

Leonurus japonicus Houtt in Traditional Chinese Medicine: A Review of Phytochemistry, Pharmacology, and Clinical Applications

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ABSTRACT: Background: *Leonurus japonicus* Houtt. grass (white *Leonurus japonicus* grass) is a perennial herbaceous plant, which is widely used in traditional Chinese medicine to treat gynecological diseases, cardiovascular protection, and inflammation management. This review integrates current knowledge of plant chemistry, pharmacology, and clinical applications to promote the integration of evidence-based and contemporary medicine. Method: A detailed literature review was conducted using PubMed, Web of Science, CNKI, and Wan Fang Data, with the search extended to December 2025. The terms “*Leonurus japonicus*”, “plant chemistry”, “pharmacology”, and “clinical application” are used. Of the 680 articles initially identified, 326 meet the criteria for full-text review because they address the applications and pharmacological mechanisms of traditional Chinese medicine. Results: Alkaloids, flavonoids, and diterpenes are only a few of the many bioactive compounds found in *Leonurus japonicus*. In traditional Chinese medicine (TCM), it is mostly used to treat hypertension, edema, menstrual problems, and to accelerate recovery after childbirth. Studies on drugs show that they can make the uterus contract, stop bleeding, protect the heart, reduce inflammation, and protect the nervous system. Preliminary clinical evidence shows that

it has the effect of preventing postpartum bleeding and relieving dysmenorrhea. Conclusion: Although preclinical evidence supports traditional applications, clinical verification is still insufficient. Future research must prioritize standardized extracts, high-quality randomized controlled trials, and mechanistic studies to fully clarify its therapeutic potential in both traditional Chinese medicine and contemporary medicine.

INTRODUCTION

Leonurus japonicus capsule, also known as *Leonurus japonicus* and White Motherwort, is a perennial herbaceous plant and belongs to the mint family. This plant has been used in medicine for hundreds of years and is often used to treat problems of the female reproductive system.¹ It can be found in many temperate regions of East Asia, including China, Japan, and South Korea.² In the theoretical framework of traditional Chinese medicine, the Japanese seven-gill eel (*L. japonicus*) is considered an important medicine for activating blood and dissolving stasis and qi. Classic medical texts, such as the Outline of Herbal Medicine (The Outline of Herbal Medicine), clarify its functions in activating blood, dissolving stasis, and adjusting menstruation.³ Because of these characteristics, the herb has long been considered a useful treatment for women's health in clinical practice.¹

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In actual traditional Chinese medicine treatment, *Leonurus japonicus* is not often used as a single-flavored medicine. On the contrary, it is often used in herbal prescriptions containing more than one herb. These preparations follow traditional treatment principles and involve combining a variety of drugs and substances to enhance therapeutic efficacy while reducing potential adverse reactions.^{4,5} *Leonurus japonicus* grass is often used in gynecological treatment to treat menstrual irregularities and regulate blood circulation. This herb is often combined with other well-known medicinal plants, such as *Angelica sinensis* (Dang Gui) and Xiang Fu, which are traditionally regarded as blood tonic and qi medicine.^{6,7}

In addition, in postpartum care, preparations containing *L. japonicus* are typically used to promote uterine recovery and reduce excessive uterine bleeding.² In addition to gynecological uses, the herb is also used to treat edema and hypertension, partly because it can act as a diuretic and help circulation.⁷ In recent years, medicinal plants have attracted great attention as a potential source of drug discovery. Therefore, *Leonurus japonicus* grass has attracted increasing interest in scientific research, and numerous studies have examined its chemical composition and pharmacological properties.⁸ Plant chemistry research has identified many types of biologically active compounds in the plant, including alkaloids such as leonurine and stachydrine, as well as flavonoids and diterpene compounds.^{4,5} Experimental evidence suggests that these constituents contribute to a variety of biological effects. For instance, some compounds may regulate uterine smooth muscle contraction via oxytocin-related signaling pathways, inhibit inflammatory signaling pathways, such as NF- κ B, and protect against oxidative stress.^{9,6} Although these findings offer scientific support for several traditional uses of *L. japonicus*, the available knowledge remains scattered across different studies.

