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# Network pharmacology-based prediction of *Farfarae Flos* and *Pseudostellaria heterophylla* in asthma treatment

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**Abstract**: **Background**: Asthma is a prevalent reversible airway disorder. Traditional Chinese medicine herbs *Farfarae Flos* and *Pseudostellaria heterophylla* may have therapeutic effects, but their mechanisms remain unclear. **Objectives**: To identify active components, key targets and molecular mechanisms of these herbs in asthma treatment via network pharmacology, molecular docking and gene expression validation. **Methods**: Active compounds and targets were screened from TCMSP (OB≥30%, DL≥0.18). Asthma-related targets were retrieved from GeneCards, DrugBank and OMIM. PPI network analysis, GO/KEGG enrichment and molecular docking were performed. PTGS2 expression was validated using GEO data. **Results**: A total of 176 targets were identified for Farfarae Flos, 74 for Pseudostellaria heterophylla and 242 for asthma, yielding 15 common targets. GO enrichment involved cytokine activity and prostaglandin-endoperoxide synthase activity; KEGG highlighted HIF-1, IL-17, C-type lectin and TNF pathways. Docking predicted that quercetin, luteolin and kaempferol had strong binding to PTGS1/PTGS2. PTGS2 expression was significantly upregulated in asthma patients versus healthy controls. **Conclusion**: These herbs may exert predicted potential activity through multi-component, multi-target and multi-pathway mechanisms, with PTGS1/PTGS2 as core targets and quercetin/luteolin/kaempferol as potential active ingredients.

**Keywords**: Asthma; *Farfarae Flos*; Molecular docking; Network pharmacology; *Pseudostellaria heterophylla*; PTGS2; Transcriptomics

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## INTRODUCTION

Asthma is a complex medical condition characterized by persistent inflammation. Because the airways are hyperresponsive and can reverse any breathing obstruction, this condition most commonly presents with recurrent symptoms such as wheezing, breathlessness, chest tightness, or coughing (Liu *et al*., 2026; Portacci *et al*., 2026). Globally, the number of individuals affected by asthma has reached around 300 million, with its occurrence showing an upward trend in a majority of nations (Rabe *et al*., 2023). In China, 3.4%-8.3% of asthma patients suffer from severe asthma (Chen *et al*., 2026). Although standard treatments such as inhaled glucocorticoids combined with long-acting $\beta_2$ receptor agonists can control symptoms in most patients, 5% to 10% of those with severe or refractory asthma respond poorly to conventional therapy (Chandrasekara and Wark, 2024). Frequent acute attacks lead to progressive damage to lung function, seriously affecting the quality of life and imposing a heavy healthcare burden (Benfante *et al*., 2023; Busse *et al*., 2022; Liu *et al*., 2026). Currently, treatment strategies for asthma mainly focus on anti-inflammation and bronchodilation, but challenges remain in clinical practice, including poor long-term medication adherence, hormone resistance and adverse drug reactions (Cazzola *et al*., 2022). Against this backdrop, the distinctive benefits of traditional Chinese medicine (TCM) in addressing asthma have garnered increasing interest in recent years, with substantial clinical data revealing that the concurrent use of various herbal components can effectively decrease the occurrence of acute asthma attacks, enhance respiratory function and reduce reliance on steroid medications (Jiang *et al*., 2026; Liu *et al*., 2025). Given these therapeutic benefits, an increasing number of patients have come to accept and actively seek TCM as a complementary treatment option to achieve better asthma control and reduce the frequency of acute exacerbations.

The chemical composition of *Farfarae Flos* is complex and a variety of active ingredients, such as terpenes, flavonoids, organic acids, alkaloids and volatile oils, have been isolated and identified (Zhou *et al*., 2024). Modern pharmacological research indicates that *Farfarae Flos* possesses various activities, including antitussive, expectorant, antioxidant, neuroprotective and anti-tumor effects, among which anti-inflammatory and anti-asthmatic effects are the most prominent (Chen *et al*., 2021). The chemical composition of *Pseudostellaria heterophylla* is rich and diverse. It mainly contains active ingredients such

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as polysaccharides, cyclic peptides, saponins, volatile oils, alkaloids and phenols. Among them, polysaccharides and cyclic peptide compounds from *Pseudostellaria heterophylla are considered characteristic active substances* (Zhang *et al*., 2026). Modern pharmacological research has shown that Pseudostellaria heterophylla has immunomodulatory, anti-inflammatory, antioxidant, myocardial-protective, anti-stress and antitussive effects (Wang *et al*., 2025). Thus, both *Farfarae Flos* and *Pseudostellaria heterophylla* possess complex chemical compositions and act on a wide range of targets. This approach helps to identify the most promising active pharmaceutical ingredients and critical targets.

