Discovery of Potential Anti-inflammatory Active Components from Miao medicine Plant Semiliquidambar Cathayensis Using Molecular Simulation Technology

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Abstract: Objective: To screen potential anti-inflammatory small molecules from Miao medicine Semiliquidambar cathayesis by molecular docking. Methods: Chemical components of Semiliquidambar cathayesis were screened from literature databases. Inflammatory-related targets were obtained by searching "inflammation" in the Genecards database. For the top 20 targets ranked by "Relevance score", target-ligand complex structures were retrieved from the Uniprot and PDB databases for molecular docking. Results: A total of 98 active components of Semiliquidambar cathayesis and 13,654 inflammation-related genes were obtained. Ten targets with high "Relevance score" and available target-ligand complex structures were screened, including MIF, TNF, SYK, TLR4, IL18, PTGS2, IL17A, IL1β, CXCL8, and NLRP3. Chemical components of Semiliquidambar cathayesis such as quercetin, catechin, isomyricitrin, and eleutheroside showed strong binding affinity to the targets, with docking scores better than -5 kcal/mol. Conclusion: Chemical components such as quercetin, catechin, isomyricitrin, and eleutheroside are potential active anti-inflammatory components of Semiliquidambar cathayesis. Further research will help clarify the material basis and action mechanism of its anti-inflammatory effect.

***Keywords*:** Miao medicine; Semiliquidambar cathayesis; Anti-inflammation; Molecular docking; Active components

1. Introduction

Semiliquidambar cathayensis H.T. Chang, an evergreen tree belonging to the Altingiaceae family, is distributed in regions such as Guizhou, Guangdong, Guangxi, Fujian, and Taiwan in China [1-3]. It is also known as Fenghegui, Banbian Fenghe, and Jiayou (a name in traditional medicine). In the Qiandongnan region of Guizhou, Semiliquidambar cathayensis is considered a highly valuable medicinal material [4]. The root, stem, leaves, and its nectar are all used for medicinal purposes, with the nectar known as "the holy medicine for rheumatism." It is sweet in taste and warm in nature, possessing the effects of dispelling wind and dampness, and promoting blood circulation [5]. The use of Semiliquidambar cathayensis in traditional medicine has a long history and confirmed efficacy, primarily used in clinical practice for treating inflammatory aspects of diseases such as rheumatoid arthritis, postnatal paralysis, hemiplegia, bruises, and cuts [6,7]. Studies have shown that Semiliquidambar cathayensis exhibits pharmacological activities including anti-inflammatory, analgesic, antiviral, antibacterial, and antioxidant effects, as well as promoting blood circulation and removing blood stasis [8,9]. It contains various active chemical components including flavonoids, alkaloids, terpenoids, phenylpropanoids, and organic acids [10,11]. Modern pharmacological research indicates the significant roles of Semiliquidambar cathayensis in anti-inflammation, pain relief, blood circulation promotion, antioxidant activity, antibacterials, and antiviral effects [12]. Inflammation is regulated by various cytokines, inflammatory mediators, and signaling pathways; it is a defensive response of the body to harmful stimuli [13]. However, excessive and persistent inflammatory responses can seriously affect the health of the organism. While Semiliquidambar cathayensis demonstrates good efficacy in treating rheumatism, its usage is largely based on folk experience, and the specific basis for its medicinal effects remains unclear. Therefore, employing molecular docking methods to explore the potential active components of Semiliquidambar cathayensis against inflammation may provide a theoretical foundation for elucidating its anti-inflammatory properties.

2. Research Methods

2.1 Collection and Structural Drawing of Chemical Constituents of Semiliquidambar cathayensis

By searching literature databases, the chemical constituents and their structures of Semiliquidambar cathayensis were

collected. The 2D structures of the small molecules were drawn using ChemDraw, converted to 3D structures, and subjected to simple MM optimization, saving the sdf structure files.

2.2 Screening and Collection of Genes and Protein Targets Related to Inflammation

Using "inflammation" as the keyword and selecting "Organism" as "Homo sapiens", inflammation-related targets were retrieved from GeneCards (https://auth.lifemapsc.com) and UniProt (https://www.uniprot.org). Genes ranked higher among the inflammation targets and for which target-ligand complexes were found in UniProt were selected for molecular docking.

2.3 Molecular Docking

2.3.1 Ligand Preparation

The sdf structure files from section 2.1 were optimized using Maestro 11.1 Ligand Preparation, generating a prepwizard. log file to prepare for ligand docking.

2.3.2 Receptor Preparation

PDB structures of each target were obtained from PDB (https://www.rcsb.org). Each structure was processed using the Schrödinger software (Maestro 11.1) through Protein Preparation Wizard (including Review and Modify, Import and Process, Optimize, Minimize, etc.), and Receptor Grid Generation.

2.3.3 Molecular Docking

The prepared ligands and receptors were subjected to molecular docking using the Ligand Docking module in Schrödinger Maestro 11.10, and the results of the molecular docking were analyzed with the Schrödinger software.

