# Action Mechanism of the TCM Combination in Cang Er Zi Nasal Relief Patch for Alleviating Nasal Inflammation Based on Network Pharmacology

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**Abstract** [**Objectives**] To investigate the mechanism of action by which the traditional Chinese medicine (TCM) compound Cang Er Zi Nasal Relief patch alleviates nasal inflammation through network pharmacology. [**Methods**] The active ingredients and target sites of the Cang Er Zi Nasal Relief patch formulation were screened and collected through a comprehensive literature review and analysis of the TCMSP database. Target sites associated with nasal inflammatory diseases were obtained from the TTD, OMIM, and GeneCards databases. String database analysis was performed to identify common targets between active ingredients and diseases. Cytoscape software was used to construct network diagrams, facilitating the identification of core active ingredients and target molecules in the herbal patch formulation. Additionally, the DAVID database was employed to perform Gene Ontology (GO) functional analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis on the identified target molecules. [**Results**] The core herbal ingredients of the Cang Er Zi Nasal Relief patch may include Baical Skullcap Root, *Centipeda minima*, Divaricate Saposhnikovia Root, Cablin Potchouli Herb, Magnoliae Flos, and Menthae Herba. The core active ingredients likely include apigenin, luteolin, oxypeucedanin, emodin, rosmarinic acid, *etc.*, which contribute to the alleviation of nasal inflammation. The core action targets may involve ESR2, TNF-α, AKT1, IL-4, MPO, and IL-6. The active ingredients in the health patch may alleviate nasal inflammation and associated symptoms like rhinorrhea, nasal itching, congestion, and dryness by targeting signaling pathways including IL-17, TNF, JAK-STAT, PI3K-Akt, and NF-κB within the body. [**Conclusions**] The clear and verifiable chain of action—"topical patches, transdermal absorption of active ingredients, regulation of core pathways, and alleviation of inflammatory symptoms"—provides robust molecular biological evidence supporting the clinical application of TCM in the external treatment of nasal disorders.

**Key words** Medicinal plants, External application of traditional Chinese medicine (TCM), Nasal inflammation, Network pharmacology, Mechanism of action

## 1 Introduction

Topical preparations of traditional Chinese medicine (TCM) are formulations designed for direct application to the skin, mucous membranes, wounds, and other external body surfaces, based on the fundamental theories of TCM[1]. These preparations embody the practical application of the TCM concept of "treating internal diseases through external means" and constitute a central element of TCM external therapies. Selecting appropriate topical dosage forms for administration not only reduces or avoids the toxic side effects associated with certain herbs but also promotes the release of active ingredients, thereby enhancing therapeutic efficacy[2]. Building upon the TCM system, innovative developments in topical preparations have effectively addressed limitations such as limited efficacy and inconvenient use associated with traditional herbal formulations, thereby achieving widespread recognition in international markets[3]. Leveraging TCM theory with modern formulation technologies to develop medicinal plants into topical dosage forms holds significant importance for advancing the large-scale application of Chinese herbal medicines.

Nasal inflammation is a prevalent condition in the field of otolaryngology. Based on the affected location, it is classified as either rhinitis or sinusitis[4]. Clinical manifestations include sneezing, nasal congestion, nasal itching, and clear nasal discharge[5]. Although rhinitis is not life-threatening, it significantly impacts daily life and severely reduces quality of life. Current treatment primarily relies on modern pharmacotherapy, such as antihistamines, corticosteroids, and leukotriene antagonists. Although these interventions effectively alleviate symptoms, they do not provide a cure for rhinitis[6]. TCM, through syndrome differentiation and treatment, offers advantages in treating rhinitis with its reversible, multi-targeted, and multi-pathway approaches[7-8].

The Cang Er Zi Nasal Relief patch, a TCM formulation developed in accordance with the principle of treating internal diseases through external means, consists of 13 herbal ingredients: Xanthii Fructus, Magnoliae Flos, Centipedae Herba, Menthae Herba, Forsythiae Fructus, Scutellariae Radix, Saposhnikoviae Radix, Dahurian Angelica Root, Cortex Moutan, Borneolum Syntheticum, Violae Herba, Pogostemon Cablin, and Coptidis Rhizoma. Through the synergistic effects of its natural ingredients, this herbal formulation assists in alleviating symptoms associated with nasal inflammation, including sneezing, nasal congestion, nasal itching, and clear nasal discharge. Additionally, it contributes to the improvement of nasal airflow sensation and enhances respiratory comfort. This study utilizes the aforementioned herbal composition as a case example to investigate the efficacy and underlying mechanisms of topical formulations derived from medicinal plants through emerging network pharmacology research methods, thereby providing scientific support for external treatment with TCM.