Therefore, the present review aims to summarize the current evidence on its phytochemistry, pharmacological activities, pharmacokinetics, and

clinical applications to provide a clearer understanding of its therapeutic potential.

MATERIALS AND METHODS

To collect studies on *Leonurus japonicus*, a literature search was conducted in four databases: PubMed, Web of Science, CNKI, and Wan Fang Data. The search covered publications available up to December 2025. Keywords used in the retrieval process included “*Leonurus japonicus*”, “White *Leonurus japonicus*”, “Yi Mu Cao”, “phytochemistry”, “pharmacology”, “clinical applications”, and “Traditional Chinese Medicine”. and “mechanism”. After the initial search, duplicate records were removed first. The remaining articles were then screened according to their titles and abstracts. Studies were retained when they focused on the phytochemical characteristics, pharmacological activities, or clinical applications of *L. japonicus* in the context of TCM. Conference abstracts, commentaries, opinion-based papers, and studies lacking sufficient methodological information were excluded. Reports that dealt exclusively with other traditional medical systems and did not involve TCM were also not considered. Following the screening procedure, 326 full-text articles were finally included in this review from an initial pool of 680 records. Information on chemical constituents, pharmacological actions, mechanisms, and clinical evidence was then extracted and organized for further analysis.

RESULTS

1. TCM Formulations Containing *Leonurus japonicus* Houtt.

Leonurus japonicus is primarily used therapeutically in established multiherb formulations.^{10,11} These composite preparations are designed to harmonize the inherent properties of the constituent herbs, thereby enhancing their therapeutic effectiveness and addressing specific TCM diagnostic classifications. According to TCM theory, Table 1 lists some of the most important TCM formulations containing *L. japonicus*, along with their main clinical indications.

Table 1. Classic TCM Formulations Containing *Leonurus japonicus*

TCM Formulation	Main Constituents (Pinyin Name)	TCM Actions	Primary TCM Indications
Yimu Shengjin Dan	Yi Mu Cao (<i>Leonurus japonicus</i>), Hong Hua (<i>Carthamus</i> , Flos), Dang Gui (<i>Angelica sinensis</i> , Radix), Chuan Xiong (<i>Chuanxiong</i> , Rhizoma), Chi Shao (<i>Paeonia rubra</i> , Radix)	Activates Blood, dispels Stasis, unblocks the Chong and Ren channels	Dysmenorrhea, amenorrhea, irregular menstruation due to Blood Stasis
Yimu Shengjin Dan	Dang Gui (<i>Angelica sinensis</i> , Radix), Chuan Xiong (<i>Chuanxiong</i> , Rhizoma), Tao Ren (<i>Persica</i> , Semen), Pao Jiang (<i>Zingiberis praeparatum</i> , Rhizoma), Yi Mu Cao (<i>Leonurus japonicus</i>)	Warms the Uterus, activates Blood, resolves Stasis, alleviates pain	Postpartum abdominal pain, lochiorrhea, and prevention of postpartum hemorrhage due to Cold and Blood Stasis
Ba Zhen Yi Mu Tang	Dang Gui (<i>Angelica sinensis</i> , Radix), Shu Di Huang (<i>Rehmannia praeparata</i> , Radix), Bai Shao (<i>Paeonia alba</i> , Radix), Chuan Xiong (<i>Chuanxiong</i> , Rhizoma), Ren Shen (<i>Ginseng</i> , Radix), Bai Zhu (<i>Atractylodes macrocephala</i> , Rhizoma), Fu Ling (<i>Poria</i>), Yi Mu Cao (<i>Leonurus japonicus</i>)	Tonifies Qi and Blood, regulates menstruation, dispels Stasis	Irregular menstruation, fatigue, and weakness in women with Qi and Blood Deficiency complicated by Blood Stasis
Yi Mu Wan	Yi Mu Cao (<i>Leonurus japonicus</i>), Dang Gui (<i>Angelica sinensis</i> , Radix), Chuan Xiong (<i>Chuanxiong</i> , Rhizoma), Chi Shao (<i>Paeonia rubra</i> , Radix), Mu Xiang (<i>Aucklandia</i> , Radix)	Promotes Blood circulation, regulates Qi, alleviates pain	Dysmenorrhea and menstrual discomfort associated with Qi Stagnation and Blood Stasis