3. Results and Analysis

3.1 Chemical Constituents of Semiliquidambar cathayensis

Using "Semiliquidambar" as a keyword, a total of 98 chemical constituents of Semiliquidambar cathayensis were collected through literature searches [14-18]. (See Table 1)

Table 1. Chemical Components of Semiliquidambar cathayesis

No.	Names	No.	Names	No.	Names
BFH001	Gallic Acid	BFH034	Niacinamide	BFH067	L-Nicotine
BFH002	Quercetin	BFH035	Isorhamnetin	BFH068	2-Hydroxy Myristic Acid
BFH003	Gallic Acid Catechin	BFH036	Lemon Bitter Compound	BFH069	Adenosine
BFH004	Catechin	BFH037	Apigenin	BFH070	Resveratrol
BFH005	Kaempferol-3-O-α-L-Rhamnoside	BFH038	Cantharidin	BFH071	D-Glucose
BFH006	Kaempferol-3-O-α-L-Furanoside	BFH039	Medicago Acid	BFH072	Vitamin D3
BFH007	Catechin-[8,7-e]-4β-(3,4-dihydroxyphenyl)-dihydro-2(3H)-pyranone	BFH040	Madecassoside	BFH073	Cholesterol
BFH008	Isoquercitrin	BFH041	Sapogenin	BFH074	Sphingosine
BFH009	Kaempferol-3-O-(2”-O-Acetyl)-β-D-Galactopyranoside	BFH042	Dictamnine	BFH075	Phytosterol
BFH010	Kaempferol	BFH043	Pinosylvin	BFH076	Glycitein
BFH011	5-O-Caffeoylquinic Acid	BFH044	Quercitannic Acid	BFH077	Coenzyme Q6
BFH012	4-Hydroxy-3-methoxyphenol 1-O-β-D-(6′-O-Galloyl)-Glucoside	BFH045	Citric Acid	BFH078	Linoleic Acid
BFH013	Mixture of 4-Hydroxy-3-methoxyphenol 1-O-β-D-(6′-O-Galloyl)-Glucoside	BFH046	D-Quinic Acid	BFH079	4-Vinylphenol
BFH014	Quercetin-3-O-β-D-Galactopyranoside	BFH047	D-Mannitol	BFH080	α-Linolenic Acid
BFH015	Isorhamnetin	BFH048	Epicatechin	BFH081	Sphinganine
BFH016	Kaempferol-3-O-β-D-Glucoside	BFH049	3-(4-Hydroxyphenyl) Propionic Acid	BFH082	3-Methylmalonic Acid
BFH017	Oleanolic Acid	BFH050	Nonanedioic Acid	BFH083	Oleamide
BFH018	Palmitic Acid	BFH051	Vanillin	BFH084	Stearamide
BFH019	β-Sitosterol	BFH052	Vitexin	BFH085	Salicylic Acid Aldehyde

No.	Names	No.	Names	No.	Names
BFH020	Stearic Acid	BFH053	4-Hydroxybenzoic Acid	BFH086	Sitosterol
BFH021	Betulinic Acid	BFH054	Dihydrokarvone-β-D-Glucoside	BFH087	Caprolactam
BFH022	Moronic Aldehyde	BFH055	Eleutheroside	BFH088	Vitamin K
BFH023	Hydroxy Gynostemma Saponin	BFH056	Macrocarpous Glycoside	BFH089	Histamine
BFH024	Lyoniside	BFH057	Hesperidin	BFH090	1-Methylhistamine
BFH025	Glutamic Acid	BFH058	Root Bark Compound	BFH091	Benzoylformic Acid
BFH026	Proline	BFH059	Patchouli Ketone	BFH092	Vitamin B6
BFH027	Hydrochloric Acid	BFH060	Genistein	BFH093	Fumaric Acid
BFH028	Proanthocyanidin B1	BFH061	Magnolol	BFH094	Serine
BFH029	Hennaquinone	BFH062	Fruit Acid	BFH095	Choline
BFH030	Sinigrin	BFH063	Gluconic Acid	BFH096	Betulinic Acid
BFH031	Soy Saponin	BFH064	Cholic Acid	BFH097	Arginine Laurate
BFH032	Coumarin	BFH065	Myristic Acid	BFH098	Carotenoid
BFH033	Kaempferol-3-O-Cloudberry Glycoside	BFH066	Histidine		

3.2 Inflammatory Protein Target Database

Using "inflammation" as the keyword, a total of 13,653 inflammation-related genes were retrieved from GeneCards, selecting the top 20 targets ranked by "Relevance score." (See Table 2)

Table 2. Information on Inflammation-Related Targets

Gene	Description	Names	POB ID	Uniprot ID	Relevance score
NLRP3	NACHT, LRR and PYD domains-containing protein 3	Proteins containing NACHT, LRR, and PYD domains	6NPY	Q96P20	56.9144
IL6	Interleukin 6	Interleukin 6	8D82	P05231	42.3858
TNF	Tumor Necrosis Factor	Tumor Necrosis Factor	2AZ5	P01375	38.4313
CRP	C-Reactive Protein	C-Reactive Protein	7PKD	P02741	35.5954
IL10	Interleukin 10	Interleukin 10	null	P22301	34.4176
TLR4	Toll Like Receptor 4	Toll-Like Receptor 4	3FXI	O00206	32.1647
CXCL8	Interleukin-8	Interleukin-8	6LFO	P10145	28.6944
IL1B	Interleukin 1 Beta	Interleukin 1 β	5R89	P01584	28.4592
NOD2	Nucleotide Binding Oligomerization Domain Containing 2	Nucleotide-Binding Oligomerization Domain 2	null	Q9HC29	26.1269
SYK	Tyrosine-protein kinase SYK	Tyrosine Protein Kinase SYK	3FQS	P43405	24.9085
PTGS2	Prostaglandin G/H synthase 2	Prostaglandin G/H Synthase 2	5F1A	P35354	21.8929
TLR2	Toll Like Receptor 2	Toll-Like Receptor 2	6NIG	O60603	21.7271
MEFV	MEFV Innate Immunity Regulator, Pyrin	MEFV, An Innate Immune Regulator, Pyrin	null	O15553	21.4813
IL17A	Interleukin 17A	Interleukin 17A	5HI3	Q16552	21.2794
IL13	Interleukin 13	Interleukin 13	3L5X	P35225	20.0036
CTLA4	Cytotoxic T-Lymphocyte Associated Protein 4	Cytotoxic T-Lymphocyte Associated Protein 4	7CIO	P16410	19.9912
HLA-DRB1	Major Histocompatibility Complex, Class II, DR Beta 1	Major Histocompatibility Complex, Class II, DR Beta 1	2G9H	P01911	19.4927
TNFRSF1A	TNF Receptor Superfamily Member 1A	TNF Receptor Superfamily Member 1A	1FT4	P19438	18.3511
IL18	Interleukin 18	Interleukin 18	3WO2	Q14116	17.6331
MIF	Macrophage Migration Inhibitory Factor	Macrophage Migration Inhibitory Factor	1GCZ	P14174	13.7927