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## 2 Materials and methods

**2.1 Screening of potential active ingredients and targets of the Cang Er Zi Nasal Relief patch** Target collection was conducted using the TCMSP (http://www.tcmspw.com/tcmsp.php). Drugs were searched using both Chinese characters and Pinyin. Given the transdermal absorption characteristics of topical medications, the screening criteria for active ingredient properties were set as follows: $DL \geqslant 0.18$ for drug-like compounds, $MW \leqslant 500$, Alogp 2 - 3. These criteria facilitated the identification of potential active pharmaceutical ingredients and their corresponding relevant targets. When *DL* was set at 0.18, the *DL* values of Violsse Herba and borneol differed significantly from those of other drugs. To ensure the adequate screening of drug ingredients and gene targets for each drug, thereby enabling a more comprehensive analysis of valuable drug-active ingredient-target pathways, *DL* screening was not applied to Violsse Herba and borneol. Subsequently, the active drug ingredients and their corresponding targets were imported into the UniProt database (https://www.uniprot.org) to retrieve the associated gene symbols. Ingredients lacking matched gene targets were excluded from further analysis. After deduplication and correction, the data were set with "human" as the attribute, followed by gene normalization and integration of potential target interactions.

The disease databases utilized in this study were the Online Mendelian Inheritance in Man (OMIM) database (https://omim.org/) and the GeneCards database (https://www.genecards.org/). The Therapeutic Target Database (TTD) was searched using the keywords "Rhinitis" and "Sinusitis" to identify targets associated with nasal inflammatory diseases. All retrieved disease targets were compiled, followed by deduplication and correction via the Uniprot database to remove duplicates. Consequently, the finalized set of disease targets for nasal inflammation were established.

**2.2 Prediction and construction of key composition targets and disease intersection targets** The identified disease and drug targets were imported into the Venny 2.1.0 online tool (https://bioinfogp.cnb.csic.es/tools/venny/index.html). Intersecting targets were extracted as potential genes involved in the anti-inflammatory effects of Cang Er Zi nasal patches. Additionally, a Venn diagram was generated to illustrate the number of disease-drug targets and the number of shared functional targets.

**2.3 Construction of the PPI network** The processed drug-disease intersection target selection analysis was imported into the String database (https://string-db.org) under the Multiple proteins section. The species filter was set to "human" and the confidence level was adjusted to 0.400 (the highest confidence threshold) to construct the protein-protein interaction (PPI) network diagram.

**2.4 GO enrichment analysis and KEGG pathway analysis** The genes from the PPI network diagram were input into the Metascape database (https://metascape.org/) after the removal of outliers, with the species restriction set to "human". GO functional and KEGG pathway enrichment analyses were conducted on the core targets, with a significance threshold set at $P < 0.01$. The results of these analyses were visualized using the MicroBioinformatics platform. For the GO analysis, the top 10 significant entries were selected and visualized as bar charts and bubble charts. For the KEGG analysis, the top 20 significant pathways were visualized as bubble charts.

## 3 Results and analysis

**3.1 Active ingredients and target sites in TCM formulations** By retrieving data from the TCMSP database, a total of 83 core active drug ingredients were screened (Table 1). Subsequently, 2 204 corresponding drug targets were predicted using Swiss-Target Prediction and the TCMSP database. The functional targets associated with these active ingredients were then deduplicated and standardized according to the UniProt database, converting them into "official symbols", which resulted in a final set of 603 drug-related targets.

**3.2 Prediction of target molecules for nasal inflammatory diseases** A total of 153 targets associated with nasal inflammatory diseases were identified in the OMIM database, 56 in the GeneCards database, and 28 in the TTD database. After deduplication and standardization using the UniProt database, 207 targets related to nasal inflammatory diseases were obtained. The intersection data in the Venn diagram (Fig. 1) indicated that drugs and nasal inflammation shared 49 common targets.

**3.3 PPI network results** A PPI network diagram was constructed using the String database to visualize the common targets shared between the investigated drugs and diseases, as shown in Fig. 2. The PPI interaction network comprises 47 nodes and 508 edges, with each edge representing an interaction relationship between nodes. Nodes with a higher number of edges are considered to correspond to more significant target proteins. Topological analysis identified the following hub targets: IL6, IL1β, IL10, TNF-α, and AKT1.

