Article published online: 2024-05-31

THIEME OPEN ACCESS

Original Article

Pharmacological Material Basis of Chushi Weiling Decoction and Its Mechanism in Eczema and Herpes Zoster Based on UPLC-Q-TOF-MS, GC-MS, and Network Pharmacology

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Pharmaceut Fronts

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Abstract

Chushi Weiling Decoction (CWD) is a classic prescription in traditional Chinese medicine used to treat dampness-heat skin diseases. However, the material composition of CWD and its therapeutic mechanism remained largely unknown. This study aimed to investigate the pharmacological material basis of CWD and their potential therapeutic effects using ultra-high performance liquid chromatography-quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS), gas chromatography-mass spectrometry (GC-MS), and network pharmacology. In this work, UPLC-Q-TOF-MS and GC-MS technologies were used to identify the main components of CWD. The UPLC-Q-TOF MS analysis was performed on a Thermo-Accucore aQ C18 (100 mm × 2.1 mm, 2.6 μm; ThermoFisher, United States) with a mobile phase consisting of acetonitrile–0.1% formic acid aqueous solution in MS^E mode. The GC-MS analysis was performed on an HP-5MS UI (0.25 mm × 30 m × 0.25 μm; Agilent, United States) of headspace injection. Treatment mechanisms of eczema and herpes zoster were explored using network pharmacology methods and enrichment analysis. Our data showed that there were 194 compounds identified using UPLC-Q-TOF-MS and 92 compounds identified using GC-MS. The mass spectrometric fragmentation rules of terpenoids, flavonoids, phenylpropanoids, phenolic acid esters, and alkaloids in CWD were summarized. Network pharmacology provided targets and pathways, and molecular docking indicated that alisol J 23-acetate, kaempferol, anomalin, and cinnamaldehyde tend to combine with target proteins in a good case at a low level of binding energy. Given the above, this study provides a reference for the material basis of CWD, and suggests that CWD may play a therapeutic role in eczema and herpes zoster by (1) anti-inflammatory, antiviral, mediating immune response; and (2) regulating steroid metabolism.

Keywords

- classic prescription
- Chushi Weiling Decoction
- network pharmacology
- molecular docking

received
November 20, 2023
accepted
April 27, 2024

DOI https://doi.org/10.1055/s-0044-1787123.
ISSN 2628-5088.

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Introduction

Chushi Weiling Decoction (CWD) is one of the first batches of 100 classic prescriptions released by the State Administration of Traditional Chinese Medicine.[1] It is a classic prescription recorded in Chen Shigong's "Orthodox Manual of External Diseases" of the Ming Dynasty and Wu Qian's "The Golden Mirror of Medicine" of the Qing Dynasty, which is used to treat dampness-heat skin diseases such as "damp sore," "fire erysipelas," and "shingles."[2–4] Modern Chinese medicine believes that "damp sore" refers to eczema, while "fire erysipelas" and "shingles" refer to skin diseases such as herpes zoster.[5,6] Eczema and herpes zoster are common skin lesions. Eczema is an inflammatory skin lesion caused by various internal and external factors, while herpes zoster is an infectious skin disease caused by the varicella-zoster virus. These two diseases have different pathologies with similar characteristics such as causing rash, blisters, erosion, exudation, itching, and pain in the affected area. Modern traditional Chinese medicine (TCM) regards CWD as the main prescription for treating eczema and herpes zoster in clinical practice, which can achieve good therapeutic effects.[7–9]

The entire recipe of CWD consists of 14 Chinese medicinal materials, including *Atractylodis Rhizoma* (Cangzhu), *Magnoliae Officinalis Cortex* (Houpo), *Citri Reticulatae Pericarpium* (Chenpi), *Glycyrrhizae Radix* et *Rhizoma* (Gancao), *Alismatis Rhizoma* (Zexie), *Poria* (Fuling), *Polyporus* (Zhuling), *Cinnamomi Cortex* (Rougui), *Atractylodis Macrocephalae Rhizoma* (Baizhu), *Gardeniae Fructus* (Zhizi), *Akebiae Caulis* (Mutong), *Saposhnikoviae Radix* (Fangfeng), *Talcum* (Huashi), and *Junci Medulla* (Dengxincao). The information and abbreviations of herbs are provided in ►**Table 1**. Among them, Cangzhu is the monarch drug, which can strengthen the spleen and dry dampness; Houpo, Chenpi, and other medicinal herbs are used as ministerial drugs to promote diuresis, promote spleen function, and remove dampness; Rougui is used as an adjuvant drug to promote Yang and Qi circulation; Gancao is a conductant drug that can clear heat and detoxify.[10–12]

Modern pharmacology and medical research have shown that Chinese medicinal herbs such as Cangzhu, Houpo, and Chenpi have therapeutic effects on eczema and herpes zoster. The terpenoids, flavonoids, and phenolic compounds from these herbs have anti-inflammatory, analgesic, and antiviral effects.[13–15] However, the material composition and therapeutic mechanism of CWD were still unclear. This study used ultra-high performance liquid chromatography-quadrupole time-of-flight mass spectrometry (UPLC-Q-TOF-MS) and gas chromatography-mass spectrometry (GC-MS) techniques to analyze the composition of CWD and identify its main components. In addition, based on network pharmacology, the

Table 1 Medical information of CWD

TCM name	Product name	Abbreviation	Origin	Lot number	Place of production	Manufacturer
Atractylodis Rhizoma	Cangzhu (stir fried with bran)	CZ	*Atractylodes Lancea* (Thunb.) DC.	220361341	Jiangsu	Beijing Kangmei Pharmaceutical Co., Ltd.
Magnoliae Officinalis Cortex	Houpo (processed with ginger juice)	HP	*Magnolia officinalis* Rehd. et Wils.	220301171	Sichuan	Kangmei Pharmaceutical Co., Ltd.
Citri Reticulatae Pericarpium	Chenpi	CP	*Citrus reticulata* cv. Chachiensis	220403921	Guangdong	Kangmei Pharmaceutical Co., Ltd.
Glycyrrhizae Radix et *Rhizoma*	Gancao	GC	*Glycyrrhiza uralensis* Fisch	210731	Xinjiang	Shanghai Kangqiao Traditional Chinese Medicine Slices Co., Ltd.
Alismatis Rhizoma	Zexie	ZX	*Alisma orientale* (Samuel) Juz.	220400501	Fujian	Kangmei Pharmaceutical Co., Ltd.
Poria	Fuling	FL	*Poria cocos* (Schw.) Wolf	210428	Anhui	Shanghai Kangqiao Traditional Chinese Medicine Slices Co., Ltd.
Polyporus	Zhuling	ZL	*Polyporus umbellatus* (Pers.) Fr.	220107	Shaanxi	Shanghai Hongqiao Traditional Chinese Medicine Slices Co., Ltd.
Cinnamomi Cortex	Rougui	RG	*Cinnamomum cassia* Presl	210203	Guangxi	Shanghai Kangqiao Traditional Chinese Medicine Slices Co., Ltd.
Atractylodis Macrocephalae Rhizoma	Baizhu (stir fried with soil)	BZ	*Atractylodes macrocephala* Koidz.	211003181	Zhejiang	Kangmei Pharmaceutical Co., Ltd.
Gardeniae Fructus	Zhizi (ground)	ZZ	*Gardenia jasminoides* Ellis.	211028	Jiangxi	Shanghai Hongqiao Traditional Chinese Medicine Slices Co., Ltd.
Akebiae Caulis	Mutong	MT	*Akebia quinata* (Houtt.) Decne.	20220701	Anhui	Guangdong Huiqun Traditional Chinese Medicine Slices Co., Ltd.
Saposhnikoviae Radix	Fangfeng	FF	*Saposhnikovia divaricata* (Trucz.) Schischk.	211117	Inner Mongolia	Shanghai Hongqiao Traditional Chinese Medicine Slices Co., Ltd.
Talcum	Huashi	HS	$[Mg_3(Si_4O_{10})(OH)_2]$	1711213	Hebei	China Shineway Pharmaceutical Group Co., Ltd.
Junci Medulla	Dengxincao	DXC	*Juncus effusus* L.	220304	Jiangsu	Shanghai Hongqiao Traditional Chinese Medicine Slices Co., Ltd.

Abbreviation: CWD, Chushi Weiling Decoction.

possible mechanism of the treatment of eczema and herpes zoster with CWD was explored. The results of this study provide a theoretical basis for clinical medication and quality control of CWD.

Material and Methods

Materials and Reagents

All 14 Chinese medicinal materials were purchased from real estate areas or main production areas (►**Table 1**), and all complied with the relevant regulations of the Chinese Pharmacopoeia 2020 Edition Part 1.[16]

The reference standards cinnamaldehyde (98.0%, lot:7713), hesperidin (95.3%, lot:110721-201115), naringin (98.0%, lot:13822), gardenoside (98.0%, lot:15277), calceolarioside B (98.0%, lot:9644), 5-*O*-methylvisammioside (98.0%, lot:14863), and prim-*O*-glucosylcimifugin (98.0%, lot:14585) were purchased from the China Institute for the Control of Food and Drug Products. Liquid chromatography-MS (LC-MS)-grade acetonitrile (ThermoFisher, United States), methanol (ThermoFisher, United States), formic acid (ThermoFisher, United States), and deionized water prepared by a Millipore Alpha-Q water purification system (Millipore, United States) were used as the mobile phase for the chromatographic separation. Other reagents were of analytical grade.

Preparation of Standards and Samples

Preparation of Standards and Samples of UPLC-Q-TOF-MS

All reference materials were dissolved in methanol to prepare solutions of cinnamaldehyde (12.4 μg/mL), hesperidin (198 μg/mL), naringin (26 μg/mL), gardenoside (31 μg/mL), calceolarioside B (45 μg/mL), 5-*O*-methylvisammioside (57 μg/mL), and prim-*O*-glucosylcimifugin (62 μg/mL).

According to the "History of Science and Technology in China: Volume of Weights and Measures," and by comparing it with the "Key Information Table of Ancient Classic Prescriptions (7 Prescriptions)," [17,18] 3.73 g of each of Cangzhu, Houpo, Chenpi, Zexie, Fuling, Zhuling, Baizhu, Zhizi, Mutong, Fangfeng, and Huashi were weighed, and 1.12 g of each of Rougui and Gancao were weighed. These materials were soaked in 400 mL of ultrapure water for 30 minutes, then 0.22 g of Dengxincao was added. All the materials were boiled over high fire and then simmered until the liquid amount was 320 mL, to obtain the complete decoction. After the above preparation, the decoction was frozen into freeze-dried powder at −55°C, 500 Pa using a Buchi Lyovapor L-200 (Buchi, Swiss).

All samples were dissolved in methanol and each was prepared into a solution of 10 mg/mL for UPLC-QTOF-MS. The sample solutions and standard solutions were filtered through 0.22 μm microporous filter membrane.

Preparation of Samples of GC-MS

The method for preparing CWD samples was the same as that of the UPLC-Q-TOF-MS mentioned above. After the preparation and lyophilization, approximately 1 g of freeze-dried powder was weighed for GC-MS of each decoction sample.

Instrumentation and Conditions

Instrumentation and Conditions of UPLC-Q-TOF-MS

The UPLC-Q-TOF MS analysis was performed using a Waters Acquity UPLC system coupled with a Xevo G2-XS QTOF mass spectrometer (Waters, United States) with an electrospray ionization ion source in MS^E mode.

The chromatographic separation process was performed on a Thermo-Accucore aQ C18 (100 mm × 2.1 mm, 2.6 μm; ThermoFisher, United States) at 25°C, with a mobile phase consisting of acetonitrile (A) and 0.1% formic acid aqueous solution (B). The gradient elution was as follows: 0–20 minutes, 5–25% eluent A; 20–30 minutes, 25–45% eluent A; 30–40 minutes, 45–70% eluent A; 40–45 minutes, 70–95% eluent A. The flow rate was 0.3 mL/min.

MS conditions were operated in both positive and negative ion modes and applied as follows: solvent gas temperature (nitrogen), 450°C; capillary voltage, 3.5 KV; an ion source temperature, 120°C; desolvation gas flow, 500 L/h; cone gas flow, 100 L/h; the low collision energy, 6 eV; the high collision energy, 25 to 60 eV.

Instrumentation and Conditions of GC-MS

The GC-MS analysis was performed using a 7890B GC-5977A MS combined instrument (Agilent, United States) in full spectrum scanning mode.

The chromatographic separation process was performed on an HP-5MS UI (0.25 mm × 30 m × 0.25 μm; Agilent, United States). The temperature gradient was as follows: 0–3 minutes, 40°C; 3–23 minutes, 40–240°C; 23–24 minutes, 240°C; 24–28 minutes, 240–280°C; 28–33 minutes, 280°C. The injection volume was 1 μL of headspace injection. The injection port temperature was 250°C, the flow rate was 1 mL/min, the split ratio was 10:1, the equilibrium temperature of the sample was 85°C, and the balance time was 30 minutes.

MS conditions were as follows: solvent gas temperature (nitrogen) was 450°C, quality scanning range was 40 to 600 Da; an ion source temperature was 230°C; and quadrupole temperature was 150°C. The solvent delay time was 4 minutes.

Data Processing and Compound Identification

Masslynx 4.1 software (Waters, United States) and UNIFI v1.8 Analysis Platform (Waters, United States) were used to analyze the mass spectra peaks of CWD in positive and negative ion modes. According to the comparison of reference standards or references, the compounds were identified by UV spectrum, retention time, excimer ion peak, molecular formula, fragment ions, and other information combined with the SciFinder database.

Methods of Research on Network Pharmacology

Active Component Collection of CWD

On the basis of confirming the ingredients of CWD, oral bioavailability (OB) and drug-likeness property (DL) parameters were analyzed using the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform

(TCMSP; https://old.tcmsp-e.com/index.php). The active ingredients of various medicinal herbs were screened with the set of OB $\geq$30% and DL $\geq$0.18 as standards based on the investigation of relevant literature. Gene names corresponding to targets were identified from the protein database Uniprot (https://www.uniprot.org). The potential targets of each active molecule were screened using the target prediction tool SwissTargetPrediction (http://swisstargetprediction.ch/).

Collection of Therapeutic Targets for Eczema and Herpes Zoster

The keywords "eczema" and "herpes zoster" were used to search through the Drugbank database (https://go.drugbank.com/), the Genecards database (https://www.genecards.org/), and the OMIM database (https://omim.org/).

Construction of Visual Network

The screened predicted targets were imported into the protein interaction analysis platform STRING 11.0 (https://version-11-0.string-db.org/). A "components-targets" network was established through Cytoscope 3.9.1 between the compound molecules and target proteins of CWD. In the network, the associations between nodes of components and targets were depicted by edges. The "degree" was used to calculate the edges linked to each node, which indicated the significance of the nodes in the network.

Gene Ontology Analysis and Pathway Enrichment (KEGG and Reactome) Analysis

Overlapping drug targets and diseases were imported into the DAVID (Database for Annotation, Visualization, and Integrated Discovery) web server (https://david.ncifcrf.gov/) and OmicShare Cloud Platform (https://www.omicshare.com/) for gene ontology (GO) biological processes and KEGG (Kyoto encyclopedia of genes and genomes) pathway enrichment analysis. The Metascape Platform (http://metascape.org/gp/index.html) was used for Reactome analysis, to explain the results of high-throughput genomics research.

Molecular Docking

The molecule structure (Mol2 structure) of the active compounds in CWD was downloaded from PubChem (https://pubchem.ncbi.nlm.nih.gov/). The 3D structure of the core protein targets was extracted from the Protein Data Bank (https://www1.rcsb.org/). Molecular docking and calculation of the binding affinity were performed using AutoDock (https://ccsb.scripps.edu/projects/).

Results and Discussion

The Analysis of UPLC-Q-TOF-MS and GC-MS

Components Determined by UPLC-Q-TOF-MS

A total of 194 components were identified from the samples of CWD by UPLC-Q-TOF-MS, including 71 terpenes, 37 flavonoids, 11 steroids, 11 phenylpropanoids, 8 alkaloids, 11 aromatics, 8 organic acids, 13 alcohols and esters, 6 simple ketones and aldehydes, and 18 other compounds. The retention time, excimer ion peak, molecular formula, herb source (in abbreviation), and other information are shown in ►**Table 2**. The ion flow diagram corresponding to peaks 1 to 194 is shown in ►**Fig. 1**.

Components Determined by GC-MS

A total of 92 components were identified from the samples of CWD by GC-MS, including 22 terpenes, 1 phenylpropanoid, 6 aromatics, 8 organic acids, 21 alcohols and esters, 20 simple ketones and aldehydes, and 14 other compounds. The results indicated that these compounds mainly come from Cangzhu, Mutong, Chenpi, etc. The retention time, ion peak, molecular formula, herb source (in abbreviation), and other information are shown in ►**Table 3**. The ion flow diagram corresponding to peaks 195 to 286 is shown in ►**Fig. 2**.

Total Components Determined of CWD

The total of 286 components from the samples of CWD included 93 terpenes, 37 flavonoids, 11 steroids, 12 phenylpropanoids, 8 alkaloids, 17 aromatics, 16 organic acids, 34 alcohols and esters, 26 simple ketones and aldehydes, and 32 other compounds.

From the perspective of medicinal herbs, there are 30 compounds in Cangzhu, 54 compounds in Houpo, 25 compounds in Chenpi, 35 compounds in Gancao, 19 compounds in Zexie, 37 compounds in Fuling, 14 compounds in Zhuling, 40 compounds in Rougui, 19 compounds in Baizhu, 33 compounds in Zhizi, 26 compounds in Mutong, 25 compounds in Fangfeng, and 2 compounds in Dengxincao in CWD.