3.3 Molecular Docking Analysis of Chemical Constituents of Semiliquidambar cathayensis and Inflammatory Targets

3.3.1 Molecular Docking Targets

Targets with high "Relevance scores" that also had corresponding target-ligand complexes identified in UniProt were selected for molecular docking (see Table 3). The chemical constituents of Semiliquidambar cathayensis were docked with the following 10 targets, and the top-ranking chemical constituents based on the docking scores were analyzed individually with their respective targets.

Table 3. Information on Inflammation Targets for Molecular Docking

Gene	Description	Names	POB ID	Uniprot ID	Relevance score
NLRP3	NACHT, LRR and PYD domains-containing protein 3	Proteins containing NACHT, LRR, and PYD domains	6NPY	Q96P20	56.9144
TNF	Tumor Necrosis Factor	Tumor Necrosis Factor	2AZ5	P01375	38.43132
TLR4	Toll Like Receptor 4	Toll-Like Receptor 4	3FXI	O00206	32.1647
CXCL8	Interleukin-8	Interleukin-8	6LFO	P10145	28.69438
IL1B	Interleukin 1 Beta	Interleukin 1 β	5R89	P01584	28.45916
SYK	Tyrosine-protein kinase SYK	Tyrosine Protein Kinase SYK	3FQS	P43405	24.90851
PTGS2	Prostaglandin G/H synthase 2	Prostaglandin G/H Synthase 2	5F1A	P35354	21.89291
IL17A	Interleukin 17A	Interleukin 17A	5HI3	Q16552	21.27944
IL18	Interleukin 18	Interleukin 18	3WO2	Q14116	17.63311
MIF	Macrophage Migration Inhibitory Factor	Macrophage Migration Inhibitory Factor	1GCZ	P14174	13.7927

3.3.2 Potential Active Compounds Targeting NLRP3

NLRP3 [19] is an inflammasome comprised of a multi-protein complex located in the cytoplasm. The NLRP3 inflammasome is primarily expressed in various cells such as macrophages, neutrophils, epithelial cells, and smooth muscle cells. Among these, NLRP3 serves as an important pattern recognition receptor in the cytoplasm, capable of detecting intracellular pathogens and metabolites, and is a core component of the inflammasome.

The results of molecular docking indicate that the top twenty scoring compounds from Semiliquidambar cathayensis, such as d-limonene-β-D-glucoside, isoangustone A, isoquercitrin, and 4-hydroxy-3-methoxyphenol 1-O-β-D-(6'-O-galloyl)-glucoside, are capable of binding to the inflammatory NLRP3 target protein. The interaction patterns between these compounds and the NLRP3 target were examined, analyzing the interactions of the mixture of d-limonene-β-D-glucoside, isoangustone A, isoquercitrin, and 4-hydroxy-3-methoxyphenol 1-O-β-D-(6'-O-galloyl)-glucoside. (See Figure 1)

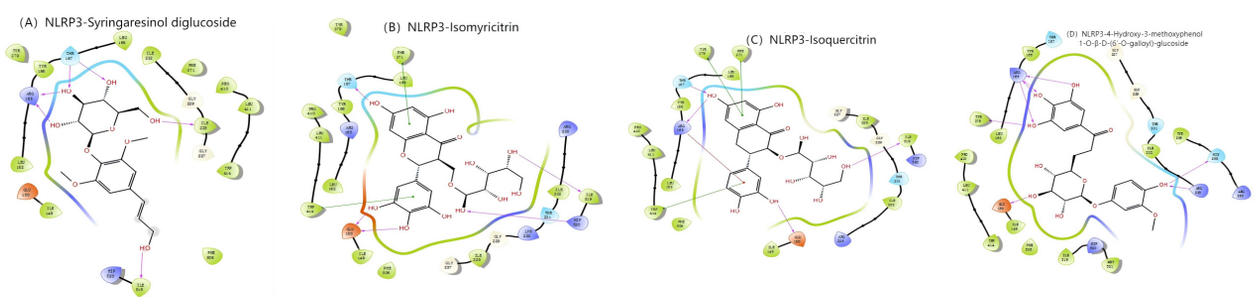

Figure 1. Interaction Pattern of NLRP3 with Chemical Components of Helicteres angustifolia

(A) NLRP3-Syringaresinol diglucoside; (B) NLRP3-Isomyricitrin; (C) NLRP3-Isoquercitrin; (D) NLRP3-4-Hydroxy-3-methoxyphenol 1-O-β-D-(6′-O-galloyl)-glucoside

(Note: •—•: Pi-Pi stacking; → :H-bong; —•: Pi-cation)

In Figure 1 (A), there are six hydrogen bonds between NLRP3 and d-limonene-β-D-glucoside, with a docking score of -9.233 kcal/mol. In Figure 1 (B), five hydrogen bonds exist between NLRP3 and isoangustone A, while strong π-π conjugation occurs between Trp414 and Phe371 with isoangustone A, resulting in a docking score of -9.136 kcal/mol. Figure 1 (C) shows four hydrogen bonds between NLRP3 and isoquercitrin, with conjugation effects between Tyr379, Phe371, and Trp414 with isoquercitrin, leading to a docking score of -9.098 kcal/mol. In Figure 1 (D), there are eight hydrogen bonds

between NLRP3 and 4-hydroxy-3-methoxyphenol 1-O-β-D-(6'-O-galloyl), with a docking score of -8.815 kcal/mol.

