



Review

## Chemical composition and biological activities of *Angelica sinensis*

Jiankun Jin, Zixuan Che, Rui Liu, Ruiqi Ma, Ying Li, Meng Zhang\*, Yu Chen\*

School of Life Science and Biopharmaceutics, Shenyang Pharmaceutical University, Shenyang 110016, China

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### Abstract

*Angelica sinensis* (*A. sinensis*), as a kind of Chinese medicine, has the effects of tonifying blood, promoting blood circulation, regulating menstrual flow, relieving pain, moistening bowel and so on. By consulting Sciencedirect database and Web of Science database, 163 related articles were found, of which 36 were related to chemical composition and pharmacological activities of *A. sinensis*. In this paper, the chemical structures and different derivatives were systematically summarized by reviewing relevant literatures, and the pharmacological effects were also summarized.

**Keywords:** *Angelica sinensis*; chemical composition; biological activity

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### 1 Introduction

*Angelica sinensis* (*A. sinensis*), also known as Danggui, is the dried root of *A. sinensis* (Oliv) Diels in the *Apiaceae* family, mainly produced in the eastern part of Gansu Province, China. It is a well-known Chinese traditional medicine and has been referred to as “blood tonic medicine” in ancient Chinese medicine due to its sweet taste, slight bitterness, and mild nature that benefits the liver, heart, and spleen meridians [1,2]. *A. sinensis*

is a perennial herb that grows to about 0.4-1 m tall and usually blooms from June to July and bears fruit from July to September. The root is cylindrical, with thick upper end and thin lower end; it is flexible, and its cross section is slightly yellowish-white or yellowish-brown [3]. Recent studies have shown that *A. sinensis* exhibits various biological activities such as antioxidant activity, anti-tumor activity, immunomodulatory effect, antidiabetic property, radioprotective effect, and anti-proliferative activity. Therefore, *A. sinensis* has great development potential. The diverse biological activities of *A. sinensis* can be attributed to the rich active ingredients, including polysaccharides, volatile oils, and organic acids [4,5]. In this paper, the chemical constituents and pharmacological effects of *A. sinensis* were reviewed in order to provide reference for further research and development of *A. sinensis*.

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\* A Author to whom correspondence should be addressed. Address: School of Life Science and Biopharmaceutics, Shenyang Pharmaceutical University, Shenyang 110016, China; Tel.: +86-18341400530 (Yu Chen), +86-18341400685 (Meng Zhang); E-mail: gzweishengwu@126.com (Yu Chen), zhangmeng123321@126.com (Meng Zhang).

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## 2 Chemical composition

Many active substances have been isolated from

*A. sinensis*, including polysaccharides, coumarins, volatile oils, organic acids, flavonoids (flavone **(1)** and flavonols **(2)**) in Fig. 1), and amino acids.



Fig. 1 The structures of flavonoids in *A. sinensis*

### 2.1 Polysaccharides

*A. sinensis* polysaccharides belong to plant polysaccharides, which are composed of at least 10 identical or different monosaccharides connected by  $\alpha$ - or  $\beta$ -glucoside bond, and widely exists in natural plants. According to their structural characteristics, *A. sinensis* polysaccharides can be divided into two types. One is homopolysaccharide, consisting of

only one type of monosaccharide unit. The other is heteropolysaccharide, consisting of two or more monosaccharides, and the main monosaccharide components of these polysaccharides include aldehydo-*D*-glucose (**(3)**), *D*-galactose (**(4)**), *L*-arabinopyranose (**(5)**), aldehydo-*L*-rhamnose (**(6)**), *L*-fucopyranose (**(7)**), *D*-Xylose (**(8)**) [6-10]. The main monosaccharide structures that constitute *A. sinensis* polysaccharides are shown in Fig. 2.

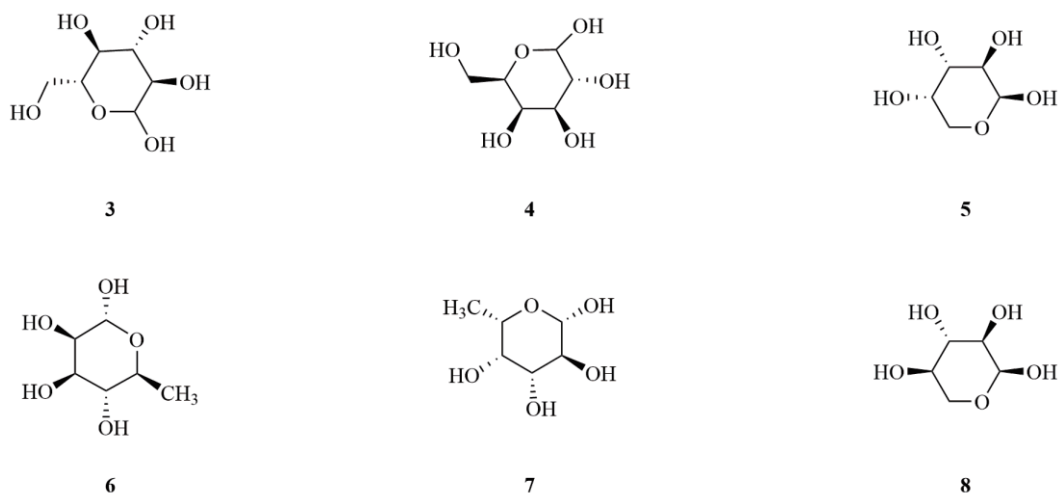


Fig. 2 The structures of the monosaccharide structures that constitute polysaccharides in *A. sinensis*

