

A Review of the Pharmacological Effects and Clinical Potential of *Angelica sinensis*

Jing Ma*, Shiyu Zhang, Wenya He, Pengliang Yun

Ningxia Medical University, Yinchuan 750002, Ningxia Province, China

*Corresponding author: Jing Ma, 18209617889@163.com

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Abstract: As one of the widely used medicinal herbs with both medicinal and dietary applications in China, *Angelica sinensis* offers the advantage of “nourishing without causing stagnation” and has a variety of pharmacological effects, making it commonly applied in clinical practice and research. In recent years, as both domestic and international scholars have delved deeper into *Angelica sinensis*, its extensive pharmacological effects have garnered attention across various sectors of society. To date, *Angelica sinensis* has been shown to possess functions such as hematopoiesis, anti-inflammation, pain relief, anti-tumor effects, and immune enhancement. It is frequently employed to address conditions like intestinal dryness, constipation, vertigo, and palpitations. Additionally, *Angelica sinensis* has demonstrated significant potential and distinct therapeutic advantages in disease intervention, functional food development, and drug innovation. This review focuses on the pharmacological effects of *Angelica sinensis*, aiming to provide valuable scientific insights for its clinical application, drug innovation, and target development.

Keywords: *Angelica sinensis*; Pharmacological effect; Research

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1. Introduction

Angelica sinensis is listed in the *Shennong Bencao Jing* (*Shennong's Classic of Materia Medica*) as a traditional Chinese herbal medicine, widely utilized in clinical practice due to its warm nature and spicy taste. In recent years, research on the chemical components and pharmacological effects of *Angelica sinensis* has become more comprehensive, with its active components and clinical efficacy gaining substantial attention. This article elaborates on the traditional efficacy and modern pharmacological effects of *Angelica sinensis*, highlighting its broad application prospects across food, pharmaceutical, and biomedical fields^[1].

2. Pharmacological activity

2.1. Pharmacological activity based on traditional efficacy

2.1.1. Invigorating and replenishing blood

The efficacy and therapeutic effects of *Angelica sinensis* are well-documented in traditional texts. In *Shennong Bencao Jing* (*Shennong's Classic of Materia Medica*), it is recorded as being effective for “treating women’s leakage and eliminating child-related issues.” According to *Bencao Qandao*, *Angelica sinensis* possesses blood-nourishing properties, making it primarily used for blood replenishment. Similarly, *Jingyue Quanshu Bencao Zheng* describes it as “the holy medicine of the blood.” Recent studies indicate that *Angelica sinensis* promotes blood circulation, improves hemorheology and microcirculation, and has anti-thrombotic functions. Therefore, in traditional Chinese medicine (TCM), *Angelica sinensis* is frequently used to treat conditions like vertigo, palpitations, blood deficiency, blood stasis, and dysmenorrhea, demonstrating favorable outcomes.

To deepen understanding of the pharmacological activity of *Angelica sinensis*, modern researchers have investigated its hematopoietic functions, particularly examining the role of *Angelica sinensis* polysaccharide (ASP) by observing hemoglobin levels in blood deficiency model rats. Interleukin-6 (IL-6) and granulocyte-macrophage colony-stimulating factor have been shown to stimulate the hematopoietic function of ASP under stimulated conditions. Further research has examined the effects of different components, such as acetophenhydrazine (APH), on blood deficiency in mice. Findings indicate that the hematopoietic potential of the water extract and alcohol precipitation supernatant (DSC) from *Angelica sinensis* is significantly stronger than that of other parts ^[2].

For example, in cases of “sports anemia,” caused by intense exercise, which induces oxidative stress and upregulates hepcidin, athletes often experience persistent “sports anemia.” Addressing this, scholars studied the efficacy of *Angelica sinensis* alcohol extract and found that it significantly improved red blood cell counts in female rats with exercise-induced anemia, thereby mitigating anemia resulting from strenuous exercise. Additionally, researchers discovered that *Angelica sinensis* alcohol extract plays an important role in regulating iron metabolism. Notably, the alcohol extract was observed to reduce serum alanine aminotransferase (ALT) levels, an indicator of liver injury, thus effectively alleviating prolonged running-induced anemia by enhancing the body’s antioxidant capacity and down-regulating hepcidin.

Renowned as a “blood tonic medicine,” *Angelica sinensis* plays a crucial role in supporting the hematopoietic system. Hematopoiesis within the body involves cellular proliferation, differentiation, and release, which contribute significantly to health maintenance. The mechanism by which *Angelica sinensis* promotes hematopoiesis is primarily through regulating the generation, proliferation, and differentiation of hematopoietic cells, as well as inhibiting apoptosis, thereby improving blood biochemical marker levels in the human body to maintain stability.