3.3.3 Potential Active Compounds Targeting TNF

TNF [20] is an inflammatory marker that promotes the formation of atherosclerosis.

The results of molecular docking indicate that the top twenty scoring compounds include coumarin, resveratrol, eleutheroside, and vitamin B6, which can interact with the inflammatory TNF target protein. The interaction patterns between these compounds and the TNF target were examined, analyzing the interactions of coumarin, resveratrol, eleutheroside, and vitamin B6. (See Figure 2)

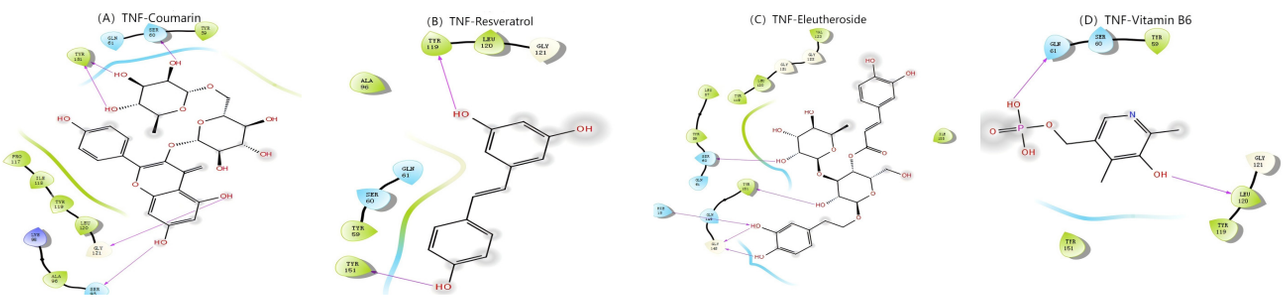

Figure 2. Interaction Patterns between TNF and Chemical Components of Semiliquidambar cathayesis

(A) TNF-Coumarin; (B) TNF-Resveratrol; (C) TNF-Eleutheroside; (D) TNF-Vitamin B6

(Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

According to Figure 2 (A), the amino acid residues Gly121 and Ser95 in TNF interact with coumarin, forming five hydrogen bonds, with a docking score of -6.463 kcal/mol. In Figure 2 (B), the amino acid residues Try119 and Try151 in TNF interact with resveratrol, resulting in two hydrogen bonds and a docking score of -5.711 kcal/mol. Figure 2 (C) shows that the amino acid residues Ser60 and Gly148 in TNF interact with eleutheroside, leading to the formation of five hydrogen bonds, with a docking score of -5.585 kcal/mol. In Figure 2 (D), the amino acid residues Gln61 and Leu120 in TNF interact with vitamin B6, resulting in two hydrogen bonds and a docking score of -5.435 kcal/mol.

3.3.4 Potential Active Compounds Targeting TLR4

TLR4 [21,22] is a crucial regulator of kidney inflammatory responses and tissue fibrosis. Excessive expression of TLR4 can adversely affect the structure and function of renal tissue, and, upon stimulation, TLR4 promotes the release of inflammatory mediators, triggering a series of inflammatory responses.

The results of molecular docking indicate that the top twenty scoring compounds, including catechin, D-mannitol, astragaloside, and vitamin B6, can interact with the inflammatory TLR4 target protein. The interaction patterns between these compounds and the TLR4 target were examined, analyzing the interactions of catechin, D-mannitol, astragaloside, and vitamin B6. (See Figure 3)

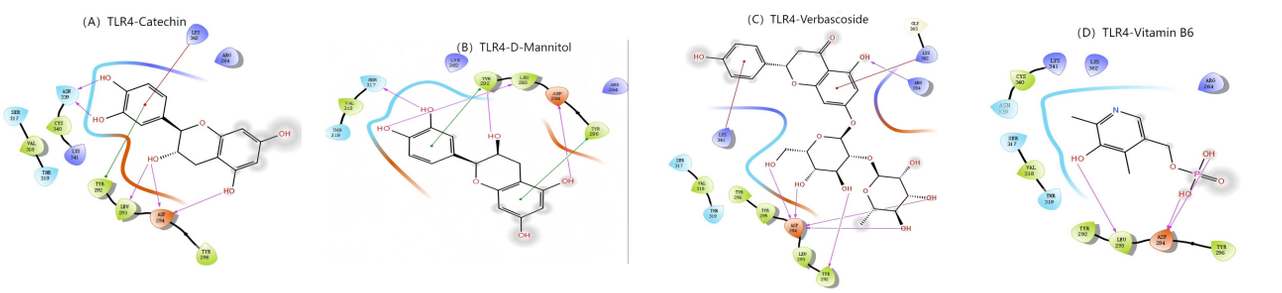

Figure 3. Interaction Pattern of TLR4 with Chemical Components of Helicteres angustifolia

(A) TLR4-Catechin; (B) TLR4-D-Mannitol; (C) TLR4-Verbascoside; (D) TLR4-Vitamin B6

((Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

In Figure 3 (A), there are five hydrogen bonds between TLR4 and catechin, with strong π-π conjugation between Tyr292 and catechin. Additionally, there is a strong cation-π interaction between Lys362 and catechin, resulting in a docking score of -5.591 kcal/mol. Figure 3 (B) shows that TLR4 forms four hydrogen bonds with D-mannitol, along with π-π conjugation between Try292 and Try296 with D-mannitol, yielding a docking score of -5.222 kcal/mol. In Figure 3 (C),

TLR4 interacts with astragaloside through six hydrogen bonds, with strong cation-π interactions between Lys362, Lys341, and astragaloside, resulting in a docking score of -5.028 kcal/mol. Finally, in Figure 3 (D), TLR4 forms three hydrogen bonds with vitamin B6, with a docking score of -5.023 kcal/mol.

