Drug Design, Development and Therapy

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Momordicae Semen: A Review of Phytochemistry, Pharmacology, Toxicology, Herbal Processing, Clinical Applications, and Q-Markers Prediction

Xin Deng[1], Yanmei Liu[1], Xiaoli Zhu[1], Hui Zhu[1], Cheng Huang[1], Yan Hong[1,2], Deling Wu[2], Yanquan Han[1–3]

[1]Grade Three-Level Laboratory of TCM Preparation, State Administration of Traditional Chinese Medicine, The First Affiliated Hospital of Anhui University of Chinese Medicine, Hefei, Anhui, People's Republic of China; [2]Anhui University of Chinese Medicine, Hefei, Anhui, People's Republic of China; [3]Zhejiang University of Traditional Chinese Medicine, Hangzhou, Zhejiang, People's Republic of China

Correspondence: Yan Hong; Yanquan Han, Email hyan2003@163.com; hyquan2003@163.com

Drug Design, Development and Therapy downloaded from https://www.dovepress.com/
For personal use only.

Abstract: Momordicae Semen (MS), a traditional Chinese medicine (TCM), is clinically used to disperse stagnation, reduce swelling, detoxify, and treat sores.. However, its therapeutic potential is limited by inherent toxicity and insufficient quality control standards that fail to reflect its therapeutic value. This review comprehensively synthesizes recent advances in MS research, encompassing phytochemistry, pharmacology, toxicology, herbal processing, and clinical applications. Phytochemical studies have identified a diverse range of bioactive compounds in MS, including triterpenoids and saponins, volatile oils, lignans, phenolic acids, flavonoids, steroids, proteins, peptides, and nitrogenous compounds. Pharmacological studies reveal its broad biological activities, such as antitumor, anti-inflammatory, antimicrobial, antiviral, antiulcer, antioxidant, immunomodulatory, hypolipidemic, hypotensive, and neuroprotective activities. Additionally, the applications of MS in TCM formulations and processed products are summarized, and prospects are examined. Furthermore, its potential quality markers (Q-markers) were systematically predicted based on the principles of specificity, measurability, efficacy correlation, traditional property, transfer and traceability, and network pharmacology. Despite these advances, critical challenges remain, including a limited understanding of its toxicological mechanisms, the processing-induced reduction of toxicity, the metabolic pathways of active constituents, and the need for comprehensive quality control standards. Addressing these issues through future research is essential to enhance the clinical utility and therapeutic potential of MS. This review provides a systematic reference and targeted directions for subsequent studies, which is crucial for realizing the safe, effective, and standardized application of MS in clinical practice and pharmaceutical development.

Keywords: Momordicae Semen, pharmacology, phytochemistry, toxicology, clinical application, Q-markers

Introduction

Momordica cochinchinensis (Lour.) Spreng. (MC) is a traditional food and herbal medicine widely distributed across regions such as Bangladesh, India, Malaysia, Myanmar, and several provinces in China, including Guangxi, Taiwan, Sichuan, and Hubei.[1] Botanically, the fruit of MC consists of four distinct parts: an exocarp (spine-adorned peel), a spongy orange mesocarp (pulp), a red aril (membrane), and brown to black seeds. Each fruit typically yields 15–20 seeds, characterized by a round, compressed, and sculpted morphology (Figure 1).