Research of Cracking Rules

To systematically and qualitatively analyze the chemical components in CWD, the MS behaviors of the samples were studied to summarize their cracking rules and characteristic fragment ions based on relevant literature.[19–40]

Mass Spectrometric Cracking Rules of Terpenoids

Terpene compounds are the general term for compounds and their derivatives with a molecular formula multiple of isoprene. Based on relevant literature, the terpenoids in CWD were preliminarily classified: in the CWD, the terpenoids in Cangzhu (compounds **3**, **27**, **45**, **47**, **49**, **51**, **58**, **63**, **73**, **81**, **84**, **92**, **158**, and **122**), Baizhu (compounds **27**, **51**, **81**, **92**, and **114**), and Mutong (compounds **71**, **136**, and **167**) were mainly sesquiterpenoids.[19–22] The terpenoids in Fuling (compounds **85**, **91, 99**, **102**, **104**, **105**, **112**, **120**, **128**, **137**, **146**, **147**, **155**, **160**, **172**, **173**, **175**, and **189**) and Zhuling (compounds **153**, **165**, **170**) were mainly lanostelane type triterpenes, while the terpenoids in Zexie (compounds **22**, **109**, **129**, **132**, **150**, **154**, **157**, **159**, **161**, **174**, **177**, and **179**) were mainly prototerpenane type tetracyclic triterpenes.[23–27] The terpenoids in Zhizi (compounds **8**, **15**, **16**, **33**, **94**, **100**, **113**, **125**, **167**, and **186**) were mainly iridoids and their glycosides.[28–30] In addition, there are also terpenoids (compounds **28**, **30**, **53**, **78**, **135**, **139**, **141**, **143**, **156**, **176**, and **180**) in other medicinal herbs.[31–33]

Table 2 Analysis and identification of components from CWD by UPLC-Q-TOF-MS

Compd.	Component name	Neutral mass (Da)	Observed *m/z*	Mass error (mDa)	Mass error (ppm)	Observed RT (min)	Adducts	Fragment ions (*m/z*, ESI^-/ESI^+)	Formula	Herb-source (in Abbreviation[a])	Ref.
1	3-Indole carboxylic acid	161.0477	162.0546	−0.3	−2.0	0.64	$[M+H]^+$	162.1524, 131.1723	$C_9H_7NO_2$	GC	36
2	Dehydroeffusal	252.0786	253.0848	−1.1	−4.3	0.66	$[M+H]^+$	253.1445, 203.1294	$C_{16}H_{12}O_3$	DXC	40
3	Butenolide B	234.1256	235.1312	−1.6	−6.9	0.66	$[M+H]^+$	235.0317, 234.1720, 219.0972, 157.1694	$C_{14}H_{18}O_3$	CZ	19
4	5,7,3′-Trimethoxyl-(−)-epicatechin	332.1260	333.1335	0.2	0.7	0.67	$[M+H]^+$	333.1335, 265.1961, 175.1598	$C_{18}H_{20}O_6$	ZZ	28,29
5	Naringin[b]	580.1792	581.1889	2.5	4.2	0.67	$[M+H]^+$	581.1134, 461.0730, 417.1751	$C_{27}H_{32}O_{14}$	CP	35
6	Quercitrin	448.1006	449.1108	3.0	6.6	0.67	$[M+H]^+$	449.1108, 303.9655, 285.0639, 275.1771, 180.9662, 165.1959, 127.1546, 109.0404	$C_{21}H_{20}O_{11}$	ZZ	28,29
7	(+)-Syringaresinol	418.1628	419.1694	−0.7	−1.6	0.68	$[M+H]^+$	419.2348	$C_{22}H_{26}O_8$	RG, HP	31,32
8	Genipin-1-*O*-gentiobioside	550.1898	549.1810	−1.5	−2.8	0.69	$[M-H]^-$	549.1810, 387.1237, 371.0946, 225.0650, 123.0331	$C_{23}H_{34}O_{15}$	ZZ	28,29
9	Picrasmalignan A	534.1890	533.1850	3.3	6.3	0.70	$[M-H]^-$	533.1850, 403.1144	$C_{30}H_{30}O_9$	RG	31
10	Liriodenine	275.0582	276.0640	−1.6	−5.6	0.72	$[M+H]^+$	276.0640	$C_{17}H_9NO_3$	HP	32
11	N-Methylisosalsoline	207.1259	208.1327	−0.5	−2.3	0.73	$[M+H]^+$	208.1327	$C_{12}H_{17}NO_2$	HP	32
12	2-Hydroxyisoxypropyl-3-hydroxy-7-isopentene-2,3-dihydrobenzofuran-5-carboxylic	306.1467	307.1526	−1.4	−4.5	0.76	$[M+H]^+$	307.1526, 291.1987, 263.2010	$C_{17}H_{22}O_5$	CZ	19
13	Aristolochic acid A	340.0583	341.0635	−2.1	−6.1	0.77	$[M+H]^+$	341.0635, 313.1517	$C_{17}H_{11}NO_7$	MT	21,22
14	Cassiferaldehyde	178.0630	179.0694	−0.9	−5.1	0.77	$[M+H]^+$	179.0694, 163.9995, 145.1784	$C_{10}H_{10}O_3$	RG	31
15	Gardenoside_qt[b]	242.1154	243.1217	−1.0	−4.1	0.77	$[M+H]^+$	243.0620	$C_{12}H_{18}O_5$	ZZ	28,29
16	Genipin	226.0841	227.0916	0.2	1.1	0.78	$[M+H]^+$	227.0916	$C_{11}H_{14}O_5$	ZZ	28,29
17	Erthro-guaiacy lglycerol	214.0841	215.0927	1.3	5.9	0.82	$[M+H]^+$	215.0927, 151.1683	$C_{10}H_{14}O_5$	RG	31
18	5′-Methoxylariciresinol	390.1679	391.1759	0.7	1.9	0.84	$[M+H]^+$	391.1759, 353.1975, 289.0502	$C_{21}H_{26}O_7$	RG	31
19	Sinapaldehyde 4-*O*-β-*D*-glucopyranoside	370.1264	371.1339	0.2	0.6	0.91	$[M+H]^+$	371.1339, 197.0718	$C_{17}H_{22}O_9$	HP	32
20	Magnoloside R	478.1686	479.1780	2.1	4.4	0.92	$[M+H]^+$	479.1780, 457.2520, 441.1270	$C_{20}H_{30}O_{13}$	HP	32
21	3-(3,4-Dimethoxyphenyl)-2-propenal	192.0786	193.0847	−1.2	−6.3	0.96	$[M+H]^+$	193.0847, 175.1160, 149.1337	$C_{11}H_{12}O_3$	RG	31
22	Sulfoorientalol C	300.1395	301.1455	−1.3	−4.5	1.07	$[M+H]^+$	301.1455, 243.0157	$C_{15}H_{24}O_4S$	ZX	27
23	Licorice glycoside A	726.2160	727.2266	3.4	4.6	1.50	$[M+H]^+$	727.2266, 711.1833, 527.1888	$C_{36}H_{38}O_{16}$	GC	36
24	11-Hydroxy-sec-*O*-β-*D*-glucosylhamaudol	472.1581	473.1638	−1.5	−3.2	1.59	$[M+H]^+$	473.1638, 429.1854, 297.3093	$C_{21}H_{28}O_{12}$	FF	37
25	Gancaonin Q	406.1780	407.1821	−3.2	−7.9	1.72	$[M+H]^+$	407.1821, 385.2041, 305.3676	$C_{25}H_{26}O_5$	GC	36
26	Prim-*O*-glucosylcimifugin[b]	468.1737	469.1790	−2.0	−4.2	1.75	$[M+H]^+$	469.1790, 443.1633, 415.1733, 385.2041	$C_{22}H_{28}O_{11}$	FF	37

(*Continued*)

Table 2 (*Continued*)

Compd.	Component name	Neutral mass (Da)	Observed *m/z*	Mass error (mDa)	Mass error (ppm)	Observed RT (min)	Adducts	Fragment ions (*m/z*, ESI^-/ESI^+)	Formula	Herb-source (in Abbreviation[a])	Ref.
27	8β-Methoxyatractylenolide I	262.1569	263.1629	−1.3	−4.8	1.92	$[M+H]^+$	263.1629, 199.1105	$C_{16}H_{22}O_3$	CZ, BZ	19,20
28	Cinncassiol A	381.1913	382.2007	2.1	5.4	2.21	$[M+H]^+$	381.1721, 339.1682, 325.1788	$C_{20}H_{30}O_7$	RG	31
29	Anomalin	426.1679	427.1717	−3.4	−8.1	2.35	$[M+H]^+$	427.1710, 263.1408, 245.0156, 217.0547	$C_{24}H_{26}O_7$	FF	38
30	Epianhydrocinnzeylanol	366.2042	367.2080	−3.5	−9.5	2.43	$[M+H]^+$	367.2080, 349.2000, 305.2243	$C_{20}H_{30}O_6$	RG	31
31	(2*S*)-2-[4-Hydroxy-3-(3-methylbut-2-enyl)phenyl]-8,8-dimethyl-2,3-dihydropyrano[2,3-f]chromen-4-one	390.1831	391.1897	−0.6	−1.6	2.49	$[M+H]^+$	391.1897, 369.2114	$C_{25}H_{26}O_4$	GC	36
32	Isochlorogenic acid A[b]	516.1268	515.1217	2.2	4.3	2.49	$[M-H]^-$	515.1217, 497.1316	$C_{25}H_{24}O_{12}$	ZZ	28,29
33	Deacetylasperulosidic acid methyl ester	404.1319	403.1231	−1.5	−3.6	2.50	$[M-H]^-$	403.1231	$C_{17}H_{24}O_{11}$	ZZ	28,29
34	Tembetarine	344.1862	345.1925	−1.0	−2.8	2.81	$[M+H]^+$	642.1540, 619.1677, 589.1520	$C_{20}H_{26}NO_4^+$	HP	32
35	Fangfengalpyrimidine	296.1372	297.1444	−0.1	−0.4	2.95	$[M+H]^+$	297.1444, 281.1784, 211.1701	$C_{14}H_{20}O_5N_2$	FF	37
36	Glycyrin	382.1416	383.1472	−1.7	−4.6	3.06	$[M+H]^+$	383.1472, 309.1640, 265.1397	$C_{22}H_{22}O_6$	GC	36
37	Magnoligan H	562.2355	561.2280	−0.3	−0.5	3.11	$[M-H]^-$	561.2280, 519.9194, 475.0555	$C_{36}H_{34}O_6$	HP	32
38	Paeonolide	460.1581	461.1668	1.5	3.1	3.17	$[M+H]^+$	460.9483, 297.1050, 167.1323, 137.1349	$C_{20}H_{28}O_{12}$	CZ	19
39	(4*E*,6*E*,12*E*)-4,6,12-Tetradecatriene-8,10-diyne-1,3,14-triol	232.1099	233.1169	−0.4	−1.5	3.26	$[M+H]^+$	233.0911, 215.0813, 193.1007, 91.1242	$C_{14}H_{16}O_3$	BZ	20
40	Nobiletin	402.1315	403.1381	−0.6	−1.5	3.45	$[M+H]^+$	413.1381, 317.1877, 301.2659	$C_{21}H_{22}O_8$	CP	35
41	Neocnidilide	194.1307	195.1392	1.3	6.6	3.50	$[M+H]^+$	195.1392, 177.1313	$C_{12}H_{18}O_2$	FF	38
42	1-Methoxyficifolinol	422.2093	423.2130	−3.6	−8.5	3.93	$[M+H]^+$	423.2130, 365.1625	$C_{26}H_{30}O_5$	GC	36
43	1,1'-Dibenzene-6',8',9'-trihydroxy-3-allyl-4-*O*-β-*D*-glucopyranoside	462.1890	463.2001	3.9	8.4	3.96	$[M+H]^+$	463.2001, 293.1686, 241.1755	$C_{24}H_{30}O_9$	HP	32
44	[(3*R*)-3,7-Dimethyloct-6-enyl] butanoate	226.1933	227.2000	−0.6	−2.7	4.31	$[M+H]^+$	227.0265, 143.0355	$C_{14}H_{26}O_2$	CP	35
45	Atractyloyne	314.1882	315.1982	2.7	8.6	4.38	$[M+H]^+$	315.1982, 261.1326	$C_{19}H_{24}O_4$	CZ	19
46	β-Hydroxyacteoside	640.2003	639.1923	−0.7	−1.2	4.51	$[M-H]^-$	639.1923, 595.2032	$C_{29}H_{36}O_{16}$	HP	32
47	Paeonioflorin	482.1788	483.1859	−0.2	−0.3	4.52	$[M+H]^+$	483.1859, 397.2006, 343.2326	$C_{23}H_{30}O_{11}$	CZ	19
48	Orientanone	348.1065	349.1138	0.0	0.1	4.60	$[M+H]^+$	349.1138, 297.4816	$C_{15}H_{24}O_5S_2$	ZX	27
49	10-epi-Atractyloside A	448.2309	449.2390	0.9	2.0	4.68	$[M+H]^+$	449.2390, 403.2103, 297.3092	$C_{21}H_{36}O_{10}$	CZ	19
50	Kanzonol Y	410.2093	411.2162	−0.4	−0.9	4.70	$[M+H]^+$	411.2162, 395.1499, 297.3092	$C_{25}H_{30}O_5$	GC	36
51	Atractylenolide III	248.1412	249.1469	−1.7	−6.7	4.81	$[M+H]^+$	249.1469, 223.1396	$C_{15}H_{20}O_3$	CZ, BZ	19,20
52	Gardenone	226.1569	227.1648	0.6	2.7	5.51	$[M+H]^+$	227.1648, 209.1573, 191.1473, 177.1319	$C_{12}H_{20}O_3$	ZZ	28,29

Table 2 (*Continued*)

Compd.	Component name	Neutral mass (Da)	Observed *m/z*	Mass error (mDa)	Mass error (ppm)	Observed RT (min)	Adducts	Fragment ions (*m/z*, ESI^-/ESI^+)	Formula	Herb-source (in Abbreviation[a])	Ref.
53	(+)-Dehydrovomifoliol	222.1256	223.1333	0.4	1.9	5.51	$[M+H]^+$	223.1333, 209.1573, 191.1473, 177.1319, 149.1367	$C_{13}H_{18}O_3$	HP	32
54	Vitexin	432.1057	433.1114	−1.5	−3.5	5.51	$[M+H]^+$	433.1114, 281.0650	$C_{21}H_{20}O_{10}$	GC	36
55	Calceolarioside B[b]	478.1475	479.1549	0.2	0.3	5.51	$[M+H]^+$	479.1550, 411.1791	$C_{23}H_{26}O_{11}$	MT	21,22
56	(*E*)-3-(3-Methoxyphenyl) acrylaldehyde	162.0681	163.0749	−0.4	−2.5	5.67	$[M+H]^+$	163.0750, 143.0357, 127.0617	$C_{10}H_{10}O_2$	RG	31
57	(±)-9-Hydroxy-10*E*, 12*Z*-octadecadienoic acid	296.2351	297.2406	−1.8	−6.2	5.84	$[M+H]^+$	297.2406, 269.1846, 211.1473, 146.1472	$C_{18}H_{32}O_3$	HP	32
58	Oxypaeoniflorin	496.1581	497.1629	−2.4	−4.9	6.18	$[M+H]^+$	497.1629, 425.1340	$C_{23}H_{28}O_{12}$	CZ	19
59	Methyl 3,4,5-trimethoxycinnamate	252.0998	251.0949	2.4	9.4	6.88	$[M-H]^-$	251.0949, 229.1132, 183.1062	$C_{13}H_{16}O_5$	CZ	19
60	Gancaonin T	398.2093	399.2145	−2.1	−5.3	7.03	$[M+H]^+$	399.2145, 297.3094	$C_{24}H_{30}O_5$	GC	36
61	Pachyman	500.2105	501.2156	−2.2	−4.3	7.24	$[M+H]^+$	501.2156, 485.2381, 439.2048	$C_{20}H_{30}O_{14}$	FL	24
62	Coniferin	342.1315	343.1411	2.3	6.8	7.2	$[M+H]^+$	343.1411, 185.1562	$C_{16}H_{22}O_8$	HP	32
63	Albiflorin	480.1632	481.1725	2.1	4.3	7.49	$[M+H]^+$	481.1725, 467.1944, 413.1339	$C_{23}H_{28}O_{11}$	CZ	19
64	Euchrenone	406.2144	407.2199	−1.8	−4.4	8.1	$[M+H]^+$	407.2199, 355.2335, 301.1431, 203.2675	$C_{25}H_{26}O_5$	GC	36
65	Xambioona	388.1675	389.1761	1.4	3.5	8.85	$[M+H]^+$	389.1761, 341.2324, 211.1702	$C_{25}H_{24}O_4$	GC	36
66	Houpulin H	436.2614	437.2673	−1.3	−3.0	9.22	$[M+H]^+$	427.2306, 355.2334	$C_{28}H_{36}O_4$	HP	32
67	Magnoflorine	342.1705	342.1773	−2.1	−6.3	9.68	$[M]^+$	342.1773, 311.2000, 297.2154, 237.2061	$C_{20}H_{24}NO_4^+$	HP	32
68	(S)-Falcarinol	244.1827	245.1906	0.6	2.4	9.69	$[M+H]^+$	245.1906, 221.1561, 203.1452	$C_{17}H_{24}O$	FF	38
69	Gancaonin R	382.2144	383.2219	0.2	0.5	9.75	$[M+H]^+$	383.2219, 307.2192, 185.1916	$C_{24}H_{30}O_4$	GC	36
70	Houpulin C	398.1882	399.1950	−0.5	−1.2	9.97	$[M+H]^+$	399.1950, 373.1039, 331.1639	$C_{27}H_{26}O_3$	HP	32
71	(4*aS*,6*aR*,6*aS*,6*bR*,8*aR*,12*aS*,14*bS*)-2,2,6a,6b,9,9,12a-Heptamethyl-1,3,4,5,6,6a,7,8,8-a,10,11,12,13,14b-tetradecahydro-picene-4a-carboxylic acid	440.3654	441.3723	−0.4	−1.0	10.02	$[M+H]^+$	441.1637, 419.1830	$C_{30}H_{48}O_2$	MT	21,22
72	Kanzonols X	394.2144	395.2200	−1.6	−4.2	10.34	$[M+H]^+$	395.2200, 331.2170, 277.2113	$C_{25}H_{30}O_4$	GC	36
73	Galloylpaeoniflorin	632.1741	633.1791	−2.3	−3.6	10.71	$[M+H]^+$	633.1526, 611.1441, 529.2185, 477.1998	$C_{30}H_{32}O_{15}$	CZ	19
74	Glyasperin A	422.1729	423.1781	−2.1	−4.9	10.72	$[M+H]^+$	423.1781, 381.2039	$C_{25}H_{26}O_6$	GC	36
75	Gancaonin H	420.1573	421.1615	−3.1	−7.4	10.88	$[M+H]^+$	421.1615, 311.2493, 207.1408	$C_{25}H_{24}O_6$	GC	36
76	(−)-Epicatechin-3-*O*-β-glucoside	464.1683	465.1780	2.5	5.4	11.35	$[M+H]^+$	465.1780, 439.2774, 297.3092, 283.2953	$C_{22}H_{24}O_{11}$	RG	31
77	Houpulin K	546.2406	547.2520	4.1	7.5	11.71	$[M+H]^+$	403.2643, 385.2346, 339.2209	$C_{36}H_{34}O_5$	HP	32