3.3.5 Potential Active Compounds Targeting CXCL8

CXCL8 [23] is a key enzyme involved in inflammation-induced oxidative stress, and its main product, PG, is an important inflammatory mediator in liver injury, playing a significant role in the onset of inflammation.

The results of molecular docking indicate that the top twenty scoring compounds, including eleutheroside, sinigrin, patchouli alcohol, and nonanedioic acid, can interact with the inflammatory CXCL8 target protein. The interaction patterns between these compounds and the CXCL8 target were examined, analyzing the interactions of eleutheroside, sinigrin, patchouli alcohol, and nonanedioic acid. (See Figure 4)

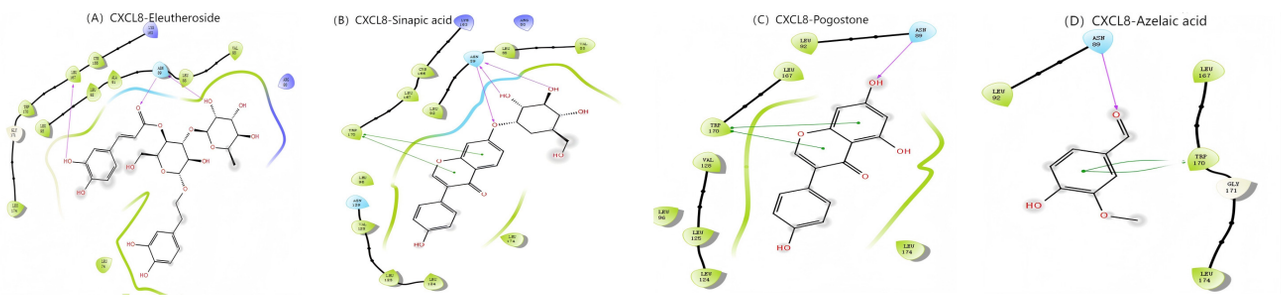

Figure 4. Interaction Pattern of CXCL8 with Chemical Components of Helicteres angustifolia

(A) CXCL8-Eleutheroside; (B) CXCL8-Sinapic acid; (C) CXCL8-Pogostone; (D) CXCL8-Azelaic acid

((Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

In Figure 4 (A), there are three hydrogen bonds between CXCL8 and eleutheroside, resulting in a docking score of -5.246 kcal/mol. Figure 4 (B) shows that CXCL8 forms three hydrogen bonds with sinigrin, along with strong π-π conjugation between Trp170 and sinigrin, yielding a docking score of -5.167 kcal/mol. In Figures 4 (C) and (D), CXCL8 interacts with patchouli alcohol and nonanedioic acid, respectively, forming one hydrogen bond with each, with docking scores of -5.013 kcal/mol and -4.830 kcal/mol.

3.3.6 Potential Active Compounds Targeting IL-1β

IL-1β [24] is a cytokine produced by activated macrophages, belonging to the interleukin family, which stimulates the proliferation, differentiation, and enhancement of function in cells involved in immune responses.

The results of molecular docking indicate that the top twenty scoring compounds, including hydrochloride, gallic acid catechin, vanillic acid, and kaempferol-3-O-β-D-pyranoglucoside, can interact with the inflammatory IL-1β target protein. The interaction patterns between these compounds and the IL-1β target were examined, analyzing the interactions of hydrochloride, gallic acid catechin, vanillic acid, and kaempferol-3-O-β-D-pyranoglucoside. (See Figure 5)

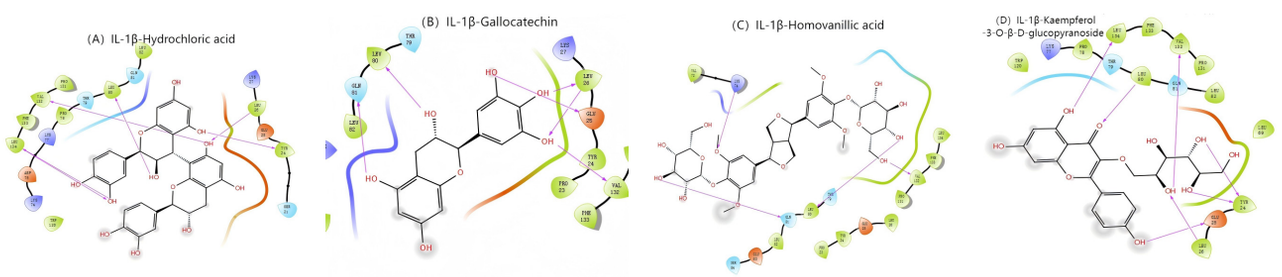

Figure 5. Interaction Pattern of IL-1β with Chemical Components of Helicteres angustifolia

(A) IL-1β-Hydrochloric acid; (B) IL-1β-Gallocatechin; (C) IL-1β-Homovanillic acid; (D) IL-1β-Kaempferol-3-O-β-D-glucopyranoside

((Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

According to Figures 5 (A, B, C, D), IL-1β forms six hydrogen bonds with hydrochloride, six hydrogen bonds with gallic acid catechin, four hydrogen bonds with vanillic acid, and seven hydrogen bonds with kaempferol-3-O-β-D-pyranoglucoside, with docking scores of -7.222 kcal/mol, -6.933 kcal/mol, -6.673 kcal/mol, and -6.469 kcal/mol, respectively.