### 2.2 Coumarins and their derivatives

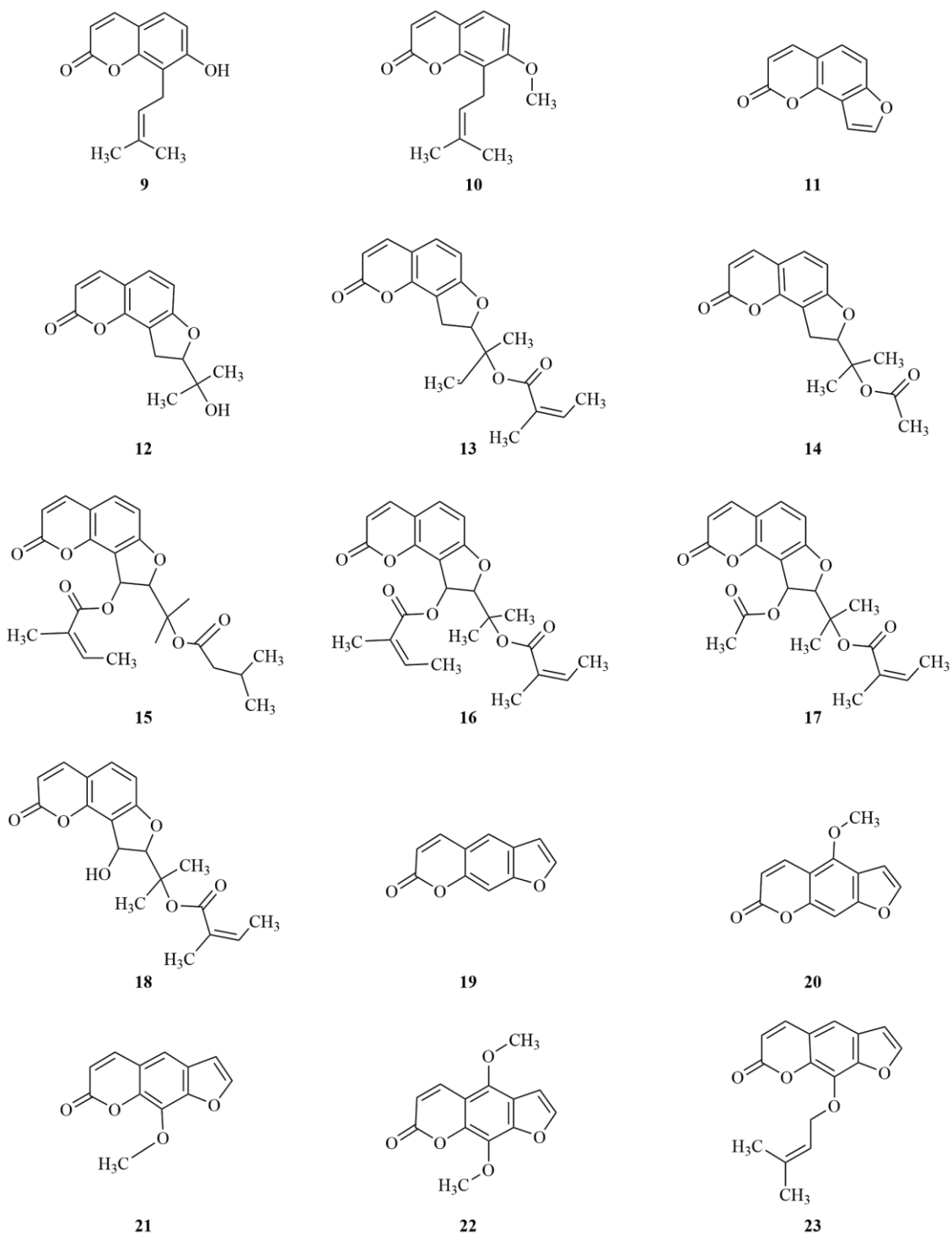
There are many kinds of coumarins isolated from *A. sinensis*, including osthenol (**(9)**), osthol (**(10)**), angelicin (**(11)**), columbianetin (**(12)**), columbianadin

(**(13)**), columbianetin acetate (**(14)**), 2'-angeloyl-3'-isovaleryl viginate (**(15)**), archangelicin (**(16)**), isoedultin (**(17)**), viginidiol-*O*-angelate (**(18)**), psoralen (**(19)**), bergapten (**(20)**), xanthotoxin (**(21)**), isopimpinellin (**(22)**), imperatorin (**(23)**), isoimperatorin



(24), phellopterin (25), cnidilin (26), byakangelicin (27), oxypeucedanin hydrate (28), byakangelicin-2'-*O*-angelate (29), byakangelicin-2'-*O*-isovalerate (30),

heraclenol-2'-*O*-angelate (31) [11-16]. The structures of coumarin and their derivatives are shown in Fig. 3.