Research indicates that IL-6, IL-10, and TNF-α are broad-spectrum cellular inflammatory mediators involved in human inflammatory and immune responses. Extensive experimental data demonstrate that IL-6 participates in various inflammatory reactions and diseases in the human body, serving as a significant pro-inflammatory factor[9-11]. IL-10 is a multi-cell-derived, multi-functional cytokine and a key anti-inflammatory factor in humans[12]. Similar to IL-6, IL-10 regulates immune functions, modulates cell growth and differentiation, and participates in inflammatory and immune responses. It is currently recognized in the medical community as an anti-inflammatory and immunosuppressive factor[13-14]. As a key anti-inflammatory cytokine secreted by Th2 cells, IL-10 suppresses the proliferation of Th1 cell and inhibits the release of inflammation-related mediators, thereby preventing mucosal edema and excessive mucus secretion. TNF-α, a multifunctional inflammatory cytokine[15], mediates the recruitment of eosinophils, lymphocytes, and neutrophils to inflammatory

**Table 1 Active ingredients in the TCM formulation of the Cang Er Zi Nasal Relief patch**

| No. | Mol ID | Molecule name | *MW* | AlogP | *DL* | No. | Mol ID | Molecule name | *MW* | AlogP | *DL* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | MOL001729 | Crysophanol | 254.25 | 2.76 | 0.21 | 43 | MOL012246 | 5, 7, 4’-Trihydroxy-8-methoxyflavanone | 302.30 | 2.28 | 0.26 |
| 2 | MOL000472 | Emodin | 270.25 | 2.49 | 0.24 | 44 | MOL012266 | Rivularin | 344.34 | 2.55 | 0.37 |
| 3 | MOL000396 | Syringaresinol | 418.48 | 2.10 | 0.72 | 45 | MOL012267 | Scutevulin | 300.28 | 2.32 | 0.27 |
| 4 | MOL008647 | Moupinamide | 313.38 | 2.86 | 0.26 | 46 | MOL011865 | Rosmarinic acid | 360.34 | 2.69 | 0.35 |
| 5 | MOL012121 | Denudadione C | 340.40 | 2.31 | 0.41 | 47 | MOL002881 | Diosmetin | 300.28 | 2.32 | 0.27 |
| 6 | MOL000310 | Denudatin B | 356.45 | 2.80 | 0.38 | 48 | MOL004328 | Naringenin | 272.27 | 2.30 | 0.21 |
| 7 | MOL000309 | Denudatin A | 340.40 | 2.61 | 0.44 | 49 | MOL000476 | Physcion | 284.28 | 2.74 | 0.27 |
| 8 | MOL000315 | Hancinone | 340.40 | 2.61 | 0.44 | 50 | MOL005190 | Eriodictyol | 288.27 | 2.03 | 0.24 |
| 9 | MOL012134 | Lariciresinol | 370.48 | 2.95 | 0.49 | 51 | MOL005573 | Genkwanin | 284.28 | 2.59 | 0.24 |
| 10 | MOL007563 | Yangambin | 446.54 | 2.60 | 0.81 | 52 | MOL000006 | Luteolin | 286.25 | 2.07 | 0.25 |
| 11 | MOL011718 | Arnicolide D | 332.43 | 2.81 | 0.33 | 53 | MOL000416 | Lariciresinol | 360.44 | 2.46 | 0.38 |
| 12 | MOL011722 | Arnicolide C | 334.45 | 2.79 | 0.32 | 54 | MOL001842 | Pinoresinol | 358.42 | 2.13 | 0.52 |
| 13 | MOL005909 | Pachypodol | 344.34 | 2.07 | 0.37 | 55 | MOL001938 | Secoisolariciresinol | 362.46 | 2.79 | 0.31 |
| 14 | MOL005910 | Retusin | 358.37 | 2.32 | 0.40 | 56 | MOL003291 | EGENINE | 383.43 | 2.85 | 0.90 |
