

# Research Progress in Modern Pharmacological Effects of Guizhi Decoction



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**Abstract:** Guizhi Decoction is a classic traditional Chinese medicine (TCM) formula composed of cassia twig (Guizhi), peony root (Shaoyao), fresh ginger (Shengjiang), jujube (Dazao), and licorice (Gancao). It functions to relieve the exterior syndrome and harmonize Ying (nutrient) and Wei (defensive) qi, primarily indicated for treating exterior wind-cold deficiency syndrome. In the formula, cassia twig serves as the monarch herb, with a pungent and warm nature to dispel cold; peony root acts as the minister herb, sour and cool to nourish yin. These two herbs are combined in equal amounts to regulate the balance of Ying (yin) and Wei (yang). Fresh ginger and jujube serve as adjuvant herbs, strengthening the spleen and stomach to promote the generation of qi and blood. Licorice, as the guiding herb, harmonizes the properties of all ingredients, collectively achieving the effects of dispelling external pathogens and harmonizing Ying-Wei. Modern research indicates that Guizhi Decoction and its individual herbs contain multiple active components, such as cinnamaldehyde from cassia twig, paeoniflorin from peony root, 6-gingerol from ginger, and glycyrrhizin from licorice. These components exert synergistic effects through multi-target and multi-pathway mechanisms. The pharmacological actions of Guizhi Decoction include anti-inflammatory, analgesic, anti-atherosclerotic, bidirectional regulation of body temperature, immunomodulatory, and antitumor effects. Clinically, it is widely used for conditions such as arthritis, asthma, cardiovascular diseases, exogenous diseases, and immune-related disorders, with significant therapeutic efficacy. Guizhi Decoction embodies the core TCM theory of "harmonizing Ying and Wei," combining exterior-relieving and tonifying effects to regulate immune function, providing an effective treatment strategy for various diseases. Future research should further explore its multi-target mechanisms and standardize its clinical application to fully realize its therapeutic potential.

**Keywords:** Guizhi Decoction; Traditional Chinese Medicine; Pharmacological Effects; Multi-target Mechanisms; Research Progress

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## 1 Herb Compatibility

The original formula of Guizhi Tang comprises 3 liang of cassia twig, 3 liang of *Paeonia lactiflora*, 3 liang of fresh ginger, 12 broken jujubes, and 2 liang of roasted licorice (Note: "liang" is a traditional Chinese weight unit, approximately 30 g per liang in modern conversion). It exerts the effects of relieving the exterior and harmonizing Ying and Wei (nutrient and defensive qi), and is well recognized as

a classic prescription for treating exterior wind-cold deficiency syndrome, characterized by symptoms such as sweating, headache, aversion to wind, fever, nasal congestion, and retching.

As the monarch herb, cassia twig is pungent and warm in nature, dispelling wind-cold and promoting blood circulation. *Paeonia lactiflora*, sour and cool in nature, nourishes yin as the minister herb. This herb pair is mixed in equal

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amounts to harmonize Ying (yin) and Wei (yang) in accordance with the theory of yin-yang balance, restoring the normal ascending and descending movement of qi in the body. Their scattered (cassia twig) and astringent (Paeonia lactiflora) properties synergistically strengthen the body resistance while dispelling pathogenic factors.

Fresh ginger and jujube act as adjuvant herbs, both tonifying the spleen and stomach. Combined, they invigorate stomach qi to promote vigorous circulation of qi and blood—when healthy qi is abundant, pathogenic factors cannot invade the body. Ginger is mobile without stagnation, assisting cassia twig in relieving the exterior and dispelling cold through diaphoresis; notably, ginger appears in 64% of the prescriptions recorded in the "Febrile Diseases" chapter of the Treatise on Typhoid Fever. Jujube, sweet in flavor and entering the Spleen Meridian (the acquired foundation of the body), tonifies the zang-fu organs. The use of 12 jujubes in the formula benefits the spleen, strengthens Wei qi, replenishes qi, and nourishes yin, while ginger prevents jujube from causing stagnation in the stomach due to its cloying nature.