(*Continued*)

Table 2 (*Continued*)

Compd.	Component name	Neutral mass (Da)	Observed *m/z*	Mass error (mDa)	Mass error (ppm)	Observed RT (min)	Adducts	Fragment ions (*m/z*, ESI^-/ESI^+)	Formula	Herb-source (in Abbreviation[a])	Ref.
78	Blumenol A	224.1412	225.1495	1.0	4.4	11.94	$[M+H]^+$	225.1495, 207.1414, 175.1156	$C_{13}H_{20}O_3$	HP	32
79	3,5-Dimethoxy-4-glucosyloxyphenylallylalcohol_qt	210.0892	209.0835	1.5	7.3	12.05	$[M-H]^-$	209.0835, 187.1010	$C_{11}H_{14}O_4$	CZ	19
80	(+)-Leptolepisol C	498.1890	497.1770	−4.7	−9.4	12.57	$[M-H]^-$	497.1770, 469.9197, 401.9299, 249.9649	$C_{27}H_{30}O_9$	RG	31
81	Atractylenolide I	230.1307	231.1388	0.8	3.5	12.57	$[M+H]^+$	231.1388, 215.1578, 189.1274, 177.1311, 145.1406	$C_{15}H_{18}O_2$	CZ, BZ	19,20
82	Isoschaftoside	564.1479	565.1540	−1.2	−2.2	12.82	$[M+H]^+$	565.1540, 527.2766, 429.2011	$C_{26}H_{28}O_{14}$	GC	36
83	(−)-Medicocarpin	432.1420	433.1498	0.5	1.1	13.09	$[M+H]^+$	433.1498, 347.1408, 291.2258, 271.1308, 183.1919	$C_{22}H_{24}O_9$	GC	36
84	Lactiflorin	462.1526	461.1465	1.2	2.6	13.64	$[M-H]^-$	461.1638, 447.1721, 381.1842	$C_{23}H_{26}O_{10}$	CZ	19
85	Poricoic acid A	498.3345	499.3412	−0.6	−1.2	15.05	$[M+H]^+$	499.3412	$C_{31}H_{46}O_5$	FL	24
86	Leonoside A	770.2633	771.2675	−3.1	−4.0	15.10	$[M+H]^+$	771.2675, 745.2080	$C_{35}H_{46}O_{19}$	HP	32
87	Cinnacasiol H	382.1992	383.2042	−2.3	−5.9	15.24	$[M+H]^+$	383.2042, 335.1576, 275.2368	$C_{20}H_{30}O_7$	RG	31
88	Decyl acetate	200.1776	201.1849	0.0	0.2	15.50	$[M+H]^+$	201.1850, 187.1868	$C_{12}H_{24}O_2$	FF	37
89	Magnoloside Y	626.2211	627.2296	1.2	2.0	16.77	$[M+H]^+$	627.2296, 583.2188	$C_{30}H_{26}O_{15}$	HP	32
90	2-Tetradecanone	212.2140	213.2227	1.4	6.7	17.41	$[M+H]^+$	213.2227	$C_{14}H_{28}O$	GC	36
91	Poricoic acid C	482.3396	483.3489	2.0	4.2	17.59	$[M+H]^+$	483.3489, 431.9511	$C_{31}H_{46}O_4$	FL	24
92	8β-Ethoxy atractylenolide III	276.1725	277.1776	−2.2	−8.1	17.75	$[M+H]^+$	277.1776, 259.1688, 205.1256	$C_{18}H_{28}O_2$	CZ, BZ	19,20
93	Dehydroabietic acid	300.2089	301.2173	1.0	3.5	18.33	$[M+H]^+$	301.2173, 269.1532	$C_{20}H_{28}O_2$	FL	24
94	Geniposide[b]	388.1370	389.1425	−1.8	−4.5	21.77	$[M+H]^+$	389.1425, 365.1651	$C_{17}H_{24}O_{10}$	ZZ	28,29
95	Paeonin	660.1457	661.1529	−0.1	−0.2	21.78	$[M+H]^+$	661.1529, 645.1854, 603.1822	$C_{28}H_{33}ClO_{16}$	CZ	19
96	Magnoloside P	774.2582	775.2691	3.6	4.6	22.09	$[M+H]^+$	775.7674, 757.3918	$C_{34}H_{46}O_{20}$	HP	32
97	(−)-15-Hydroxy-T-muurolol	218.1671	219.1734	−1.0	−4.5	22.53	$[M+H]^+$	219.1663, 207.1403, 147.1930, 123.1908	$C_{15}H_{22}O$	RG	31
98	Crocin I[b]	976.3788	977.3900	4.	4.1	22.57	$[M+H]^+$	977.3900, 831.3745, 655.3856	$C_{44}H_{64}O_{24}$	ZZ	28,29
99	Dehydrotumulosic acid	484.3553	485.3640	1.4	3.0	23.01	$[M+H]^+$	485.3640, 467.3574, 447.9464, 271.1655	$C_{31}H_{48}O_4$	FL	24
100	Croceic acid	328.1675	327.1611	0.9	2.8	23.32	$[M-H]^-$	327.1611, 309.1694	$C_{20}H_{24}O_4$	ZZ	28,29
101	(−)-Myrtenal	150.1045	151.1117	0.0	0.0	23.49	$[M+H]^+$	151.1117, 121.1606	$C_{10}H_{14}O$	HP	32
102	Poricoic acid CE	510.3709	511.3764	−1.8	−3.6	23.55	$[M+H]^+$	511.3764, 451.3655, 397.0895, 375.1113	$C_{33}H_{50}O_4$	FL	24
103	Icariside F2	402.1526	403.1564	−3.5	−8.7	24.00	$[M+H]^+$	403.1564, 315.1757	$C_{18}H_{26}O_{10}$	CZ, BZ	19,20
104	3-(2-Hydroxyacetoxy)-5α,8α-peroxydehydro-tumulosic acid	572.3349	573.3462	4.0	6.9	24.12	$[M+H]^+$	573.3462, 555.1128, 469.1532	$C_{33}H_{48}O_8$	FL	24

Table 2 (*Continued*)

Compd.	Component name	Neutral mass (Da)	Observed *m/z*	Mass error (mDa)	Mass error (ppm)	Observed RT (min)	Adducts	Fragment ions (*m/z*, ESI^-/ESI^+)	Formula	Herb-source (in Abbreviation[a])	Ref.
105	24-Methylene-3-oxol anost-8-en-21-oic acid	468.3604	469.3699	2.2	4.8	24.13	$[M+H]^+$	469.1532, 429.1674	$C_{31}H_{48}O_3$	FL	24
106	(−)-Epoxycaryophyllene	220.1827	221.1895	−0.5	−2.1	24.21	$[M+H]^+$	221.1895, 191.0765	$C_{15}H_{24}O$	HP	32
107	Cinnamoid E	234.1620	235.1692	−0.1	−0.4	24.29	$[M+H]^+$	235.1692, 185.1523	$C_{15}H_{22}O_2$	RG	31
108	β-Eudesmol	224.2140	225.2226	1.3	6.0	24.40	$[M+H]^+$	225.2226, 199.0994	$C_{15}H_{28}O$	CZ, BZ, HP, FF	19,20,32,38
109	23-*O*-Methylalisol A	504.3815	505.3870	−1.8	−3.5	24.42	$[M+H]^+$	505.3870, 487.3789, 469.3716	$C_{31}H_{52}O_5$	ZX	27
110	5-*O*-Methylvisamminol[b]	290.1154	289.1097	1.6	5.4	24.55	$[M-H]^-$	289.1097, 243.1042, 221.1214	$C_{16}H_{18}O_5$	FF	37
111	Geranylacetone	194.1671	195.1763	1.9	9.8	24.60	$[M+H]^+$	195.1734, 179.2052	$C_{13}H_{22}O$	FF	38
112	Tumulosic acid	486.3709	487.3803	2.1	4.4	24.66	$[M+H]^+$	487.3803, 469.3732	$C_{31}H_{50}O_4$	FL	24
113	Shanzhiside	392.1319	393.1405	1.4	3.5	24.79	$[M+H]^+$	393.1405, 225.0653	$C_{16}H_{24}O_{11}$	ZZ	28,29
114	Eudesma-4(14)-en-1,6-diol	240.2089	241.2153	−0.9	−3.8	26.27	$[M+H]^+$	241.2153, 197.2770	$C_{15}H_{28}O_2$	BZ	20
115	Kanzonol H	424.2250	425.2340	1.8	4.1	26.41	$[M+H]^+$	425.2282, 371.2043	$C_{26}H_{32}O_5$	GC	36
116	Syringin	372.1420	373.1502	0.9	2.4	27.12	$[M+H]^+$	373.1502, 357.1291	$C_{17}H_{24}O_9$	CZ	19
117	Undecyl acetate	214.1933	215.2013	0.8	3.7	27.26	$[M+H]^+$	215.2014, 159.1566	$C_{13}H_{26}O_2$	FL	24
118	2,5,5-Trimethylhepta-1,6-diene	138.1409	139.1489	0.7	5.2	27.45	$[M+H]^+$	139.1489, 103.1270	$C_{10}H_{18}$	CP	35
119	4-Keto-Magnoflorine	356.1498	357.1576	0.5	1.4	27.71	$[M+H]^+$	357.1576, 343.3559	$C_{20}H_{22}NO_5^+$	HP	32
120	16-Deoxyporicoic acid B	468.3240	469.3291	−2.1	−4.5	27.87	$[M+H]^+$	469.3291, 365.1646, 259.2386	$C_{30}H_{44}O_4$	FL	24
121	(22*E*)-Ergosta-7,22 -dien-3β,5α,6β-ol	430.3447	431.3530	1.0	2.4	28.00	$[M+H]^+$	431.3530, 413.1703, 387.2134, 343.1938	$C_{28}H_{46}O_3$	FL, ZL	24,26
122	Cedrol	222.1984	223.2059	0.2	1.0	28.12	$[M+H]^+$	223.2059, 197.1910	$C_{15}H_{28}O$	CZ	19
123	Cinnamoid D	236.1776	237.1842	−0.7	−2.9	28.16	$[M+H]^+$	237.2576, 219.1752, 165.0047	$C_{15}H_{24}O_2$	RG	31
124	Glyasperin D	370.1780	371.1829	−2.4	−6.5	28.17	$[M+H]^+$	371.1829	$C_{22}H_{26}O_5$	GC	36
125	Asperuloside_qt	252.0634	253.0694	−1.2	−4.9	28.25	$[M+H]^+$	253.0694, 225.9753	$C_{12}H_{12}O_6$	ZZ	28,29
126	Magnocurarine	314.1756	315.1817	−1.2	−3.7	28.97	$[M+H]^+$	315.1817	$C_{19}H_{24}NO_3^+$	HP	32
127	(2*R*)-2-[3,4-Dihydroxy-5-(3-methyl-but-2-enyl)phenyl]-5,7-dihydroxy-8-(3-methylbut-2-enyl)chroman-4-one	424.1886	425.1949	−0.9	−2.2	29.57	$[M+H]^+$	425.1949, 409.2286, 355.2137, 299.2554	$C_{25}H_{28}O_6$	GC	36
128	15-Hydroxy-7-oxoabieta-8,11, 13-trien-18-oic acid	330.1831	331.1916	1.2	3.7	29.57	$[M+H]^+$	331.1916, 299.2554	$C_{20}H_{26}O_4$	FL	24
129	10-*O*-Methyl-alismoxide	252.2089	253.214	−1.5	−5.8	29.85	$[M+H]^+$	253.2147, 179.2194	$C_{16}H_{28}O_2$	ZX	27
130	Houpulin F	420.2665	421.2731	−0.7	−1.6	30.44	$[M+H]^+$	421.2731, 341.3293, 271.3299	$C_{28}H_{36}O_3$	HP	32
131	Dauricine	624.3199	625.3290	1.8	2.9	30.85	$[M+H]^+$	625.3290, 205.2191, 189.1632, 161.1524	$C_{38}H_{44}N_2O_6$	MT	21,22
132	16-Oxo-alisol A	504.3451	505.3518	−0.6	−1.1	30.88	$[M+H]^+$	505.3518, 483.1921, 467.2456	$C_{30}H_{48}O_6$	ZX	27

(*Continued*)

Table 2 (*Continued*)

Compd.	Component name	Neutral mass (Da)	Observed *m/z*	Mass error (mDa)	Mass error (ppm)	Observed RT (min)	Adducts	Fragment ions (*m/z*, ESI^-/ESI^+)	Formula	Herb-source (in Abbreviation[a])	Ref.
133	Caryolane-1,9β-diol	238.1933	239.2011	0.5	2.2	31.07	$[M+H]^+$	239.2011, 193.1995	$C_{15}H_{26}O_2$	RG	31
134	Houpulin J	402.2559	403.2641	1.0	2.4	31.51	$[M+H]^+$	403.2641, 385.2346, 371.2216, 355.3386, 337.3595	$C_{28}H_{34}O_2$	HP	32
135	Cinncassiol D1	352.2250	353.2333	1.0	2.9	32.02	$[M+H]^+$	353.2333, 335.3303	$C_{20}H_{32}O_5$	RG	31
136	Akebonic acid	440.3291	441.3379	1.5	3.5	33.10	$[M+H]^+$	441.3379, 409.2314	$C_{29}H_{44}O_3$	MT	21,22
137	Poricoic acid D	514.3294	513.3193	−2.9	−5.6	33.33	$[M-H]^-$	513.3193	$C_{32}H_{48}O_7$	FL	24
138	Ergosta-7-en-3,5,6-triol	432.3604	433.3671	−0.5	−1.2	33.51	$[M+H]^+$	433.3671, 417.3971, 313.2673	$C_{28}H_{48}O_3$	ZL	26
139	Uralsaponin B	822.4038	823.4070	−4.0	−4.9	33.67	$[M+H]^+$	803.4070, 779.3923, 765.5055	$C_{42}H_{62}O_{16}$	GC	36
140	Kanzonols L	490.2355	491.2425	−0.3	−0.7	33.75	$[M+H]^+$	491.2425, 475.2702, 327.1432	$C_{30}H_{34}O_6$	GC	36
141	Cinncassiol D4-2-*O*-monoacetate	366.2406	367.2471	−0.8	−2.3	33.88	$[M+H]^+$	367.2471, 319.3628	$C_{21}H_{34}O_5$	RG	31
142	Hydroxytetracosanoic acid	384.3604	385.3677	0.1	0.2	34.33	$[M+H]^+$	385.3677, 299.2268	$C_{24}H_{48}O_3$	ZL	26
143	Cinncassiol D3	368.2199	369.2283	1.1	2.9	34.37	$[M+H]^+$	369.2283, 319.1751	$C_{20}H_{32}O_6$	RG	31
144	(22*E*)-Ergosta-6,8(14),22-trien-3β-ol	396.3392	397.3451	−1.4	−3.6	34.61	$[M+H]^+$	397.3451, 381.3475, 365.3563, 279.1637	$C_{28}H_{44}O$	FL	24
145	2-Lauroleic acid	198.1620	199.1701	0.8	4.2	35.10	$[M+H]^+$	199.1701, 185.1708, 161.1730	$C_{12}H_{22}O_2$	FL	24
146	Poricoic acid DM	528.3451	529.3472	−5.2	−9.8	35.42	$[M+H]^+$	529.3472	$C_{32}H_{48}O_6$	FL	24
147	Poricoic acid B	484.3189	485.3290	2.8	5.9	35.56	$[M+H]^+$	485.3290, 467.3383, 411.1554, 325.2855	$C_{30}H_{44}O_5$	FL	24
148	(22*E*)-Er-gosta-5,7,9(11), 22 -tetraen-3β-ol	394.3236	395.3306	−0.3	−0.7	35.61	$[M+H]^+$	395.3306, 327.3144, 305.2249	$C_{28}H_{42}O$	FL	24
149	Oleanolic acid-28-*O*-beta-*D*-glucopyranoside	618.4132	619.4167	−3.8	−6.1	35.75	$[M+H]^+$	619.4167, 535.3676, 475.3616	$C_{36}H_{58}O_8$	HP	32
150	Alisol A 23,24-diacetate	574.3870	575.3991	4.9	8.5	35.85	$[M+H]^+$	575.3984, 553.3695, 493.3624	$C_{34}H_{54}O_7$	ZX	27
151	Crepenynic acid	278.2246	279.2295	−2.3	−8.3	35.92	$[M+H]^+$	279.2296, 237.2577	$C_{18}H_{30}O_2$	BZ	20
152	Citromitin	404.1471	403.1393	−0.5	−1.3	36.64	$[M-H]^-$	403.1393	$C_{20}H_{20}O_7$	CP	35
153	Polyporusterone F	462.3345	463.3445	2.7	5.8	36.68	$[M+H]^+$	463.3445, 413.3189, 319.2897	$C_{28}H_{46}O_5$	ZL	26
154	11,25-Anhydroalisol F	452.3291	453.3365	0.2	0.5	36.90	$[M+H]^+$	453.3365, 429.3682, 413.2441, 302.3736	$C_{30}H_{44}O_3$	ZX	27
155	Daedaleanic acid B	488.3502	489.3558	−1.6	−3.4	37.76	$[M+H]^+$	489.3558, 473.3861, 341.3287	$C_{30}H_{48}O_5$	FL	24
156	24-Hydroxy-11-deoxyglycyrrhetic acid	458.3396	459.3494	2.5	5.5	37.81	$[M+H]^+$	459.3494, 421.3847	$C_{29}H_{46}O_4$	GC	36
157	Alisol J 23-acetate	526.3294	527.3362	−0.5	−1.0	38.10	$[M+H]^+$	527.3362, 487.3979, 475.3038	$C_{32}H_{46}O_6$	ZX	27
158	Stigmasterol 3-*O*-beta-*D*-glucopyranoside	574.4233	575.4328	2.2	3.8	38.56	$[M+H]^+$	575.4328, 545.4279, 537.3829, 343.2842	$C_{35}H_{58}O_6$	CZ	19
159	16,23-Oxido-alisol B	470.3396	471.3465	−0.4	−0.8	39.07	$[M+H]^+$	471.3456, 399.3606	$C_{30}H_{46}O_4$	ZX	27

Table 2 (*Continued*)

