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ARTICLE

Network-pharmacology and molecular docking-based investigation of mechanism of *Sophora flavescens* on cancer and inflammation

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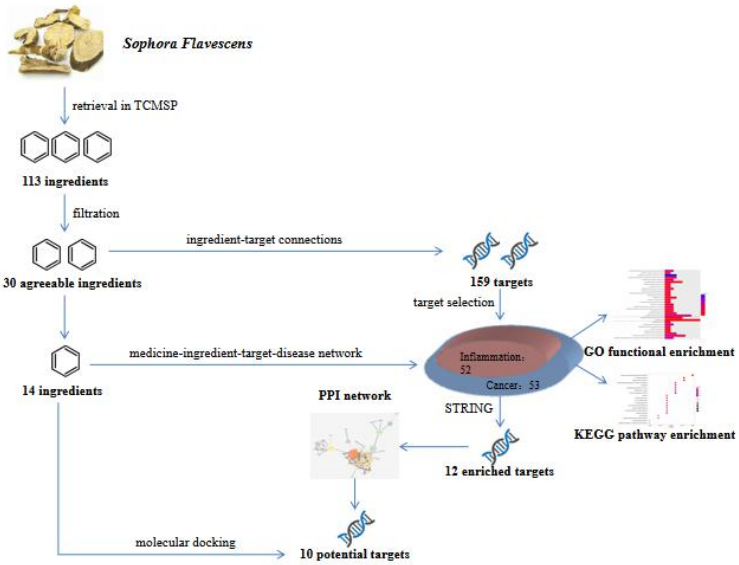
Highlights

We used TCMSP, GeneCards, TTD, OMIM, STRING, PubChem databases, and SybylX-2.0, Cystoscope softwares to analyze and predict the possible anti-cancer and anti-inflammatory targets and pathways of Kushen (*Sophora flavescens, SF*). The study provides a theoretical basis for further mechanism study of *SF* in the prevention and treatment of cancer and inflammation.

Traditionality

Sophora flavescens, the dried root of a Leguminosae plant, has long been clinically used for anti-inflammation as traditional antipyretic medicine in many countries. *SF* displays the efficacy of eliminating heat and dehumidification, therefore it can treat damp-heat-related endopyretic syndrome. Modern research highlights its growth inhibitory activity against various types of cancer. Nowadays, *SF* and its preparations such as Kushen Letion, Fufang Kushen Letion/Injection, Matrine Injection are clinically used to treat different cancer, dermatosis, gynecologic diseases and digestive system diseases**.**



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Abstract

Objective: In order to explore the systematical regulatory mechanism of Kushen (*Sophora flavescens, SF*) on inflammation and cancer, we analyzed inter-molecular interactions between herbal ingredients of *SF* and human inflammation and cancer through network-pharmacology and molecular docking-based approaches.

Methods: Firstly, ingredients and potential targets were obtained from Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform, GeneCards database, Therapeutic Targets Database and Online Mendelian Inheritance in Man database. Then, protein-protein interaction network and medicine-ingredient-target-disease network were established and analyzed via STRING and Cytoscape. Surflex-dock was performed by SybylX-2.0. Finally, functional enrichment and pathway enrichment were achieved by Gene Ontology database and Kyoto Encyclopedia of Genes and Genomes database.

Results: The results showed that 113 components of *SF* and 53 potential targets were related in the study. *SF* exerts anti-inflammatory and anti-cancer mechanism through key targets located in nucleus, such as JUN, MYC, RELA, NCOA, PPARG which may trigger the NF-κB pathway, the Bcl-2/Bax pathway and other pathways to effect DNA transcriptional activity.

Conclusions: The study predicted the mechanism of *SF* on cancer and inflammation. According to the results, we suggest that the ingredients of *SF* effect on DNA binding and transcription in nuclear receptors-like JUN, MYC, RELA, NCOA, PPARG. the receptors trigger several pathways including NF-κB pathway, the Bcl-2/Bax pathway and others. Eventually, it regulates inflammatory factors and cell proliferation, senescence and apoptosis.

Keywords: Network-pharmacology, Molecular docking, Sophora flavescens, Cancer, Inflammation

Abbreviations: SF, *Sophora flavescens*; TCMSP, Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform; TTD, Therapeutic Targets Database; OMIM, Online Mendelian Inheritance in Man; PPI, protein-protein interaction; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes; TCM, Traditional Chinese Medicine; OB, oral bioavailability; DL, drug-likeness; CC, Cellular Component; MF, Molecular Function; BP, Biological Process.

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Competing interests: The authors declare that there is no conflict of interests regarding the publication of this paper.

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Background

Cancer has been threatening human's life for a long time. According to the statistics, The increase in cancer incident cases have been incredibly reached to 52% over the recent decade and the majority of cancer disability-adjusted life-years came from years of life lost, and only 3% came from years lived with disability[1]. It is well accepted that inflammation reaction, as the protective process of human body, is implicated in cancer. It is widely approved that inflammation promotes oncogenesis. Inflammation involves an array of cellular factors, biological processes and systemic reactions. As a consequence, cancer often follows inflammation with its proliferation pathways and reactions[2]. And they usually act coordinately, which ultimately allows cancer to progress[3-5]. However, it also participates in cancer rejection. The dynamic switch is dependent on the length of inflammatory process. Acute inflammation benefits human body as a protective reaction from microbial infection, tissue damage and oncogenesis[6]. Chronic inflammation triggers oncogenesis and provides a more positive micro-environment to cancer through inflammatory factors which promote cell proliferation and angiogenesis[7]. NF-κB, one of the major inflammatory factors, promotes cell proliferation with a carcinogenic micro-environment by activating chemokines, NOS, COX-2, TNF-α and other genes in nucleus[8]. Besides, CXCR4/CXCL12 axis has been demonstrated as a vital inducer of cancer metastasis[9, 10]. Generally, inflammation links cancer through a dual-directional regulatory effect on micro-environment.