| 15 | MOL000008 | Apigenin | 270.25 | 2.33 | 0.21 | 57 | MOL003298 | Forsythialan B | 388.45 | 2.00 | 0.45 |
| 16 | MOL002083 | Tricin | 330.31 | 2.30 | 0.34 | 58 | MOL003306 | ACon1_001697 | 372.45 | 2.38 | 0.57 |
| 17 | MOL001689 | Acacetin | 284.28 | 2.59 | 0.24 | 59 | MOL003322 | FORSYTHINOL | 372.45 | 2.38 | 0.57 |
| 18 | MOL000173 | Wogonin | 284.28 | 2.59 | 0.23 | 60 | MOL003370 | Onjixanthone I | 302.30 | 2.65 | 0.30 |
| 19 | MOL000228 | (2R)-7-hydroxy-5-Methoxy-2-phenylchroman-4-one | 270.30 | 2.82 | 0.20 | 61 | MOL000791 | Bicuculline | 367.38 | 2.83 | 0.88 |
| 20 | MOL002560 | Chrysin | 254.25 | 2.60 | 0.18 | 62 | MOL011747 | Lledebouriellol | 374.42 | 2.80 | 0.51 |
| 21 | MOL002714 | Baicalein | 270.25 | 2.33 | 0.21 | 63 | MOL011753 | 5-O-Methylvisamminol | 290.34 | 2.02 | 0.25 |
| 22 | MOL002737 | Scutellarein | 286.25 | 2.07 | 0.24 | 64 | MOL009356 | Tectochrysin | 268.28 | 2.85 | 0.20 |
| 23 | MOL002908 | 5, 8, 2’-Trihydroxy-7-methoxyflavone | 300.28 | 2.32 | 0.27 | 65 | MOL005791 | Oxypeucedanin | 286.30 | 2.00 | 0.30 |
| 24 | MOL002910 | Carthamidin | 288.27 | 2.03 | 0.24 | 66 | MOL005792 | {5-[2’(R)-Hydroxy-3’-methyl-3’-butenyl-oxy] furocoumarin} | 286.30 | 2.74 | 0.26 |
| 25 | MOL002913 | Dihydrobaicalin | 272.27 | 2.30 | 0.21 | 67 | MOL005793 | 9-{[(2R)-3, 3-dimethyloxiran-2-yl] methoxy} furo [3,2-g] chromen-7-one | 286.30 | 2.49 | 0.29 |
| 26 | MOL002914 | Eriodyctiol | 288.27 | 2.03 | 0.24 | 68 | MOL005800 | Byakangelicol | 316.33 | 2.47 | 0.36 |
| 27 | MOL002915 | Salvigenin | 328.34 | 2.82 | 0.33 | 69 | MOL005888 | Ombuin | 330.31 | 2.01 | 0.34 |
| 28 | MOL002917 | 5, 2’, 6’-Trihydroxy-7, 8-dimethoxyflavone | 330.31 | 2.30 | 0.33 | 70 | MOL005890 | Pachypodol | 356.40 | 2.99 | 0.40 |
| 29 | MOL002918 | Ganhuangenin | 346.31 | 2.03 | 0.37 | 71 | MOL005908 | 3,5-Dihydroxy-4’,7-dimethoxyflavone | 314.31 | 2.27 | 0.30 |
| 30 | MOL002925 | 5,7,2’,6’-Tetrahydroxyflavone | 286.25 | 2.07 | 0.24 | 72 | MOL005911 | 5-Hydroxy-7, 4’-dimethoxyflavanon | 300.33 | 2.80 | 0.27 |
| 31 | MOL002926 | Dihydrooroxylin A | 286.30 | 2.55 | 0.23 | 73 | MOL005912 | 5-Hydroxy-7・3’,4’-trimethoxyflavanone | 330.36 | 2.78 | 0.33 |
| 32 | MOL002927 | Skullcapflavone II | 374.37 | 2.54 | 0.44 | 74 | MOL005916 | Irisolidone | 314.31 | 2.30 | 0.30 |
| 33 | MOL002928 | Oroxylin A | 284.28 | 2.59 | 0.23 | 75 | MOL013352 | Obacunone | 454.56 | 2.68 | 0.77 |
| 34 | MOL002932 | Panicolin | 314.31 | 2.57 | 0.29 | 76 | MOL002904 | Berlambine | 351.38 | 2.49 | 0.82 |
| 35 | MOL002933 | 5, 7, 4’-Trihydroxy-8-methoxyflavone | 300.28 | 2.32 | 0.27 | 77 | MOL001845 | Clemastanin B_qt | 360.44 | 2.46 | 0.38 |
| 36 | MOL002936 | 5, 8-Dihydroxy-6, 7-dimethoxyflavone | 314.31 | 2.57 | 0.29 | 78 | MOL000118 | Alpha-Terpineol | 154.28 | 2.42 | 0.03 |

(To be continued)