Compd.	Component name	Neutral mass (Da)	Observed *m/z*	Mass error (mDa)	Mass error (ppm)	Observed RT (min)	Adducts	Fragment ions (*m/z*, ESI^-/ESI^+)	Formula	Herb-source (in Abbreviation[a])	Ref.
160	26-Hydroxyporicoic acid DM	544.3400	545.3496	2.3	4.3	39.08	$[M+H]^+$	545.3496, 499.3533, 461.3603	$C_{32}H_{48}O_7$	FL	24
161	Alisol B diacetate	556.3764	557.3873	3.6	6.5	39.51	$[M+H]^+$	557.3918, 531.4154	$C_{34}H_{52}O_6$	ZX	27
162	Stigmast-4-ene-3,6-dione	426.3498	427.3558	−1.3	−2.9	39.56	$[M+H]^+$	429.3558, 349.3443, 299.3168	$C_{29}H_{46}O_2$	ZZ	28,29
163	(22*E*)-Ergosta-7,22 -dien-3β-ol	398.3549	399.3621	0.0	0.0	40.24	$[M+H]^+$	399.3621, 345.3486, 301.3576	$C_{28}H_{46}O$	FL, ZL	24,25
164	Glyasperin E	444.1573	445.1657	1.1	2.5	40.40	$[M+H]^+$	445.1657, 429.3067, 301.2096	$C_{27}H_{24}O_6$	GC	36
165	Polyporoid C	494.3244	495.3276	−4.0	−8.1	40.99	$[M+H]^+$	495.3276, 439.3856	$C_{28}H_{46}O_7$	ZL	26
166	3β-Hydroxystigmasta-5,22-dien-7-one	424.3341	425.3378	−3.6	−8.5	41.79	$[M+H]^+$	425.3378, 399.4010, 257.2334	$C_{29}H_{44}O_2$	HP	32
167	Stigmasterol	412.3705	413.3751	−2.7	−6.6	42.15	$[M+H]^+$	413.3751, 399.3317, 313.2665	$C_{29}H_{48}O$	MT, ZZ	21,22,28,29
168	Hesperidin[b]	610.1898	611.1940	−3.1	−5.0	42.17	$[M+H]^+$	611.1940, 441.3571, 297.3090	$C_{28}H_{34}O_{15}$	CP	35
169	Heptadecane	240.2817	241.2897	0.7	3.0	42.38	$[M+H]^+$	241.2897	$C_{17}H_{36}$	BZ	20
170	Polyporusterone A	478.3294	479.3336	−3.1	−6.5	42.87	$[M+H]^+$	479.3336, 441.3643	$C_{28}H_{46}O_6$	ZL	25,26
171	4,22-Stigmastadiene-3-one	410.3549	411.3608	−1.4	−3.3	43.49	$[M+H]^+$	411.3608, 387.3042, 297.3090	$C_{29}H_{46}O$	HP	32
172	3α-Pachymic acid	528.3815	529.3891	0.3	0.6	43.51	$[M+H]^+$	529.3891, 485.3752, 441.3631	$C_{33}H_{52}O_5$	FL	24
173	Poricoic acid ZG	502.3294	503.3363	−0.4	−0.8	43.81	$[M+H]^+$	503.3363, 419.3841	$C_{30}H_{46}O_6$	FL	24
174	11-Deoxy 13,17-epoxy-alisol A	490.3658	491.3706	−2.5	−5.0	43.82	$[M+H]^+$	491.3707, 463.3458, 439.2510, 333.1403	$C_{30}H_{50}O_5$	ZX	27
175	Eburicoic acid	470.3760	471.3858	2.5	5.4	44.19	$[M+H]^+$	471.3858, 447.4211, 433.2019	$C_{31}H_{50}O_3$	FL	24
176	Cinnacaslol glucoside	544.2520	545.2608	1.6	2.9	44.42	$[M+H]^+$	545.2608, 523.5031, 441.3846	$C_{26}H_{40}O_{12}$	RG	31
177	13,17-Epoxy-alisol A	506.3607	507.3688	0.8	1.5	44.65	$[M+H]^+$	507.3688, 493.3894, 365.4323, 283.2955	$C_{30}H_{50}O_6$	ZX	27
178	Kaempferol[b]	286.0477	287.0556	0.6	2.2	44.82	$[M+H]^+$	287.0557, 269.9386	$C_{15}H_{10}O_6$	ZZ	28,29
179	25-*O*-Ethylalisol A	518.3971	519.4084	4.0	7.7	44.85	$[M+H]^+$	519.4084, 467.4148	$C_{32}H_{54}O_5$	ZX	27
180	Oplopanane	192.1878	193.1960	0.9	4.5	45.02	$[M+H]^+$	193.2343, 177.2408	$C_{14}H_{24}$	HP	32
181	beta-Sitosterol-3-*O*-β-*D*-xylopyranoside	546.4284	547.4303	−5.4	−9.9	45.05	$[M+H]^+$	547.4303, 519.3270, 505.3836	$C_{34}H_{58}O_5$	MT	21,22
182	(4*E*,6*E*,12*E*)-Tetradecatriene-8, 10-diyne-1,3-diyl diacetate	300.1362	301.1437	0.2	0.8	45.82	$[M+H]^+$	301.1437, 261.2044, 217.1814, 173.1560	$C_{18}H_{20}O_4$	BZ	20
183	8-Methylheptadecane	254.2974	255.3038	−0.	−3.4	45.98	$[M+H]^+$	255.3051, 241.1753	$C_{18}H_{38}$	RG	31
184	2,4-Di-*t*-butylphenol	206.1671	207.1749	0.6	2.8	45.99	$[M+H]^+$	207.1749, 189.0352, 147.0085	$C_{14}H_{22}O$	CP	35
185	5-Allyl-5′-(1″-hydroxyallyloxy)biphenyl-2,2’-diol	298.1205	299.1284	0.6	1.9	46.00	$[M+H]^+$	297.3135, 283.2956, 255.2339	$C_{18}H_{18}O_4$	HP	32
186	Squalene	410.3913	411.4005	2.0	4.9	46.00	$[M+H]^+$	411.3562	$C_{30}H_{50}$	ZZ	28,29
187	Myristic acid	228.2089	229.2164	0.2	1.0	46.00	$[M+H]^+$	229.2164, 215.2060, 201.1866	$C_{14}H_{28}O_2$	ZZ	28,29
188	Palmitoleic acid	254.2246	255.2304	−1.5	−5.8	46.00	$[M+H]^+$	255.2304	$C_{16}H_{30}O_2$	ZZ	28,29

(*Continued*)

Table 2 (*Continued*)

Compd.	Component name	Neutral mass (Da)	Observed *m/z*	Mass error (mDa)	Mass error (ppm)	Observed RT (min)	Adducts	Fragment ions (*m/z*, ESI^-/ESI^+)	Formula	Herb-source (in Abbreviation[a])	Ref.
189	Acetyl Eburicoic Acid	512.3866	513.3924	−1.4	−2.7	46.01	$[M+H]^+$	513.4417, 495.4774, 359.3011	$C_{33}H_{52}O_4$	FL	24
190	Heneicosane	296.3443	297.3526	1.0	3.5	46.01	$[M+H]^+$	297.3095, 283.2956	$C_{21}H_{44}$	ZZ	28,29
191	Licorisoflavan A	438.2406	439.2451	−2.8	−6.3	46.02	$[M+H]^+$	439.2524, 383.1993, 311.3788	$C_{27}H_{34}O_5$	GC	36
192	Procyanidin B2	578.1424	579.1471	−2.6	−4.5	46.07	$[M+H]^+$	579.1022, 551.3563, 495.3051	$C_{30}H_{26}O_{12}$	RG	31
193	(2*E*)-1-Butoxy-2-hexene	156.1514	157.1593	0.6	3.8	46.07	$[M+H]^+$	157.1593	$C_{10}H_{20}O$	GC	36
194	Gancaonin C	354.1103	355.1191	1.5	4.2	46.19	$[M+H]^+$	355.1191	$C_{20}H_{18}O_6$	GC	36

Abbreviation: CWD, Chushi Weiling Decoction.
[a]Abbreviations: CZ, Cangzhu; HP, Houpo; CP, Chenpi; GC, Gancao; ZX, Zexie; FL, Fuling; ZL, Zhuling; RG, Rougui; BZ, Baizhu; ZZ, Zhizi; MT, Mutong; FF, Fangfeng; DXC, Dengxincao.
[b]Compared with reference substance.

There are three main rules for the cleavage of terpenoids: (1) when a compound forms a glycoside, it can lose all saccharides first, to obtain fragment ions. For example, genipin-1-*O*-gentiobioside (**8**; *m/z* 549.18096 $[M-H]^-$) of Zhizi is an iridoid glycoside compound containing one group of gentian disaccharide (i.e., two molecules of glucose). In its secondary mass spectrometry, genipin-1-*O*-gentiobioside sequentially lost two glucose groups, generating fragment ions of *m/z* 387.12365 $[M - H - Glc]^-$ and 225.06502 $[M - H - 2Glc]^-$. (2) Terpene skeletons are prone to lose neutral groups such as CO, CO_2, and H_2O. (3) If the terpenoid skeleton forms a six-membered ring with unsaturated double bonds during mass spectrometry cleavage, it is prone to RDA cleavage. During the cracking process of genipin-1-*O*-gentiobioside, a six-membered ring containing unsaturated double bonds was generated, to obtain fragment ions of *m/z* 123.03313 (►**Fig. 3**) through RDA cracking. This is consistent with the reference.[29,30]

Atractylenolide I (**81**; *m/z* 231.13876 $[M+H]^+$) in Cangzhu and Baizhu is a sesquiterpene lactone. In the positive ion mode, the ester bond broke on the five-membered lactone ring, to generate fragment ions of *m/z* 189.12743. Then, fragment ions of *m/z* 163.11331 or 145.14062 were generated through the cracking progress of the six-membered ring (►**Fig. 4**).

Mass Spectrometric Cracking Rules of Flavonoids

Flavonoids are widely distributed in the plant kingdom, often forming glycosides through *O*-glycosidic bonds. Based on relevant literature,[28–36] the flavonoids in CWD were preliminarily classified. There were a total of 37 confirmed flavonoids in CWD (compounds **4**–**6**, **23**–**26**, **31**, **32**, **36**, **40**, **50**, **54**, **60**, **64**, **65**, **69**, **72**, **74**-**76**, **80**, **82**, **95**, **98**, **110**, **115**, **124**, **127**, **140**, **152**, **164**, **168**, **178**, **191**, **192**, and **194**), mainly from medicinal herbs such as Chenpi, Fangfeng, Gancao, Rougui, and Zhizi. Through research on the cleavage patterns of flavonoids in CWD, we found that: (1) loss of saccharide groups tends to occur in flavonoid glycosides. (2) RDA cleavage reaction tends to occur on the C-ring of flavonoids. (3) Neutrality loss of CO, CO_2, and H_2O often occurs. These rules are consistent with reference.[34,35]

Taking quercitrin (**6**; *m/z* 449.11080 $[M+H]^+$) contained in Zhizi as an example, in the positive ion mode, the loss of rhamnose (*m/z* 146) occurred, generating fragment ions of *m/z* 303.96551 $[M+H-Rha]^+$. Quercetin fragment ions continued to have RDA cleavage at positions $^{1,3}A$ of the C-ring, generating $^{1,3}A$ ions at *m/z* 153.06728. In addition, RDA cleavage could also occur at positions $^{1,2}A$; $^{0,2}A$; $^{1,4}A$; or $^{0,4}A$ of the C-ring (►**Fig. 5**). This cleavage pathway was believed to be reliable by comparing with reference.[34]

Mass Spectrometric Cracking Rules of Phenylpropanoids

Phenylpropanoid compounds include phenylpropanoic acids, coumarins, and lignans. Based on relevant literature,[31–33,37] the phenylpropanoids in CWD were preliminarily classified. The phenylpropanoid compounds (compounds **7**, **17**, **29**, **55**, **62**, **66**, **70**, **77**, **86**, **130**, **134**, and **261**) in CWD mainly came from Houpo, Fangfeng, and Rougui. Phenylpropanoic acid ester bonds are prone to cleavage to generate phenylpropanoic

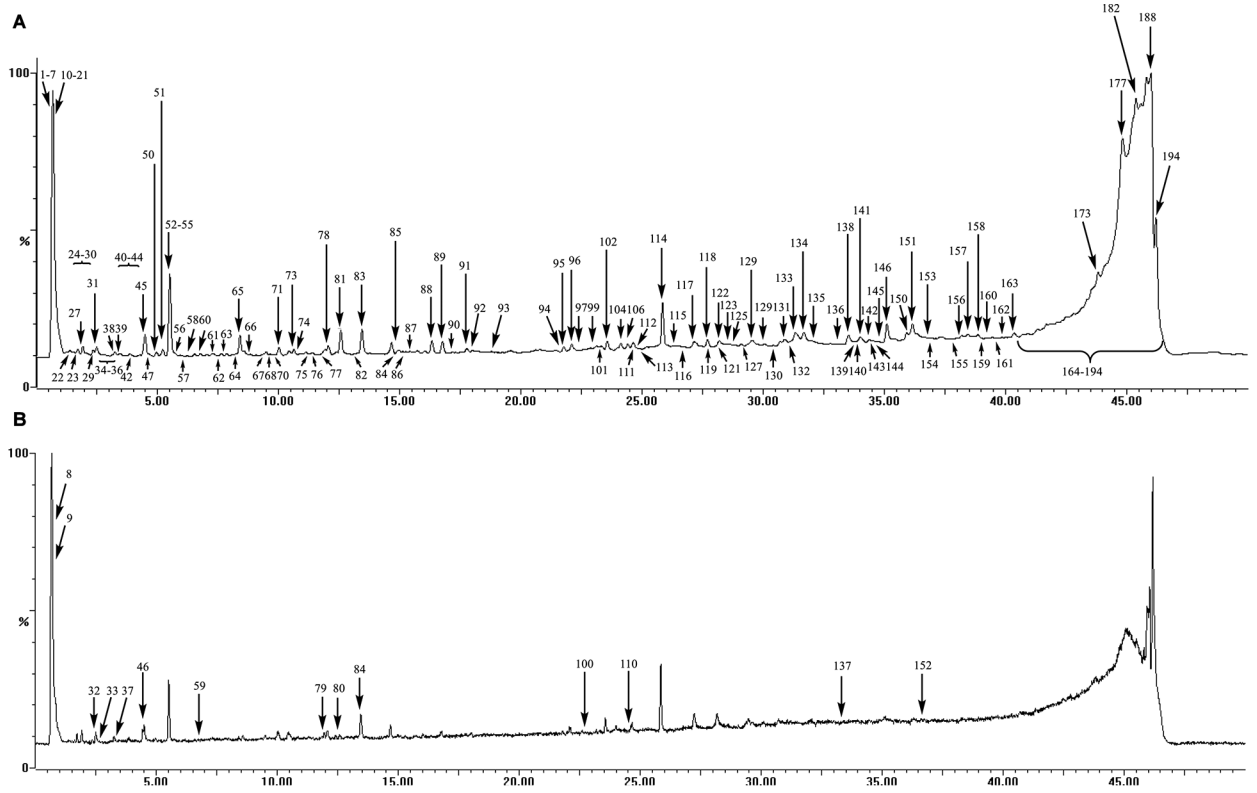


Fig. 1 Total ion flow diagram of CWD components in (**A**) positive ion mode and (**B**) negative ion mode of UPLC-Q-TOF-MS. CWD, Chushi Weiling Decoction.

Table 3 Analysis and identification of components from CWD by GC-MS

Compd.	Component Name	Observed RT (min)	Observed *m/z*	Fragment Ions (*m/z*)	Formula	Herb-source (in Abbreviation*)
195	2-Hydroxyethyl acrylate	5.0	116.047	88.030, 72.990, 55.020	$C_5H_8O_3$	FF
196	2,3-Butanediol	5.2	90.068	75.020, 57.040	$C_4H_{10}O_2$	CZ, HP, ZX
197	3-Furaldehyde	5.7	96.021	96.000, 66.990	$C_5H_4O_2$	FF, FL, CP, CZ
198	3-Methylvaleric Acid	6.2	116.084	87.000, 60.020	$C_6H_{12}O_2$	BZ
199	2-Methylidenecyclopropane-1-carboxylic acid	6.3	98.037	98.010, 86.970, 74.020	$C_5H_6O_2$	HP
200	Pentanoic acid	7.0	102.068	86.960, 73.000, 60.010	$C_5H_{10}O_2$	RG
201	3,3-Dimethylacrylic acid	7.1	100.052	100.030, 82.010, 60.020	$C_5H_8O_2$	MT
202	2-Valerylfuran	7.3	152.084	133.010, 109.990, 94.980, 59.980	$C_9H_{12}O_2$	HP
203	Tetrahydropyran	7.5	86.073	108.050, 86.000, 72.990, 56.020	$C_5H_{10}O$	HP, RG
204	Carene	7.7	136.234	136.080, 122.020	$C_{10}H_{16}$	MT
205	4-Methylanisole	7.8	122.073	122.030, 107.010, 79.000, 55.020	$C_8H_{10}O$	HP
206	Benzaldehyde	8.3	106.042	106.010, 94.990, 77.010	C_7H_6O	FF, RG, MT
207	5-Methyl-2-furaldehyde	8.3	110.037	109.990, 81.010	$C_6H_6O_2$	GC, CP, ZL
208	5-Ethyl-2-methyl-2,3-dihydro-furan	8.4	112.089	111.930, 72.000, 54.980	$C_7H_{12}O$	CP
209	Methylal	8.5	76.094	76.020, 30.120	$C_3H_8O_2$	BZ
210	2,4-Dihydroxy-2,5-dimethyl-3(2*H*)-furan-3-one	8.7	144.042	144.000, 100.990, 87.010, 73.000, 55.020	$C_6H_8O_4$	FF
211	2-Amylfuran	8.8	138.207	138.040, 108.980, 82.040, 68.100	$C_9H_{14}O$	ZL
212	Hexanoic acid	9.0	116.084	87.020, 73.020, 60.020	$C_6H_{12}O_2$	FF, ZX, ZL
213	α-Phellandrene	9.1	136.234	136.050, 122.010, 107.980	$C_{10}H_{16}$	MT

(*Continued*)

Table 3 (*Continued*)