2. Phytochemistry

Phytochemical research on *Leonurus japonicus* has revealed complex chemical constituents closely linked to its medicinal properties. More than 200 chemical constituents have been isolated and identified from this plant. There are four main types of compounds: alkaloids, diterpenes, flavonoids, and phenolic acids.^{12,9} Alkaloids are widely regarded as the main components of *Leonurus japonicus*. In particular, because of its diverse pharmacological properties^{11,13}, it is a chemical marker often used to assess quality and has attracted considerable scientific interest. The plant also contains other alkaloids, notably leonurine and stachydrine, which are considered to have distinct biological effects, particularly cardioprotective and neuroprotective activities.^{14,10}

Diterpene compounds are another important class of chemicals found in *L. japonicus*. Many of these molecules have half-alkane skeletons and are associated with different pharmacological activities. Leonuketal, a unique spiral diterpene, is considered to be a specific chemical marker of the species.^{9,15} These compounds exhibit significant anti-inflammatory and antioxidant effects, in part by inhibiting the nuclear factor- κ B (NF- κ B) signaling pathway.¹⁶ Recent phytochemical research has discovered several new isopentane diterpene compounds, including primoxen A-D, which have a significant inhibitory effect on the production of nitric oxide in activated macrophages.^{17,18}

Flavonoids are another important component of *L. japonicus*. More than 50 flavonoids and glycosides have been recorded in plants.^{9,15} Rutin, quercetin, phenol, and their glycoside derivatives are examples

of such compounds. It is believed that these flavonoids contribute significantly to the antioxidant, anti-inflammatory, and vascular protective effects of herbal medicine.²⁰ In recent years, with the development of phytochemical analysis, some previously undescribed flavonol glycosides characteristic of this species have been isolated, most notably the rare syringyl-acylated flavonol glycosides leonurusoides A–E.²¹

In addition to these main chemicals, *L. japonicus* also contains many other chemicals. These include phenolic acid components such as caffeic acid and chlorogenic acid, essential oil components such as β -thuyacin and cycloene ether terpenes, and sterol²², and so on. The presence of these structurally diverse compounds creates a complex plant chemical system, which may explain why the herb can handle multiple conditions simultaneously. Some people think these parts may work together to make the plant more biologically active overall.

3. Pharmacological Activities

Numerous experimental studies have investigated the biological activity of *Leonurus japonicus*. At present, the available data indicate that the plant contains a variety of biologically active compounds and can interact with diverse biological targets and signaling pathways. Therefore, the extracts obtained from *L. japonicus* and the isolated compounds exhibit a wide range of pharmacological effects across gynecology, cardiovascular, inflammatory, and nervous systems.^{23,24} The diversity of these biological activities is largely due to their complex chemical components, especially alkaloids, such as ephylloids and hydrazides, as well

as flavonoids and diterpene compounds. Since these components can affect multiple molecular pathways simultaneously, *L. japonicus* is often regarded as a model of multi-target medicinal plants in traditional Chinese medicine research. From a gynecological perspective, *L. japonicus* exhibits significant uterine contractile activity, supporting its long-term use in postpartum recovery and the management of menstrual disorders.²⁵ Experimental research shows that plant extracts can induce dose-dependent contraction of uterine smooth muscle. These observed effects are believed to be mediated by oxytocin receptor activation and regulation of the epinephrine signaling pathway.²⁴ Among the identified ingredients, alkaloids, particularly leonurine and stachydrine, appear to be particularly important, as they regulate intracellular calcium mobilization and promote prostaglandin synthesis.^{23,25}