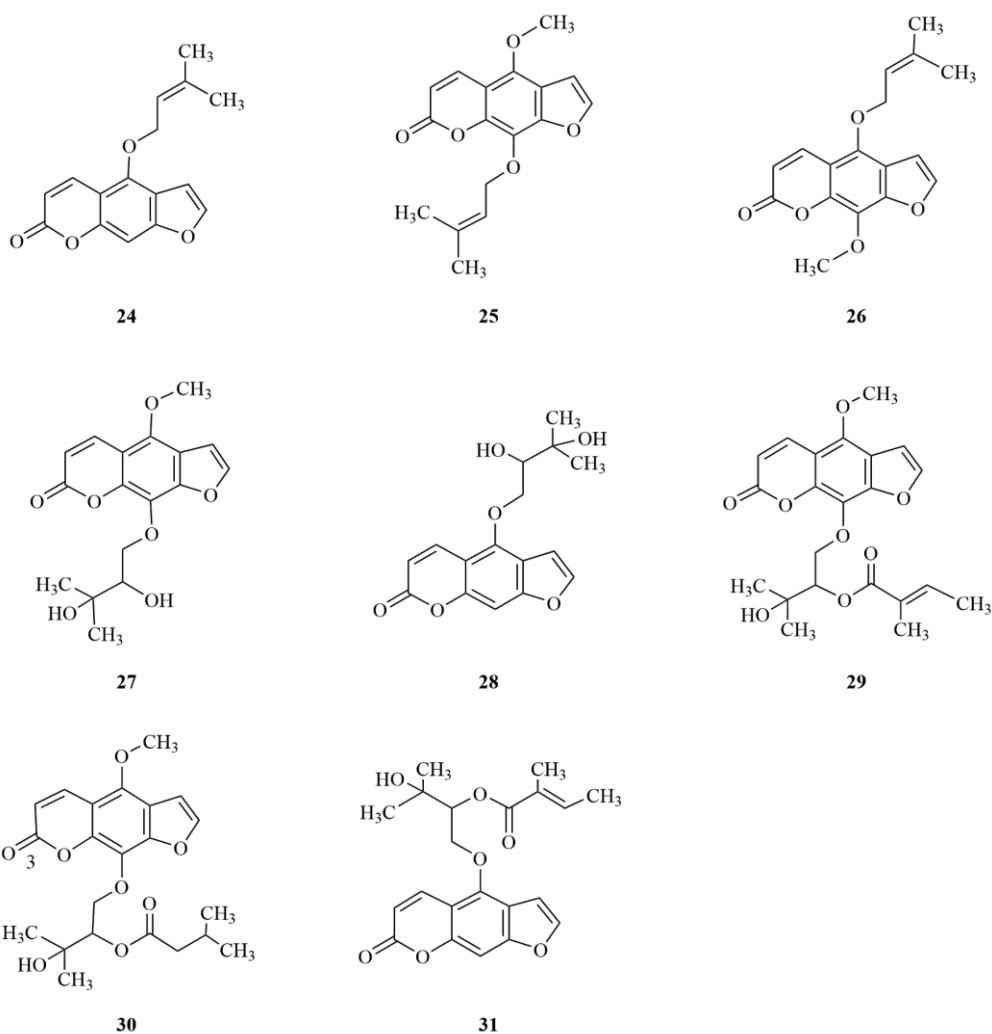
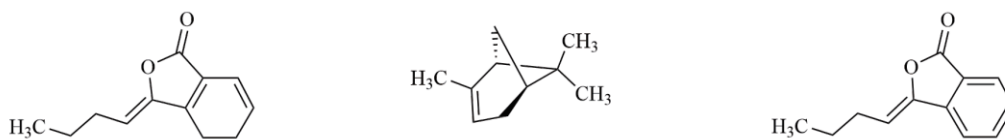


Fig. 3 The structures of coumarins and their derivatives in *A. sinensis*

### 2.3 Volatile oil

The essential oil of *A. sinensis* is the primary active components of *A. sinensis*, mainly composed of various compounds such as phthalides, terpenes, and alkanes (Fig. 4). These components are numerous and diverse in structure, including ligustilide (**32**), (-)- $\alpha$ -pinene (**33**), 3-butylidene-(3Z)-

1(3H)-isobenzofuranone (**34**), senkyunolide A (**35**), senkyunolide H (**36**), senkyunolide I (**37**), levistolide A (**38**), 3-(4-Hydroxy-3-methoxyphenyl)allyl 3-(4-hydroxy-3-methoxyphenyl)acrylate (**39**), (*E*)- $\beta$ -ocimene (**40**), (-)- $\beta$ -elemene (**41**), 1-Vinyl-1-methyl-2-(1-methylethenyl)-4-(1-methylideneethylidene)cyclohexane (**42**) [17-23]. The structures of *A. sinensis* volatile oils are shown in Fig. 4.