Compd.	Component Name	Observed RT (min)	Observed *m/z*	Fragment Ions (*m/z*)	Formula	Herb-source (in Abbreviation*)
214	α-Terpinene	9.3	136.234	136.000, 121.000, 93.200	$C_{10}H_{16}$	FL
215	Pyrrole-2-carboxaldehyde	9.3	95.037	94.990, 72.960, 60.020	C_5H_5NO	FF
216	Cymene	9.4	134.110	123.050, 119.040, 104.970, 91.000, 72.930	$C_{10}H_{14}$	HP, FL
217	*D*-Limonene	9.5	136.125	136.080, 107.050, 93.050, 79.050	$C_{10}H_{16}$	FL, CP, MT
218	Eucalyptol	9.6	154.249	154.100, 139.000	$C_{10}H_{18}O$	FL, HP
219	2-Ethyl-5-propylcyclopentanone	9.6	154.136	154.120, 123.920, 112.000, 84.050	$C_{10}H_{18}O$	FF
220	1-Phenylpropane-1,2-diol	9.6	152.190	152.070, 136.020, 119.980	$C_9H_{12}O_2$	CP
221	m-Cresol	9.7	108.058	108.030, 79.020	C_7H_8O	GC
222	3,5,5-Trimethylcyclohex-3-en-1-one	9.7	138.207	138.040, 95.980	$C_9H_{14}O$	ZZ
223	Phenylacetaldehyde	9.8	120.058	120.000, 91.030, 65.020	C_8H_8O	RG, FF, CP, HP, ZZ, ZL
224	Salicylaldehyde	9.8	122.121	122.030, 93.010, 76.000	$C_7H_6O_2$	FL
225	γ-Caprolactone	10.0	114.068	85.000, 55.030	$C_6H_{10}O_2$	CP
226	Ethyl 4-ethyloxy-2-oxobut-3-enoate	10.0	172.074	136.000, 99.050, 71.080	$C_8H_{12}O_4$	CP
227	γ-Terpinene	10.0	136.234	136.020, 121.100, 93.050	$C_{10}H_{16}$	FL
228	2-Acetylpyrrole	10.1	109.053	109.930, 94.010, 66.020	C_6H_7NO	FF, HP
229	*n*-Heptanoic acid	10.4	130.099	127.920, 87.020, 73.010, 60.020	$C_7H_{14}O_2$	RG
230	Terpinolene	10.5	136.234	136.080, 121.050	$C_{10}H_{16}$	FL
231	Linalool	10.7	154.136	121.010, 93.030, 71.030	$C_{10}H_{18}O$	ZZ
232	Isophorone	11.1	138.104	123.070, 126.030, 82.030	$C_9H_{14}O$	GC, ZZ
233	3-Phenylpropanal	11.7	134.073	134.040, 115.020, 103.050	$C_9H_{10}O$	RG, CP, ZZ
234	Menthol	11.9	156.151	134.020, 123.080, 109.050, 95.050, 85.080	$C_{10}H_{20}O$	GC, RG, ZZ, MT, BZ, CZ, FL, ZL
235	Octanoic acid	12.0	144.211	144.010, 99.030	$C_8H_{16}O_2$	FF
236	Thymol	12.1	150.104	135.040, 122.000	$C_{10}H_{14}O$	RG, CP, HP
237	Terpineol	12.2	154.136	136.080, 121.020, 84.980	$C_{10}H_{18}O$	CP
238	Safranal	12.3	150.104	135.030, 121.060, 107.040, 79.030	$C_{10}H_{14}O$	ZZ
239	3,5,5-Trimethyl-4-methylen-2-cyclo-hexen-1-on	12.6	150.218	150.120, 135.010, 107.960	$C_{10}H_{14}O$	ZZ
240	5-Hydroxymethylfurfural	12.7	126.032	135.040, 108.960, 69.020	$C_6H_6O_3$	CP, MT, ZX
241	3-Phenylpropanol	12.8	136.089	117.040, 103.010, 72.940	$C_9H_{12}O$	RG
242	5-Indanol	13.1	134.175	134.010, 118.970	$C_9H_{10}O$	HP
243	p-Allylphenol	13.1	134.073	134.030, 118.990, 105.010, 72.960	$C_9H_{10}O$	RG, HP
244	R-γ-Decalactone	13.2	170.131	133.970, 109.960, 95.030	$C_{10}H_{18}O_2$	FF
245	Nonanoic acid	13.2	158.131	127.030, 115.020, 98.020	$C_9H_{18}O_2$	FF, RG
246	Cinnamaldehyde**	13.4	132.058	131.030, 114.980, 77.030	C_9H_8O	RG, GC, FL, HP, CP, BZ, ZZ
247	1,3,3-Trimethyl-2-vinyl-1-cyclohexene	13.7	150.141	135.010, 121.000, 106.980, 76.920	$C_{11}H_{18}$	GC, ZZ
248	Cinnamyl alcohol	13.8	134.073	115.010, 92.030, 78.000	$C_9H_{10}O$	RG
249	o-Acetyl-p-cresol	13.9	150.068	135.010, 107.020	$C_9H_{10}O_2$	ZZ
250	2-Methoxy-4-vinylphenol	13.9	150.174	135.070, 118.990, 88.970	$C_9H_{10}O_2$	CP
251	4′-Hydroxy-2′-methylacetophenone	13.9	150.174	150.120, 136.010, 117.960, 89.960	$C_9H_{10}O_2$	ZZ
252	1-Butyl-3-methylcyclohex-2-en-1-ol	14.0	168.151	134.970, 120.930, 77.000	$C_{11}H_{20}O$	HP
253	4,4,6-Trimethylcyclohex-2-en-1-ol	14.3	140.120	125.070, 84.010	$C_9H_{16}O$	ZZ
254	Apricolin	14.6	156.115	128.010, 85.000	$C_9H_{16}O_2$	CP

Table 3 (*Continued*)

Compd.	Component Name	Observed RT (min)	Observed *m/z*	Fragment Ions (*m/z*)	Formula	Herb-source (in Abbreviation*)
255	2-Methoxyphenylacetone	14.7	164.084	135.0500, 121.020, 91.050	$C_{10}H_{12}O_2$	RG
256	Modhephene	15.0	204.351	204.160, 189.960, 161.960	$C_{15}H_{24}$	MT
257	Berkheyaradulene	15.0	204.350	204.120, 190.020, 175.980	$C_{15}H_{24}$	MT
258	Vanillin	15.1	152.047	136.920, 122.940, 78.980	$C_8H_8O_3$	CP, DXC, HP
259	*trans*-Caryophyllene	15.5	204.351	204.120, 192.000, 134.020	$C_{15}H_{24}$	MT
260	γ-Elemene	15.6	204.351	204.140, 191.980, 135.960	$C_{15}H_{24}$	MT
261	Coumarin	15.7	146.037	134.010, 118.010,	$C_9H_6O_2$	FF, RG, HP
262	Paeonol	15.7	166.174	166.060, 148.980, 134.000, 106.090	$C_9H_{10}O_3$	ZL
263	Massoia lactone	16.1	168.115	123.000, 97.010, 67.990	$C_{10}H_{16}O_2$	RG, HP
264	γ-Selinene	16.1	204.351	204.120, 190.000, 175.960	$C_{15}H_{24}$	MT
265	α-Curcumene	16.2	202.335	202.070, 175.990, 118.020, 89.950	$C_{15}H_{22}$	MT
266	Pentanoic acid, 5-hydroxy-, 2,4-bis(1,1-dimethylethyl)phenyl ester	16.5	306.219	252.910, 191.090, 109.080	$C_{19}H_{30}O_3$	GC
267	β-Sesquiphellandrene	16.7	204.351	204.120, 192.020	$C_{15}H_{24}$	MT
268	Dihydroactinidiolide	16.9	180.115	179.990, 137.070, 111.020	$C_{11}H_{16}O_2$	CP
269	Valencene	16.9	204.351	204.160, 189.980, 161.960, 136.010	$C_{15}H_{24}$	MT
270	γ-Eudesmol	18.0	222.366	222.130, 206.020, 177.980	$C_{15}H_{26}O$	HP
271	*trans*-Isoelemicin	18.1	208.254	208.050, 178.030, 147.980	$C_{12}H_{16}O_3$	HP
272	Agarospirol	18.1	222.366	222.100, 206.010, 178.980, 126.020	$C_{15}H_{26}O$	MT, BZ, CZ
273	β-Eudesmol	18.3	222.198	204.130, 189.120, 149.080	$C_{15}H_{26}O$	BZ, CZ, FF, HP, MT
274	α-Eudesmol	18.3	222.366	222.100, 206.010, 178.980	$C_{15}H_{26}O$	HP
275	Atractylon	18.4	216.319	202.100, 178.020, 136.100	$C_{15}H_{20}O$	CZ, BZ, MT
276	Sandacanol	18.7	208.183	176.120, 161.100, 90.950, 69.010	$C_{14}H_{24}O$	RG
277	1-[(1*S*,3a*R*,4*R*,7*S*,7a*S*)-4-Hydroxy-4-methyl-7-propan-2-yl-1,2,3,3a,5,6,7,7a-octahydroinden-1-yl]ethanone	19.2	238.193	238.140, 205.070, 153.050, 135.050	$C_{15}H_{26}O_2$	ZX, CZ
278	Longifolenaldehyde	19.5	220.183	220.160, 206.950, 121.070, 104.990, 95.020	$C_{15}H_{24}O$	ZX
279	Senkyunolide J	19.5	226.121	182.060, 152.030, 125.980, 111.040	$C_{12}H_{18}O_4$	FF
280	Isospathulenol	19.6	220.183	220.150, 205.120, 162.110, 119.070	$C_{15}H_{24}O$	ZX
281	1-epi-Cubenol	19.8	222.198	206.990, 179.080, 162.070, 147.090, 135.020	$C_{15}H_{26}O$	RG
282	Tetridamine	19.9	165.127	165.020, 149.100, 119.990	$C_9H_{15}N_3$	MT
283	Cryptomeridiol	20.1	240.209	204.140, 149.090	$C_{15}H_{28}O_2$	CZ, HP
284	Diisobutyl phthalate	20.5	278.344	278.120, 223.010, 149.030, 103.960	$C_{16}H_{22}O_4$	CP
285	7,9-Ditert-butyl-1-oxaspiro[4.5]deca-6,9-diene-2,8-dione	21.0	276.173	261.050, 232.080, 217.100, 205.060, 175.050	$C_{17}H_{24}O_3$	FL, ZL
286	β-Cyclocostunolide	22.6	232.318	232.140, 217.990, 204.000	$C_{15}H_{20}O_2$	BZ

Abbreviation: CWD, Chushi Weiling Decoction; RT, retention time.

*Abbreviation: CZ, Cangzhu; HP, Houpo; CP, Chenpi; GC, Gancao, ZX, Zexie; FL, Fuling; ZL, Zhuling; RG, Rougui; BZ, Baizhu; ZZ, Zhizi; MT, Mutong; FF, Fangfeng; DXC, Dengxincao.

**Compared with reference substance.

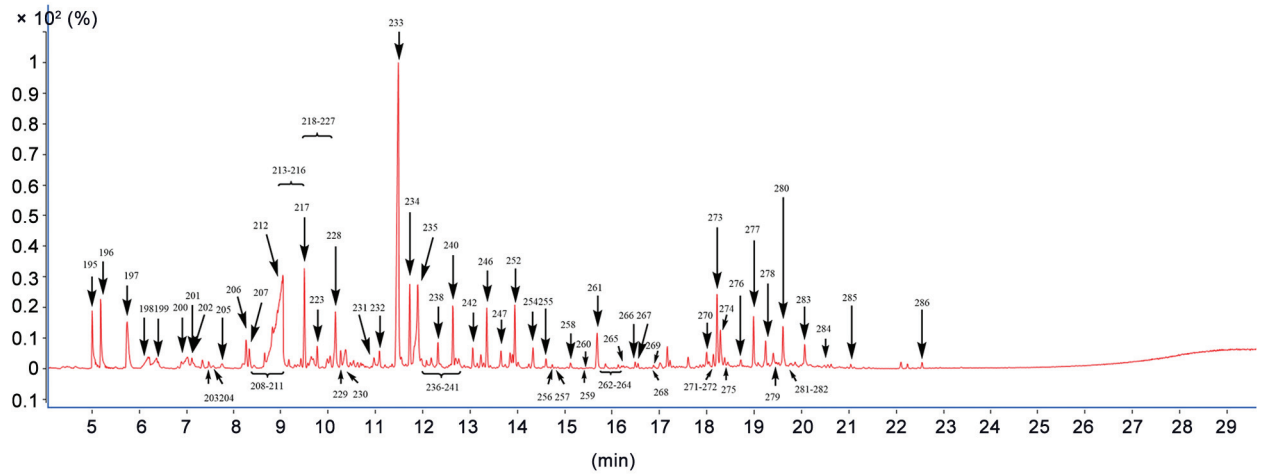
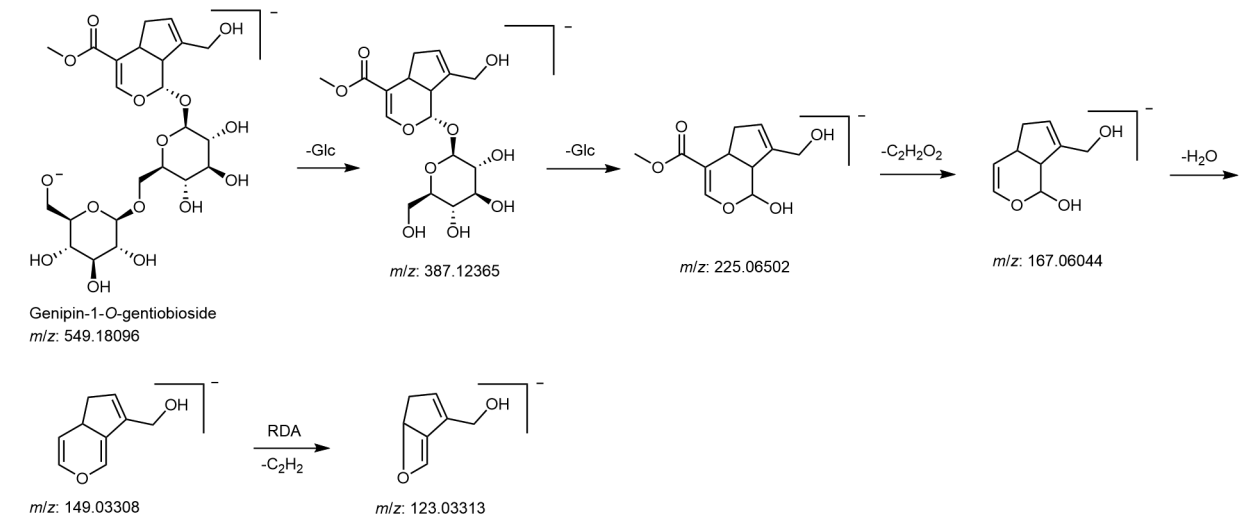


Fig. 2 Total ion flow diagram of CWD components in GC-MS. CWD, Chushi Weiling Decoction.



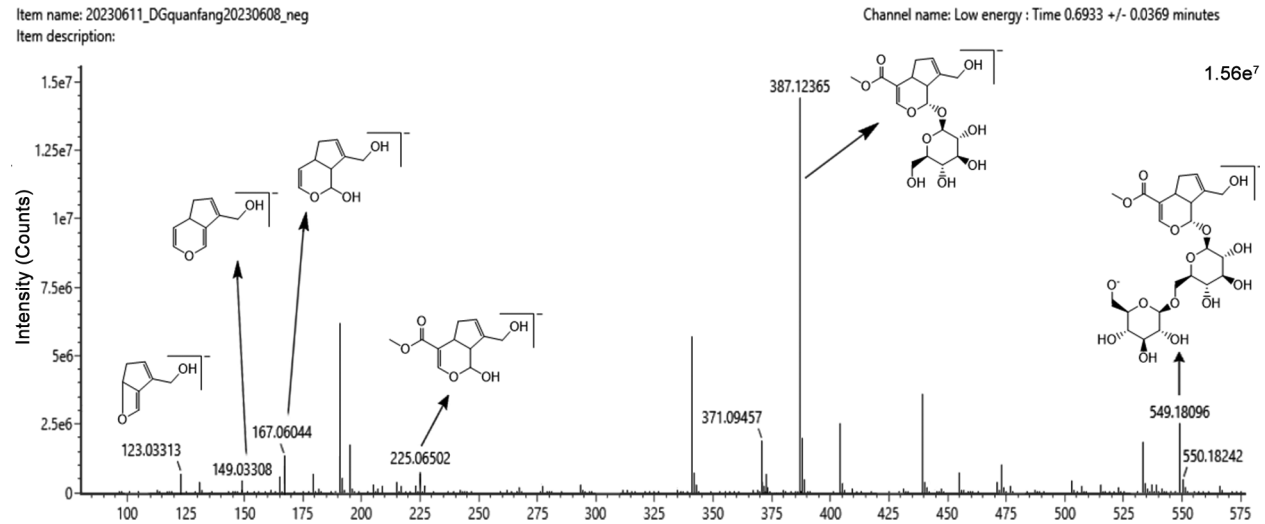


Fig. 3 Mass fragmentation pathways and secondary mass spectra of genipin-1-*O*-gentiobioside.