To meet the challenge, research on mechanisms and regulations of cancer and inflammation has last for several generations and great progress has made by mechanism study and drug discovery. Despite the rapid advances in new drug screening and chemical synthesis technologies, it has been increasingly difficult to search for highly efficient compounds with single target. Since cancer and inflammation have sophisticated formation pathways and work via several, specific points and pathways, which trapped us for a long time, a single approach is not enough to cure inflammation-related cancer.

Traditional Chinese Medicine (TCM) displays its unique advantages on the treatment of cancer and inflammation, such as low toxicity, side effect and availability of a wide range of sources. The function characteristics of TCM include multi-ingredient, multi-target and synergistic mechanism[11-13]. *Sophora flavescens* (*SF*), also known as Kushen in Chinese, is one of most important TCM. *SF* is bitter in taste and cold in nature. Besides China, it has also been widely used in many countries, such as Japan, Korea. Accumulating studies performed by different laboratories have demonstrated that *SF* exerts broad-spectrum pharmacological activities, including anti-inflammatory, anti-infectious and anti-tumor effects. It is reported that *SF* is able to inhibit both microbial growth and its enzymes for cell wall protein anchoring and virulence[14]. The anti-inflammatory effect of *SF* is associated with inhibiting the pro-inflammatory environment through blockage of NF-κB translocation to nuclear[15]. Moreover, *SF* significantly inhibit inflammation and infiltration of macrophages through suppressing the release of pro-inflammatory mediators and expression of adhesion molecule LFA-1 and chemoattractant protein MCP-1/CCL2[16].

Besides, it is also found that *SF* has potential inhibitory ability on cancer. *SF* induces apoptosis in cancer cells through inhibition of cAMP-PDE, mTOR and Akt[17]. Additionally, activating caspase proteases and increasing Bax/Bcl-2 ratio are also key mechanisms of anti-cancer effect of *SF*[18]. Although there are many researches on anti-inflammatory and anti-tumor mechanism of *SF*, most of them focus on certain chemical components and targets, which barely matches to the comprehensive trait of *SF* and cannot provide an overall description.

Network-pharmacology is a kind of comprehensive and predictive research method. It works through citing, comparing, connecting and analyzing data from multiple databases and published references. It aims to study the relationships among drugs, drug-target moleculars (e.g. proteins, RNAs) and diseases. With the rapid progress in bioinformatics, network pharmacology has been applied in many aspects of TCM, such as predicting new drug targets, action mechanism, new drug discovery, drug evaluation for PD/PK, safety and toxicology, quality control, and bioinformatics[19]. Besides, the network-pharmacological methods are able to intuitively trace out the relation of different herbs and their interaction with targets, which may extend their applications in multi-drug combined therapies[20, 21]. Additionally, network pharmacology was also employed to elucidate the multi-active mechanism of a medicinal composition and to predict some key compounds and targets. Consequently, network pharmacology is considered to be a promising approach towards understanding of multiple ingredients and multiple targets of a disease.

In the study, we comprehensively reveal the effect

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of *SF* on inflammation and cancer by network pharmacology. Our study reveals that *SF* inhibits cancer and inflammation through multi-target, multi-pathway and synergistic processes.

Methods

Compound Library Construction and Drug-Likeness Screening.

Active compounds of *SF* were obtained from traditional Chinese medicine systems pharmacology (TCMSP) database ((http://lsp.nwu.edu.cn/tcmsp.php). We inputted "kushen" and "*Sophora flavescens*" in the searching table and filtered the ingredients with ADME indexes including oral bioavailability (OB), drug-likeness (DL) and Caco-2 permiability (Caco-2) according to the oral delivery method of herbal medicine[22, 23]. Ultimately, we set up the filtration rank as OB greater than or equal to 30 percent, DL greater than or equal to 0.18, Caco-2 greater than or equal to 0.40.

Prediction of *SF* Targets.

Key terms "Inflammation", "Neoplasm", "Malignant Tumor" and "Cancer" were inputted in GeneCards database, TTD database and OMIM database to retrieved targets of these diseases. At the meantime, targets of the filtered ingredients were obtained by retrieval in TCMSP. The bi-directional retrieval was accomplished by exporting all outcomes from databases and extracting the overlapped targets. To improve accuracy, Uniprot was used to correct the targets' names and symbols.

Construction of Protein-Protein Interaction (PPI) Network.

The STRING database was utilized to acquire the information of targets interaction in "Homo sapiens" with "high" interaction score predicted by active interaction sources-textmiming, experiments, databases, co-expression, neighborhood, gene fusion and co-occurrence. Then, Cytoscape was utilized to establish a ingredients-targets interaction network which is predicted by degree, betweenness centrality and combine score[24, 25].

Molecular Docking.