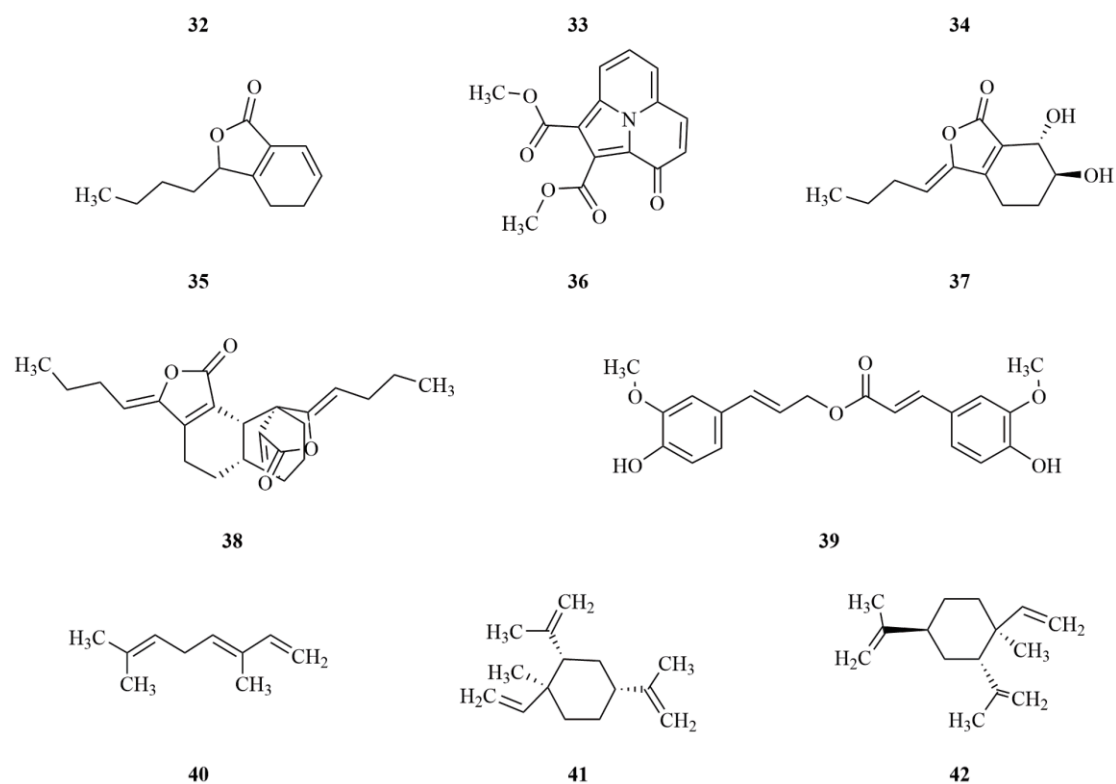
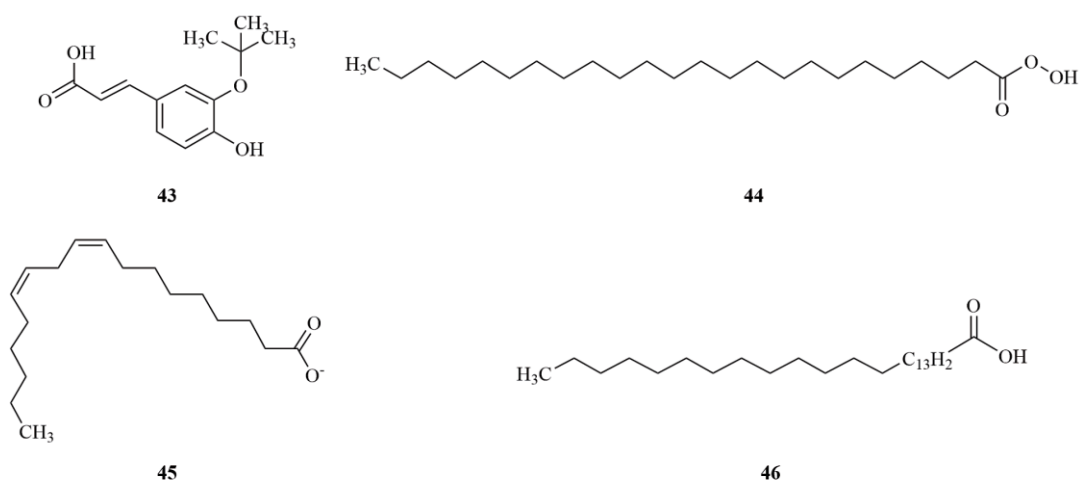