This study integrates network pharmacology with molecular docking to systematically explore the potential active components, key targets and associated signaling pathways of Farfarae Flos and Pseudostellaria heterophylla in the treatment of asthma, with particular emphasis on the prostaglandin endoperoxide synthase (PTGS) family.

## MATERIALS AND METHODS

***Drug-disease target screening***

To elucidate the pharmacological effects of Farfarae Flos and Pseudostellaria heterophylla, a multidimensional and integrated analytical approach was employed in this study. First, the chemical components of these two herbs were obtained from the Traditional Chinese Medicine Systems Pharmacology Database (TCMSP, <https://www.tcmsp-e.com/>). Compounds were screened according to ADME (Absorption, Distribution, Metabolism and Excretion) criteria and those with an oral bioavailability (OB) ≥ 30% and drug-likeness (DL) ≥ 0.18 were retained. Subsequently, the corresponding therapeutic targets of these components were collected. Target gene names were standardized using the UniProt database (http://www.uniprot.org/).

The asthma-related targets were detected by searching the GeneCards database (relevance score ≥10), DrugBank and Online Mendelian Inheritance in Man (OMIM) using the keyword “asthma; the Farfarae Flos target points, Pseudostellariae heterophylla target points and asthma-related targets were imported into the Venn2.1 online tool for intersection analysis. The 15 "common potential targets" in this study are defined as the intersection of the three, namely (*Farfarae Flos* target ∩ *Pseudostellariae* target) ∩ asthma-related target. In other words, the targets that enter subsequent analysis must meet the following two conditions at the same time: (i) present in the active ingredient targets of the two medicinal materials, *Farfarae Flos* and *Pseudostellariae* heterophylla; (ii) simultaneously included in the asthma target databases such as GeneCards and OMIM.

***Establish protein–protein interaction (PPI) network***

To investigate possible relationships among common genes, the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) database was used, with the species set to “Homo sapiens”. A cutoff value of ≥ 0.4 was used to construct the PPI network. Following export of the network data in Tab-Separated Values (TSV) format, it was further refined by using Cytoscape 3.8.1. Topological analysis uses the following three indicators to evaluate the importance of each node in the network: (i) degree centrality (Degree Centrality); (ii) betweenness centrality (Betweenness Centrality); (iii) closeness centrality (Closeness Centrality). After this processing stage, the software was also applied to calculate node attributes and produce the visual displays of molecular interactions.

***Enrichment analysis***

To better understand the biological functions and signaling pathways associated with the 15 common potential targets, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were performed using the Database for Annotation, Visualization and Integrated Discovery (DAVID) (https://david.ncifcrf.gov/). GO analysis covers three subcategories: Biological Process (BP), Cellular Component (CC) and Molecular Function (MF). The statistical significance threshold was set at an adjusted p-value < 0.05. Since enrichment analysis involves the simultaneous testing of multiple GO/KEGG entries, the Benjamini-Hochberg (BH) method was applied to correct the original p-values for multiple testing in order to control the False Discovery Rate (FDR) and the FDR-corrected p-values were reported. Finally, GO/KEGG entries with corrected p-value <0.05 and enriched gene number ≥ 2 were selected as significant enrichment results; in order to clearly display the core enrichment direction, the top 19 BP entries, the top 5 CC entries, the top 8 MF entries and the top 20 KEGG pathways in the results section were visually presented in the results section.

***Molecular docking***

The 3D structures of PTGS1 (PDB ID: 6Y3C) and PTGS2 (PDB ID: 5IKR) were retrieved from the PDB and prepared using PyMOL by removing water molecules, redundant ligands and non-functional residues, followed by hydrogen addition and structure optimization. Ligands were retrieved from PubChem, converted using OpenBabel and prepared in AutoDockTools, where Gasteiger charges and rotatable bonds were assigned. To validate the docking protocol, redocking of the native co-crystallized ligands was performed for both PTGS1 and PTGS2. The Root Mean Square Deviation (RMSD) between the redocked poses and the crystallographic conformations was calculated and values below 2.0 Å confirmed the reliability of the docking parameters and scoring function.