According to the analysis results of the network, current knowledge and literature support, we extracted the potential key targets in the pathway. The Protein Database was used to obtain 3D structures of the targets. And the Scifinder and ChemDraw were used to obtain structures of relevant ingredients. Finally, SybylX-2.0 was used to accomplish the surflex-docking.

Gene Ontology (GO) Functional Enrichment and Kyoto Encyclopedia of Genes and Genomes (KEGG) Pathway Enrichment.

We performed functional enrichment of selected targets via GO database with the screening condition of identifier as official gene symbol, species as human, $P < 0.05$ and FDR < 0.05[26]. To determine the certain pathways that the ingredients affected on, we enriched the pathway through KEGG Mapper of KEGG database. Then, referring to current knowledge of the diseases and literature support, we remapped an integrative pathway through which *SF* exerts its effect.

Results

Ingredients of *SF*.

We obtained 113 ingredients of *SF* through retrieval in TCMSP at first. After filtration with OB, DL and Caco-2, 30 agreeable ingredients were selected and listed in Table 1.

Potential Targets of Active Components of *SF*.

TCMSP was used to download all 159 relevant targets of the active ingredients. GeneCards database, TTD database and OMIM database provided 77277 drug targets in the treatment of Inflammation, Neoplasm, Malignant Tumor and Cancer (Table 2). 53 cancer-relevant targets and 52 inflammation-relevant targets were selected from the outcomes via comparison. Interestingly, after comparison of the target lists, we noticed that all inflammation-related targets were included in cancer (Figure 1). To explore the mechanism of *SF* on cancer and inflammation and the potential mechanism connection between cancer and inflammation, we analyzed the targets both associated with inflammation and cancer.

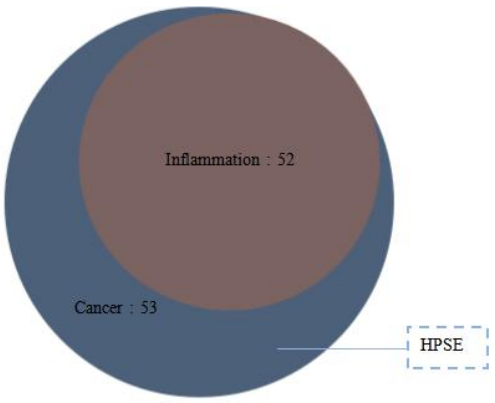

Figure 1. Comparison of cancer and inflammation. The disease-related genes were displayed by numbers and radius. The blue cycle representing neoplasm contains 53 gene. The red cycle representing inflammation only contains 52 gene, excepting HPSE. The Venn indicates a therapeutic relation between neoplasm and inflammation.

Table 1 Active components of Sophora flavescens and their parameters.

ID	Molecule Name	OB (%)	Caco-2	DL
1484	inermine	75.18	0.89	0.54
3542	8-Isopentenyl-kaempferol	38.04	0.53	0.39
3627	sophocarpine	64.26	0.99	0.25
3648	inermin	65.83	0.91	0.54
3673	wighteone	42.80	0.64	0.36
3676	sophoramine	42.16	1.43	0.25
3680	sophoridine	60.07	1.13	0.25
0392	formononetin	69.67	0.78	0.21
4941	(2R)-7-hydroxy-2-(4-hydroxyphenyl)chroman-4-one	71.12	0.41	0.18
5944	matrine	63.77	1.39	0.25
6561	(+)-14α-hydroxymatrine	35.73	0.53	0.29
6562	(+)-7,11-dehydromatrine,(leontalbinine)	62.08	1.06	0.25
6563	(+)-9α-hydroxymatrine	32.04	0.61	0.29
6564	(+)-allomatrine	58.87	1.08	0.25
6565	AIDS211310	68.68	1.15	0.25
6566	(+)-lehmannine	58.34	1.21	0.25
6568	isosophocarpine	61.57	1.39	0.25
6569	(-)-14β-hydroxymatrine	37.26	0.77	0.29
6571	anagyrine	62.01	1.16	0.24
6572	1,4-diazaindan-type,alkaloid,flavascensine	34.64	1.13	0.24
6573	13,14-dehydrosophoridine	65.34	1.06	0.25
6583	7,11-dehydromatrine	44.43	1.11	0.25
6596	glyceollin	97.27	0.53	0.76
3347	hyperforin	44.03	0.87	0.60
6604	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	48.09	0.80	0.39
6613	kushenin	47.62	0.71	0.38
6627	lehmanine	62.23	1.18	0.25
6628	(+)-lupanine	52.71	1.16	0.24
0456	phaseolin	78.20	1.09	0.73
6649	sophranol	55.42	0.60	0.28

Table 2 Targets retrieval

Sources	Retrieval manner	Quantity
TCMSP	Ingredients	159
GeneCards	“Inflammation”	9006
	“Neoplasm”	20589
	“Malignant Tumor”	12632
	“Cancer”	24239
TTD	“Inflammation”	125
	“Neoplasm”	21
	“Malignant Tumor”	0
	“Cancer”	1888
OMIM	“Inflammation”	8
	“Neoplasm”	3
	“Malignant Tumor”	128
	“Cancer”	166

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The PPI Analysis.
The data of PPI was obtained from STRING platform. The top 12 enriched targets were displayed in a barplot (Figure 2). JUN, a protein-coding gene, is related with the Oxytocin signaling pathway and possessed the highest enrichment score. The CCR5 pathway in macrophages plays a significant role in the sequence-specific DNA binding process. Besides, IL-6 and MYC were also highly enriched. IL6 gene encodes a cytokine and functions in inflammation and the maturation of B cells. Additionally, this gene is implicated in a wide variety of inflammation-associated diseases which is related to the Th1 differentiation pathway. MYC encodes a nuclear phosphoprotein and plays a role in the cell cycle progression, apoptosis and cellular transformation. It is associated with protein metabolism pathways and the NGF pathway.