Fig. 4 The structures of volatile oil in *A. sinensis*

#### 2.4 Organic acids

Ferulic acid is the indicative component used for the quality control of *A. sinensis* in the current Chinese Pharmacopoeia. It is widely recognized for its extensive applications in medicine, the food industry, and the cosmetics sector. The structures of

organic acid compounds in *A. sinensis* are shown in Fig. 5, including ferulic acid (43), methyl tetracosane acid (44), linoleic acid (45), palmitic acid (46), oleic acid (47), succinic acid (48), ethyl p-Anisate acid (49), vanillic acid (50) [23-25]. The structures of organic acids are shown in Fig. 5.



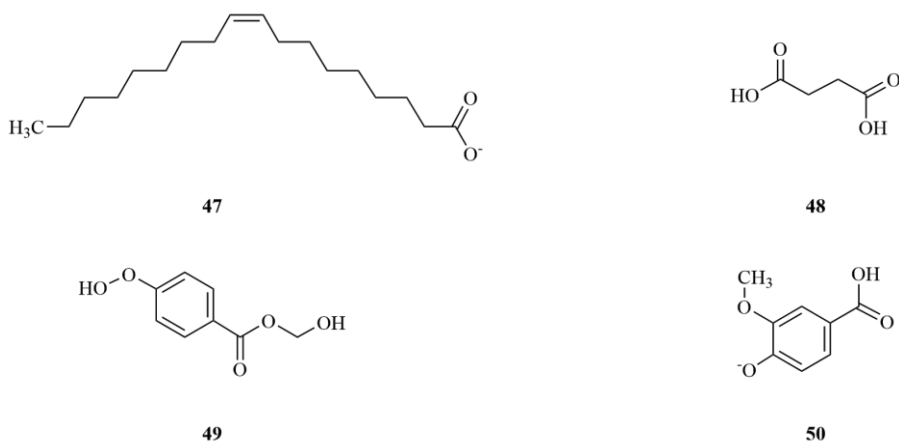


Fig. 5 The structures of organic acids in *A. sinensis*

### 2.5 Amino acids

*A. sinensis* is rich in amino acids. Various amino acids can be extracted from *A. sinensis* in Fig. 6, including arginine (51), *L*-glutamic acid

(52), *L*-aspartic acid (53), *L*-lysine (54), valine (55), *L*-threonine (56), proline (57), alanine (58), serine (59) [25-27]. The structures of amino acids are shown in Fig. 6.

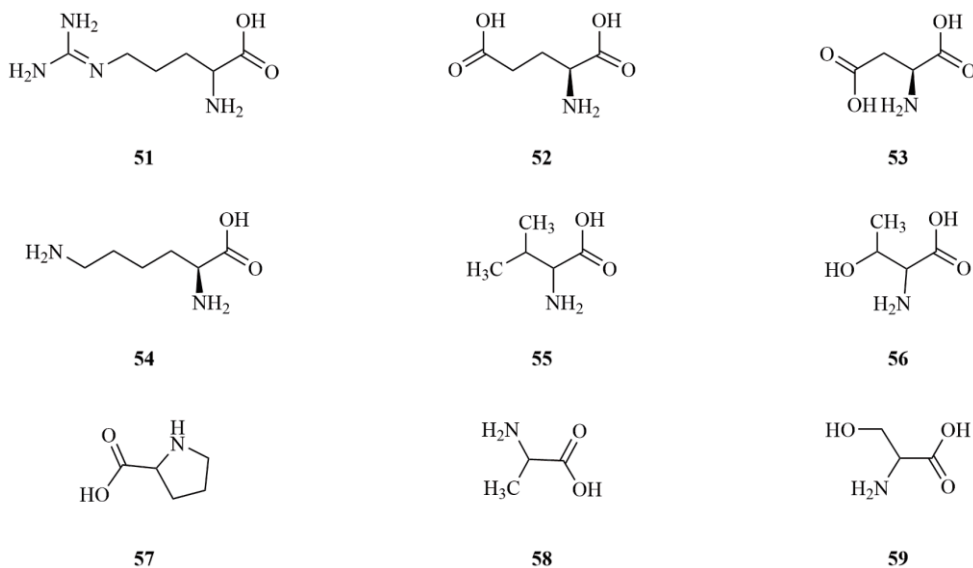


Fig. 6 The structures of amino acids in *A. sinensis*

## 3 Pharmacological activities

By searching relevant literature, six physiological activities of *A. sinensis* were obtained, namely promoting hematopoiesis and anti-anemia

effects, lowering blood lipid and anti-atherosclerosis, affecting smooth muscle, immune function, anti-tumor effect and antioxidant and anti-aging effect, as shown in Fig. 7.