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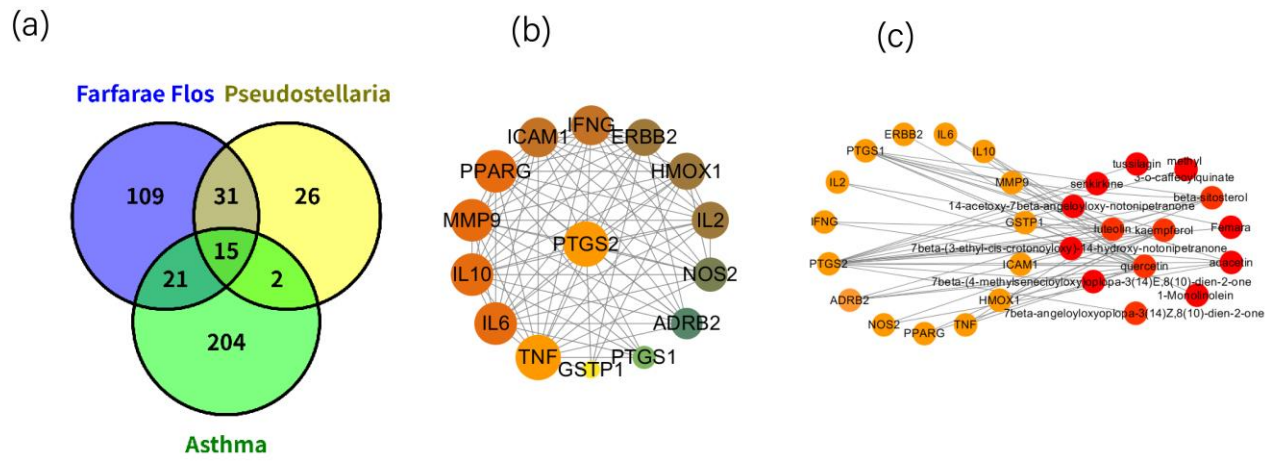



**Fig. 1**: Identification of potential targets and network analysis of Farfarae Flos and Pseudostellaria heterophylla against asthma. (a) Venn diagram. illustrating the overlap between drug targets for each herb and asthma-related genes. The intersection represents the common potential targets of the herbs for treating asthma; (b) PPI network of the 15 common targets. In this network, nodes correspond to target proteins, while edges signify their interactions. Nodes are color-coded and sized according to their degree of connectivity (larger = higher degree), indicating their topological importance in the network; (c) Drug-component-target-disease network. This network visualizes the multi-compound, multi-target relationships. Colour distinguishes different entity types (orange: active components; red: targets). Edges indicate direct interactions between connected nodes.

Celecoxib and aspirin were used as positive control ligands to benchmark the docking protocol against known PTGS inhibitors. The coordinates of the native co-crystallized ligand defined the active pocket. Docking was performed using AutoDock Vina with a grid box (center: 35, 30, 30; size: 20 × 20 × 20 A) and exhaustiveness = 64. Each ligand-receptor pair underwent 10 independent docking runs to ensure stability. The lowest binding energy (kcal/mol) and RMSD values were reported. Visualization and interaction analysis were conducted in PyMOL. A heatmap of binding affinities was generated using GraphPad Prism 10.1.2.

***Transcriptomic validation***

To validate the expression of core targets, two independent asthma transcriptomic datasets were obtained from the GEO database: GSE64913 (primary validation set) and GSE27876 (independent corroboration set). Differential expression analysis was performed using the GEO2R online tool. For each dataset, probe IDs were mapped to gene symbols using official platform annotation files and multiple probes for the same gene were averaged. Batch effects were minimized by selecting datasets from the same platform and confirming sample comparability through phenotype annotation. For each target, an independent-samples t-test was used to compare mean expression levels between the asthma and healthy groups.

## RESULTS

***Identification of potential targets***

After conducting database searches, the number of potential targets was determined to be 176 for Farfarae Flos, 74 for Pseudostellaria heterophylla and 242 for asthma-related conditions. Overlap analysis using Venny 2.1 identified 15 common potential targets, including PTGS1, PTGS2, Adrenergic Receptor Beta 2 (ADRB2), Nitric Oxide Synthase 2 (NOS2), Tumor Necrosis Factor (TNF), etc. (Fig. 1a; Table S1). Subsequently, to delve into the relationship between these 15 potential targets and their associated active components, Cytoscape 3.8.1 was employed to construct both the PPI network and the drug-ingredient-target-disease network visualization (Figs. 1b and 1c; Table S2). To further prioritize the core targets for subsequent validation, the network topological features of the 15 shared targets were evaluated based on the PPI network. Among them, PTGS2 and PTGS1 ranked highest in degree centrality and betweenness centrality (first and second, respectively) and were therefore selected as the core targets for further molecular docking and Molecular Dynamics (MD) Simulation.