Furthermore, various flavonoid constituents (such as luteolin, rutin, and quercetin) have exhibited estrogenic regulatory characteristics. Research findings indicate that these substances might engage with estrogen receptors, thereby promoting the expression of genes responsive to estrogen.¹² In ovariectomized rat models, long-term administration of *L. japonicus* extracts has been shown to promote endometrial proliferation and increase uterine weight, suggesting potential therapeutic value in managing menopausal symptoms.²⁴ Furthermore, the traditional application of this herb for dysmenorrhea has been supported by experimental findings showing that it can reduce prostaglandin F2 α production and suppress inflammatory mediators in endometrial tissues, thereby alleviating uterine spasms.^{26,22}

Another important pharmacological property of *L. japonicus* is its ability to protect the heart and blood vessels.^{27,26} In experimental hypertension models, plant extracts have shown considerable blood pressure-lowering effects. These effects seem to act through several mechanisms, including blocking calcium channels, inhibiting angiotensin-converting enzyme (ACE), and dilating blood vessels via nitric oxide.^{27,28} Stachydrine, an alkaloid, has been identified as a key component, demonstrating significant ability to relax vascular smooth muscle.^{29,24} Anti-thrombotic properties include inhibition of platelet aggregation by disrupting arachidonic acid metabolism and reducing thromboxane A2

A lot of research has been done on the anti-inflammatory and immunomodulatory effects.³⁰ In both acute and chronic inflammation models, extracts exhibit a substantial reduction in edema and inflammatory cell infiltration through mechanisms involving suppression

of NF- κ B activation and subsequent downregulation of pro-inflammatory cytokines such as TNF- α , IL-6, and IL-1 β .^{10,26} The diterpenoid constituents exhibit significant suppression of COX-2 and iNOS expression in activated macrophages.^{33,34} In autoimmune inflammation models, *L. japonicus* extracts have demonstrated efficacy in reducing joint swelling and cartilage damage, in part by modulating the balance between Th1 and Th2 cytokines.^{33,34} Recent research indicates that the extracts may facilitate macrophage polarization towards the anti-inflammatory M2 phenotype, potentially aiding in the resolution of chronic inflammatory responses.^{35,17}

Recent pharmacological investigations have demonstrated that *L. japonicus* may confer protective effects in various neurological disorder models.^{36,19} In experimental stroke models, pretreatment with plant extracts has demonstrated efficacy in reducing infarct volume and improving neurological outcomes, presumably via increased cerebral blood flow and the prevention of excitotoxic neuronal damage.^{37,15} Leonurine, a principal alkaloid present in the plant, has exhibited considerable neuroprotective properties. Mechanistic investigations indicate that it may mitigate glutamate-induced neurotoxicity by regulating NMDA receptor function and preserving intracellular calcium homeostasis.^{33,38} In depression models, extended administration of *L. japonicus* extracts has produced antidepressant-like effects, apparently associated with the modulation of monoamine neurotransmitter systems.¹⁹ Moreover, experimental studies suggest that the plant may provide protective effects in Alzheimer's disease models by inhibiting b-amyloid aggregation and reducing neuroinflammation.³⁹

Besides the major pharmacological effects mentioned above, *L. japonicus* has also been reported to have other biological effects, such as diuretic, antimicrobial, anticancer, and hepatoprotective activities.^{39,26} It is important to note that many pharmacological studies have used crude plant extracts, which makes it difficult to link specific biological effects to particular compounds. Even though synergistic interactions between different parts of the herb may make it more effective as a medicine, they also make it harder to standardize and control quality in clinical settings.^{40,26}