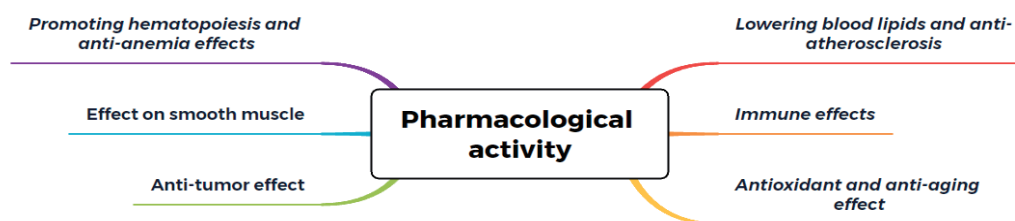


Fig. 7 Pharmacological activities of *A. sinensis*

### 3.1 Promoting hematopoiesis and anti-anemia effects

Hu et al. investigated the potential of *A. sinensis* polysaccharide (ASP) in mobilizing hematopoietic stem/progenitor cells (HSPC) and its role in restoring hematopoietic function in mice with hematopoietic failure. This investigation involved the intravenous administration of peripheral blood mononuclear cells (PBMC) from male BALB/c mice, mobilized by ASP, into female mice that had been irradiated with 8.5 G-60 G  $\gamma$  rays. Changes in levels of white blood cells (WBC), hemoglobin (HGB), and platelets (PLT) in the peripheral blood of recipient mice were monitored, alongside their survival at the 30-day mark. The source of hematopoietic reconstitution was identified through polymerase chain reaction (PCR) analysis. The findings indicated that WBC, PLT, HGB levels, and the 30-day survival rate of the ASP group were notably higher than that of the control and NS groups ( $P < 0.05$ ). Y chromosome PCR analysis confirmed that the regenerated hematopoietic cells of the surviving mice in the ASP group originated from male donors. It was observed that transplantation of ASP-mobilized peripheral blood HSPCs effectively restored long-term hematopoietic failure in mice [28].

Wang et al. investigated the regulatory mechanism of ASP on the proliferation of hematopoietic progenitor cells in order to elucidate the biological mechanism of ASP in regulating hematopoietic progenitor cell proliferation and “blood tonic”. By assessing the effects of ASP on the

proliferation and cloning of hematopoietic progenitor cells through *in vitro* culture techniques and the detection of hematopoietic growth factors, they found that ASP significantly enhanced the proliferation and differentiation of myeloid hematopoietic progenitor cells (BFU-E, CFU-E, CFU-GM, and CFU-MK) in normal or anemic mice. The culture medium of fibroblasts, macrophages, spleen cells, and skeletal muscle induced by ASP was found to enhance the colony yield of hematopoietic progenitor cells. It was concluded that the mechanism of ASP promoting hematopoietic growth may be related to the direct or indirect stimulation of macrophages, fibroblasts, and lymphocytes in the hematopoietic microenvironment, leading to the secretion of highly active hematopoietic growth factors [29].

### 3.2 Lowering blood lipid and anti-atherosclerosis

Wang et al. examined the impact of *A. sinensis* on cellular damage caused by hyperlipidemia, aiming to investigate the potential anti-atherosclerosis effects of *A. sinensis* and its underlying mechanisms. Human umbilical vein endothelial cells (ECV304) were subjected to hyperlipidemia as an injurious factor. The study utilized scanning electron microscopy to observe the ultrastructure of the cells and spectrophotometry to measure the nitric oxide (NO) levels in the cell culture medium. Immunocytochemistry was employed to assess the expression of intercellular adhesion molecule-1 (ICAM-1), basic fibroblast growth factor (bFGF), and transforming growth factor  $\beta$ 1 (TGF $\beta$ 1).



Following a 24-h incubation with hyperlipidemia serum, significant damage to the endothelial cells' ultrastructure was observed, along with increased expression of ICAM-1 and bFGF on the cell surface, decreased NO levels in the cell culture medium, and reduced expression of TGF $\beta$ 1. The addition of *A. sinensis* reversed these effects of hyperlipidemia on endothelial cells. The modulation of ICAM-1, bFGF, TGF $\beta$ 1, and NO expression in endothelial cells by *A. sinensis* may be attributed to its anti-atherosclerosis properties [30].