***GO and KEGG pathway enrichment analysis***

To determine the functional roles of these 15 shared targets, a detailed functional enrichment analysis was carried out. GO enrichment analysis results predicted that these targets are involved in various biological functions, including cytokine activity, prostaglandin-endoperoxide synthase activity, negative regulation of apoptotic process and immune response (Figs. 2a-2c; Table S3). KEGG enrichment analysis results predicted that the HIF-1, IL-17 and TNF signaling pathways were significantly enriched (Fig. 2d; Table S4).

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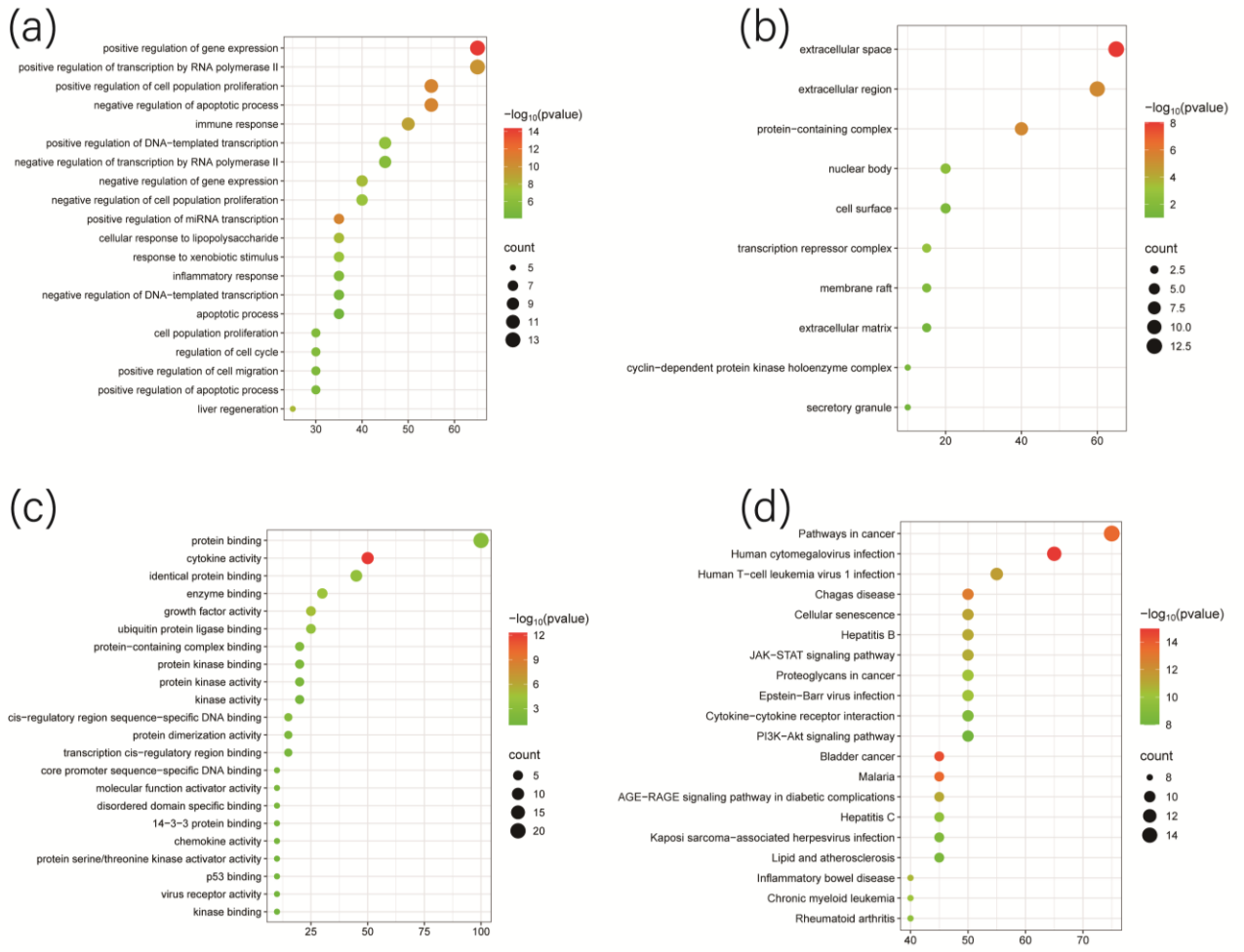



**Fig. 2**: GO functional and KEGG pathway enrichment analyses. (a) GO biological process (BP) enrichment analysis; (b) GO cellular component (CC) enrichment analysis; (c) GO molecular function (MF) enrichment analysis; (d) KEGG pathway enrichment analysis.