4. Pharmacokinetics and Toxicology

Recent studies have examined the pharmacokinetic properties of various active constituents derived from *Leonurus japonicus*. Experimental data from animal models show that *Leonurus japonicus* contains the main alkaloid, which is absorbed relatively quickly after oral administration and usually reaches its peak within 1-2 hours. It has been reported that its oral

bioavailability is about 35–40%, indicating that some compounds are metabolized by the body before reaching the bloodstream.^{43,26} Distribution studies show that leonurine and similar alkaloids can enter several major organs, including the liver, kidneys, and heart.⁴⁴ The liver is the part where metabolic changes occur the most. Cytochrome P450 enzymes such as CYP3A4 and CYP2D6 participate in it, and the II combination reaction occurs.²⁶ Renal excretion is the principal route of elimination. Studies on rodents have found that their elimination half-life is about 4 to 6 hours. Toxicological investigations typically indicate that formulations derived from *Leonurus japonicus* exhibit a comparatively positive safety profile when administered within established dosage parameters. Acute toxicity assessments in rodent models revealed that the median lethal dose (LD₅₀) of standardized extracts exceeded 2000 mg/kg, indicating a low degree of acute toxicity.²² Subacute toxicity studies further showed that daily administration of the extracts at doses up to 500 mg/kg did not cause any obvious adverse effects in experimental animals.⁴² However, long-term exposure to higher doses has occasionally been associated with mild and reversible liver toxicity in chronic experiments lasting up to six months.⁴⁶ Additional safety assessments have also examined potential reproductive and genetic toxicity. Current evidence suggests that recommended doses do not significantly affect fertility or embryonic development, and genotoxicity tests have generally produced negative results.^{40,39} Nevertheless, possible herb–drug interactions should still be considered in clinical practice. Because some constituents may influence cytochrome P450 enzymes such as CYP3A4 and CYP2D6, caution may be warranted when *L. japonicus* is co-administered with medications metabolized via these pathways, including certain anticoagulants and antihypertensive drugs.^{47,42}

5. Clinical Applications

Leonurus japonicus has been used in traditional Chinese medicine for a long time to treat blood flow and women's health problems. This is closely related to its application in clinical practice. Recent pharmacological studies have confirmed many traditional indications, and an increasing number of clinical trials have tested their expected therapeutic effects across various medical conditions. Gynecological diseases remain the most common clinical use, although there are many other uses. During the postpartum period, preparations containing *L. japonicus* are often used to promote uterine recovery and reduce excessive bleeding.^{47,25} In modern combined traditional Chinese and Western medicine, these therapies are usually administered as

herbal extracts or injectable preparations.

A number of clinical studies have evaluated the efficacy of *Leonurus japonicus* in postpartum recovery and menstrual disorders. In studies involving postpartum women, the use of *Leonurus japonicus* preparations is associated with accelerated uterine recovery and reduced malignant dew discharge in the initial stage of recovery.^{49,28} Observational studies show that menstrual disorders, especially in patients with primary dysmenorrhea, have milder pain and better symptoms after taking *Leonurus japonicus* preparations. Some studies have also shown that treatment can reduce prostaglandin F2 α levels. This means that the herb may help relieve strong uterine contractions and the inflammation associated with the period.^{43,24}

In addition to gynecological disorders, *Leonurus japonicus* has been studied for its possible cardiovascular advantages. Clinical observations suggest that herbal preparations may facilitate modest reductions in blood pressure when employed as adjunctive therapy for patients with mild hypertension.^{30,46} In a clinical study lasting around 12 weeks, patients administered *Leonurus japonicus* extract demonstrated significant reductions in both systolic and diastolic blood pressure relative to baseline measurements. These clinical observations align with pharmacological studies indicating that bioactive compounds in *L. japonicus* may affect vascular function via multiple mechanisms, including the inhibition of angiotensin-converting enzyme (ACE) activity and nitric oxide-mediated vasodilation.^{30,46,47,26} In addition, the herb has been reported to provide symptomatic benefits for certain patients with cardiac arrhythmias, including improvements in heart rate variability. However, clinical evidence in this area remains limited, and further well-designed clinical trials are required to clarify its therapeutic role.