Cytoscape analysis.
Cytoscape was used to analyze the PPI network based on the date from STRING. The outcome displayed with the color of nodes, size of nodes and width of edge separately standing for degree, betweenness centrality and combine score (Figure 3). The results were quite similar to that of PPI analysis. JUN possess the highest score in degree and centrality. Moreover, MYC, IL6, CXCL8, MAPK14 and PTGS2 possessed relatively higher score in degree, and NCOA1, PTGS2, CXCL8 and other proteins possessed relatively higher score in centrality.

Medicine-Ingredient-Target-Disease Network.
A general outlook of relationships among *SF*, its ingredients, potential targets, inflammation and cancer were displayed by Cytoscape (Figure 4). According to the results, it was obvious that *SF* showed mechanism on inflammation and cancer in a multi-target, multi-pathway and synergistic process.

Molecular Docking.
According to the results of PPI analysis, we eventually selected 10 potential targets. The Surflex-dock between related ingredients and potential targets was accomplished though analyzing molecules structures, preparing molecules and docking functions via SybylX-2.0 (Table 3). The results indicated that the most of active ingredients of *SF* had effective binding (total score>5) with different targets (Figure 5). What's more, some of them had stronger combination with targets (total score>7)[27, 28]. Additionally, a particular ingredient could affect multiple targets and a target could also be affected by different ingredients, which indicates the effect of TCM on diseases is characterized by multi-ingredients, multi-targets and synergistic process.

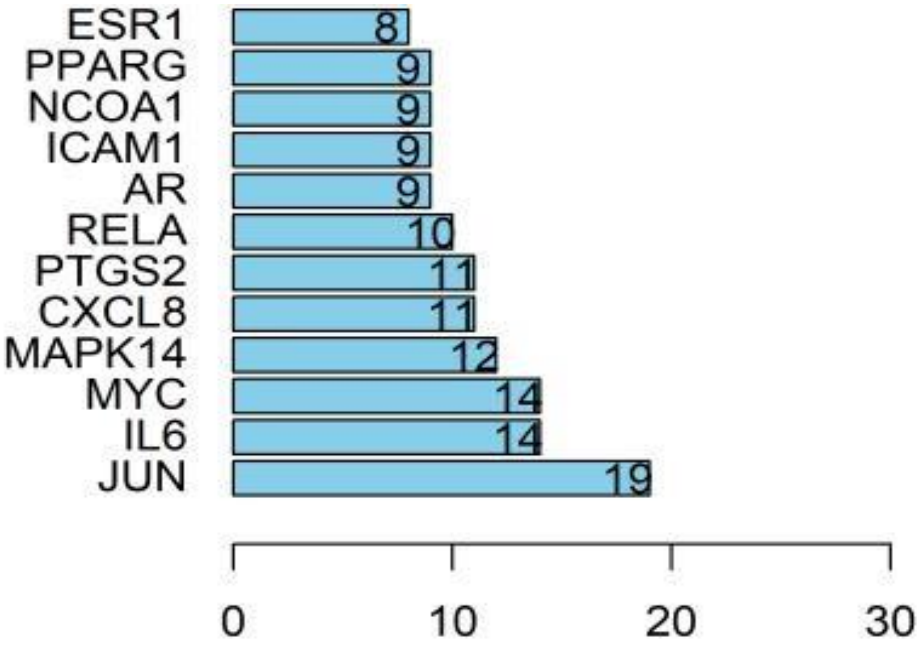

Figure 2. The top 12 enriched targets. The genes were organized by counting the numbers of interaction between genes.