(Continued)

| No. | Mol ID | Molecule name | *MW* | AlogP | *DL* | No. | Mol ID | Molecule name | *MW* | AlogP | *DL* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 37 | MOL002937 | DIHYDROOROXYLIN | 286.30 | 2.55 | 0.23 | 79 | MOL000122 | 1,8-cineole | 154.28 | 2.15 | 0.05 |
| 38 | MOL000525 | Norwogonin | 270.25 | 2.33 | 0.21 | 80 | MOL000709 | (S)-Matsutake alcohol | 128.24 | 2.53 | 0.01 |
| 39 | MOL000552 | 5, 2'-Dihydroxy-6, 7, 8-trimethoxyflavone | 344.34 | 2.55 | 0.35 | 81 | MOL000019 | D-Camphene | 136.26 | 2.93 | 0.04 |
| 40 | MOL008206 | Moslosooflavone | 298.31 | 2.84 | 0.25 | 82 | MOL006866 | Isosafrole | 162.20 | 2.55 | 0.05 |
| 41 | MOL012240 | 2',3',5,7-tetrahydroxyflavone | 286.25 | 2.07 | 0.24 | 83 | MOL000905 | (-)-beta-Pinene | 136.26 | 2.93 | 0.05 |
| 42 | MOL012245 | 5,7,4'-trihydroxy-6-methoxyflavanone | 302.30 | 2.28 | 0.27 |  |  |  |  |  |  |

sites, stimulating these cells to produce factors such as IL-6 and IL-8. TNF-α also promotes Ig secretion by stimulating B-cell proliferation. During the body's inflammatory response, macrophages release large amounts of TNF-α, activating surface adhesion receptors on neutrophils and endothelial cells while promoting the release of inflammatory factors[16-17]. As a key pro-inflammatory factor, IL-1β plays a crucial role in inducing Th2 inflammatory responses[18-20]. Research indicates that the intensity of inflammation in asthma airway epithelial cells is partially regulated through IL-1β release[21]. Furthermore, inhibition of IL-1β significantly reduces airway inflammatory responses in asthmatic mice[22-23].

**3.4 Drug-active ingredient-target analysis results** Based on TCM, identified potential drug active ingredients, and their intersecting targets, a visual network diagram of TCM formulations was constructed using Cytoscape 3.10.1, as shown in Fig. 3. The network comprises 99 nodes and 201 connections. Green V-shaped nodes represent drugs, pink diamond-shaped nodes denote the active ingredients of each drug, and blue circular nodes indicate potential target molecules. The size of each node reflects its degree value, with an average node degree of approximately 4. Notably, 35 nodes exhibit a degree exceeding the average betweenness centrality.

The screening results are shown in Table 2. The data indicate that Scutellariae Radix, Pogostemon Cablin, Centipedae Herba, Saposhnikoviae Radix, and Magnoliae Flos may be the core Chinese herbs responsible for the pharmacological effects of this herbal formulation. Apigenin, luteolin, oxypeucedanin, pachypodol, moupinamide, tectochrysin, emodin, and rosmarinic acid may be the core active ingredients responsible for the pharmacological effects of this herbal formulation. Additionally, ESR2, EGFR, ADORA2A, TNF, TP53, AKT1, IL4, MPO, and IL6 may represent the core targets for the pharmacological effects of this herbal formulation.

**Table 2 Key nodes and topological features in the TCM-active ingredients-target network**

| No. | Node name | Node type | Degree | Betweenness centrality | No. | Node name | Node type | Degree | Betweenness centrality |
|---|---|---|---|---|---|---|---|---|---|
| 1 | ESR2 | Target | 22 | 0.217 3 | 19 | Denudadione C | Compound | 7 | 0.066 9 |
| 2 | Apigenin | Compound | 17 | 0.178 7 | 20 | Alpinetin | Compound | 6 | 0.021 9 |
| 3 | Baical Skullcap Root | Plant | 15 | 0.128 1 | 21 | Naringenin | Compound | 6 | 0.057 2 |
| 4 | Luteolin | Compound | 13 | 0.091 1 | 22 | AKT1 | Target | 6 | 0.029 1 |
| 5 | Oxypeucedanin | Compound | 12 | 0.071 9 | 23 | *Centipeda minima* | Plant | 5 | 0.031 0 |
| 6 | 5,8,2'-Trihydroxy-7-methoxyflavone | Compound | 11 | 0.119 3 | 24 | Chrysin | Compound | 5 | 0.021 8 |
| 7 | Pachypodol | Compound | 11 | 0.105 5 | 25 | Divaricate Saposhnikovia Root | Plant | 5 | 0.003 5 |
| 8 | Moupinamide | Compound | 10 | 0.104 6 | 26 | IL4 | Target | 5 | 0.042 5 |
| 9 | Tectochrysin | Compound | 10 | 0.077 0 | 27 | MPO | Target | 5 | 0.041 3 |
| 10 | Emodin | Compound | 9 | 0.078 2 | 28 | Magnoliae Flos | Plant | 4 | 0.060 0 |
| 11 | Rosmarinic acid | Compound | 8 | 0.104 9 | 29 | Denudatin B | Compound | 4 | 0.080 3 |
| 12 | Cablin Potchouli Herb | Plant | 8 | 0.042 7 | 30 | Baicalein | Compound | 4 | 0.016 3 |
| 13 | EGFR | Target | 8 | 0.128 4 | 31 | Irisolidone | Compound | 4 | 0.022 4 |
| 14 | ADORAA | Target | 8 | 0.109 2 | 32 | IL6 | Target | 4 | 0.007 5 |
| 15 | Menthae Herba | Plant | 7 | 0.092 6 | 33 | ESRRA | Target | 4 | 0.020 5 |
| 16 | 9-[[(2R)-3,3-dimethyloxiran-2-yl]methoxy]furo[3,2-g]chromen-7-one | Compound | 7 | 0.057 5 | 34 | ALOX5 | Target | 4 | 0.020 8 |
| 17 | TNF | Target | 7 | 0.066 8 | 35 | PLA2G1B | Target | 4 | 0.008 6 |
| 18 | TP53 | Target | 7 | 0.033 0 |  |  |  |  |  |

