. In a comparative study on the antioxidant activity of various components of A. officinarum extract, [Lin et al. \(2017\)](#page-23-29) discovered that the diphenylheptanes exhibited antioxidant activity both in vitro and in vivo. [Xia et al. \(2009\)](#page-24-21) found that the total flavonoids of A. officinarum can act as antioxidants by

inhibiting reactive oxygen free radicals and decreasing the catalytic activity of metal ions in vitro. In the HepG2 oxidative damage model induced by H_2O_2 , diphenylheptane in A. officinarum showed significant antioxidant activity. The extract of A. officinarum could potentially prevent oxidative stress damage by activating the Keap1/Nrf2/ARE signaling pathway. The antioxidant mechanism of the extract of A. officinarum is shown in [Figure 5B.](#page-21-0)

5.4 Antibacterial effect

The *in vitro* antibacterial experiment conducted by [Zhao et al.](#page-24-15) [\(2007\)](#page-24-15) showed that the chloroform and ethyl acetate extracts of A. officinarum exhibited anti-Candida albicans activity. The chloroform extract of A. officinarum, at a concentration of 20 mg/mL, demonstrated strong activity. [Qin et al. \(2015\)](#page-23-30) showed that both the alcohol extract and water extract of A. officinarum had a good inhibitory effect on methicillin-resistant Staphylococcus aureus, but had no significant inhibitory effect on Pseudomonas aeruginosa, Candida albicans, Acinetobacter, or Escherichia coli. Flavonoids are the most important antibacterial components of A. officinarum. [Ouyang et al. \(2018\)](#page-23-31) studied the impact of galangin on the antibacterial activity against vancomycinintermediate S. aureus. The study results showed that galangin had

significant inhibitory activity against ATCC25293, N315, and Mu50, with a minimum inhibitory concentration (MIC) of 32 mg/L. The results of further studies showed that galangin inhibited the growth of bacteria by inhibiting the activity of cell wall hydrolase. At the same time, the effect of quercetin on P. aeruginosa PAO1 was also studied ([Ouyang et al., 2016](#page-23-32)). The results showed that 16 mg/L of quercetin could significantly inhibit the biofilm formation, the quorum sensing system, and independent factors of P. aeruginosa. This suggests that quercetin may have the potential to treat biofilm-associated infections.

5.5 Improve memory ability

Alzheimer's disease (AD) is a chronic degenerative disease of the central nervous system in middle-aged and elderly individuals. Its main clinical manifestation is cognitive dysfunction. Huang Liping ([Huang et al., 2022](#page-22-30)) has shown that galangin can improve learning and memory impairment in APP/PS1 mice. It may inhibit the activity of acetylcholinesterase (AChE) in the brain through the cholinergic pathway, increasing the level of ACh and improving learning and memory function. On the other hand, it may play a role in protecting hippocampal neurons by regulating the Akt/MEF2D/ Beclin-1 signaling pathway and clearing abnormal proteins in

TABLE 7 Study on pharmacological effects of A. officinarum.