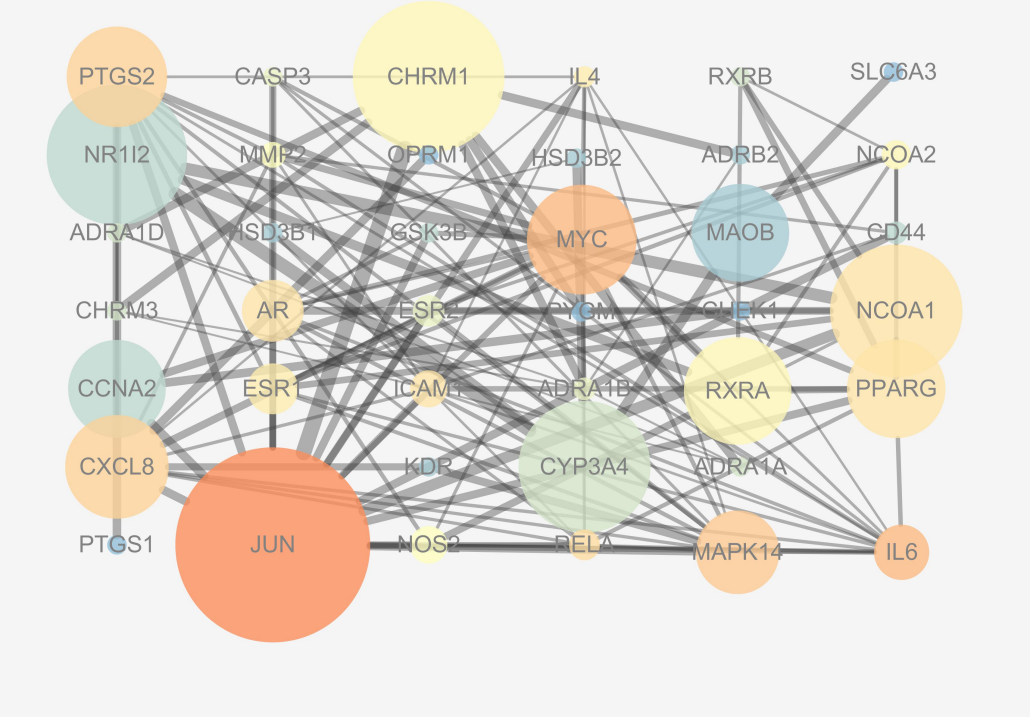

Figure 3. Cytoscape analysis. Color indicates degree, warmer to higher degree and cooler to lower one. Size of nodes indicates betweenness centrality, larger one standing for a higher score and vice versa. Width of edge indicates combine score, wider one standing for a higher score and narrower for lower.

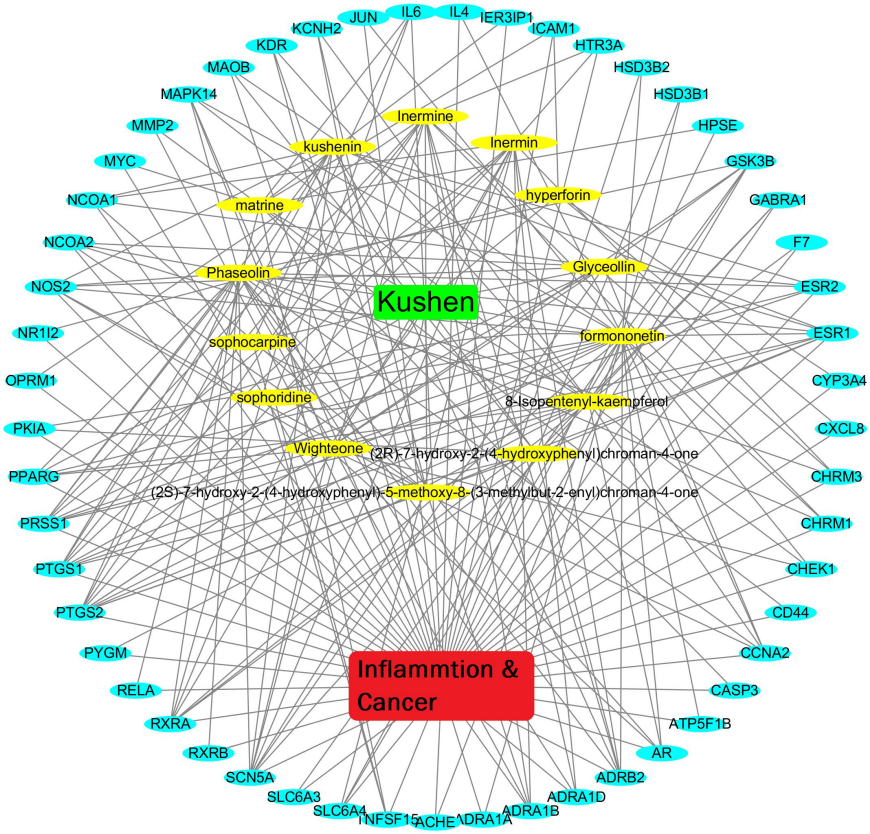

Figure 4. Medicine-ingredient-target-disease network. The figure is organized in "herbal medicine-inredient-target-disease" order. Green frame indicates to *SF* (Kushen), yellow to its ingredients, blue to the target genes and red to inflammation and neoplasm.

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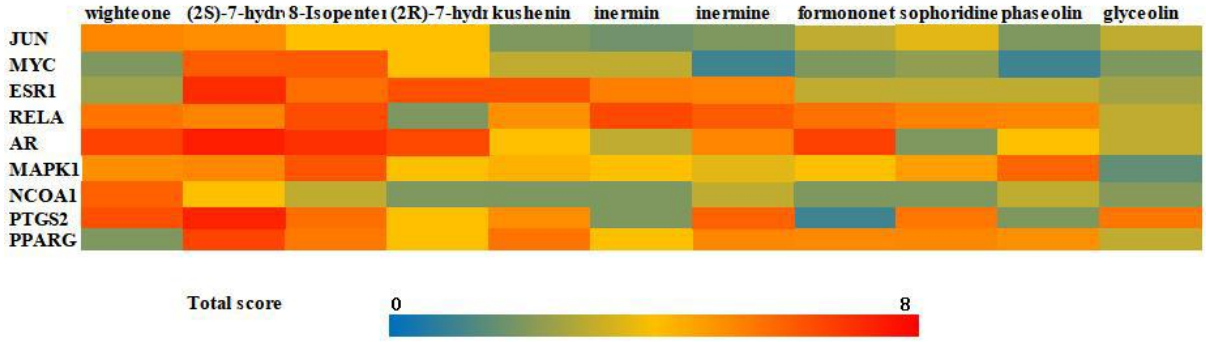

Figure 5. **Heat Map of Molecule Docking**. The color indicates the total score as the docking results. Blue represents low score indicating less probability of docking. Red represents high score indicating high probability.