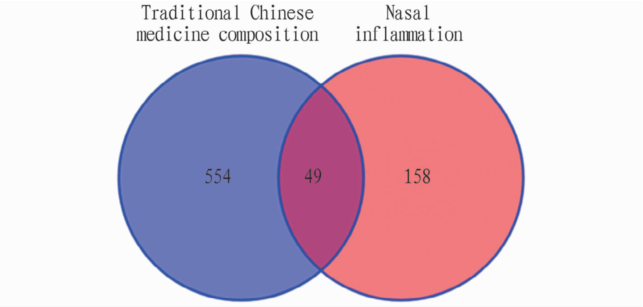

**Fig. 1** Venn diagram of common targets between TCM compositions and nasal inflammation

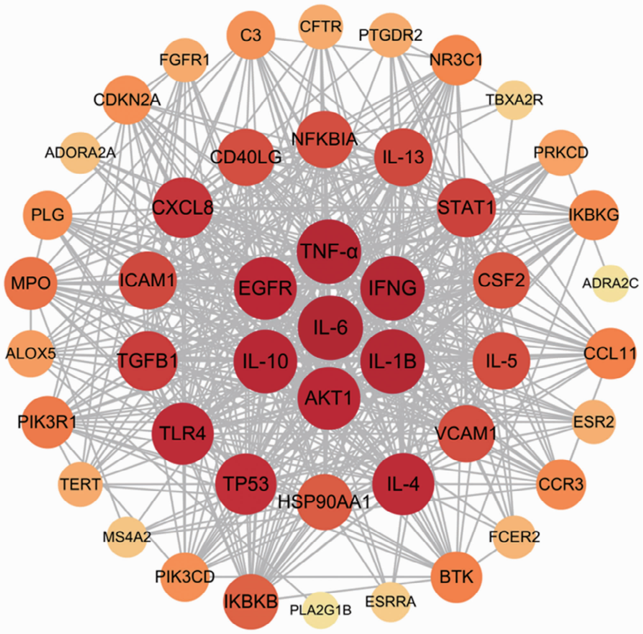

**Fig. 2** PPI network diagram

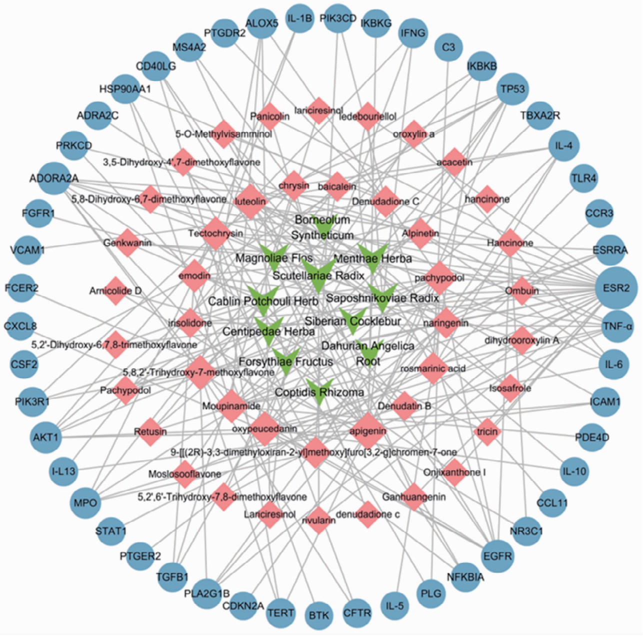

**Fig. 3** TCM-active ingredients-target network diagram

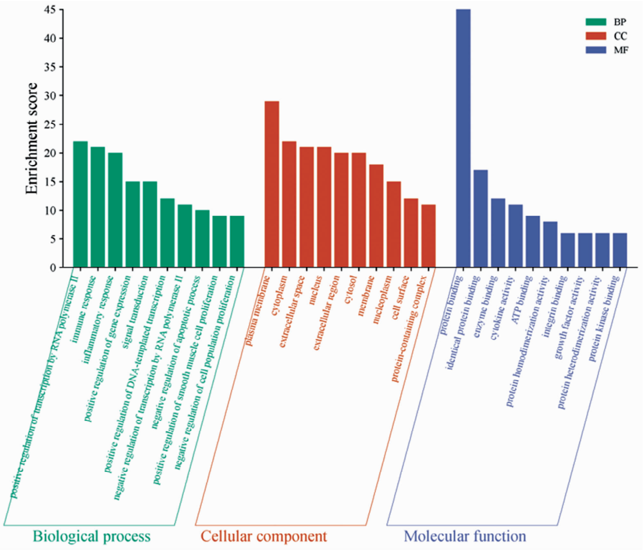

**Fig. 4** GO functional analysis diagram of potential targets for the active ingredients in the TCM formulation

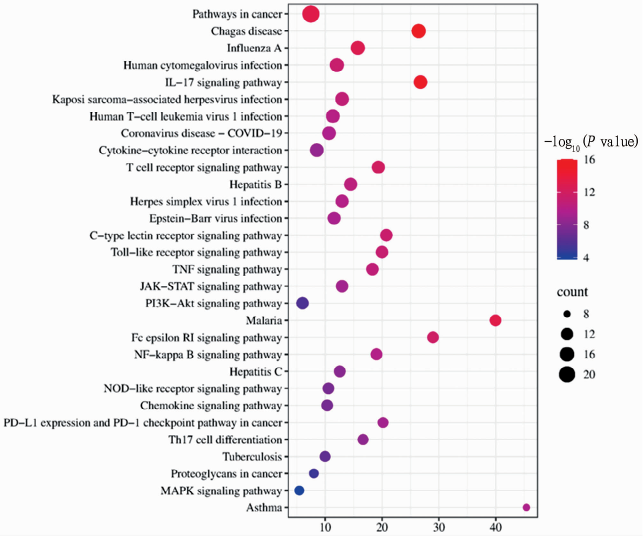

**Fig. 5** KEGG pathway enrichment diagram of potential targets for active ingredients in TCM formulations

Research indicates that Scutellariae Radix serves as the active anti-inflammatory ingredient in the TCM formulations "Shuangxin Biyuan Powder", "Biyuan Shu Oral Liquid", and "Biyuantongqiao Granules" and the decoction "Bai Guo Huang Qin Tang". Its primary ingredient, baicalin, inhibits multiple inflammatory mediators[24], demonstrating potent anti-inflammatory effects while regulating the Th1/Th2 balance to mitigate allergic reactions[25]. The anti-inflammatory active ingredients in Centipeda Herba are predominantly volatile oil compounds. Research indicates[26] that the volatile oil of Centipedae Herba exhibits potent anti-inflammatory activity. It not only suppresses inflammatory responses triggered by various pro-inflammatory substances but also mitigates inflammation by decreasing capillary permeability and and reducing the levels of pro-inflammatory factors in inflamed areas[27-28]. Apigenin alleviates TGF-β1-induced remodeling of the nasal mucosa and inferior turbinate tissue by inhibiting the MAPK/NF-κB pathway, thereby preventing and treating nasal inflammation[29]. Luteolin promotes Th1 cell differentiation by inhibiting abnormal activation of the TLR4/NF-κB pathway, thereby restoring the Th1/Th2 balance and exerting therapeutic effects against nasal inflammation[30]. Oxypeucedanin alleviates nasal inflammation by suppressing the activation of the PI3K/AKT/NF-κB and MAPK signaling pathways[31]. Rosmarinic acid significantly suppresses house dust mite allergen-induced allergic asthma and inhibits allergen-specific IgG1 expression, demonstrating potent anti-allergic effects. Besides, it suppresses seasonal allergic rhinoconjunctivitis[32]. Numerous studies confirm that emodin effectively treats various inflammations, including nasal inflammation, while also enhancing human immunity beyond its anti-inflammatory properties[33].