3.3.7 Potential Active Compounds Targeting SYK

SYK [25] is involved in signal transduction in various cell types and serves as a key mediator of immune receptor signaling in inflammatory cells.

The results of molecular docking indicate that the top twenty scoring compounds, including coumarin, kaempferol-3-O-β-D-pyranoglucoside, astragaloside, and vitamin K, can interact with the inflammatory SYK target protein. The interaction patterns between these compounds and the SYK target were examined, analyzing the interactions of coumarin, kaempferol-3-O-β-D-pyranoglucoside, astragaloside, and vitamin K. (See Figure 6)

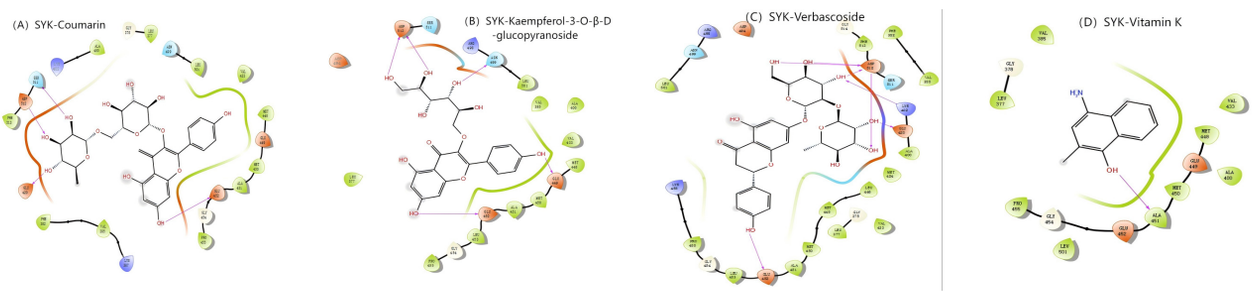

Figure 6. Interaction Pattern of SYK with Chemical Components of Helicteres angustifolia

(A) SYK-Coumarin; (B) SYK-Kaempferol-3-O-β-D-glucopyranoside; (C) SYK-Verbascoside; (D) SYK-Vitamin K

(Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

According to Figures 6 (A, B, C, D), SYK forms four hydrogen bonds with coumarin, five hydrogen bonds with kaempferol-3-O-β-D-pyranoglucoside, seven hydrogen bonds with astragaloside, and one hydrogen bond with vitamin K, with docking scores of -8.720 kcal/mol, -8.404 kcal/mol, -8.325 kcal/mol, and -8.215 kcal/mol, respectively.

3.3.8 Potential Active Compounds Targeting PTGS2

PTGS2 [26] is a key enzyme involved in inflammation-induced oxidative stress, and its main product, PG, is an important inflammatory mediator in liver injury, playing a significant role in the onset of inflammation.

The results of molecular docking indicate that the top twenty scoring compounds, including coumarin, quercetin-3-O-β-D-pyranogalactoside, kaempferol-3-O-β-D-pyranoglucoside, and kaempferol-3-O-(2"-O-acetyl)-β-D-pyranogalactoside, can interact with the inflammatory PTGS2 target protein. The interaction patterns between these compounds and the PTGS2 target were examined, analyzing the interactions of coumarin, quercetin-3-O-β-D-pyranogalactoside, kaempferol-3-O-β-D-pyranoglucoside, and kaempferol-3-O-(2"-O-acetyl)-β-D-pyranogalactoside. (See Figure 7)

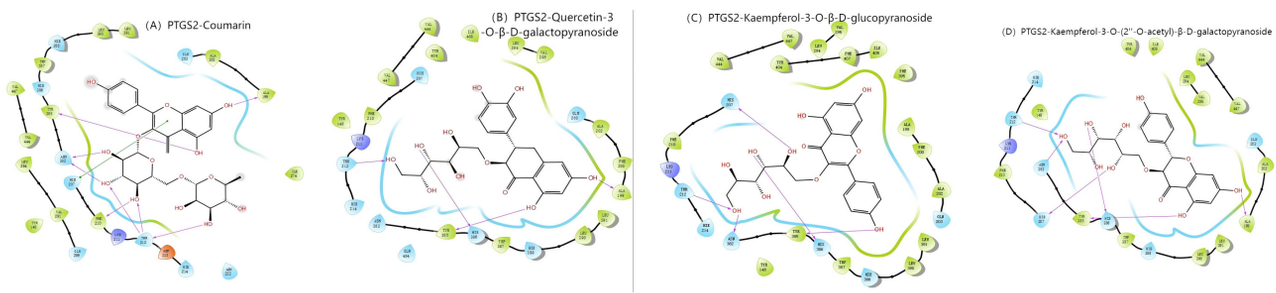

Figure 7. Interaction Pattern of PTGS2 with Chemical Components of Helicteres angustifolia

(A) PTGS2-Coumarin; (B) PTGS2-Quercetin-3-O-β-D-galactopyranoside; (C) PTGS2-Kaempferol-3-O-β-D-glucopyranoside; (D) PTGS2-Kaempferol-3-O-(2"-O-acetyl)-β-D-galactopyranoside

(Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

Figure 7 (A) shows that PTGS2 forms eight hydrogen bonds with coumarin, and there is strong π-π conjugation between HIS207 and coumarin, with a docking score of -10.359 kcal/mol. Additionally, Figures 7 (B, C, D) demonstrate that PTGS2 forms four hydrogen bonds with quercetin-3-O-β-D-pyranogalactoside, five hydrogen bonds with kaempferol-3-O-β-D-pyranoglucoside, and six hydrogen bonds with kaempferol-3-O-(2"-O-acetyl)-β-D-pyranogalactoside, with docking scores of -9.947 kcal/mol, -9.543 kcal/mol, and -9.207 kcal/mol, respectively.