***Molecular docking***

Molecular docking prediction results predicted that quercetin, luteolin and kaempferol all predicted potential binding abilities to the active pockets of PTGS1 and PTGS2 (Figs. 3a–g). For PTGS1, the predicted binding energies of the three compounds are −7.8, −8.0 and −7.6 kcal/mol, respectively; for PTGS2, they are −8.5, −8.5 and −8.0 kcal/mol, respectively. All predicted binding energies are below −7.0 kcal/mol, indicating that all three have good theoretical binding affinities. However, it should be pointed out that the binding energy difference between each compound is small (< 0.5 kcal/mol), which is within the inherent error range of the molecular docking calculation method, so it is not appropriate to rank the affinities of different compounds based on this. The corresponding PDB IDs and detailed molecular docking data are presented in table1.

***MD simulation***

To validate the reliability of the docking parameters, redocking of the co-crystallized ligands into PTGS1 and PTGS2 was performed. The RMSD values were 1.754 Å and 0.739 Å, respectively, both below the accepted threshold of 2.0 Å, confirming the reproducibility of the docking protocol. Additionally, docking of the known PTGS inhibitors aspirin and celecoxib yielded binding energies of −5.8 and −6.3 kcal/mol, respectively, providing a reference context for our candidate compounds. Furthermore, a 100 ns MD simulation of the quercetin-PTGS2 complex revealed stable binding throughout the trajectory, with backbone RMSD below 3.5 Å (Figs. 4a-4f; Table S5).

***Transcriptomic analysis***

PTGS2 expression was analyzed in two independent GEO datasets: GSE64913 and GSE27876. In both datasets, PTGS2 was significantly upregulated in asthma patients compared with healthy controls ($p < 0.05$). Detailed expression data are summarized in table 2.