Licorice, honored as "Guolao" (the "eldest of herbs" in traditional Chinese medicine, TCM), is a common Chinese herb used to harmonize the properties of other herbs in prescriptions. Regardless of whether the paired herbs are yin or yang in nature, or scattered or astringent in property, licorice enhances the circulation of qi and blood, and replenishes deficiencies simultaneously. In summary, cassia twig and Paeonia lactiflora regulate Ying and Wei; ginger and jujube tonify the spleen and stomach; and licorice protects the body's vital essence. The combination of these five herbs is effective in treating exogenous infections, asthma, immune disorders, and cardiovascular diseases caused by Ying-Wei disharmony and invasion of wind-cold pathogens.

## 2 Chemical Composition and Pharmacological Actions

The chemical components of TCM form the material basis of their efficacy. Studies have confirmed that both the GD compound and its individual herbs can effectively inhibit the expression of inflammatory factors and improve the body's immune function. Unlike single chemical drugs, TCM formulas exert synergistic effects through multi-target and multi-pathway regulation. Using ultra-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF/MS), a total of 71

compounds were detected in the plasma and urine of rats administered with GD [1], including 1 from cassia twig, 16 from Paeonia lactiflora, 17 from fresh ginger, 4 from jujube, and 33 from licorice. Cinnamaldehyde, the main active ingredient of cassia twig, accounts for 70%–80% of its volatile oil and is identified as the characteristic component of cassia twig [2], exerting antipyretic, analgesic, antibacterial, anti-inflammatory, and antitumor effects. Paeoniflorin, accounting for 90% of the active ingredients in Paeonia lactiflora, has broad anti-inflammatory, analgesic, and immunomodulatory effects [3]. 6-Gingerol, the main source of ginger's pungent flavor [4], exerts anti-inflammatory, analgesic, anticancer, and cardiogenic effects [5]. Liquiritin, the most abundant active ingredient in licorice saponins, has wide applications in multiple therapeutic fields [6]; glycyrrhizin (a specific component of licorice) exhibits anti-inflammatory, antiviral, and antitumor pharmacological effects. Jujube contains a variety of chemical constituents, including primary metabolites (sugars, amino acids, proteins) and secondary metabolites such as saponins, flavonoids, alkaloids, and triterpenoids [7]. It exerts inhibitory effects in central nervous system, anticancer activity, immune enhancement, and liver protection by increasing the number of immune cells, thereby improving the body's immune capacity and disease resistance.

### 2.1 Anti-inflammatory Effects

All individual herbs in GD possess anti-inflammatory properties. In vitro studies have shown that inflammatory mediators induce increased PGE2 activity in cells; however, cinnamaldehyde and gingerol inhibit PGE2 activity, while paeoniflorin and glycyrrhizin suppress the release of inflammatory factors (e.g., TNF- $\alpha$  and IL-1 $\beta$ ) after GD intervention [8–11]. In animal experiments, GD effectively reduced skin allergic reactions and scratching frequency in mice, confirming its favorable anti-inflammatory efficacy and potential as a therapeutic alternative for inflammatory conditions. The anti-inflammatory effects of GD are mainly mediated through the PGE2, IL-1 $\beta$ , and TNF- $\alpha$  signaling pathways.

### 2.2 Analgesic Effects

Inflammatory mediators such as IL-6 activate nociceptive neurons and enhance inflammatory responses, thereby inducing pain. Studies have demonstrated that GD administration reduces serum inflammatory factor levels and alleviates pain sensation. Quercetin, abundant in all herbs of

GD (cassia twig, *Paeonia lactiflora*, ginger, jujube, and licorice), exerts significant analgesic effects in pain model mice [12]. Researchers measured NO and PGE2 levels in paw skin tissue of pain model mice and detected the expression of COX-2 and iNOS via Western blot (WB). Results showed that cinnamaldehyde in GD decreased IL-1 $\beta$  and TNF- $\alpha$  expression in model mice, while the combination of peony and licorice reduced NO and PGE2 levels—these effects significantly decreased abdominal writhing frequency and pain scores [13]. Additionally, paeoniflorin improves muscle coordination [14], suggesting that these components regulate pain through multiple mechanisms, including modulation of related receptors, anti-inflammatory effects, and antioxidant activity.