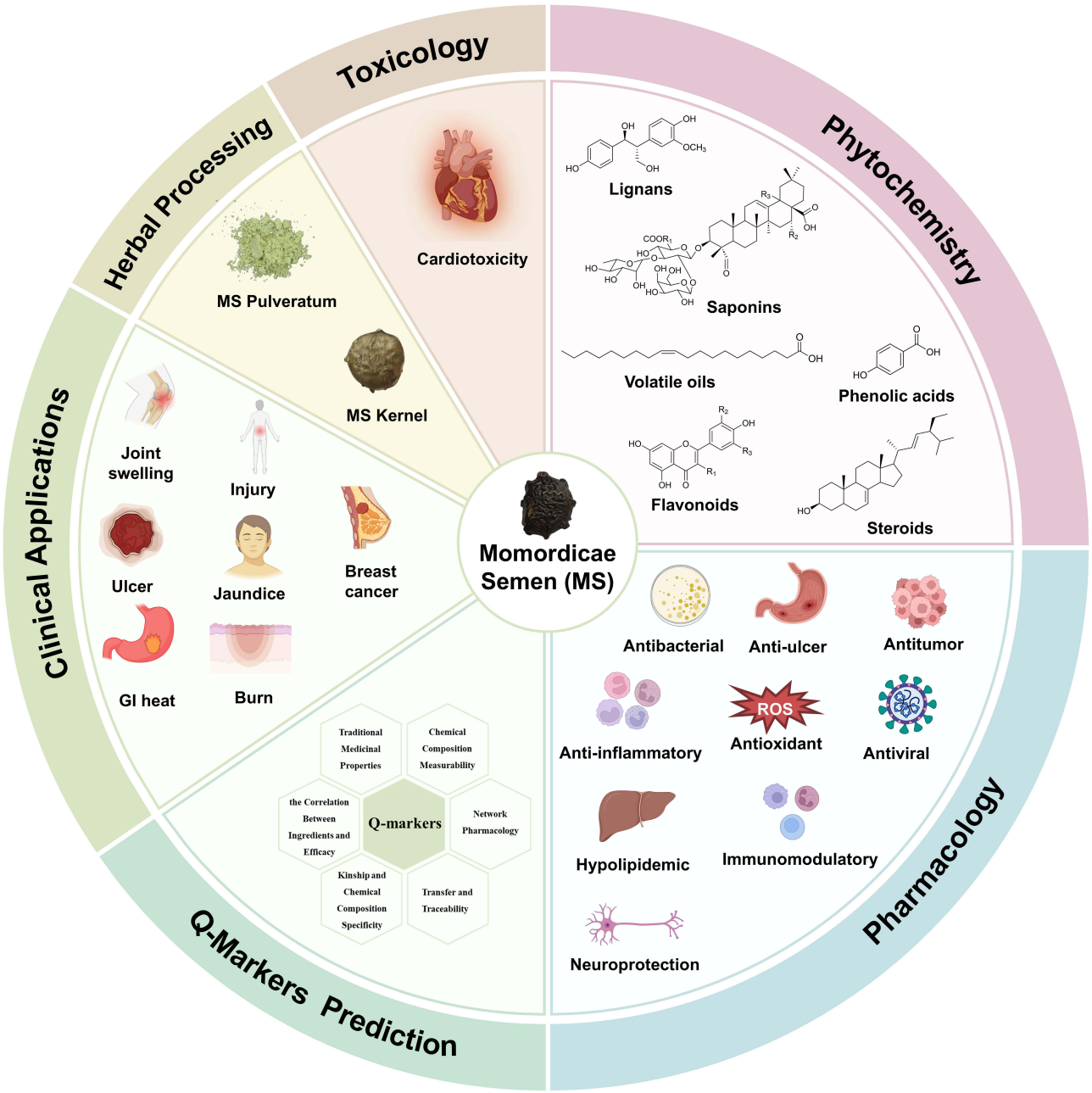
Momordicae Semen (MS), the dried ripe seed of MC, is recorded as a medicinal part in the *Chinese Pharmacopoeia* with the functions of dissipating binds, dispersing swelling, expelling toxins, and treating sores. It is used to treat sores, ulcers, swelling, toxins, acute mastitis, scrofula, hemorrhoids, fistula, dry ringworm, and favus. Additionally, MS holds significant value in ethnomedicine, particularly as an integral component of traditional Mongolian Medicine.

However, MS is inherently toxic, and its raw form is rarely administered directly. To reduce toxicity, MS is usually processed or combined with other herbs. Despite its therapeutic potential, the *Chinese Pharmacopoeia* (2025) currently

Received: 20 July 2025
Accepted: 30 October 2025
Published: 22 November 2025

© 2025 Deng et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms.php and incorporate the Creative Commons Attribution – Non Commercial (unported, v4.0) License (http://creativecommons.org/licenses/by-nc/4.0/). By accessing the work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission from Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please see paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php).

Graphical Abstract



employs only the content of gypsogenin 3-O-β-D-glucuronopyranoside as the quality standard for MS. This unidimensional approach inaccurately reflects the therapeutic value of this medicinal herb.

While previous reviews have primarily summarized the chemical constituents and pharmacological activities of MS,[2] this review systematically evaluates its phytochemistry, pharmacology, toxicology, herbal processing, and clinical applications. Furthermore, it identifies Q-markers to establish a comprehensive quality evaluation system, aiming to provide a theoretical foundation for the safe and effective clinical use of MS.