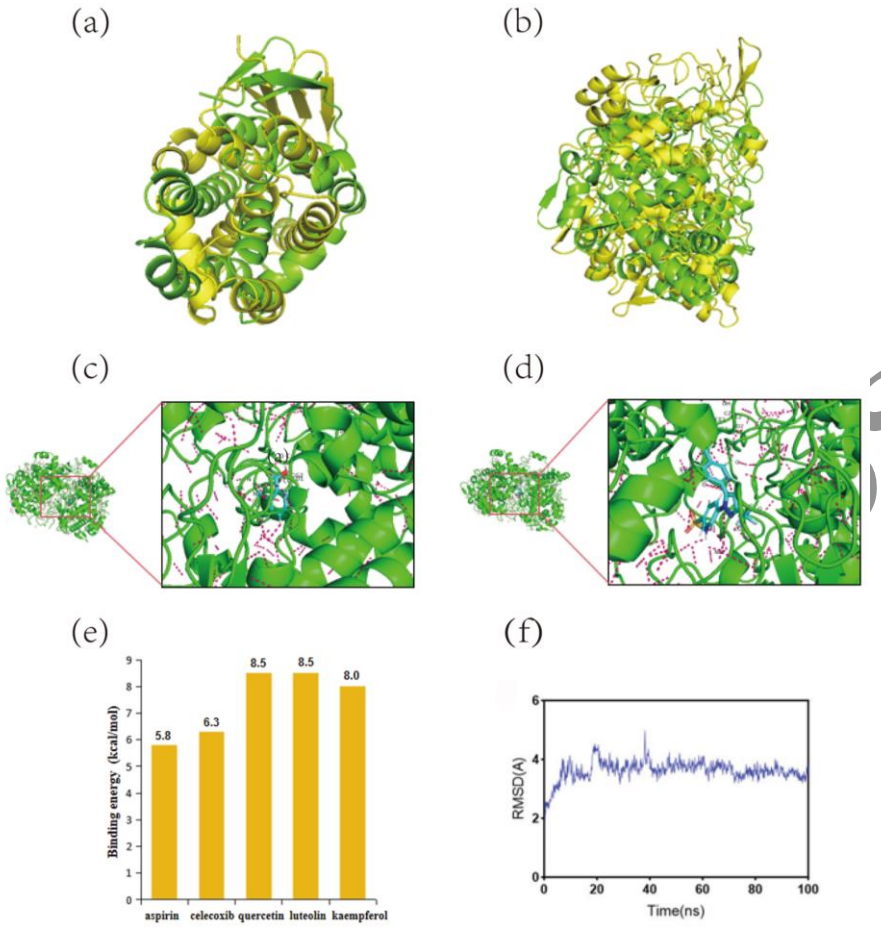



**Fig. 4**: Validation of docking protocol and dynamic stability assessment. (a-b) Redocking validation of PTGS1 (PDB ID: 6Y3C) and Redocking validation of PTGS2 (PDB ID:5IKR); Co-crystallized ligands (green) and redocked poses (yellow) are superimposed, with RMSD values of 1.754 Å and 0.739Å, respectively; (c) aspirin-PTGS2, The molecular docking energy is -5.8kcal/mol; (d)celecoxib-PTGS2, The molecular docking energy is -6.3kcal/mol; (e) Comparative predicted binding energies of positive-control inhibitors (aspirin and celecoxib) and three flavonoid compounds against PTGS2. (f) RMSD trajectory of the quercetin-PTGS2 complex over 100 ns MD simulation, showing equilibration and stable binding (Throughout the entire production process, the main chain RMSD is approximately equal to 3.5a).

**Table 1**: Summary of molecular docking results.

| Target protein | PDB ID | Binding energy (kcal/mol) / quercetin | Binding energy (kcal/mol) / luteolin | Binding energy (kcal/mol) / kaempferol |
|---|---|---|---|---|
| ADRB2 | 6KR8 | -6.8 | -7.3 | -6.7 |
| NOS2 | 5XN3 | -6 | -5.9 | -5.4 |
| PPARG | 2Q59 | -6.6 | -6.7 | -7.2 |
| TNF | 2E7A | -6.2 | -5.5 | -6 |
| PTGS1 | 6Y3C | -7.8 | -8 | -7.6 |
| HMOX1 | 1N3U | -6 | -6.1 | -6.4 |
| ICAM1 | 1D3L | -4.9 | -5.7 | -5.1 |
| GSTP1 | 5DAL | -5.8 | -6.9 | -6.7 |
| MMP2 | 1GKD | -6.1 | -6.6 | -6 |
| PTGS2 | 5IKR | -8.5 | -8.5 | -8 |
| IL10 | 2H24 | -6.2 | -6 | -5.9 |
| IL6 | 1ALU | -7.7 | -7.9 | -8.3 |
| ERBB2 | 7PCD | -7.1 | -6.5 | -7.5 |
| IL2 | 1IRL | -6 | -5.5 | -5.1 |
| IFNG | 1HIG | -4.5 | -6.4 | -5.7 |

Molecular docking and binding ability: > -5kcal/mol: relatively weak; -5 to -7kcal/mol: Moderate; < -7kcal/mol: relatively strong. Lower (more negative) values indicate higher affinity.

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**Table 2**: PTGS2 expression in healthy controls and asthma patients (GSE64913 and GSE27876 datasets).

| | Gene expression in healthy people | Gene expression in asthma patients | *p*. value |
|---|---|---|---|
| GSE64913 | 3.66 ± 0.09 | 4.50 ± 0.23 | 0.001 |
| GSE27876 | 8918.84 ± 446.3 | 11922.17 ± 1007.3 | 0.02 |

Values are presented as mean ± SD. P values were calculated using independent samples t-test.

## DISCUSSION

Asthma is a chronic inflammatory disorder of the airways with high heterogeneity (Siu *et al*., 2026). Due to differences in genetic background, environmental exposure and immune response patterns, asthma patients exhibit significant individual heterogeneity, which contributes to the complex pathogenesis and positions asthma as a major global public health challenge(Walls and Marshall, 2026). Traditional Chinese medicine has extensive clinical experience treating asthma and provides distinct benefits in therapy based on pattern differentiation. *Farfarae Flos* and *Pseudostellaria heterophylla* are TCM formulas used for asthma.

Network pharmacology analysis identified the key active ingredients of *Farfarae Flos* and *Pseudostellaria heterophylla*, including quercetin, luteolin and kaempferol. Previous studies have reported that quercetin attenuates bronchial inflammation and structural airway changes in asthmatic mice by blocking the TGF-β1/SMAD signaling cascade(Fang *et al*., 2023). Kaempferol, which exhibits multiple biological functions, encompasses anti-inflammatory, antioxidant and immunomodulatory properties(Zhao *et al*., 2026). Luteolin, another bioactive flavonoid, can markedly suppress the activation of classical inflammatory signaling cascades, such as NF-κB and MAPK, thereby lowering the expression of inflammatory genes and consequently reducing the secretion of pro-inflammatory cytokines such as TNF-α, IL-1β and IL-6(Singh., 2026).