### 2.3 Anti-atherosclerotic Effects

Atherosclerosis pathogenesis involves multiple factors, including overexpression of nuclear factor- $\kappa$ B (NF- $\kappa$ B), interleukins (IL-1 $\beta$ , IL-6), and matrix metalloproteinase 9 (MMP9), which activate tumor necrosis factor (TNF) and exacerbate atherosclerosis. Excessive nitric oxide (NO) production increases myocardial oxygen consumption, promotes cellular inflammatory responses, and ultimately triggers myocardial infarction [15]. In a high-fat diet-induced atherosclerotic mouse model, GD administration downregulated TLR4 expression. In a rat model of acute myocardial infarction (established by left coronary artery ligation), intragastric administration of cinnamaldehyde (a key component of GD) prolonged coagulation time and reduced mortality caused by thrombosis. Furthermore, paeoniflorin downregulated NF- $\kappa$ B activity, TNF- $\alpha$ , IL-1 $\beta$ , IL-6 levels, and iNOS protein expression, while upregulating HDL-C levels and modulating the NF- $\kappa$ B pathway [16]. These findings confirm that GD exerts anti-atherosclerotic effects primarily through regulating the Nox4/NF- $\kappa$ B and AMPK pathways, inhibiting atherosclerosis and inflammatory responses, protecting cardiac function, and eliminating excessive free radicals to reduce oxidative stress. Collectively, GD exerts cardiovascular protective effects via multi-target mechanisms, including anti-inflammation, antioxidation, and lipid metabolism regulation [17].

### 2.4 Body Temperature Regulation

GD exerts a bidirectional regulatory effect on body temperature: it warms yang to transform qi and warms the heart,

raising abnormally low body temperature and lowering abnormally high body temperature through diaphoresis and pathogen elimination. PKA and PKC promote heat production by regulating cellular activities; IL-1 $\beta$  (a major pyrogen) is released from peripheral cells, sends signals to the brain, and induces fever through multiple pathways. During fever, the activity and mRNA expression of cyclooxygenase (COX) and prostaglandin E2 (PGE2) increase, along with TRPV4 (a temperature sensor) expression. In a rat model, intragastric GD administration inhibited hypothalamic PKA and PKC activity, reducing febrile responses and decreasing body temperature in febrile model rats. In a hypothermic rat model (established by antadine injection), GD extract increased body temperature. These results indicate that the bidirectional temperature regulation of GD may be associated with PKA and PKC involvement in fever induction.

### 2.5 Immune Regulation

In TCM theory, Wei qi corresponds to immune cells in Western medicine, while Ying qi corresponds to blood—sufficient Ying and Wei qi ensure normal immune system function. Disruption of Ying-Wei balance and immune decline predispose the body to pathogenic invasion. In a mouse model of immune deficiency, GD administration restored T cell levels to normal, suggesting that GD regulates cellular immune function by increasing T cell numbers. This mechanism underpins its efficacy in autoimmune diseases such as allergic rhinitis and skin allergic disorders.

### 2.6 Antitumor Effects

Ying-Wei disharmony impairs triple energizer (san Jiao) qi transformation, leading to turbidity stagnation, blood stasis, and ultimately tumorigenesis. Studies have found that 6-gingerol activates caspase-3 (a key mediator of apoptosis), inducing cancer cell apoptosis and inhibiting malignant tumor metastasis [18]. Quercetin and chalcone (major components of GD) exert anticancer effects by inhibiting viral protein expression, improving energy metabolism, and reducing cancer cell activation—these effects are associated with modulation of inflammatory, immune, and oxidative stress pathways [19, 20].

Table 1 Mechanisms of GD Components in Regulating Disease-Related Signaling Pathways

| TCM Herb                   | Chemical Composition                                                 | Regulated Signaling Pathways/Factors                                | Action Mechanism                                                    |
|----------------------------|----------------------------------------------------------------------|---------------------------------------------------------------------|---------------------------------------------------------------------|
| Cassia twig [21, 22]       | Cinnamaldehyde, cinnamyl alcohol, cinnamic acid, coumarin, quercetin | NO, TNF- $\alpha$ , IL-1 $\beta$ , IL-6, PGE2                       | Reduced inflammatory response, immune regulation                    |
| Paeonia lactiflora [23-26] | Paeoniflorin, benzoylpaeoniflorin, oleanolic acid                    | TLR4, NF- $\kappa$ B, PGE2, NO, TNF- $\alpha$ , IL-1 $\beta$ , IL-6 | Reduced oxidative stress, inhibited apoptosis, reduced inflammation |
| Ginger [27-29]             | Quercetin, 6-gingerol, 8-gingerol                                    | TNF- $\alpha$ , IL-1 $\beta$ , NF- $\kappa$ B                       | Reduced oxidative stress, reduced inflammation                      |
| Jujube [30]                | Oleanolic acid, rutin                                                | IL-6, TNF- $\alpha$                                                 | Immune regulation, reduced oxidative stress                         |
| Licorice [31-33]           | Oleanolic acid, glycyrrhizin, liquiritin, quercetin                  | MAPK, NF- $\kappa$ B, NO, IL-1 $\beta$ , IL-6, PGE2                 | Immune regulation, reduced inflammation, inhibited apoptosis        |