3.3.9 Potential Active Compounds Targeting IL-17A

IL-17A [27] is considered an important pathogenic factor. In many inflammation-related diseases, such as viral herpes, inhibiting IL-17A can significantly reduce the inflammatory response it causes, greatly increasing survival rates.

The results of molecular docking indicate that the top twenty scoring compounds, including 4-hydroxy-3-methoxyphenol 1-O-β-D-(6'-O-galloyl)-glucoside, sinigrin, coumarin, and eleutheroside, can interact with the inflammatory IL-17A target protein. The interaction patterns between these compounds and the IL-17A target were examined, analyzing the interactions of 4-hydroxy-3-methoxyphenol 1-O-β-D-(6'-O-galloyl)-glucoside, sinigrin, coumarin, and eleutheroside. (See Figure 8)

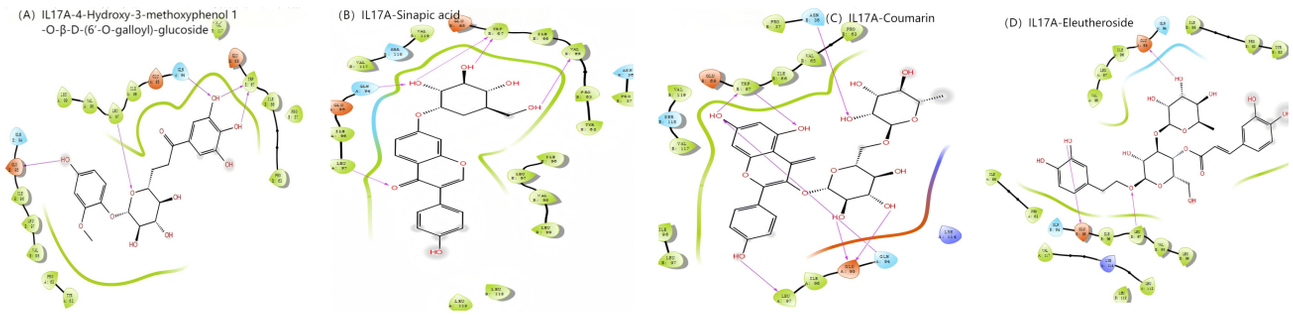

Figure 8. Interaction Pattern of IL-17A with Chemical Components of Helicteres angustifolia

(A) IL17A-4-Hydroxy-3-methoxyphenol 1-O-β-D-(6′-O-galloyl)-glucoside; (B) IL17A-Sinapic acid; (C) IL17A-Coumarin; (D) IL17A-Eleutheroside

(Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

According to Figures 8 (A, B, C, D), IL-17A forms five hydrogen bonds with 4-hydroxy-3-methoxyphenol 1-O-β-D-(6'-O-galloyl)-glucoside, five hydrogen bonds with sinigrin, seven hydrogen bonds with coumarin, and three hydrogen bonds with eleutheroside, with docking scores of -8.141 kcal/mol, -7.690 kcal/mol, -7.619 kcal/mol, and -7.528 kcal/mol, respectively.

3.3.10 Potential Active Compounds Targeting IL-18

IL-18 [28] is a recently discovered multifunctional pro-inflammatory factor that promotes inflammation and apoptosis. It can effectively induce the production of γ-interferon, playing a significant regulatory role in the body's immune and inflammatory responses.

The results of molecular docking indicate that the top twenty scoring compounds, including vanillic acid, eleutheroside, sinigrin, and 3-aldehydesalicylic acid, can interact with the inflammatory IL-18 target protein. The interaction patterns between these compounds and the IL-18 target were examined, analyzing the interactions of vanillic acid, eleutheroside, sinigrin, and 3-aldehydesalicylic acid. (See Figure 9)

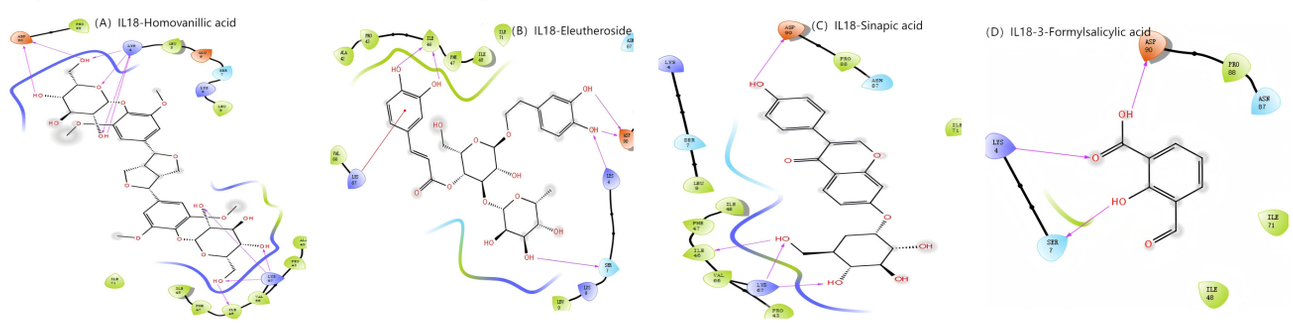

Figure 9. Interaction Pattern of IL-18 with Chemical Components of Helicteres angustifolia

(A) IL18-Homovanillic acid; (B) IL18-Eleutheroside; (C) IL18-Sinapic acid; (D) IL18-3-Formylsalicylic acid

(Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

In Figures 9 (A, B, C, D), IL-18 forms ten hydrogen bonds with vanillic acid, six hydrogen bonds with eleutheroside, four hydrogen bonds with sinigrin, and three hydrogen bonds with 3-aldehydesalicylic acid. Additionally, there is a strong cation-π interaction between Lys67 and eleutheroside, with docking scores of -5.924 kcal/mol, -5.868 kcal/mol, -4.955 kcal/mol, and -4.868 kcal/mol, respectively.