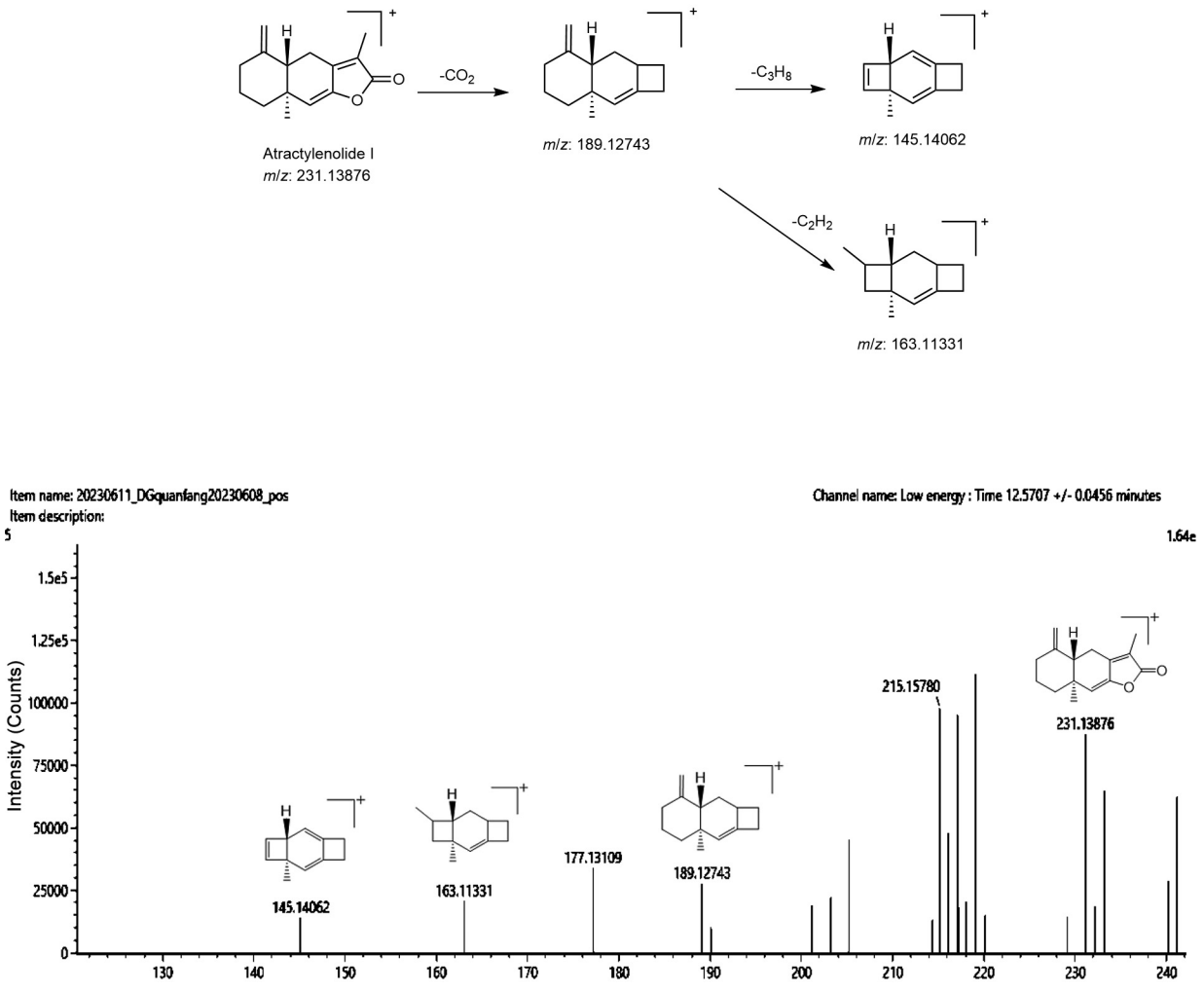


Fig. 4 Mass fragmentation pathways and secondary mass spectra of atractylenolide I.

acid fragment ions. Different characteristic skeleton fragment ions are generated due to different mother nucleus structures: fragment ions of *m/z* 179, 161, and 135 can be inferred to contain caffeoyl fragment ions, and *m/z* 193, 175, and 160 can be inferred to contain ferulic acid fragments ions, and *m/z* 163 and 119 can be inferred to contain *para*-coumarin acid fragment ions, which was consistent with the pyrolysis rule of phenylpropanoids in the positive ion mode described in the literature.[36,38] The fragment ions often have a neutral loss of CO, H_2O, and CO_2.

Anomalin (**29**; *m/z* 427.17103 $[M+H]^+$) contained in Fangfeng is a derivative of pyranocoumarin with a total of three ester bonds. In the positive ion mode, anomalin was prone to ester bond cleavage and neutral loss of 2-methyl-2-butenoic acid groups (►**Fig. 6**), which can be referred to in the literature.[38]

Mass Spectrometric Cracking Rules of Phenols, Acids, and Esters

Under the conditions of dissociation, the main mass spectrometry cleavage pathway of phenolic compounds is the loss of substituents in the structure. Based on relevant literature,[26–36] the phenols, acids, and esters in CWD were preliminarily classified. There were a total of 44 confirmed phenolic, acid, and ester compounds in CWD (compounds **1**, **18**, **21**, **37**, **38**, **41**, **44**, **56**, **57**, **59**, **83**, **87–89**, **93**, **96**, **116**, **117**, **142**, **145**, **151**, **182**, **184**, **187**, **195**, **198-201**, **212**, **221**, **225**, **226**, **228**, **230**, **236**, **244**, **245**, **250**, **254**, **266**, **270**, **279**, and **284**). In the secondary mass spectrometry of phenolic glycosides, high-abundance fragment ions often originate from the loss of saccharides. Carboxylic acids and their ester compounds are prone to α-cracking, neutral loss of R or OR' groups (depending on which bond of the O atom breaks), and loss of CO, generating $[R+H]^+$ and $[OR'+H]^+$ fragment ions in positive ion mode. Generally speaking, the ion peak intensity generated by aromatic compounds and their esters is stronger than that of fatty acids and their esters.[20–24]

Taking paeonolide (**38**; *m/z* 460.94828 $[M+H]^+$), a component in Cangzhu, as an example, it has paeonol as a aglycone and contains a nonreducing terminal 1-α-arabinopyranoside. During the dissociation process, paeonolide gradually removed saccharide groups and generated fragment ions of *m/z* 167.13227. Afterward, fragment ions of *m/z* 137.13492 and phenol fragments were generated (►**Fig. 7**).[30]

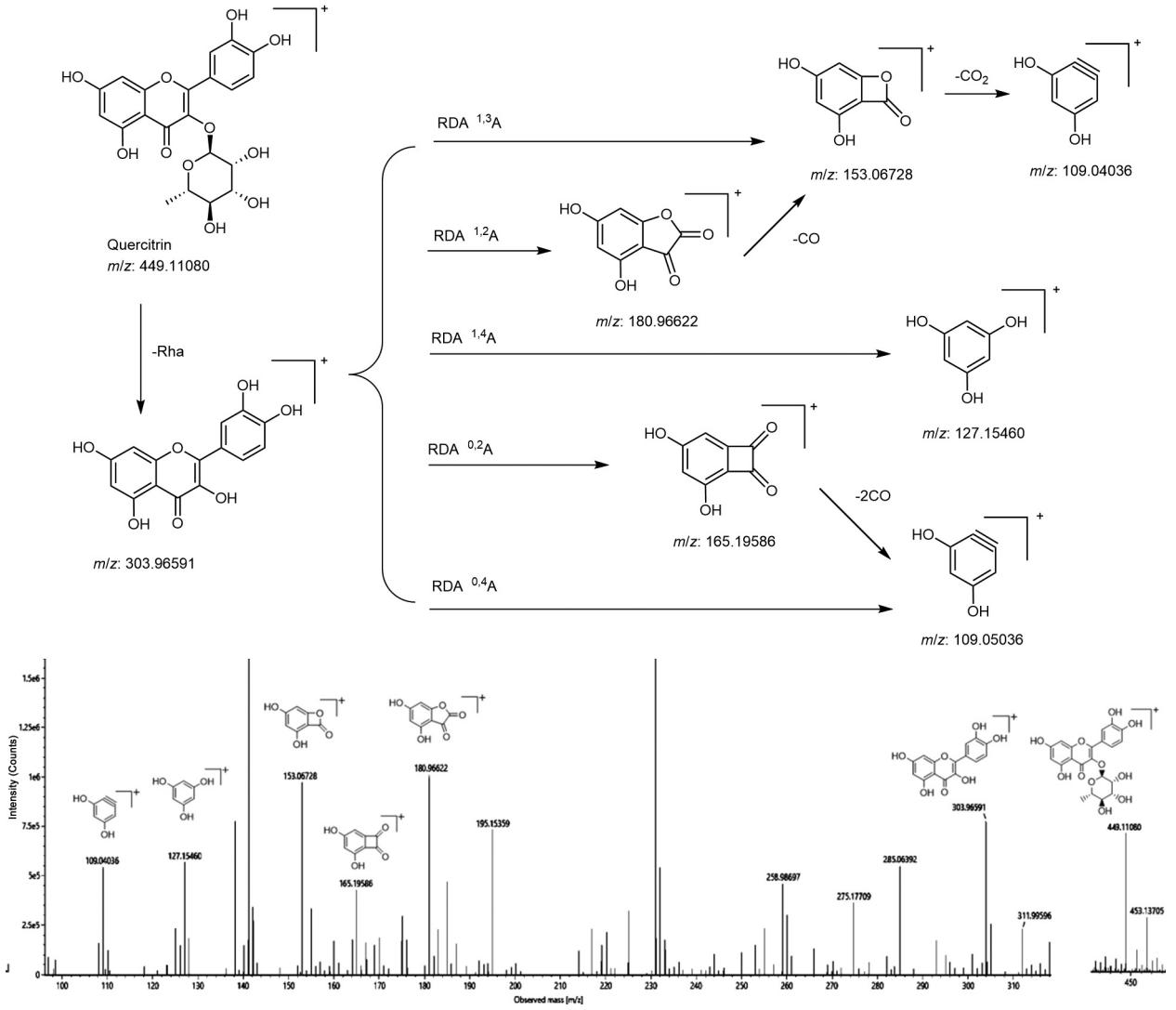


Fig. 5 Mass fragmentation pathways and secondary mass spectra of quercetin.

Mass Spectrometric Cracking Rules of Alkaloids

Alkaloids are a class of natural compounds containing basic nitrogen atoms, often with nitrogen heterocyclic structures. Based on relevant literature,[21,22,33,37–39] the alkaloids in CWD were preliminarily classified and the cracking rules of alkaloids were summarized. The alkaloid components (compounds **10**, **11**, **34**, **35**, **67**, **119**, **126**, and **131**) in CWD mainly included aporphine alkaloids, isoquinoline alkaloids, and other alkaloids, which are mainly from Houpo, Mutong, and Fangfeng. Alkaloids have various cleavage patterns based on the different C–N skeleton structures, among which the most important fragmentation patterns are four: (1) the groups connected to N atoms are prone to loss, generating fragments such as CH_2, CH_4, NH_2, NH_4, etc. (2) When the alkaloid contains hydroxyl substitutions, it can cause neutral loss of H_2O and methylene. When the alkaloid contains carboxyl substituents, it can cause a loss of CO_2. The alkaloid skeleton with multiple hydroxyl groups in the side chain is prone to breakage and dehydration rearrangement. (3) When the alkaloid has a tetrahydroisoquinoline structure, an RDA cleavage reaction can occur, producing complementary fragment ions. (4) After the cleavage of benzyl isoquinoline alkaloids, benzyl fragment ions will be produced, resulting in typical peaks that are different from other types of alkaloids.

Dauricine (**131**; *m/z* 625.32900 $[M+H]^+$) in Mutong is a type of bis benzyl tetrahydroisoquinoline alkaloid. In the positive ion mode, the cleavage at positions C-1 and C-1a would produce benzyl fragment ions at *m/z* 107.12712, which was a typical fragment ion different from the aporphine alkaloids mentioned above.[39] In the secondary mass spectrometry, after the loss of benzyl fragment ions, the mother nucleus fragment ions of dauricine, *m/z* 205.21913, continued to generate fragments ions of *m/z* 189.16320 and 161.15241 (►**Fig. 8**).

Results on Network Pharmacology

Active Component and Targets Collection in CWD

After the screening (OB $\geq$ 30%, DL $\geq$ 0.18) and searching in relevant literature data, 143 chemical components for CWD were obtained from TCMSP. Furthermore, 1,051 targets for

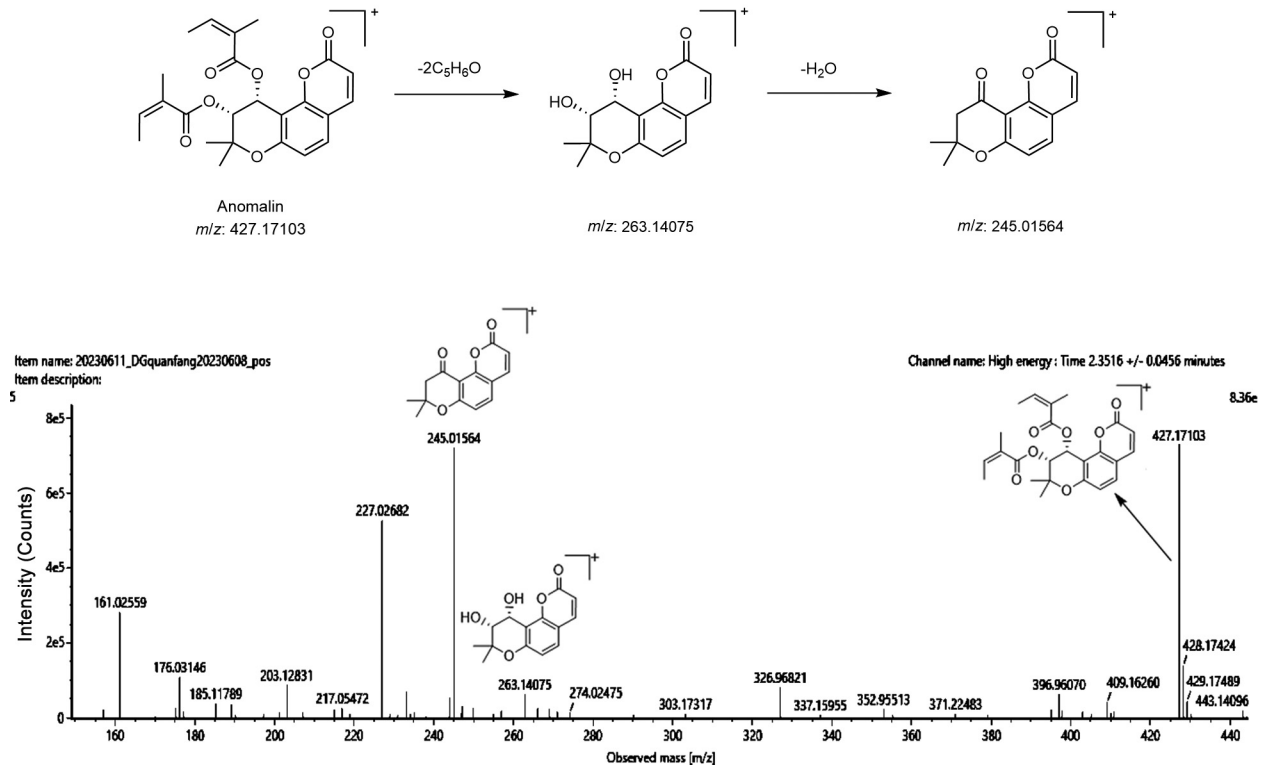


Fig. 6 Mass fragmentation pathways and secondary mass spectra of anomalin.

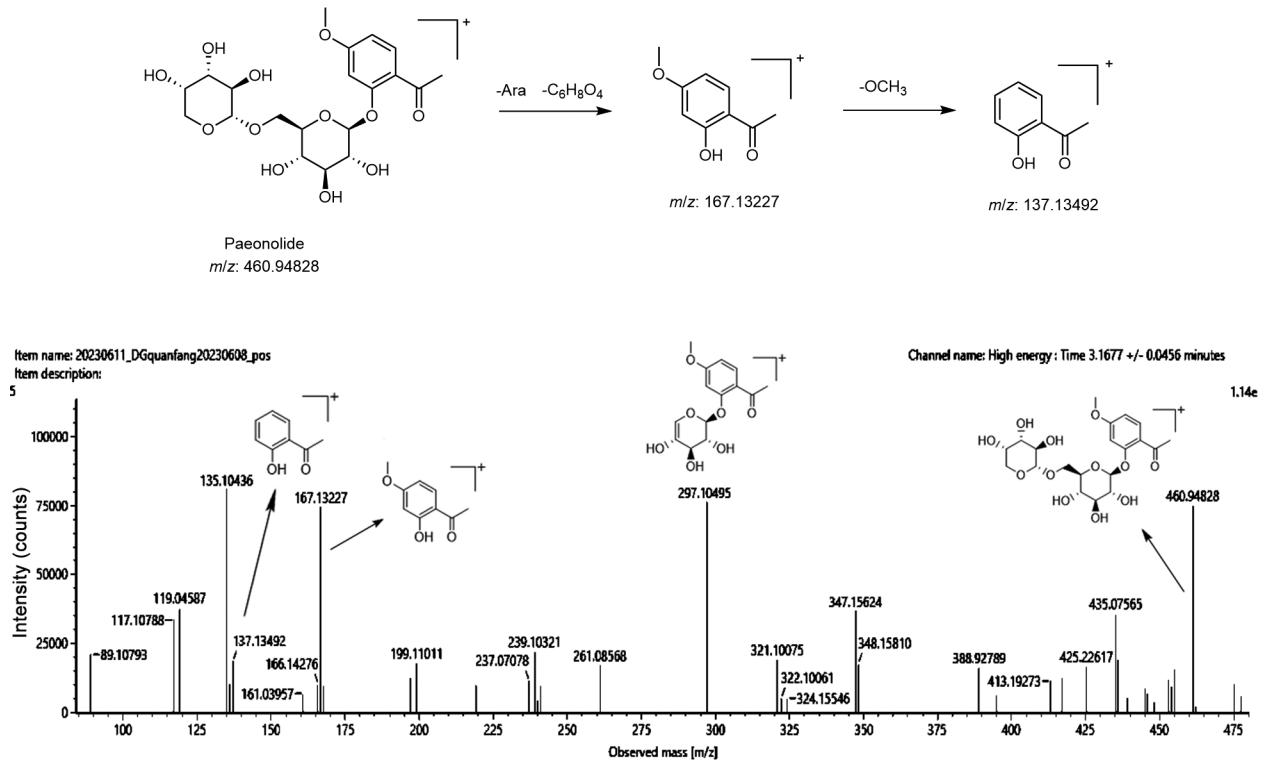


Fig. 7 Mass fragmentation pathways and secondary mass spectra of paeonolide.