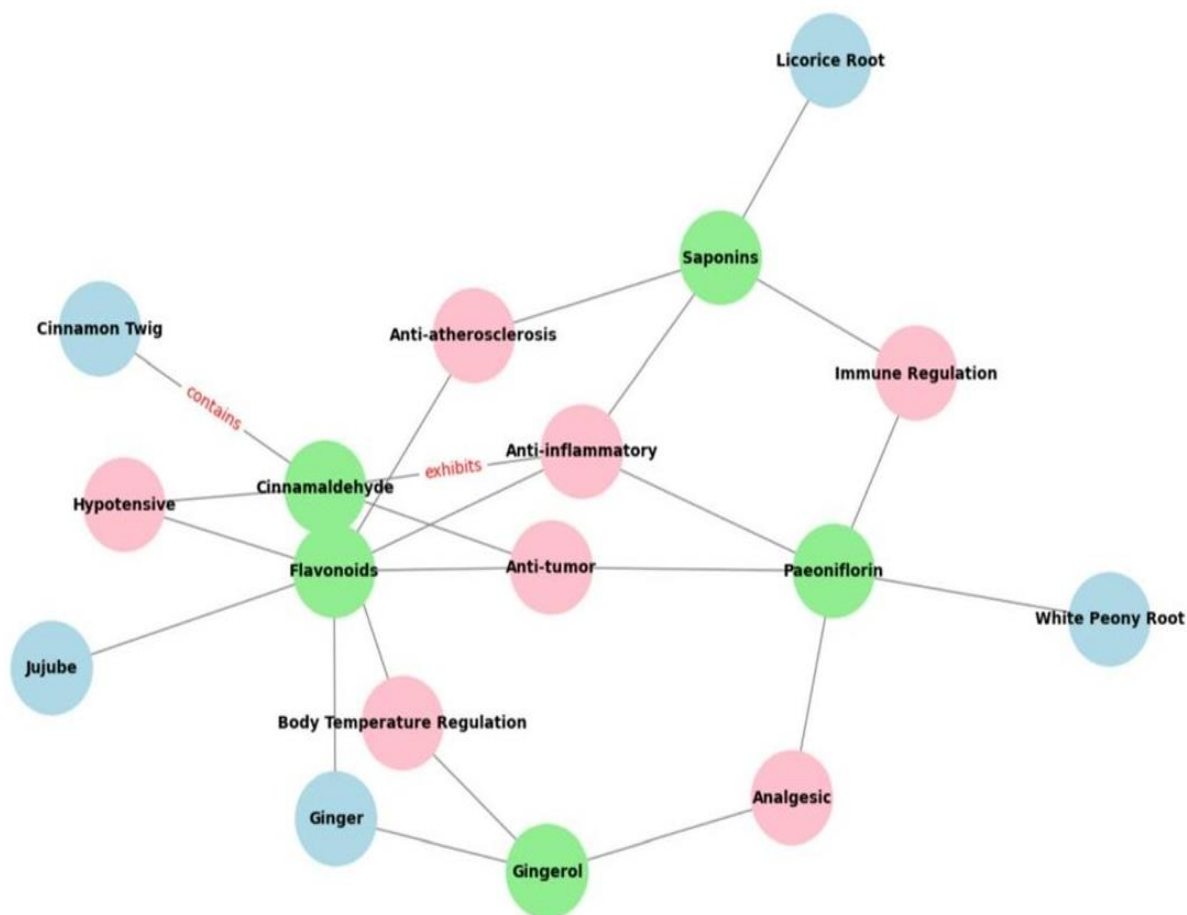


Figure 1 Cinnamon Twig Decoction: Herbs, Active Compounds, and Pharmacological Effects