Table 3. Molecular docking

Target	ID	Name	Å	Total Score
JUN	6i0j	wighteone	1.35	5.20
	6i0j	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	1.35	5.04
MYC	6u6w	8-Isopentenyl-kaempferol	1.20	6.14
	6u6w	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	1.20	6.10
ESR1	6vig	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	1.45	7.10
	6vig	(2R)-7-hydroxy-2-(4-hydroxyphenyl)chroman-4-one	1.45	6.32
	6vig	kushenin	1.45	6.30
	6vig	8-iIsopentenyl-kaempferol	1.45	5.71
	6vig	inermin	1.45	5.37
	6vig	inermine	1.45	5.27
RELA	4kv1	inermin	1.50	6.49
	4kv1	8-isopentenyl-kaempferol	1.50	6.41
	4kv1	inermine	1.50	6.11
	4kv1	formononetin	1.50	5.66
	4kv1	wighteone	1.50	5.57
	4kv1	sophoridine	1.50	5.30
	4kv1	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	1.50	5.23
	4kv1	phaseolin	1.50	5.21
	4kv1	kushenin	1.50	5.02
AR	4lbs	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	0.76	7.39
	4lbs	8-isopentenyl-kaempferol	0.76	7.01
	4lbs	formononetin	0.76	6.65
	4lbs	wighteone	0.76	6.63
	4lbs	(2R)-7-hydroxy-2-(4-hydroxyphenyl)chroman-4-one	0.76	6.51
	4lbs	inermine	0.76	5.21
MAPK 14	3lff	8-isopentenyl-kaempferol	1.50	6.26
	3lff	phaseolin	1.50	5.88
	3lff	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	1.50	5.17
	3lff	wighteone	1.50	5.04
NCOA1	6gev	wighteone	1.54	6.02

PTGS2	5f19	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	2.04	7.26
	5f19	wighteone	2.04	6.34
	5f19	inermine	2.04	5.96
	5f19	8-isopentenyl-kaempferol	2.04	5.71
	5f19	glyceolin	2.04	5.56
	5f19	sophoridine	2.04	5.54
	5f19	kushenin	2.04	5.04
PPARG	6ms7	(2S)-7-hydroxy-2-(4-hydroxyphenyl)-5-methoxy-8-(3-methylbut-2-enyl)chroman-4-one	1.43	6.59
	6ms7	kushenin	1.43	5.59
	6ms7	8-isopentenyl-kaempferol	1.43	5.52
	6ms7	sophocarpine	1.43	5.20
	6ms7	inermin	1.43	5.19
	6ms7	formononetin	1.43	5.15
	6ms7	phaseolin	1.43	

GO Functional Enrichment and KEGG Pathway Enrichment.

Results of cellular component (CC), molecular function (MF) and biological process (BP) were obtained from GO functional enrichment (Figure 6). According to the results, most targets locate in nucleus. The main molecular functions of the targets included transcriptional regulation (DNA-templated), positive regulation of cytosolic calcium ion concentration, sequence-specific DNA binding, positive regulation of transcription from RNA polymerase II promoter and inflammatory response. The main biological processes in which the targets participate are regulations of alpha 1-adrenergic receptor activity, steroid hormone receptor activity, and transcription factor activity (sequence-specific DNA binding).