More recently, increasing attention has been directed toward the potential neurological and psychiatric effects of *Leonurus japonicus*. Preliminary clinical observations suggest that preparations containing this herb may help alleviate anxiety symptoms in some patients with generalized anxiety disorder. Improvements in Hamilton Anxiety Rating Scale scores have been reported after several weeks of treatment.^{41,37,47}

Furthermore, only a few clinical studies have examined the potential antidepressant effects of *Leonurus japonicus* wort preparations. In one study, lasting about six weeks, patients with mild to moderate depression who were given an extract of *L. japonicus* showed measurable decreases in their Hamilton

Depression Rating Scale scores. Some studies also suggested that the therapeutic effects observed were comparable to those produced by low-dose selective serotonin reuptake inhibitors (SSRIs), while the incidence of adverse reactions appeared to be relatively lower.^{37,25}

DISCUSSION

The evidence summarized in this review highlights the close relationship between the traditional therapeutic uses of *Leonurus japonicus* and the pharmacological findings reported in modern scientific studies. Growing evidence indicates that the biological activities of this herb are closely associated with its diverse bioactive constituents, particularly alkaloids such as leonurine and stachydrine, as well as several anti-inflammatory diterpenoid compounds.^{47,26,24} These compounds have demonstrated interactions with various molecular targets and signaling pathways, potentially elucidating the historical application of *L. japonicus* in conditions commonly referred to in Traditional Chinese Medicine as “blood stasis” or “Qi stagnation.” Such pathological concepts are frequently linked to disorders such as dysmenorrhea, cardiovascular diseases, and inflammatory conditions.^{47,26}

Although considerable progress has been made in experimental research, clinical evidence supporting the therapeutic effects of *Leonurus japonicus* remains relatively limited. Many current studies rely on *in vitro* experiments or animal models. Although these methods have produced important meronological insights, they cannot fully simulate the complexity of human physiological and pathological states. Therefore, it is necessary to conduct additional clinical research to determine whether the pharmacological effects observed in the experimental setting translate into consistent treatment outcomes in the clinical setting. Another problem is ensuring that the herbal preparations are the same. Most drugs have only one active ingredient, but *L. japonicus* is believed to work by combining the effects of several different chemical constituents. Although this multi-component nature reflects the overall treatment principle of traditional Chinese medicine, it poses challenges to the development of standardized extracts with a unified chemical composition and reliable clinical efficacy.^{27,43,35}

In addition, further research is needed to clarify the specific role of individual compounds in *Leonurus japonicus*. Many pharmacological studies focus primarily on crude extracts, making it challenging to determine the exact contribution of any specific component to the observed biological activity. Although the study of whole extracts may reveal potential

synergy among components, the study of isolated compounds remains essential for determining the specific mechanism of action and identifying candidate drugs.^{40,26} The latest advances in analytical technology and systems biology may provide new opportunities to meet these challenges. Methods such as metabolomics, proteomics, and network pharmacology can facilitate the study of complex interactions among various biologically active ingredients and biological targets. By integrating these modern research strategies, a more comprehensive understanding of the multi-target treatment mechanism related to *L. japonicus* may be achieved.³⁵

CONCLUSION

In a word, *Leonurus japonicus* demonstrates how a traditional medicinal plant rooted in traditional Chinese medicine can enhance modern drug treatment. Many of its biologically active components produce a wide range of pharmacological effects that are closely related to its use in regulating blood flow, relieving blood stasis, and improving women’s health. Although the preclinical data are extensive and encouraging, the transition from traditional to evidence-based treatments remains incomplete. To solve this problem, it is necessary to focus on rigorous clinical verification, establish advanced standardization protocols, and apply contemporary scientific methods to elucidate its intricate mechanisms. By combining traditional knowledge with scientific progress, *Leonurus japonicus* has considerable potential to improve health outcomes, underscoring the need for ongoing collaborative research to fully realize its therapeutic potential.

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