## 3 Clinical Research

### 3.1 Arthritis

Arthritis is characterized by joint tissue damage caused by chronic inflammation and injury, with significant clinical harm [34]. Inflammatory factors (IL-1 $\beta$ , PGE2, TNF- $\alpha$ ) stimulate erythrocyte deposition, inducing joint inflammation [35]. In a study using a complete Freund's adjuvant-induced arthritis mouse model, animals were divided into a

GD administration group and a normal saline control group. At the end of the experiment, serum TNF- $\alpha$ , IL-1 $\beta$  activity, and PGE2 levels were significantly lower in the GD group than in the control group [36], confirming that GD alleviates inflammatory arthritis by inhibiting inflammatory factor expression. In TCM theory, arthritis is attributed to wind-cold-dampness obstruction, leading to blood stasis and insufficient qi-blood nourishment of joints. The liver governs tendons (which attach to bones and converge at joints); Paeonia lactiflora in GD enters the Liver Meridian, soothing the liver and relieving acute pain [37]. Combined

with cassia twig and ginger (warm in nature, promoting blood circulation and removing stasis, warming meridians and unblocking yang [38]), this herb pair enhances the effects of promoting blood circulation, resolving stasis, and unblocking collaterals, thereby inhibiting joint inflammation.

## 3.2 Asthma

Asthma is a common chronic respiratory disease characterized by cough, wheezing, shortness of breath, and chest tightness. The lungs are "delicate" organs prone to pathogenic invasion, and asthma is driven by sustained inflammatory responses of immune cells—abnormal activation of MAPK and NF- $\kappa$ B pathways by inflammatory factors exacerbates asthma symptoms. In an *in vitro* study of mouse alveolar macrophages (with an induced inflammation model), GD intervention reduced IL-1 $\beta$ , IL-6, and TNF- $\alpha$  levels [39]. UPLC-Q-TOF/MS analysis confirmed that GD is rich in flavonoids and triterpenoid saponins; its key active components (ursolic acid, quercetin, glycyrrhizin) exert anti-asthmatic effects via antihistamine activity, inhibition of inflammatory pathways, and modulation of MAPK signaling. In TCM theory, lung qi disharmony is the core pathogenesis of asthma. Volatile oils in GD (e.g., cinnamaldehyde) exert anti-asthmatic effects with minimal adverse reactions [40], regulating asthmatic inflammatory responses, alleviating cough and wheezing, restoring qi circulation, and reducing airway spasm.

## 3.3 Cardiovascular Diseases

### 3.3.1 Myocardial Ischemia

The cardiovascular system (heart, blood vessels, and lymphatic vessels) circulates blood, delivers nutrients, and nourishes tissues. Myocardial ischemia is a pathological state where oxygen supply fails to meet metabolic demands due to impaired nutrient delivery, potentially progressing to acute myocardial infarction (complicated by arrhythmia, shock, or heart failure). Western medicine primarily uses vasodilators for treatment, which carry risks of bleeding and liver/kidney damage. In TCM theory, myocardial ischemia is mainly caused by cold stasis and vascular stenosis, leading to blood flow obstruction; treatment focuses on promoting blood circulation, resolving stasis, and warming the heart. In GD, cassia twig increases coronary blood flow, while ginger warms the heart—together, they promote venous circulation.

The heart governs blood vessels, and blood production/circulation depend on the spleen and heart [41, 42]; jujube enters the Heart and Spleen Meridians, tonifying blood vessels, warming and nourishing blood, and preventing recurrent myocardial ischemia. The formula alleviates myocardial ischemia and vascular obstruction, improves cardiac function, and enhances blood flow/metabolism, making it effective for myocardial ischemia caused by vascular stenosis, obstruction, or blood stasis.

### 3.3.2 Hypertension

Hypertension is a cardiovascular disease that, if uncontrolled, leads to complications such as myocardial infarction and heart failure [43]. Autonomic nervous imbalance (overactivation of the sympathetic nervous system) is a key pathogenic factor [44]. In TCM theory, hypertension is rooted in a combination of deficiency and excess; liver fire stirring wind causes qi imbalance, leading to headache, dizziness, and blurred vision [45]. Treatment focuses on pacifying the liver, extinguishing wind, and regulating Ying-Wei. *Paeonia lactiflora* in GD enters the Liver Meridian (sour in flavor, descending in nature), reducing liver fire and soothing the liver. Its active component (paeoniflorin) dilates blood vessels by increasing NO levels [46]; combined with volatile oils (cinnamaldehyde, gingerol), it enhances smooth muscle relaxation and reduces angiotensin levels. A 1:1 combination of cassia twig and *Paeonia lactiflora* reduces nerve growth factor (NGF), growth-associated protein 43 (GAP43), and tyrosine hydroxylase (TH) levels, inhibiting sympathetic overactivity and exerting antihypertensive effects. Unlike Western medicine (which uses receptor blockers), TCM treats hypertension based on syndrome differentiation, regulating zang-fu function and overcoming the limitation of lifelong medication [47].