2.1.2. Regulating menstruation and relieving pain

Mingyi Bielu (*Other Records of Famous Doctors*) describes *Angelica sinensis* as “primarily warming and analgesic.” In clinical practice, beyond its use in treating gynecological dysmenorrhea, it is also effective in alleviating headaches, arthralgia, and neuralgia. Researchers have investigated the analgesic effects of certain chemical components of *Angelica sinensis*, focusing on anti-inflammatory pathways. Nerve growth factor (NGF) is known to play a role in pain enhancement, and ligustilide, an essential oil component of *Angelica sinensis*, has shown therapeutic effects on prostatitis in mouse models. This compound can effectively reduce

the expression of inflammatory substances in prostatitis tissue, thereby increasing the pain threshold in model mice by reducing the frequency of writhing behavior.

In TCM gynecology, *Angelica sinensis* is frequently used to treat dysmenorrhea in women. Dysmenorrhea is primarily caused by “hypothalamic-pituitary-ovarian axis disorder,” which *Angelica sinensis* can alleviate by inhibiting estrogen production. Additionally, severe contractions of the uterine smooth muscle contribute to dysmenorrhea, causing abdominal pain before and after menstruation. Experimental studies on the pharmacological effect of *Angelica sinensis* on menstrual pain relief found that model mice treated with its volatile oil exhibited significantly fewer writhing movements compared to those given normal saline [3]. Furthermore, due to the reduction of oxytocin, the amplitude and frequency of uterine smooth muscle contractions were markedly decreased.

In conclusion, the essential oil of *Angelica sinensis* effectively regulates menstruation and alleviates pain, showing a clear therapeutic effect on uterine smooth muscle spasms. Some researchers have further explored the effects of *Angelica sinensis* essential oil components on uterine contractility, discovering its bidirectional nature: small doses stimulate, while large doses inhibit uterine contraction. Through extensive efficacy screening, researchers identified the most effective component for inhibiting uterine contractions: neutral, non-phenolic fraction A3.

2.2. Pharmacological activity based on dilatational effect

2.2.1. Antitumor activity

Angelica sinensis polysaccharide, the primary active component of *Angelica sinensis*, exhibits significant antitumor effects through its pharmacological mechanisms. Both *in vivo* and *in vitro* experiments show that *Angelica sinensis* has notable antitumor activity. *In vivo*, ASP primarily inhibits tumor cell growth and metastasis by effectively stimulating the host immune system and inhibiting cancer cell adhesion. Scholars have reported that ASP can inhibit human leukemia K562 cells in a dose-dependent manner by promoting erythropoietin-mediated signal transduction and activating specific protein signaling pathways.

In vitro studies have identified a new *Angelica sinensis* component, polysaccharide APS-1d, which significantly inhibits cancer cell proliferation and induces apoptosis. Research has demonstrated that APS-1d shows anticancer activity against human cervical cancer HeLa cells by activating the intrinsic mitochondrial pathway to curb proliferation and promote apoptosis. Additionally, ASP has been effective in inducing apoptosis in T47D breast cancer cells by increasing the overexpression of cyclic adenosine response element-binding protein.

2.2.2. Liver protection

Various factors, such as unhealthy habits, alcohol, drug abuse, chemical exposure, and hyperlipidemia, can cause liver damage, disrupting the body’s metabolic regulation and leading to an imbalance in energy regulation across organs. Studies indicate that ASP plays a significant role in liver protection, positively impacting liver damage caused by various factors. In research on rats exposed to cadmium-induced immune and liver injury, a specific dose of ASP was found to alleviate liver damage, improve immune function, and enhance enzyme activity regulation to varying degrees. Studies also show that ASP effectively slows chronic liver fibrosis both *in vivo* and *in vitro*, achieving liver protection through its anti-inflammatory and antioxidant mechanisms. Furthermore, its cholesterol-lowering properties help reduce liver strain by decreasing fat accumulation and

regeneration, thereby promoting liver function protection.

Additionally, extensive experimental studies have demonstrated that the TCM compound preparation, *Astragalus-Angelica* mixture, exhibits beneficial effects, such as delaying chronic renal failure and improving protein and lipid metabolism. For instance, the *Astragalus-Angelica* mixture has been shown to enhance renal function and reduce the tubulointerstitial damage index in rats with chronic purinase-induced sclerosis. Chronic kidney disease often results in interstitial fibrosis and increased renal tubular epithelial cell atrophy. *Astragalus-Angelica* mixture provides a similar therapeutic effect to enalapril in treating this condition, although it does not exert its effects by blocking the renin-angiotensin system within the kidney. Instead, it protects the kidney by inhibiting the overexpression of transforming growth factor- β and osteopontin rather than activating renal cells.

2.2.3. Anti-Alzheimer's disease

Alzheimer's disease (AD), a common neurodegenerative disorder, impairs cognitive functions in older adults, affecting their independent thinking and memory and leading to a diminished quality of life. The pathological hallmark of Alzheimer's is amyloid- β (A β), which reduces the viability of neural 2A cells in a concentration-dependent manner. To address this cause of Alzheimer's, researchers administered a specific dose of *Angelica sinensis* extract to a small group of patients with neural cell dysfunction. The extract significantly reduced lesions caused by amyloid- β and helped prevent neurotoxicity induced by this marker. This illustrates the critical role of *Angelica sinensis* extract in inhibiting amyloid- β , emphasizing its unique value in anti-Alzheimer's research. Additionally, research has shown that the mediating pathway of *Angelica sinensis* extract involves phosphatidylinositol 3-kinase/protein kinase B/glycogen synthase kinase-3 β signaling, which reduces amyloid- β toxicity and protects the nervous system. Further studies on rat models with hippocampal inflammation suggest that ASP improves memory deficits in Alzheimer's rats by inhibiting inflammatory factors and reducing neuronal apoptosis^[4].