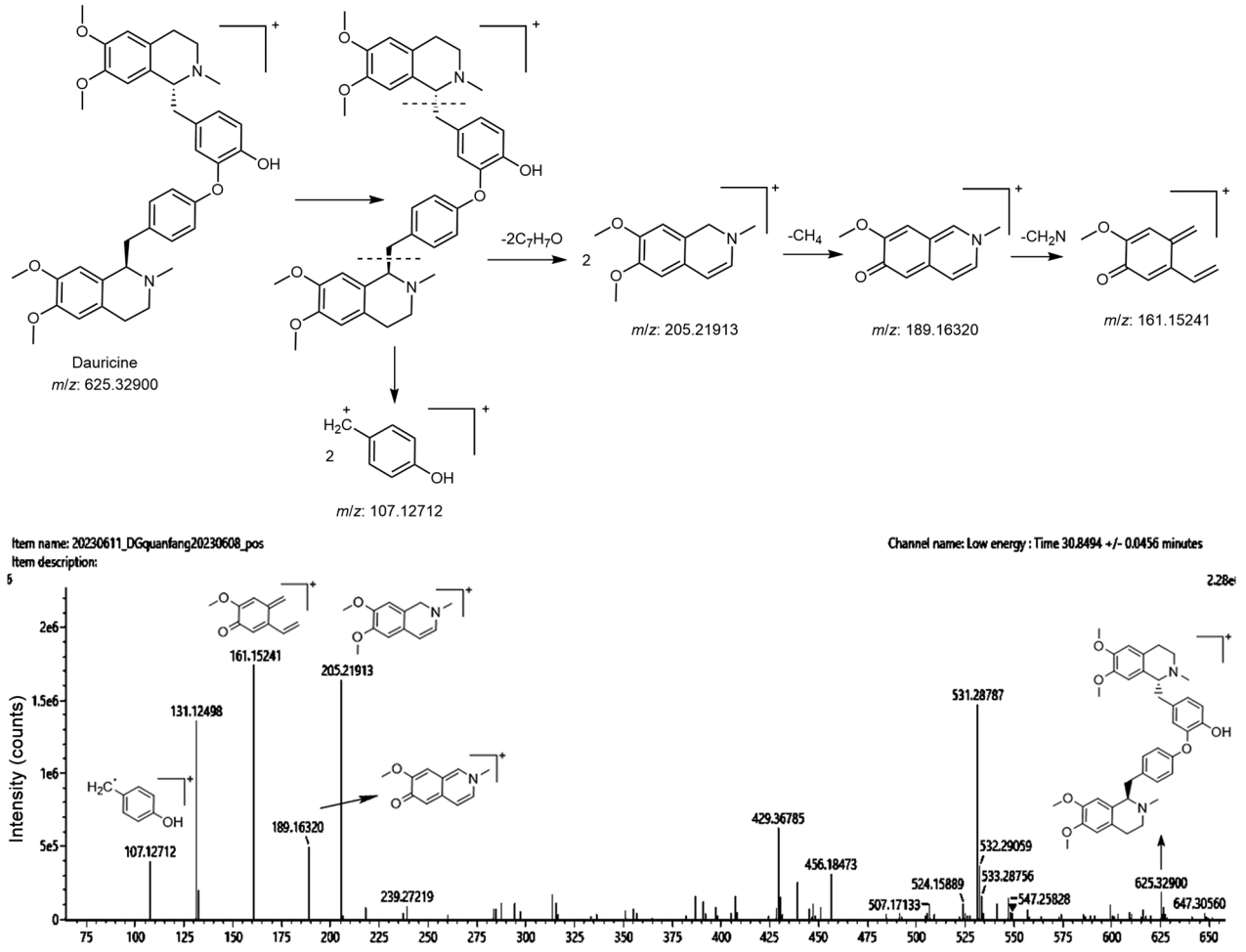


Fig. 8 Mass fragmentation pathways and secondary mass spectra of dauricine.

CWD were predicted by SwissTargetPrediction. A total of 4,174 related targets of "eczema" and "herpes zoster" were selected from the Drugbank database, the Genecards database, and the OMIM database. Finally, 1,051 targets of CWD and 4,174 disease-related targets were mapped to the Venn. A total of 362 overlapping targets were obtained.

Analysis of the PPI Network and "Compounds–Targets" Network

A total of 362 intersection targets were inputted into STRING 11.0, and the results show that the network consists of 6,280 edges, with an average degree value of 34.7 and an average local clustering coefficient of 0.501, $p < 1.0E\text{-}16$.

Nodes with a degree value less than 25 were deleted, and 48 core target proteins were used to form the protein–protein interaction (PPI) core network, then isolated targets without interaction were removed, as shown in ►**Fig. 9**. In the PPI network diagram, different colored lines between targets represent different evidence, with *green* representing adjacent genes, *red* representing fusion genes, and *blue* representing co-occurrence genes. The thicker the connecting lines, the stronger the interaction between proteins, indicating more interactions between proteins rather than the expected interactions of a random set of proteins extracted from the genome. The top 10 core targets for degree ranking were CYP19A1 (cytochrome P450 family 19 subfamily A member 1), AR (androgen receptor), HMGCR (3-hydroxy-3-methylglutaryl-coenzyme A reductase), ESR1 (estrogen receptor 1), PTGS2 (prostaglandin-endoperoxide synthase 2), ALOX5 (arachidonate 5-lipoxygenase), SHBG (sex hormone-binding globulin), NOS2 (nitric oxide synthase 2), ADORA3 (adenosine A3 receptor), and NR3C1 (nuclear receptor subfamily 3 group C member 1).

Screening of Active Ingredients

According to the "compounds–targets" network, the compounds with the highest degree ranking indicated that they were more likely to participate in a certain treatment process and related signaling pathways, and had stronger interactions with target proteins. By intersecting 143 core components in network pharmacology with 287 components of CWD, 25 overlapping components were obtained, with their numbers and degree values shown in ►**Table 4**. This indicates that these components may have therapeutic effects on eczema and herpes zoster.

Gene Ontology and KEGG Pathway Enrichment Analysis

GO and KEGG pathway enrichment analysis was performed on key intersection target genes to obtain the top 25 GO and KEGG signaling pathways, and they were annotated

separately. Based on the PPI network, pathway enrichment analysis used protein interaction and metabolic pathway information to predict the therapeutic mechanism of CWD. This is a method beneficial for studying the holistic nature of CWD from a multi-pathway and multi-target perspective and can transform the overall effects of TCM decoction into descriptions used in modern pharmacology.

As shown in ►**Fig. 10**, GO enrichment analysis revealed a total of 52 pathways, and the enrichment results showed that the biological process mainly included pathways such as

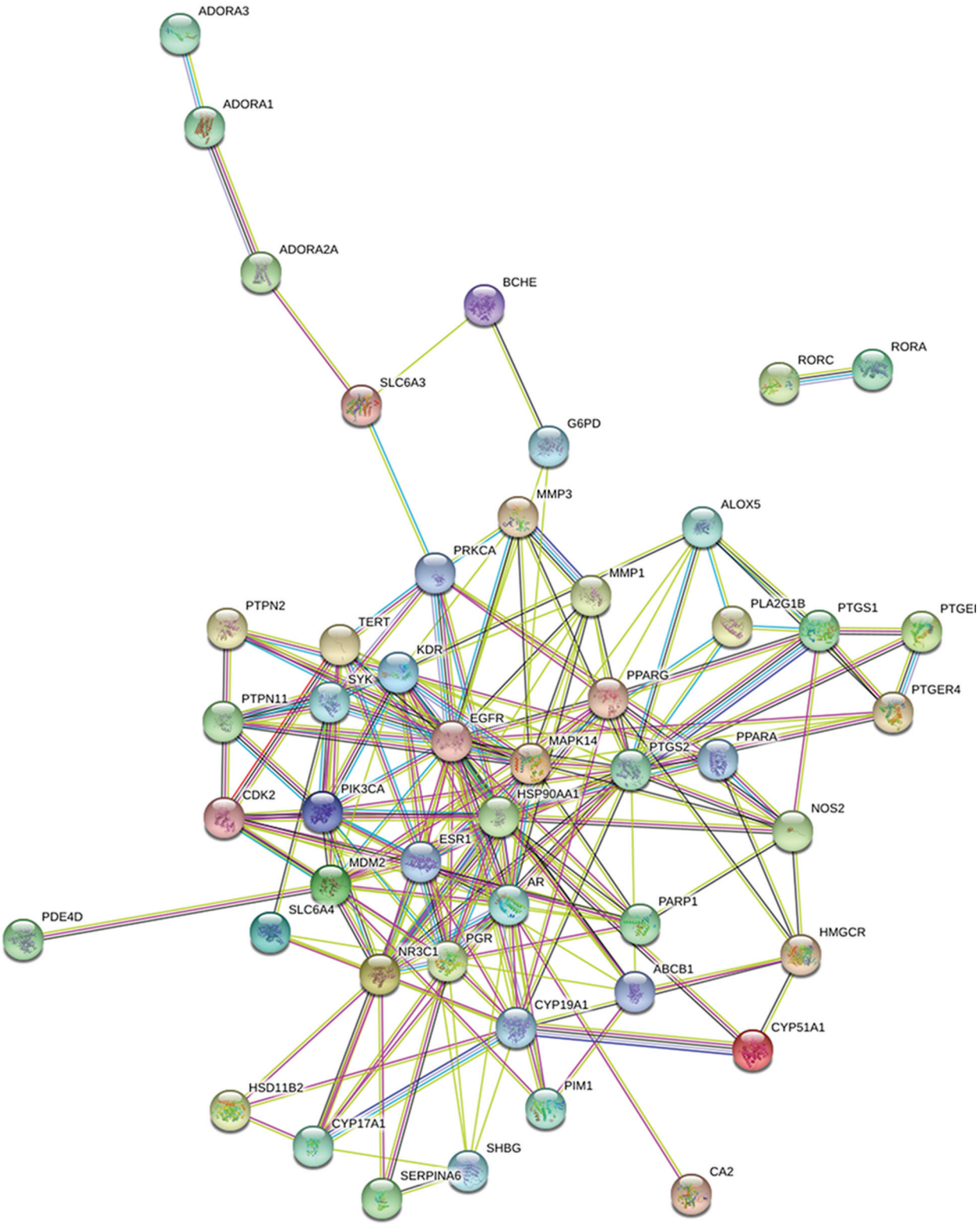


Fig. 9 The PPI network of protein interaction relationships. PPI, protein–protein interaction.

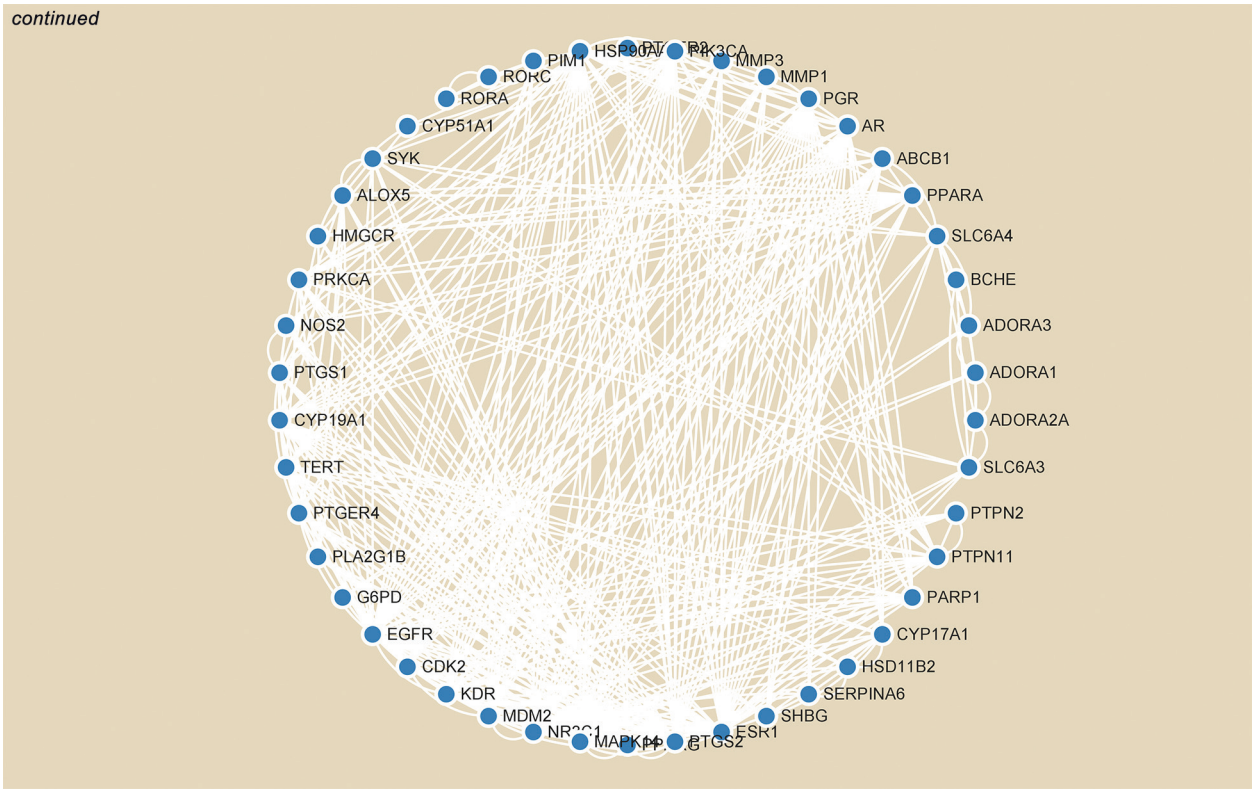


Fig. 9 (Continued)

biological regulation, single organism process, cellular process, response to stimuli, and regulation of biological process; cellular component mainly included pathways such as cell, cell part, organelle, membrane and organelle part; molecular function mainly included pathways such as binding, catalytic activity, signal transducer activity, molecular transducer activity, and nucleic acid binding transcription factor activity.

KEGG enrichment analysis resulted in a total of 194 pathways (►**Fig. 11**), covering multiple aspects such as metabolism, genetic information processing, environmental information processing, cellular processes, organismal systems, and human diseases. The top 25 mainly included the pathways in cancer, prostate cancer, proteoglycans in cancer, the vascular endothelial growth factor signaling pathway, the C-type lectin receptor signaling pathway, and human cytomegalovirus infection.

Reactome Enrichment Analysis

Using the Metascape platform, Reactome analysis covered a total of 15 pathways (►**Fig. 12**), including signaling by interleukins, nuclear receptor transcription pathway, metabolism of lipids, signaling by receptor tyrosine kinases, and metabolism of steroids (►**Table 5**).

Molecular Docking Analysis

Based on the above research, alisol J 23-acetate (**157**), kaempferol (**178**), anomalin (**29**), icariside F2 (**103**), and cinnamaldehyde (**246**) (►**Fig. 13**) with high degree values were selected. These five components belong to naturally occurring major active constituents in the monarch drug Cangzhu, ministerial drugs Zhizi, Zexie, Fangfeng, and adjuvant drug Rougui of CWD, which have representative structures as terpene, flavonoid, phenylpropanoid, aromatic glycoside, and aldehyde.[27–31] Therefore, they were used to molecularly dock with core targets CYP19A1, AR, and HMGCR (HMG-CoA) (►**Fig. 14**) using autodock software. The mode with the lowest binding energy was selected for plotting. The dark part represents the 3D conformation of the target protein, while the highlighted part represents the ligand molecular structure in ►**Fig. 15**. The results showed that the molecular docking binding energies of CYP19A1, AR, HMGCR with alisol J 23-acetate (**157**), kaempferol (**178**), anomalin (**29**), cinnamaldehyde (**246**) were the lowest, mostly lower than −5.00 kcal/mol, indicating strong binding activity between these active ingredients and the targets (►**Table 6**).

Discussion

CWD is commonly used in the treatment of eczema and herpes zoster. It clears heat removes dampness, and strengthens the spleen and diuresis. Nevertheless, there is still insufficient research on the material basis and pharmacology of CWD. This study integrates the research results of UPLC-Q-TOF-MS, GC-MS, network pharmacology, and molecular docking to provide a basis for further research.

Through analysis from the PPI network and pathway enrichment (KEGG, GO, and Reactome) of CWD, it was found that the main target proteins of CWD in the treatment of eczema and herpes zoster were CYP19A1, AR, HMGCR, ESR1, PTGS2, etc. Based on the interactions and metabolic pathway information involved in these proteins, enrichment analysis can be summarized as follows: CWD may regulate C-type

Table 4 Overlapping components of material basis and network pharmacology

Compd.	Component name	Herb-source (in Abbreviation[a])	Average shortest path length	Closeness centrality	Stress	Degree
157	Alisol J 23-acetate	ZX	2.547	0.393	1026334	50
170	Polyporusterone A	ZL	2.567	0.390	991250	48
178	Kaempferol	ZZ	2.555	0.391	887930	47
29	Anomalin	FF	2.575	0.388	992448	47
99	Dehydrotumulosic acid	FL	2.594	0.385	737238	46
151	Crepenynic acid	BZ	2.650	0.377	677680	40
120	16-Deoxyporicoic acid B	FL	2.626	0.381	463502	39
12	2-Hydroxyisoxypropyl-3-hydroxy-7-isopentene-2, 3-dihydrobenzofuran-5-carboxylic	CZ	2.746	0.364	808492	34
162	Stigmast-4-ene-3,6-dione	RG	2.642	0.378	500454	33
167	Stigmasterol	MT, ZZ	2.757	0.363	172222	22
94	Geniposide	ZZ	2.813	0.355	210508	17
17	Erthro-guaiacy lglycerol	RG	2.813	0.355	243830	16
103	Icariside F2	CZ, BZ	2.944	0.340	304602	15
92	8β-Ethoxy atractylenolide III	CZ, BZ	2.905	0.344	227614	15
168	Hesperidin	CP	2.781	0.360	157740	13
149	Oleanolic acid-28-*O*-β-*D*-glucopyranoside	HP	2.920	0.342	51986	12
40	Nobiletin	CP	2.765	0.362	72624	11
173	Poricoic acid ZG	FL	2.940	0.340	34882	10
152	Citromitin	CP	2.797	0.357	47464	9
80	(+)-Leptolepisol C	RG	3.091	0.323	35944	9
58	Oxypaeoniflorin	CZ	3.131	0.319	25476	7
19	Sinapaldehyde 4-*O*-β-*D*-glucopyranoside	HP	3.258	0.307	27060	4
45	Atractyloyne	CZ	3.469	0.288	3016	4
116	Syringin	CZ	3.183	0.314	1620	3
65	Xambioona	GC	4.010	0.249	0	1

[a]Abbreviation: CZ, Cangzhu; HP, Houpo; CP, Chenpi; GC, Gancao; ZX, Zexie; FL, Fuling; ZL, Zhuling; RG, Rougui; BZ, Baizhu; ZZ, Zhizi; MT, Mutong; FF, Fangfeng.

lectin receptor signaling pathway, human cytomegalovirus infection, interleukin-17 signaling pathway, inflammatory mediators of TRP channel, serotonergic synapses, arachidonic acid metabolism, and Fc-ε-biological pathways such as the RI signaling pathway, to act on anti-inflammatory and antiviral mechanisms. The target proteins above have been proven to be key enzymes in metabolic pathways such as the synthesis of estrogen, synthesis of cholesterol, prostaglandin biosynthesis, and arachidonic acid metabolism.[41–44] This result indicates CWD may have the potential to regulate immune response mechanisms, which are usually the most important in the treatment of eczema and herpes zoster diseases.

From the perspective of active ingredients, some researchers have confirmed that natural products from 14 Chinese medicinal materials in CWD such as oxypaeoniflorin (**58**), kaempferol (**178**), geniposide (**94**), icariside F2 (**103**), and hesperidin (**168**), have anti-inflammatory, antibacterial, and anti-infective effects.[45–49] These components can reduce the expression level of inflammatory factors and reduce vascular permeability. Molecular docking also showed good binding activity of the above natural products with target proteins CYP19A1, AR, and HMGCR (HMG-CoA). These results to some extent mutually verified the analysis of the PPI network and pathway enrichment.