## 3.4 Exogenous Diseases

Ying-Wei balance is critical for normal bodily function. The Huangdi Neijing (China's first medical theoretical monograph) states: "When Wei qi is insufficient, pathogenic factors stagnate". GD is a representative prescription for treating exterior wind-cold deficiency syndrome (symptoms: headache, fever, sweating, floating and slow/weak pulse) and remains widely used in modern clinical practice for exogenous diseases [48]. Ginger (warm and dispersive in nature) is a core herb for diaphoresis; combined with cassia twig, it warms the body, dispels pathogens via sweating, and harmonizes Ying-Wei. In animal

models, GD administration reduces inflammatory factor expression, while cinnamaldehyde decreases PGE2 and TRPV4 levels (cinnamaldehyde inhibits cyclooxygenase, which catalyzes PGE2 production from arachidonic acid, exerting antipyretic effects) [49]. Additionally, cAMP signaling (a thermoregulatory factor) is inhibited during fever and activated during hypothermia—GD modulates this pathway to restore normal body temperature.

## 3.5 Immune Diseases

### 3.5.1 Allergic Rhinitis

Allergic rhinitis in TCM is attributed to kidney yang deficiency and external wind invasion, leading to spleen-lung deficiency; treatment focuses on restoring spleen-lung transportation and transformation. GD warms yang and regulates zang-fu function, improving rhinitis symptoms with a low recurrence rate in clinical screening [50]. In a guinea pig model of allergic rhinitis (established by sensitizer injection), GD administration significantly reduced nasal secretions and sneezing frequency, suggesting that GD modulates Ying-Wei balance and immune function in early-stage allergic rhinitis.

### 3.5.2 Urticaria

Urticaria is an immune disease caused by multiple factors (physiological, emotional, environmental), with immune deficiency, yin-yang imbalance, and external pathogen invasion as key pathogenesis [51]. TCM classifies its etiology as internal/external wind: external wind (yang pathogen) invades the Taiyang Meridian, while internal wind arises from abnormal Taiyang qi transformation, leading to migratory wind rash and pruritus [52]. Western medicine uses antihistamines (effective but with side effects on organs), while TCM focuses on tonifying the spleen (the foundation of acquired health) [53, 54]. Jujube (red in color, sweet in flavor, entering the Heart Meridian) is rich in amino acids, alkaloids, polyphenols, and vitamins, exerting immunomodulatory effects [55]. The Huangdi Neijing notes that "five grains nourish the body and prevent pathogenic invasion"—normal spleen-stomach function tonifies the zang-fu organs, nourishes blood/meridians, and strengthens the body barrier. Jujube combined with licorice harmonizes Ying-Wei, tonifies the spleen-stomach, and stabilizes the middle energizer; paired with *Paeonia lactiflora*, it nourishes stomach yin and soothes liver yang. *Cassia twig* and ginger promote yang and dispel pathogens.

Clinical case analysis shows that GD treatment achieves a high recovery rate and significant efficacy in urticaria, with immunomodulation as a core therapeutic mechanism.

## 4 Summary

As a classic TCM prescription, Guizhi Decoction contains active components including volatile oils, glycosides, flavonoids, and phenolics, exerting anti-inflammatory, analgesic, antipyretic, anti-asthmatic, and anti-atherosclerotic effects. Guided by TCM theory, GD combines dispersing and tonifying herbs to dispel exterior pathogens while regulating immune function. Clinically, it is widely used for exogenous diseases, immune allergic disorders, cardiovascular diseases, and chronic inflammatory conditions. Further research on its multi-target mechanisms and clinical application standardization will help unlock the full therapeutic potential of this classical prescription.

## Conflicts of Interest

All authors declare no conflicts of interest regarding the publication of this paper.

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