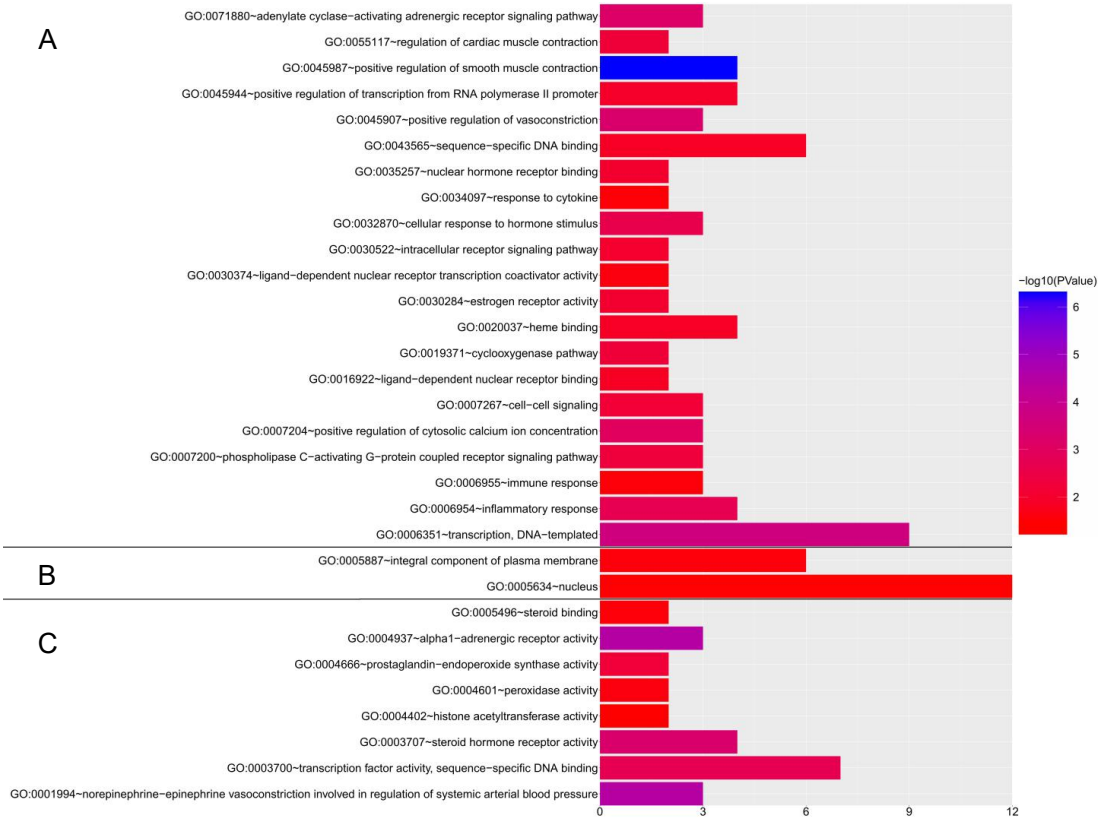

Figure 6. GO functional enrichment. The color indicates the *P* value. Cooler ones represent higher significant. The length indicates the enrichment score. **(A)**. Results of molecular function (MF). **(B)**. Results of cellular component (CC). **(C)**. Results of biological process (BP).

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Several pathways were exported from KEGG pathway enrichment. The top 20 highly enriched pathways were listed and drawn comprehensively in a map (Figure 7, Figure 8). They were virus infection related pathways, IL-17 signaling pathway, Th17 cell differentiation pathway, TNF signaling pathway, AGE-RACE signaling pathway, thyroid hormone signaling pathway and Estrogen signaling pathway. The pathways referred to immune system, endocrine system, digestive system, respiratory system and mainly regulate inflammatory factors, cell proliferation, senescence and apoptosis (Figure 8).

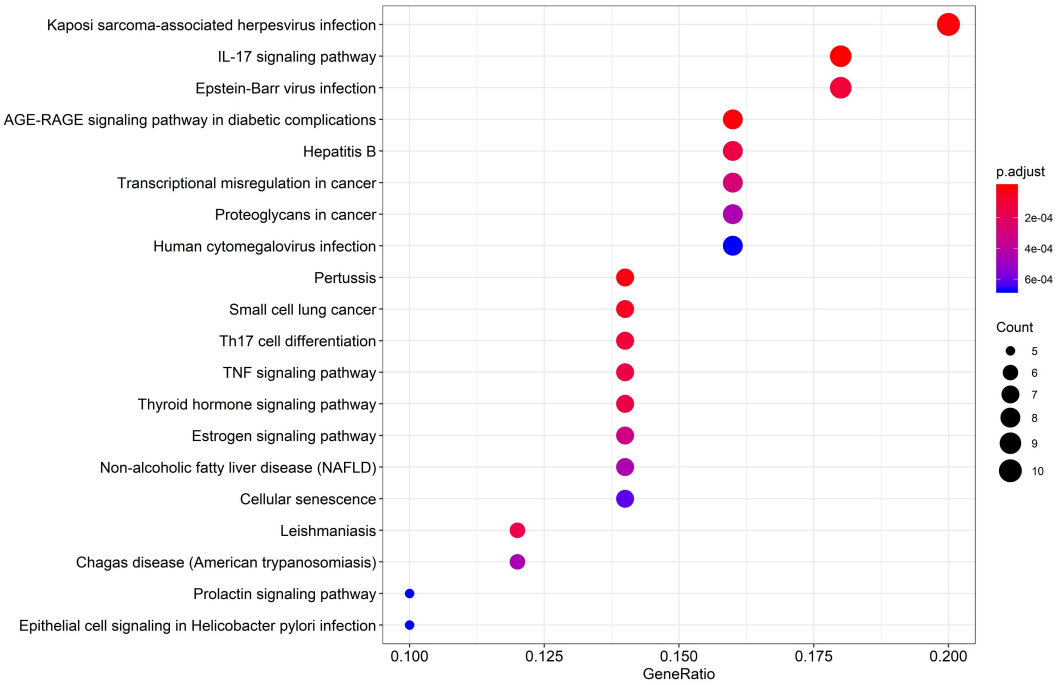

Figure 7. KEGG pathway enrichment. Each pathway was enriched by the number of its related genes. The correlation of the enrichment value was measured by their Person correlation coefficients. Red indicates high significant and blue indicates low significant. The distance to ordinate directly indicates the gene ratio. And the size of nodes indicates the count.