**3.5 Analysis of GO enrichment and KEGG pathway analysis results for key targets** GO functional enrichment analysis conducted via the Metascape database yielded 130 enrichment results, comprising 97 biological processes, 27 cellular components, and 6 molecular functions. The top 10 entries from the BP, CC, and MF categories of the GO enrichment results were selected. Based on these selections, bar charts and bubble charts were generated using the MicroBioinformatics platform, as shown in Fig. 4. The vertical axis of the GO enrichment analysis bar chart represents the enrichment score, while the horizontal axis displays the pathway names. Higher enrichment scores indicate greater levels of enrichment.

Analysis results from GO indicate that the active compounds in TCM patches may exert their effects by regulating biological processes such as the positive regulation of transcription by RNA polymerase II, immune responses, inflammatory responses, and the positive regulation of gene expression. These compounds participate in biological processes occurring in the cytoplasm, extracellular space, cell nucleus, and extracellular regions, thereby influencing protein complexes, protein binding, enzyme binding, and cytokine activity to exert their therapeutic effects.

KEGG pathway enrichment analysis conducted using the DAVID database identified 139 significantly enriched pathways ($P < 0.01$). The pathway data were imported into MicroBioinformatics, where a combined filter based on $P$-values and gene enrichment counts selected 30 pathways for visualization in a bubble chart. As shown in Fig. 5, the key targets involved in the health-promoting effects of Chinese herbal medicated patches primarily participate in signaling pathways including IL-17, TNF, JAK-STAT, PI3K-Akt, and NF-κB.

Research indicates that the NF-κB signaling pathway promotes the release of inflammatory mediators and immune cell infiltration by activating MyD88-dependent pathways, representing a key component in the pathophysiology of rhinitis[34]. The JAK/STAT signaling pathway plays a pivotal role in the pathophysiology of rhinitis by mediating Th cell differentiation and the transcription of inflammation-related genes. The PI3K/Akt signaling pathway activates Akt by catalyzing the production of PIP3, thereby mediating eosinophil recruitment, goblet cell proliferation, and the release of pro-inflammatory factors such as IL-4 and IL-5, contributing to airway hyperresponsiveness and mucosal damage in allergic rhinitis[34]. Therefore, the active ingredients in the health patch may exert anti-inflammatory effects on nasal inflammation by targeting multiple pathways throughout the body.

## 4 Conclusions

**4.1 The rationality of the "sovereign, minister, assistant, and messenger" combination in TCM formulations** The primary advantage of TCM formulations lies in the synergistic combination of "sovereign, minister, assistant, and messenger" herbs. Through topological analysis in network pharmacology, this study identifies Scutellariae Radix and Pogostemon Cablin as core herbs. Scutellariae Radix, primarily functioning to clear heat and dry dampness (sovereign herb), simultaneously regulates multiple inflammatory targets, including ESR2 and TNF. Pogostemon Cablin (minister herb) assists in dispelling dampness and unblocking orifices, enhancing pathway regulation through components such as pogostemon flavanol. Besides, Centipedae Herba, Saposhnikoviae Radix, and Magnoliae Flos (auxiliary herbs) further expand target coverage by dispelling cold to open orifices and dispelling wind to resolve exterior syndromes, thereby forming a synergistic network of "multiple ingredients-multiple targets-multiple pathways". This outcome closely aligns with TCM's "sovereign, minister, assistant, and messenger" theory, providing objective experimental evidence supporting the modern biological interpretation of Chinese herbal formulations. It also offers a reference paradigm for optimizing the formulation of similar externally applied Chinese herbal preparations.

**4.2 Molecular mechanisms of TCM external treatment for nasal inflammation** TCM external therapies often face insufficient clinical credibility due to "unclear mechanisms of action". This study addresses this gap through a multidimensional analysis. On the one hand, core ingredients such as apigenin and luteolin—selected based on the characteristics of topical formulation—exhibit physicochemical properties ($MW \leqslant 500$, Alogp 2 – 3) that meet transdermal absorption requirements. On the other hand, KEGG pathway enrichment analysis confirms that these components directly target pathological pathways involved in nasal inflammation by inhibiting NF-κB (reducing IL-6 and TNF-α release) and the PI3K-Akt pathway (suppressing eosinophil recruitment), ultimately alleviating nasal mucosal hyperemia and edema. The entire chain of action—topical patch, transdermal absorption of active ingredients, regulation of core pathways, and improvement of inflammatory symptoms—is clearly demonstrable, providing robust molecular biological evidence supporting the clinical application of TCM in the external treatment of nasal diseases.

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