KEGG enrichment analysis predicted that common targets were significantly enriched in HIF-1, IL-17, C-type lectin receptor and TNF signaling pathways. Notably, the screened flavonoids, such as quercetin and luteolin, have been reported to alleviate airway inflammation by inhibiting the HIF-1α pathway and by modulating the Th17/Treg balance to suppress IL-17 production. More importantly, these pathways do not act in isolation: the TNF, HIF-1α and IL-17 pathways are cross-regulated and C-type lectin receptor signaling contributes to the allergen response by promoting Th2/Th17 differentiation. In the PPI network, PTGS2 (degree centrality = 14) is widely connected to the upstream and downstream genes of the above pathways, suggesting that it may be a key node mediating the coordinated regulation of multiple pathways. It should be emphasized that the primary basis for core target nomination was network topological centrality (degree and betweenness centrality), ensuring that target selection was driven by system-level connectivity rather than by computational binding energies. Accordingly, molecular docking and MD simulations served strictly as post-selection validation approaches to evaluate binding modes and dynamic stability and played no role in the initial target screening process.

In summary, the anti-asthma effect of this drug may be due to the coordinated regulation of the above-mentioned pathway network by multiple active ingredients. It is worth noting that although the OB/DL threshold used for active ingredient screening has certain limitations—such as the possibility of excluding ingredients with low bioavailability but still efficacy—the candidate ingredients screened in this study are all the main pharmacodynamic substances of this formula and are well connected with the core targets, suggesting that the current screening has captured the core substance basis of anti-asthmatic activity.

The role of PTGS2 (COX-2) and its downstream metabolite prostaglandin E2 (PGE2) in asthma is far from simple "pro-inflammatory" or "anti-inflammatory" effects, but rather a highly complex, context-dependent regulatory network. Multiple studies have demonstrated that endogenous PGE2 derived from COX-2 plays an important protective role in the airways: PGE2 inhibits eosinophil chemotaxis via the EP2 receptor and it also suppresses ILC2 activation and type 2 cytokine production through the EP4/cAMP signaling pathway. However, PTGS2/PGE2 also has a potential pathogenic role in asthma. On the other hand, PGE2 may also drive pathological processes under certain conditions. Chronic and sustained high concentrations of PGE2 can promote Th2-type immune bias, enhance eosinophil infiltration, induce excessive airway mucus secretion and stimulate smooth muscle proliferation, thereby exacerbating airway hyperresponsiveness and remodeling. In this study, the transcription level of PTGS2 was observed to be significantly up-regulated in asthma patients based on the GEO database and quercetin, luteolin and kaempferol were predicted through molecular docking to have better binding affinity to PTGS2. These findings only suggest that PTGS2 is a candidate relevant target in asthma. In view of the bidirectional regulatory characteristics of the PTGS2/PGE2 pathway, future research should not stop at simple intervention of PTGS2 expression level or enzyme activity, but should further explore the differential functions of different EP receptor subtypes in different stages of asthma and in different cell types.

In the GSE64913 dataset, PTGS2 expression (probe 204748_at) predicted an upward trend in the asthma group and the difference was statistically significant ($p=0.0014$). This finding was further cross-validated in the independent cohort GSE27876 ($p<0.05$), suggesting that PTGS2 expression changes are consistent across different asthma cohorts and may serve as a potential key target for asthma. Mechanistically, PTGS2 expression is very low in the resting state but is rapidly induced in airway epithelial cells, smooth muscle cells, macrophages and fibroblasts upon exposure to pro-inflammatory factors or oxidative stress. Activated PTGS2 catalyzes the conversion of arachidonic acid to lipid mediators such as prostaglandin E2 (PGE2) (Cebulla *et al*., 2023; Martín-Vázquez *et al*., 2023). Notably, the functional consequences of PTGS2/PGE2 signaling in asthma are highly context-dependent: acute low concentrations of PGE2 may induce bronchodilation, whereas chronic sustained high concentrations promote Th2-biased immune responses, enhance eosinophil infiltration, induce excessive airway mucus secretion and stimulate smooth muscle proliferation, thereby exacerbating airway hyperresponsiveness and remodeling(Almeida *et al*., 2024; Bok *et al*., 2025).

In contrast, PTGS1 participates in normal physiological processes such as safeguarding the gastric mucosa, promoting platelet clumping and controlling renal blood flow(Barekat *et al*., 2026). PTGS1 activity is significantly enhanced in mast cells from patients with allergic asthma and inhibition of PTGS1 can reduce antigen-induced TXA2 production and airway contraction (Johnsson *et al*., 2021). Molecular docking findings indicated that the primary bioactive components (quercetin, luteolin and kaempferol) possessed favorable predicted binding affinities towards PTGS2 and PTGS1. These computational findings suggest that these compounds may modulate the upstream signaling of the aforementioned inflammatory pathways through targeting PTGS1/PTGS2, potentially achieving multi-target and multi-level effects.