2.2.4. Cardiovascular protection

Studies on chronic cardiotoxicity in mice indicate that *Angelica sinensis* water extract effectively improves heart performance and lowers mortality rates in model mice. The ASP water extract maintained normal levels of AST in serum and antioxidant activity in the organs of these mice, helping alleviate arrhythmia and conduction abnormalities, while also supporting the myofibrils in maintaining their activity. In studies on hypoxia-induced injury of H9c2 cardiomyocytes, ASP exhibited a protective effect, with treated cells showing increased survival and proliferation rates compared to the model group. *Angelica sinensis* plays a significant role in treating cardiovascular diseases and regulating angiogenesis, as it contains both anti-angiogenic and pro-angiogenic components, offering new directions in the development of angiogenesis regulators. Therefore, in TCM clinical practice, it is essential for medical staff and researchers to harness the pharmacological benefits of *Angelica sinensis* appropriately.

3. The antioxidant effect and mechanism of *Angelica sinensis*

The antioxidant effect of *Angelica sinensis* is notably distinct in current clinical applications. Throughout various endogenous and exogenous processes, the human body produces a large amount of reactive nitrogen oxides. When there is an imbalance between these reactive nitrogen oxides and the body's antioxidant defense

system, oxidative stress occurs. Clinically, antioxidants are frequently used to treat diseases related to oxidative stress. The antioxidant effect of ASP is primarily demonstrated by its antioxidant properties *in vitro*, which protect rat chondrocytes from oxidative stress damage. Studies have shown that ephedrine reduces antioxidant capacity in mouse liver tissue and activates tumor necrosis factor in mice.

In treating liver injury in mice, researchers found that ASP effectively counteracted liver damage caused by jute exposure, improving the organ's antioxidant capacity. Additionally, ASP has been shown to protect neurons from oxidase-induced cytotoxicity, effectively decreasing the number of apoptotic cells in the body and significantly raising reactive oxygen species levels in cells. Overall, ASP exhibits a strong antioxidant capacity, providing promising avenues for the development of natural antioxidant drugs.

4. The antihypertensive effect and mechanism of *Angelica sinensis*

Essential hypertension is a common chronic disease that can induce organ damage in the heart, brain, kidneys, and other areas, making it a significant risk factor for cardiovascular disease mortality. Studies have shown that *Angelica* alcohol extract can help maintain cellular balance by regulating mitogen-activated protein kinase, leading to a spontaneous reduction in blood pressure in hypertensive rats. This not only improves endothelial function and reverses ventricular remodeling in hypertensive rats but also effectively treats liver and kidney damage, enhancing the vitality of the affected animals.

Additionally, the pathogenesis of hypertension often involves vascular endothelial dysfunction. Some researchers have explored how *Angelica sinensis* might regulate vascular endothelial function to reduce hypertension incidence. In animal experiments, scholars discovered that the essential oil of *Angelica sinensis* exhibits pharmacological properties that spontaneously regulate hypertension in rats, acting through various intracellular enzyme signaling pathways. One critical mechanism involves reducing renin and angiotensin levels in blood vessels, as the renin-angiotensin-aldosterone system is closely linked to antihypertensive effects. By lowering renin and angiotensin levels, the essential oil of *Angelica sinensis* offers promising potential in developing new antihypertensive medications ^[5].

Furthermore, *Angelica sinensis* promotes antihypertensive effects by regulating lipid metabolism, inhibiting atherosclerosis, and facilitating blood pressure reduction. For instance, when using the essential oil of *Angelica sinensis* to up-regulate enzyme and gene expression levels, researchers found that it holds significant value in improving lipid metabolism in hypertensive rats. This effectively curtails atherosclerosis, contributing to blood pressure reduction and supporting *Angelica sinensis* as a valuable agent in antihypertensive treatment.

5. Conclusion

With advancements in modern science and technology, extraction, separation, and identification techniques for TCM have greatly improved, significantly enriching research on the chemical composition and pharmacological actions of TCM in our country. The pharmacological studies of *Angelica sinensis* not only reflect the profound and excellent culture of TCM but also substantiate the scientific basis of TCM theories. However, research on the pharmacological effects of *Angelica sinensis* remains somewhat limited. In recent years, academia has focused heavily on studying components within the essential oil of *Angelica sinensis* and examining the clinical activities and pharmacological effects of its different components. Unfortunately, the chemical components

of traditional decoctions have not been extensively analyzed. As an important clinical medicine, increased attention to the traditional decoction of *Angelica sinensis* could effectively broaden the research scope on its chemical composition and enhance the credibility of its pharmacological effects.

Disclosure statement

The authors declare no conflict of interest.

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