Besides, research has shown that natural steroid compounds in Chinese herbal medicine can exert therapeutic effects through these receptor signaling pathways, meanwhile, steroid hormone-like regulatory effects are also an important way to treat immune diseases.[50–52] Atractylodin and atractylone (atractyloyne, **45**) contained in Cangzhu also have diuretic effects.[45,46] Alisol (Alisol J 23-acetate, **157**) in Zexie can significantly increase liver tissue SOD content, inhibit leukotriene production and β-hexosaminase release,

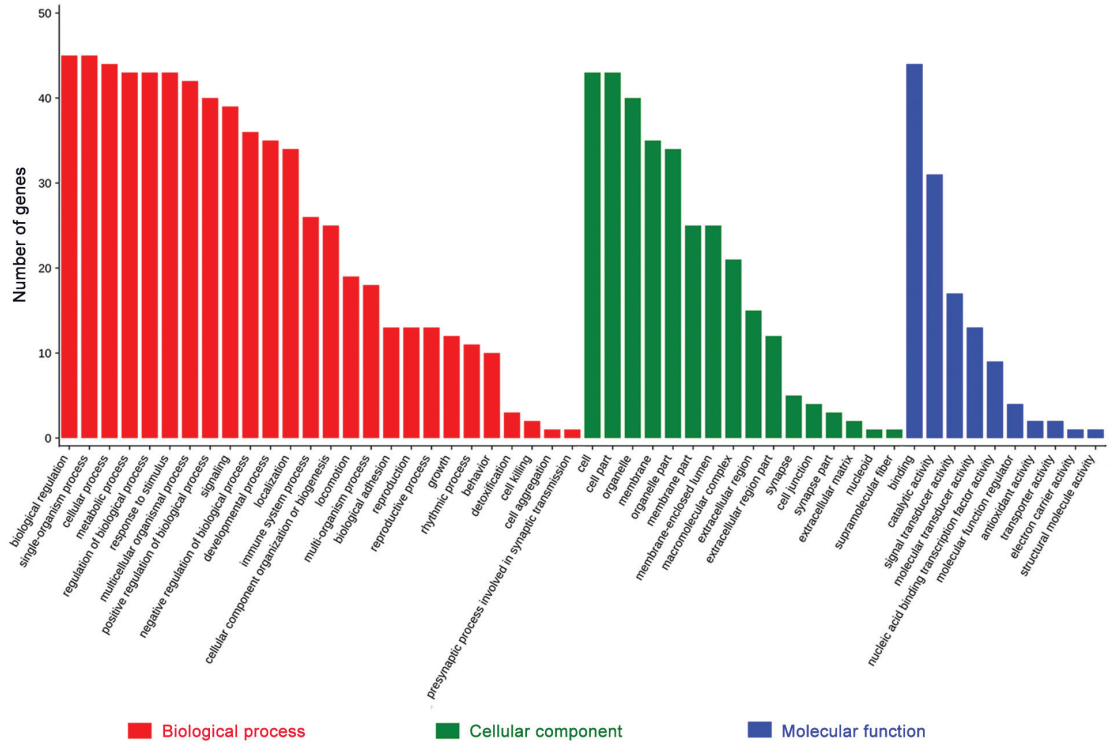


Fig. 10 Visualization and annotation of GO pathway enrichment analysis (top 25).

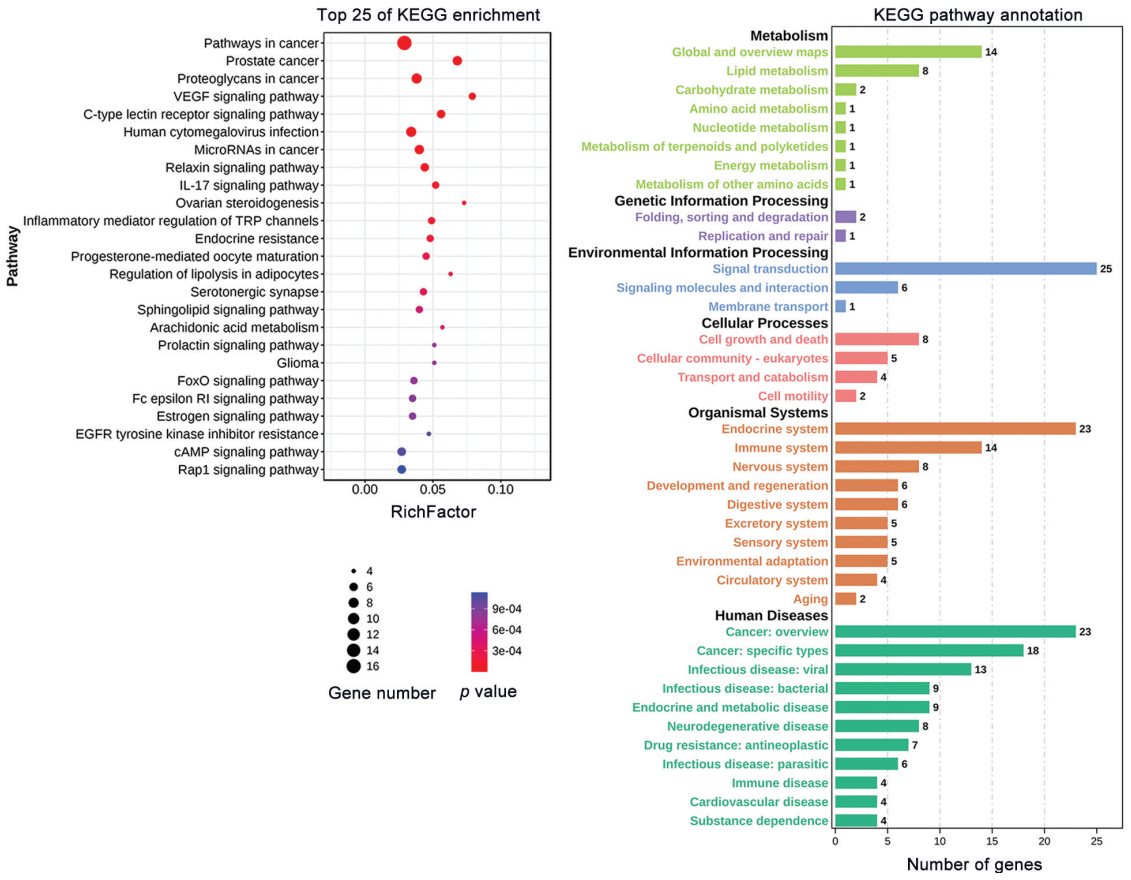


Fig. 11 Visualization and annotation of KEGG pathway enrichment analysis (top 25).

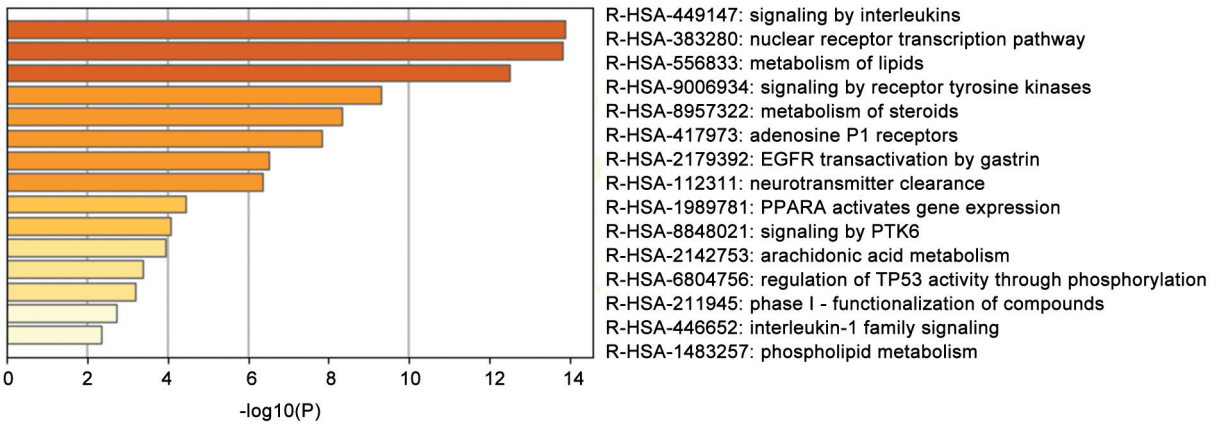


Fig. 12 Visualization and annotation of Reactome enrichment analysis.

Table 5 Reactome pathways (top 5)

Category	GO ID	Description	Count	%	Log10(*P*)	Log10(*q*)
Reactome Gene Sets	R-HSA-449147	Signaling by Interleukins	14	29.17	−13.89	−10.7
Reactome Gene Sets	R-HSA-383280	Nuclear receptor transcription pathway	8	16.67	−13.81	−10.7
Reactome Gene Sets	R-HSA-556833	Metabolism of lipids	15	31.25	−12.49	−9.78
Reactome Gene Sets	R-HSA-9006934	Signaling by receptor tyrosine kinases	11	22.92	−9.32	−6.86
Reactome Gene Sets	R-HSA-8957322	Metabolism of steroids	7	14.58	−8.32	−5.91

Note: Log10(*P*) describes the significant level of gene enrichment, the smaller the value, the higher the significance; Log10(*q*) describes corrected Log10(*P*) value.

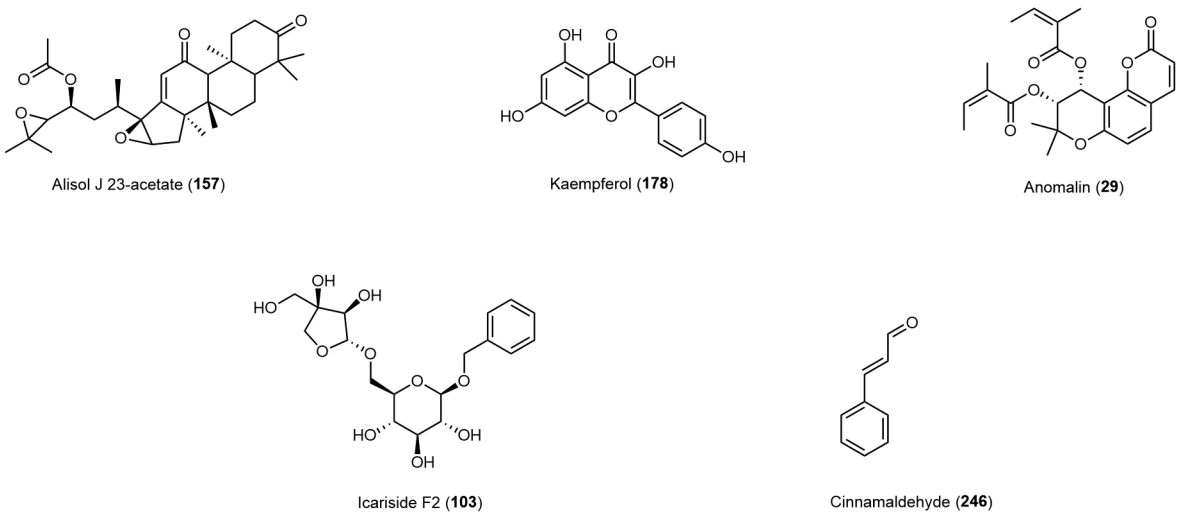


Fig. 13 Chemical structures of alisol J 23-acetate (**157**), kaempferol (**178**), anomalin (**29**), icariside F2 (**103**), and cinnamaldehyde (**246**).

reduce oxidative damage, and inhibit delayed allergic reactions.[53] Polyporusterone (polyporusterone A, **170**) and poricoic acid (16-deoxyporicoic acid B, **120**; poricoic acid ZG, **173**) in Fuling and Zhuling can regulate blood lipids and reduce sodium and water retention. The sterones and sterols (ergone, cerevisterol) in Fuling have been proven to have diuretic functions, while increasing urine output, they can also increase the excretion of electrolytes such as K^+, Na^+, and Cl^-. Fuling extract poricoic acid can play a similar role as an aldosterone antagonist.[54,55] The pharmacological effects of these compounds are consistent with the "dehumidification" and "diuretic" effects of CWD and can reflect the possible steroid hormone-like regulatory effects to adjust the water-electrolyte metabolism.

In summary, all the analyses and examples indicate that CWD may have therapeutic effects on eczema and herpes zoster through the above core proteins, pathways, and ingredients from Chinese medicinal materials.

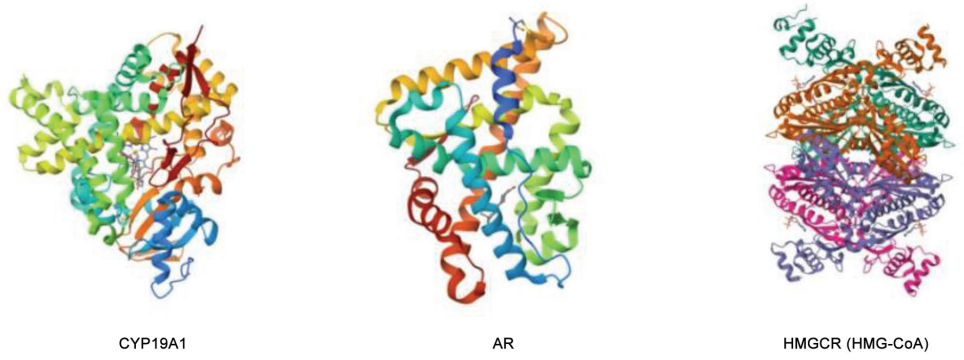


Fig. 14 Target protein conformation of CYP19A1, AR, and HMGCR (HMG-CoA).

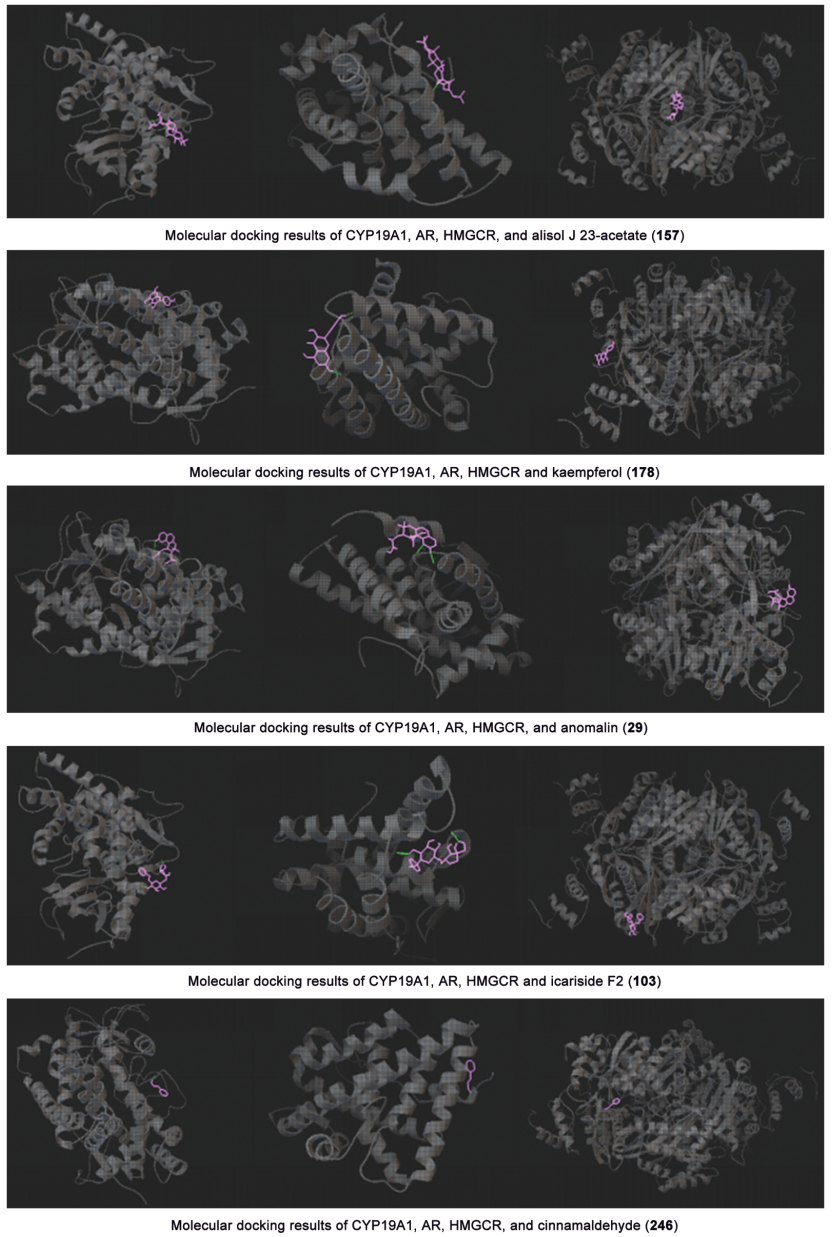


Fig. 15 Molecular docking results. The 3D conformation of target protein CYP19A1, AR, and HMGCR was presented from left to right, respectively.

Table 6 The lowest binding energy of molecular docking between CYP19A1, AR, HMGCR, and different components

The lowest binding energy (kcal·mol^{-1})	CYP19A1	AR	HMGCR
Alisol J 23-acetate	−7.19	−6.16	−5.77
Kaempferol	−5.95	−5.00	−5.17
Anomalin	−7.08	−4.60	−5.38
Icariside F2	−2.78	−1.87	−1.83
Cinnamaldehyde	−4.38	−4.81	−5.32

Conclusion

This study conducted a systematic chemical composition analysis of the classic prescription, CWD. The material basis of CWD was preliminarily characterized by UPLC-Q-TOF-MS and GC-MS techniques. A total of 286 chemical components were identified. The mass spectrometry fragmentation patterns of some terpenoids, flavonoids, phenylpropanoids, phenolic esters, and alkaloids in CWD were summarized. Through subsequent research, 25 overlapping components in material basis and network pharmacology were selected, to provide a basis for further research on the quality standards of CWD.

At the same time, network pharmacology, GO, KEGG, and Reactome enrichment analysis reveal that potential therapeutic mechanisms of action of CWD might be: (1) anti-inflammatory, antiviral, and mediated immune response; (2) regulating steroid metabolism. Meanwhile, molecular docking indicated that alisol J 23-acetate, kaempferol, anomalin, and cinnamaldehyde of CWD tend to combine with core target proteins at a low level of binding energy.

This study provides ideas and methods for the basic research of CWD and gives evidence support for clinical medication.

Conflict of Interest

None declared.

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