Li et al. investigated the impact of *A. sinensis* on aortic atherosclerosis induced by high fat in rabbits. By studying the effects of *A. sinensis* on experimental high-fat-induced aortic atherosclerosis in rabbits, the researchers explored the mechanisms underlying the anti-atherosclerosis properties of *A. sinensis*. Healthy rabbits were divided into a normal control group (fed a normal diet), a high-fat group (fed a high-fat diet), and an *A. sinensis* treatment group (fed a high-fat diet supplemented with *A. sinensis* injection). After a 10-week feeding period, the rabbits were euthanized. The study assessed the aortic atherosclerotic plaque area, observed the aorta's ultrastructure using transmission electron microscopy, and measured the nitric oxide (NO) content in the aorta strips using the Griess reaction method. The results showed that *A. sinensis* significantly reduced the atherosclerotic plaque area, inhibited foam cell formation in the arterial wall, and increased NO content in the aorta. In conclusion, *A. sinensis* demonstrated the ability to counteract high lipid-induced atherosclerosis formation, potentially through its protective effects on endothelial cells, inhibition of foam cell formation, and modulation of NO production [31].

### 3.3 Effect on smooth muscle

Liu et al. conducted a study to investigate the impact of *A. sinensis* essential oil on the

contraction of isolated uterine smooth muscle in rats. The researchers observed the effects of *A. sinensis* essential oil on uterine smooth muscle contraction by examining the reactions of uterine smooth muscle strips in the presence of oxytocin and a high potassium depolarization solution. The results indicated that *A. sinensis* essential oil dose-dependently inhibited the contraction of uterine smooth muscle induced by oxytocin and calcium in the high potassium depolarizing solution. The cumulative dose-effect curve of calcium chloride shifted to the right, with a decrease in maximum effect, suggesting non-competitive inhibition. Furthermore, the essential oil inhibited both intracellular and extracellular calcium contractile components of uterine smooth muscle. In conclusion, the inhibitory effect of *A. sinensis* essential oil on rat uterine smooth muscle strips may be attributed to its antagonistic action against calcium [32].

In another study, Wu et al. investigated the effects of the volatile oil of *A. sinensis* on isolated trachea, duodenum, and vascular smooth muscle. The research aimed to explore the tissue selectivity and mechanism of action of the volatile oil. Smooth muscle samples from the trachea, duodenum, and blood vessels were prepared *in vivo*, and changes in muscle tension were recorded and analyzed using a physiological signals acquisition and analysis system. The results showed that *A. sinensis* volatile oil at concentrations of 0.001% to 0.1% had a significant relaxation effect on the resting trachea, duodenum, and thoracic aorta smooth muscle. Additionally, 0.01% of *A. sinensis* volatile oil reduced the precontraction of tracheal smooth muscle induced by various substances, and weakened the effects of these substances on duodenal smooth muscle precontraction. Moreover, 0.001% of *A. sinensis* volatile oil exhibited an antagonistic effect on aortic smooth muscle contraction induced by norepinephrine and potassium chloride. In conclusion, the volatile oil of *A. sinensis* has a broad



diastolic effect on three types of smooth muscles, with its mechanism possibly linked to the inhibition of voltage-dependent calcium channels [33].

### 3.4 Immune effects

Feng et al. conducted a study on the immunomodulatory effects of *A. sinensis* in mice [34]. Polysaccharides, as vital regulators of biological responses, exhibit promising applications in anti-tumor, anti-aging, and immune regulation. Previous research has demonstrated the diverse effects of *A. sinensis* polysaccharides, including anti-radiation, anti-tumor, and hematopoietic promotion. Nevertheless, the specific immunomodulatory effects and underlying mechanisms of *A. sinensis* polysaccharides require further elucidation [35]. In their investigation, *A. sinensis* [Oliv. Diels] sourced from Minxian county, Gansu Province, was utilized for the isolation and purification of *A. sinensis* polysaccharides. The study shows that ASP-3, the primary component of *A. sinensis* polysaccharides, is a homogeneous polysaccharide characterized by a low weight average molecular weight and narrow range, suggesting it has potential medicinal value. *A. sinensis* polysaccharide was found to enhance the non-specific immune function in normal mice, counteract immunosuppression induced by cyclophosphamide and hydrocortisone, and exhibit a potent inhibitory effect on humoral immune function. Additionally, ASP-3 was observed to boost the activities of macrophages and T lymphocytes while suppressing B cell proliferation. These findings indicate that *A. sinensis* polysaccharides stimulates non-specific and cellular immunity in mice by directly activating macrophages and T lymphocytes, with its inhibition of humoral immunity potentially linked to the direct suppression of B lymphocytes. Furthermore, the elevation of IL-2 and IFN- $\gamma$  levels by *A. sinensis* polysaccharides may be closely associated with its regulation of immune function [36].