While discussing the therapeutic potential of *Farfarae Flos*, its safety issues cannot be ignored. *Farfarae Flos* contains a variety of pyrrolizidine alkaloids (PAs), mainly including senkirkine, senecionine and their N-oxides. This type of alkaloid has clear hepatotoxicity and can cause severe liver damage such as hepatic veno-occlusive disease. It should be emphasized that the active ingredients screened in this study (quercetin, luteolin and kaempferol) are all flavonoids and do not belong to the pyrrolizidine alkaloids, so they are not involved in the above-mentioned hepatotoxicity risks. However, given that Farfarae Flos itself contains hepatotoxic pyrrolizidine alkaloids, strict control of pyrrolizidine alkaloid content and quality standards must be implemented if preparation development or clinical translation is undertaken in the future. It is recommended that current research on quality standards be consulted to establish a limit-setting method for pyrrolizidine alkaloids in Farfarae Flos, thereby ensuring clinical drug safety.

Several limitations of this study should be acknowledged. First, all findings are computational predictions and require further verification through *in-vitro* enzyme activity assays, cell-based functional studies and animal models of asthma. Second, the transcriptomic validation was limited to observing PTGS2 expression levels in two public datasets, which only supports disease association and does not validate the proposed multi-target, multi-pathway mechanisms. Third, although a GeneCards relevance score threshold of $\geq 10$ was chosen to balance target set size and biological relevance, this cutoff may exclude genes with lower scores but critical roles in specific asthma subtypes, tissues, or pathological stages; the GeneCards scoring system itself is inherently biased by the volume of existing literature, potentially over-representing well-studied genes while under-covering newly discovered or rare genes. Future studies integrating multi-tissue transcriptomic data from asthma patients could identify tissue- and state-specifically expressed disease genes, providing a more comprehensive target profile. In addition, integrating multiple TCM databases with ADMET prediction platforms and including literature-reported active ingredients as supplementary candidates would further expand the compound spectrum and provide a more complete pharmacodynamic profile of this herb pair. Fourth, the intersection strategy [(*Farfarae Flos* targets $\cap$ *Pseudostellaria heterophylla* targets) $\cap$ asthma targets] was adopted to focus on synergistic mechanisms of the herb pair; although consistent with the study's aim, it may exclude targets identified by only one of the two herbs. Fifth, molecular docking results represent binding predictions rather than functional inhibition and the modest binding energy differences among compounds should not be interpreted as a ranking of biological activity. One limitation of this study is the absence of a negative control in the molecular docking analysis, which would help exclude non-specific binding. Future studies incorporating structurally unrelated compounds as negative controls in COX enzyme assays will further validate the specificity of flavonoid–PTGS binding. Finally, although the active ingredients identified in this study are flavonoids and do not carry the hepatotoxicity risk associated with pyrrolizidine alkaloids, the crude herb *Farfarae Flos* itself contains such alkaloids and future translational development must implement strict quality control measures.

Collectively, these computational findings provide a testable hypothesis for the anti-asthmatic mechanisms of the *Farfarae Flos* and *Pseudostellaria heterophylla*, warranting further experimental investigation.

## CONCLUSION

In summary, this study used a strategy that combined network pharmacology, molecular docking and transcriptome analysis to predict the potential active ingredients and candidate targets (PTGS1 and PTGS2) of *Farfarae Flos* and *Pseudostellaria heterophylla* for the treatment of asthma. However, it should be emphasized that all findings in this study are computational prediction results and cannot yet be used as pharmacodynamic evidence. The predicted binding affinity and pathway correlation need to be further verified through *in-vitro* enzyme activity experiments, cell function studies and asthma animal models.

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***Authors' contributions***
Yunlai Wu: Conceptualization, validation, formal analysis and writing-original draft preparation; Mengbo Yang: Software, validation, investigation and data curation; Ting Wang: Visualization; Xianyan Wang: Visualization; Yu Li: Conceptualization, methodology, resources, supervision, project administration and writing-review and editing; Shaoqing Wang: Visualization; Lijun Han: Visualization; Yue Ming: Visualization; Ting Cao: Visualization; Xingjiang Li: Software, validation, investigation and data curation; Yuhang Li: Visualization; All authors have read and agreed to the published version of the manuscript.

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***Data availability statements***
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

***Ethical approval***
Not applicable.

***Conflict of interest***
The authors declare no conflict of interest.

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