3.3.11 Potential Active Compounds Targeting MIF

MIF [29], as a multifunctional cytokine, regulates both innate and adaptive immune responses. It is present in various cells under pathological and physiological conditions and participates in multiple disease processes, including inflammatory arthritis, multiple sclerosis, and sepsis.

The results of molecular docking indicate that the top twenty scoring compounds, including soy saponins, quercetin, catechin gallate, and proanthocyanidin B1, can interact with the inflammatory MIF target protein. The interaction patterns between these compounds and the MIF target were examined, analyzing soy saponins, quercetin, catechin gallate, and proanthocyanidin B1. (See Figure 10)

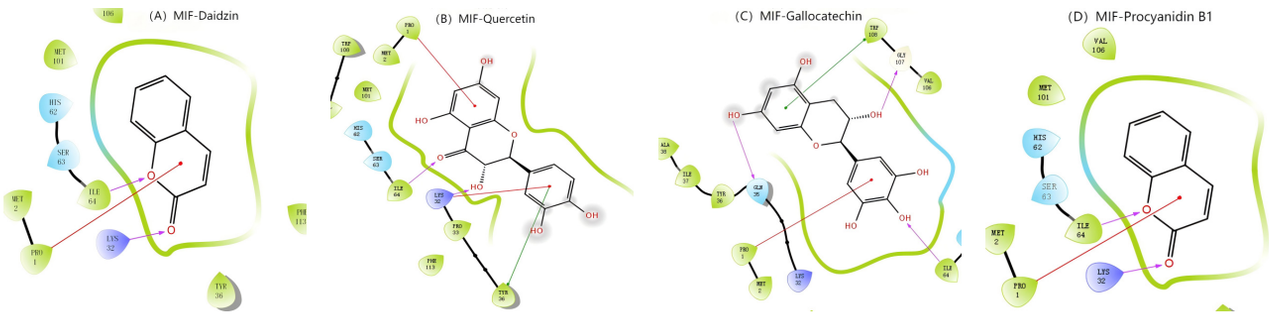

Figure 10. Interaction Pattern of MIF with Chemical Components of Helicteres angustifolia

(A) MIF-Daidzin; (B) MIF-Quercetin; (C) MIF-Gallocatechin; (D) MIF-Procyanidin B1

(Note: •—•: Pi-Pi stacking; → :H-bong ; —•: Pi-cation)

Figure 10 (A) shows that MIF forms two hydrogen bonds with soy saponins, and there is a strong cation-π interaction between Pro1 and soy saponins, with a docking score of -6.599 kcal/mol. In Figure 10 (B), it can be seen that MIF forms two hydrogen bonds with quercetin, and there is potential π-π conjugation between Tyr36 and quercetin. Additionally, strong cation-π interactions exist between Pro1, Lys32, and quercetin, with a docking score of -6.411 kcal/mol. In Figures 10 (C, D), MIF forms three hydrogen bonds with catechin gallate and one hydrogen bond with proanthocyanidin B1. Furthermore, there is a good cation-π interaction between Pro1 and catechin gallate, as well as potential π-π conjugation with Trp108, with docking scores of -6.409 kcal/mol and -6.324 kcal/mol, respectively.

4. Conclusions and Discussion

A total of 98 chemical components in Semiliquidambar cathayesis were subjected to molecular docking with 10 inflammatory target proteins (NLRP3, TNF, TLR4, CXCL8, IL1B, SYK, PTGS2, IL17A, IL18, MIF). The results showed that the chemical components of Semiliquidambar cathayesis interact with one or more amino acid residues in the active pockets of different target proteins, forming hydrogen bonds, π-π conjugation, or cation-π interactions, thus establishing stable docking models.

The chemical components in Semiliquidambar cathayesis exhibited good binding affinity with the inflammatory protein targets, with docking scores all below -5 kcal/mol, suggesting the presence of potentially good anti-inflammatory active components. Quercetin showed strong interactions with NLRP3, TNF, IL1B, SYK, and MIF; catechin exhibited intense interactions with targets such as TLR4, CXCL8, IL1B, and IL17A; isoquercitrin interacted with targets like NLRP3, CXCL8, IL1B, PTGS2, and IL17A; and eleutheroside interacted with targets TNF, TLR4, CXCL8, PTGS2, IL17A, and IL18. Compounds such as quercetin, catechin, isoquercitrin, and eleutheroside are flavonoid natural compounds that demonstrate good binding activity with inflammatory targets, suggesting they may be potential anti-inflammatory active components of Semiliquidambar cathayesis [30].

Coumarin showed strong effects on targets such as TNF, TLR4, IL1B, SYK, PTGS2, and IL17A, and as a natural phenylpropanoid compound, it may also serve as a potential anti-inflammatory active component of Semiliquidambar cathayesis. Sinigrin displayed good binding activity with targets CXCL8, IL17A, and IL18, and given that sinigrin [31] possesses a phenolic hydroxyl structure with broad pharmacological effects, it may also be a potential anti-inflammatory agent. This study, by collecting and further isolating the chemical components of Semiliquidambar cathayesis, utilized molecular docking techniques to explore its potential anti-inflammatory active components, providing a theoretical basis for clinical applications in anti-inflammatory treatment.

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