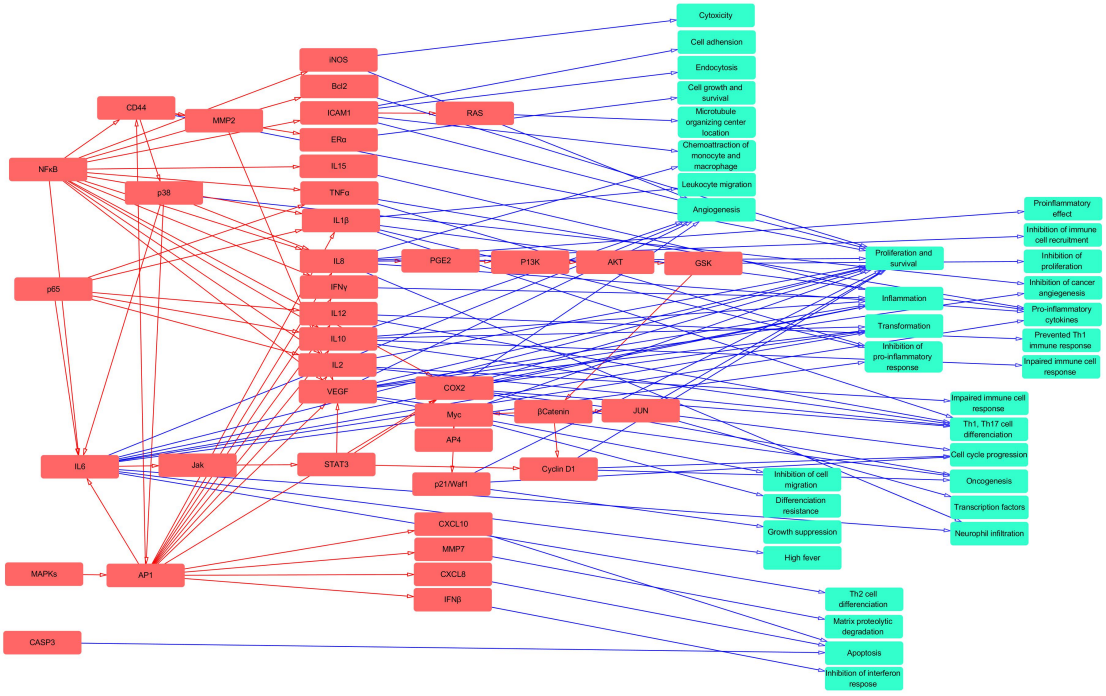

Figure 8. Comprehensive pathway map of anti-cancer and anti-inflammation mechanism of *SF*

Discussion

As one of the representative herbs of TCM, *SF* has received extensive investigation in modern pharmacology due to its effects on diseases induced by inflammation, such as cancer[16-18]. To better understand the mechanisms behind the clinical applications of *SF*, we built an integrated analytical platform based on network pharmacology, including target prediction, PPI network, topology analysis, gene enrichment analysis, and molecular docking. Using this platform, we revealed the underlying mechanisms of anti-inflammatory effects and therapeutic potential in cancer treatment of *SF*. This study indicates that *SF* displays effects on cancer and inflammation through multi-target, multi-pathway and synergistic processes.

According to ingredient-target interaction, the medicine-ingredient-target-disease network and outcomes of surflex-dock, it is obvious that a ingredient of *SF* could affect multiple targets while any single target could also be affected by different ingredients. Regarding the results od PPI and Cytoscape, JUN, IL6, MYC, MAPK14, CXCL8, PTGS2, RELA, AR, ICAM1, NCOA1, PPARG, ESR1 were considered as the potential targets. The targets' potential effect on cancer and inflammation can be seen in relevant previous researches on the targets[35-54]. Generally, *SF* mainly interferes DNA transcriptional activity to regulate inflammatory factors and cell proliferation, senescence and apoptosis. Besides, the enrichment of functions and pathways showed the DNA-binding activity, cycle-regulatory effect and inflammation-regulatory effect of *SF*. The results reflects the functional characteristics of *SF* on diseases including multi-ingredients, multi-targets and synergistic mechanism, like other herbal medicines[29-32]. Moreover, during the research, we noticed that all selected targets of inflammation belong to the cancer's, and sex hormone targets, like ESR1, NCoA1, AR are critical in the diseases. In this case, we speculated that *SF* may have a potent anti-cancer activity, especially on sex hormone related cancers, like breast cancer, cervical cancer, prostate cancer and et al.

According to our results, we drew a comprehensive map of the pathways through which *SF* works on cancer and inflammation (Figure 8). The NF-κB pathway, broadly relevant to ingredients-effected pathways, seems like one of the significant regulators which is indirectly affected by ingredients of *SF*. NF-κB is often activated in inflammatory process and hyperactivation of NF-κB can also affect EGFR and other factors which are necessary for cancer cell invasion [8,34]. In the map, we predict that NF-κB has broad-spectrum effects on inflammatory factors and cancer related factors, such as IL1, IL6, IL8, TNF-α, COX-2, Bcl-2, VEGF, ICAM1 and other factors, directly or indirectly. It is widely accepted that these factors prevent the body from inflammation and oncogenesis and dysregulated factors will induce oncogenesis by providing an environment to cancer cell for proliferation and metastasis.

The study does have limitations because of the imperfect databases which lack some aspects of data. However, the network pharmacology properly matches to herbal medicines' study and current investigation on medicine[33]. On one hand, it has a wide coverage of data and displays connections between multiple molecules, which is suitable for herbal medicine. On the other hand, it is valid in speculation of the capacity of herbs and pharmacological discovery field.

Conclusion

In this study, we deduce the potential targets, pathways and relevant ingredients of *SF* in anti-cancer and anti-inflammation process, which indicates that the effects of *SF* on cancer and inflammation are characterized by multi-ingredients, multi-targets and synergistic process. Additionally, the study also provides ideas and methods for further research and development of *SF* and other traditional Chinese medicines as well.

Data Availability

The data used to support the findings of this study are included within the article.

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