Pharmacological effects Extracts, compounds Model Dosage/ concentration Effects/mechanisms Reference Total flavonoids of A. officinarum In vivo: BALB/c mice; ethanol-induced gastric ulcers model *in vivo* and in vitro; gastric mucosal epithelial cells in vitro High, middle, and low dose: 126.8 mg/kg, 63.4 mg/kg, 31.7 mg/kg The total flavonoids of A. officinarum effectively decreased the ulcer index, decreased the release of inflammatory mediators (IL-1β, IL-6, TNF- α and PGE2), increased the content of nitric oxide, and improved the secretion of GAS and MTL [Lin et al. \(2020\)](#page-23-39) Inhibition of gastrointestinal motility A. officinarum decoction and its different parts Kunming mouse; New Zealand rabbit High and low dose: 8 g/kg and 4 g/kg for 7 days The main antispasmodic and analgesic components of A. officinarum are flavonoids and diarylheptanoids, in which the gastrointestinal spasmolysis is stronger than that of flavonoids. and the analgesic effect of diarylheptanoids is stronger [Gui et al. \(2021\)](#page-22-15) Different active parts of A. officinarum Ten New Zealand rabbits, both male and female 0.05 g/L The active components of A. officinarum extract could inhibit the spontaneous movement of intestinal muscle in a dosedependent manner and each active component could inhibit intestinal spasm induced by acetylcholine [Cheng et al.](#page-22-16) (2015) A. officinarum New Zealand rabbit; NIH mouse; SD rat $0.2 \text{ mL}/10 \text{ g}$ The supercritical extract of A. officinarum can inhibit the excitation of intestinal smooth muscle induced by neostigmine and antagonize muscarinic receptors [Wu et al.](#page-24-23) [\(2004b\)](#page-24-23) Analgesic and antiinflammatory Total flavonoids of A. officinarum NIH mouse; SD rat Low, medium, and high doses: 16.6, 33.2, and 66.4 g/kg The total flavonoids of A. officinarum had an obvious inhibitory effect on the acute inflammation model and pain in mice induced by acetic acid and heat stimulation [Chen et al.](#page-22-22) [\(2009\)](#page-22-22) Total flavonoids of A. officinarum SD rats, NIH mice; acetic acid-induced IBS model rats High, middle, and low dose: 2, 1, 0.5 g/kg, for two consecutive weeks, once a day The total flavonoids of A. officinarum can effectively reduce the visceral sensitivity of IBS rats induced by acetic acid and inhibit the pain induced by heat stimulation, acetic acid, and formaldehyde in mice [Liang et al.](#page-22-23) (2013) Galangin KM mouse; NRK-52E cell; mouse UAN model Low, medium and high doses: 100, 200, 400 mg/kg, once a day for 15 days Galangin can significantly inhibit the activation of NLRP3 inflammasomes and the release of inflammatory factors IL-1β and IL-18 in NRK-52E cells [Lu et al. \(2020\)](#page-23-40) Galangin Female BALB/c mice; asthma model 15.5 mg/kg, once a day for 4 days Galangin can exert its antiinflammatory effect by inhibiting the activity of NF-κB and down-regulating the expression of MCP-1, Eotaxin, CXCL10, and VCAM-1 mRNA in human airway smooth muscle cells induced by TNF-α [Cha \(2015\)](#page-22-24) Galangin Female BALB/c mice; establishment of mouse asthma model sensitized and challenged by ovalbumin 10 mg/kg Galangin can reduce the expression of TNF-α and decrease airway inflammation in asthmatic mice [Gu and Wu](#page-22-33) [\(2017\)](#page-22-33)

TABLE 7 (Continued) Study on pharmacological effects of A. officinarum.

TABLE 7 (Continued) Study on pharmacological effects of A. officinarum.