### 3.5 Anti-tumor effect

Cao et al. conducted a study on the structure analysis and antitumor properties of *A. sinensis* polysaccharide ASP-2a. The researchers isolated and purified the crude polysaccharide of *A. sinensis* using anion exchange cellulose column and gel column chromatography, resulting in the extraction of white flocculent polysaccharide ASP-2a [37]. The structure of ASP-2a was examined through high efficiency size-exclusion chromatography, infrared spectrum analysis, gas chromatography, and uronic acid reduction. *In vivo* experiments using a mouse sarcoma S-180 transplantation model were conducted to evaluate the tumor inhibition rate, spleen index, and thymus index of ASP-2a. The results show that ASP-2a is a homogeneous compound with a weight average relative molecular weight of  $7.4 \times 10^5$  Da. It consists of arabinose, galactose, rhamnose, glucose and galacturonic acid in a ratio of 38.2, representing a novel acid polysaccharide isolated from *A. sinensis* for the first time. Furthermore, the study demonstrated that ASP-2a had a certain inhibitory effect on sarcoma S-180 tumor-bearing mice and significantly enhanced the thymus index and spleen index of the tumor-bearing mice [38].

### 3.6 Antioxidant and anti-aging effect

Hua et al. conducted a study to examine the impact of *A. sinensis* polysaccharides on the activation and expression of JAK2 and STAT3 in K562 leukemia cells. The researchers utilized immunocytochemistry and confocal laser scanning microscopy to assess the STAT3 expression in K562 cells treated with *A. sinensis* polysaccharides at a concentration of 200 mg/L over various time intervals. Western blotting was employed to analyze the levels of JAK2, Phospho-STAT3, and STAT3 expression in both the cytoplasm and nucleus. The findings revealed a significant decrease in STAT3



expression in the nucleus of K562 cells after 12 h of *A. sinensis* polysaccharides treatment, while there was a notable increase in the cytoplasm [39]. Subsequent treatment for 72 h resulted in decreased STAT3 expression in the cell nucleus compared to the control group, with no significant difference observed in the cytoplasm. Western blot analysis showed that the expression of STAT3 in cytoplasmic increased at 12, 24, 36, and 48 h, but decreased compared to the control group. The phosphorylation level of STAT3 was consistently lower than that of the control group at all time points, and no significant change was observed in JAK2 expression. In conclusion, it was found that *A. sinensis* polysaccharides inhibited proliferation, enhanced differentiation, and induced apoptosis in K562 cells, with its mechanism closely associated with the activation of JAK2/STAT3 signal transduction molecules and nuclear translocation [40].

Long et al investigated the free radical scavenging and antioxidant properties of angelicolactone [41]. The study involved assessing the scavenging effects of angelicolide on 1-1-diphenylpicophenylhydrazide free radical (DPPH $\cdot$ ) and  $\cdot$ OH, its self-reducing capacity, and its protective role against lipid peroxidation induced by linoleic acid and H<sub>2</sub>O<sub>2</sub> *in vitro*. The results demonstrated that angelicolactone exhibited significant scavenging effects on DPPH $\cdot$  and  $\cdot$ OH, with IC<sub>50</sub> values of 2.0 and 7.6 mg/mL, respectively. Angelicolactone at concentrations of 1, 4, and 16 mg/mL displayed inhibitory effects on the spontaneous oxidation of linoleic acid and H<sub>2</sub>O<sub>2</sub>-induced oxidative hemolysis of red blood cells in a dose-dependent manner. Moreover, angelicolactone exhibited a certain reducing capacity across different concentration gradients. In conclusion, angelicolactone was found to possess free radical scavenging and antioxidant properties [42].

#### 4 Conclusion

When affected by temperature, light and

other factors, the components in *A. sinensis* tend to change and transform, so the structures of these components are diverse. At present, hundreds of components have been obtained in *A. sinensis*, and there are still reports of new compounds. Phenols, polysaccharides, flavonoids, alcohols and other components have various biological activities, such as anti-tumor, neuroprotective, spasmolytic and analgesic properties. With the continuous development of science and technology, new pharmacological activities of other components in *A. sinensis* have been continuously discovered. *A. sinensis* polysaccharides, as one of the primary bioactive compounds in *A. sinensis*, are known for their low toxicity and good safety profile. They consist of pectin polysaccharides, neutral polysaccharides, and weak acidic polysaccharides. However, due to challenges of low yield and complex purification processes of natural *A. sinensis* polysaccharides, current research primarily focuses on the biological activities of *A. sinensis* heteropolysaccharides or their derivatives. These heteropolysaccharides are composed of arabinose, galactose, and glucose. Modern pharmacological research shows that *A. sinensis* polysaccharides not only enhance immune function and possess antioxidant properties but also mitigate pathological changes in vital human organs. They exhibit various pharmacological activities including anti-tumor effects, radiation protection, and hepatoprotective effects-indicating significant potential for therapeutic applications. Comprehensive understanding of the structure of *A. sinensis* polysaccharides is crucial for studying their biological activities. This knowledge not only helps to explore their mechanisms of action but also helps to develop more effective analogs or derivatives as novel drugs for treating relevant diseases in clinical settings. Based on the wide clinical application of *A. sinensis* and the complexity of the composition and activity of *A. sinensis*, it is worthwhile to further study the composition of *A.*



*sinensis*. It is believed that in the near future, with the deepening of research, *A. sinensis* will play a greater role in human health.

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