Pharmacological effects Extracts/ compounds Model Dosage/ concentration Effects/mechanisms Reference Galangin C57 male mice 25 mg/kg lasted until 4 weeks after operation Galangin attenuates cardiac fibrosis induced by AB by reducing cardiac oxidative stress and inhibiting the transformation of cardiac fibroblasts into myofibroblasts [Yang et al.](#page-24-26) (2020) Galangin Male KM mice; NRK-52E cells Low, medium, and high doses: 100,200,400 mg/kg Galangin can significantly inhibit the activation of NLRP3 inflammasomes and the release of IL-1β and IL-18 in NRK-52E cells [Lu et al. \(2020\)](#page-23-40) Galangin Female Spraguee-Dawley rats; bilateral ovariectomy model 300 mg/(kg·d), last for 12 weeks The ethanol extract of AOH can significantly reverse bone loss, in part by increasing bone formation and inhibiting bone resorption associated with its antioxidant effect [Su et al. \(2016\)](#page-23-44) A. officinarum oil Staphylococcus aureus, Escherichia coli, Bacillus subtilis, Saccharomyces cerevisiae 0.02 g/mL The peroxide value (POV) and acid value (AV) of peanut oil of A. officinarum volatile oil were lower [Huang et al.](#page-22-36) [\(2015\)](#page-22-36) Different components of A. officinarum extract HepG2 hepatoma cell line; HepG2 oxidative damage model induced by H_2O_2 in human hepatoma cell line High, medium, and low doses: 300, 200 and 100 mg, administered continuously for 30 days The diphenylheptane fraction of A. officinarum extract showed antioxidant-related activity in vitro and in vivo, followed by flavonoids [Lin et al. \(2017\)](#page-23-29) Anti-liver injury A. officinarum Kunming mice, half male and half female; alcoholinduced acute alcoholic liver injury model in mice Low, medium, and high dose: 1, 2, and 4 g/kg A. officinarum may have a protective effect on alcoholic liver injury in mice by scavenging free radicals and providing antioxidant effect. However, its active components and specific mechanism need to be further studied [Zhou et al.](#page-24-27) [\(2012\)](#page-24-27) Galangin C57BL/6 mice; concanavalin A (ConA) induced hepatitis model 25 mg/kg or 50 mg/kg Galangin inhibits NF-κB and STAT1 signal transduction, resulting in a decrease in the expression and secretion of many inflammatory mediators [Luo et al. \(2015\)](#page-23-45) Hypoglycemic A. officinarum ICR male mice 200 mg/kg An 80% ethanol elution site can significantly reduce the blood glucose level of acute hyperglycemic mice [C et al. \(2017\)](#page-22-37) A. officinarum and its extract Male New Zealand White Rabbit 4 g/kg After oral administration of 3 and 4 g/kg A officinarum root powder for 4–8 h, the blood glucose level of normal rabbits decreased significantly [Akhtar et al.](#page-22-38) (2002) A. officinarum extract Male Wistar rats; type 2 diabetic rats induced by nicotinamide/ streptozotocin as model 100, 200, and 500 mg/kg for 28 days The rhizome extract of A. officinarum exhibits antidiabetic effects in rats with type 2 diabetes [Heidari et al.](#page-22-39) [\(2022\)](#page-22-39) Hypolipidemic Total flavonoids of A. officinarum (TFAO) Male SD rats $\overline{}$ Low, medium, and high doses: 100, 200, 200, and 300 mg TFAO has significant effects on regulating blood lipids, antioxidation and protecting liver, and can regulate the expression of obesity-related factors, which may be the mechanism of its slimming and lipid-lowering effect [Fang et al. \(2015\)](#page-22-40)

TABLE 7 (Continued) Study on pharmacological effects of A. officinarum.

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hippocampal neurons through autophagy and chaperone-mediated autophagy (CMA). This can reduce the deposition of amyloid-β (Aβ) and the formation of tau protein. It can be concluded that galangin may improve the learning and memory impairment of APP/PS1 mice by regulating the Akt/MEF2D/Beclin-1 signaling pathway. In the PC12 cell injury model stimulated by H2O2, A. officinarum extract can significantly reduce the lactate dehydrogenase leakage rate, decrease the content of MDA, and increase the activities of SOD and GSH-Px ([Zhai et al., 2014b](#page-24-29)).

5.6 Anti-tumor effect

The anti-tumor mechanism of A. officinarum can be reflected in regulating the cell cycle, inducing tumor cell apoptosis and autophagy, inhibiting tumor cell migration and invasion, and reversing drug resistance in tumors. [Luo and Liu \(2020\)](#page-23-48) found that galangin has a broad-spectrum anti-tumor effect. Its inhibitory effect on different tumor cells varies and depends on time and concentration. Galangin can strongly inhibit the genotoxicity of chemical toxic substances in vivo and in vitro, making it a potential preventive drug for cancer.

[Zhang et al. \(2012\)](#page-24-31) found that A. officinarum can induce apoptosis by activating mitochondrial apoptosis, caspases, and causing changes in the levels of Bcl-2 in various liver cancer cell lines. Additionally, kaempferol derived from A. officinarum has the ability to induce apoptosis in HCCLM3 and Huh7 cells by controlling the ATM/ CHEK2/KNL1 signaling pathway.

5.7 Other functions

In addition to the above pharmacological effects, A. officinarum has anti-liver injury, hypoglycemic, hypolipidemic, and anticoagulant effects. [Zhou et al. \(2012\)](#page-24-27) showed that A. officinarum can protect the function of hepatocytes in mice after an acute alcoholic liver injury. The results showed that A. officinarum could significantly reduce the concentrations of alanine aminotransferase (ALT) and aspartate transaminase (AST) in the serum of mice after injury, indicating that A. officinarum has a certain hepatoprotective effect. Its pharmacological mechanism may be to protect liver cells by scavenging free radicals and reducing the degree of damage caused by alcohol. [Akhtar et al. \(2002\)](#page-22-38) showed that the extract of A. officinarum has a significant hypoglycemic effect. In the hypoglycemic experiment on normal male New Zealand rabbits, oral A. officinarum powder at a dose of 3 g/kg significantly reduced blood glucose levels. The methanol and

water extracts showed even more pronounced hypoglycemic effects. When the oral dose was increased to 4 g/kg, there was a significant decrease in blood glucose levels of rabbits after 8 h. However, A. officinarum powder and its extract had no effect on rabbits with diabetes induced by alloxan. Therefore, its hypoglycemic effect may be achieved by promoting insulin secretion from the pancreas in the body. Obese patients are often accompanied by abnormal fat metabolism, which can lead to high blood total cholesterol (TC) and/or triglyceride (TG) levels. [Fang et al. \(2015\)](#page-22-40) showed that middle and high doses of total flavonoids from A. officinarum play a significant role in controlling body mass, fat accumulation, and cholesterol metabolism, as well as reducing the levels of serum leptin and plasma neuropeptide Y in nutritionally obese rats with hyperlipidemia. A study ([Luo et al., 2015](#page-23-45)) has shown that galangin has an obvious inhibitory effect on thrombosis in rats, demonstrating a certain anticoagulant effect. The potential mechanism may be to improve the blood flow state of rats by participating in the endogenous coagulation system.

6 Conclusion and prospection

A. officinarum is an important traditional Chinese medicine for both medicine and food. Using modern research methods, the pharmacological effects of its active compounds have been clearly

described, and the mechanisms of anti-gastric ulcer, inhibition of gastrointestinal motility, antioxidant effect, antibacterial, antiinflammatory, and analgesia have been gradually clarified. The treatment of traditional digestive tract diseases has been expanded to a certain extent, broadening its scope of clinical application. So far, 337 compounds have been isolated from A. officinarum. Among them, galangin is a very important active compound extracted from A. officinarum. The pharmacological effects of galangin are very extensive. However, most pharmacological effects are currently only verified in cell and animal models, and there is a lack of clinical study data to support them. In addition, the mechanism of pharmacological action of galangin is not fully understood. Most studies are limited to the pharmacodynamic level or a few specific targets or pathways, and are unable to elucidate the general mechanism of action or the connection between the various targets and pathways. In the future, based on existing research, network pharmacology, bioinformatics, and multi-omics analysis can be used to comprehensively and deeply analyze the molecular mechanisms, genes, and signaling pathways of galangin. Further studies are needed to explore the extracts of A. officinarum for any potential toxicities, side effects, and contraindications. With the continuous discovery of the structure of the active components of A. officinarum and the in-depth study of its pharmacological activity, its pharmacodynamic mechanism is gradually becoming clear. The research scope of the pharmacological activity of A. officinarum has been continuously expanded by the vast number of scientific research works, and its medicinal value will be further developed and applied.

Author contributions

XL: Conceptualization, Funding acquisition, Writing–original draft, Writing–review and editing. JW: Software, Writing–original draft. KZ: Writing–original draft. TX: Writing–original draft. JZ: Writing–review and editing. XX: Writing–original draft. QL: Writing–original draft. XL: Conceptualization, Funding acquisition, Writing–review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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