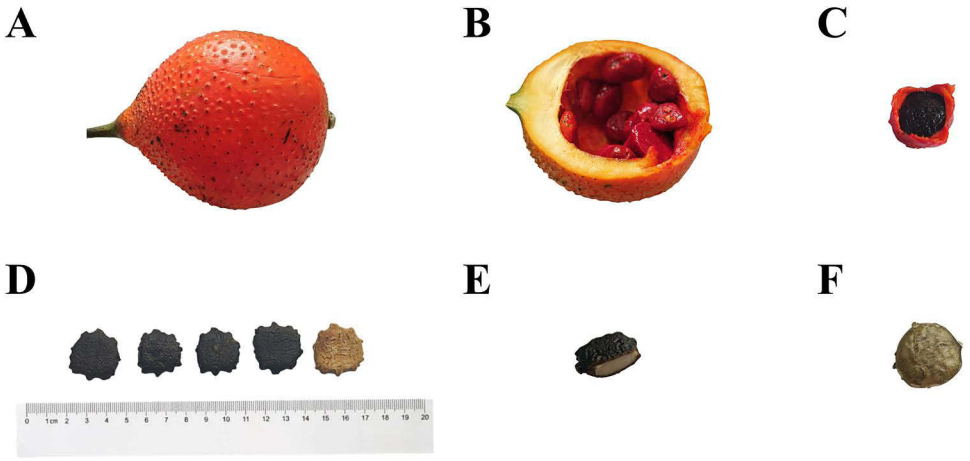


Figure 1 Morphological and anatomical features of *Momordica cochinchinensis* (**A**) Whole fruit exterior. (**B**) Transverse section of the fruit. (**C**) Enlarged view of the aril surrounding the seed. (**D**) Dried seed with a ridged surface. (**E**) Transverse section of the seed. (**F**) Isolated seed kernel.

Materials and Methods

Literature for this comprehensive review on MS was compiled from various databases, including PubMed, China National Knowledge Infrastructure (CNKI), Google Scholar, SciFinder, ScienceDirect, and Web of Science, spanning two decades. Retrieval based on the following keywords: "*Momordica cochinchinensis*", "Momordicae Semen". All chemical structures were drawn using ChemDraw software.

The literature about MS was scrutinized, merging the candidate components of Q-markers with data from the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP) database (oral bioavailability [OB] ≥ 0.30, drug-likeness [DL] ≥ 0.18). The SwissADME platform (http://swissadme.ch) was employed to screen the active ingredients of MS, selecting those with high gastrointestinal (GI) absorption and two or more "Yes" in drug-likeness (DL) parameters as active components.[3,4] Predicted Q-markers targets were analyzed via SwissTargetPrediction, and the resulting targets were mapped onto the STRING database (https://cn.string-db.org/) to construct a protein-protein interaction (PPI) network. Core targets were identified using the cytoHubba plugin in Cytoscape. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were conducted via DAVID (https://david.ncifcrf.gov/home.jsp), with results visualized using bioinformatics tools. Finally, a "component-target-pathway" network was constructed using Cytoscape 3.10.1, and candidate Q-markers were prioritized based on the number of edges connected to the component nodes.

Results and Discussion

Phytochemistry

MS contains a diverse array of chemical components. Comprehensive phytochemical analyses have identified triterpenes and saponin derivatives, volatile oils, lignans, phenolic acids, flavonoids, steroids, proteins, peptides, nitrogenous compounds, and other compounds.

Triterpenoids and Saponins

Triterpenes and saponins, a class of bioactive compounds abundant in MS, primarily consist of cucurbitane-type tetracyclic and oleanane-type pentacyclic triterpenoids. These compounds represent characteristic components of MS, distinguished by their complex structures and limited distribution. Modern pharmacological studies have revealed that MS saponins exhibit diverse pharmacological activities, including anti-inflammatory, cytotoxic, immunomodulatory, and nephroprotective effects.[5] Notably, new evidence indicates that these saponins may simultaneously act as the primary toxic constituents in MS, revealing their dual pharmacological and toxicological roles. The triterpenoids and saponins isolated from MS are systematically cataloged in Table 1, and their corresponding structures are illustrated in Figure 2.

https://doi.org/10.2147/DDDT.S555032

Table 1 Triterpenoids and Saponins in MS (1–49)

NO.	Compound Name	Ref.
1	Mubezhiside A	[6]
2	Mubezhiside B	[6]
3	Mubezhiside C	[6]
4	Mubezhiside D	[6]
5	Mubezhiside E	[6]
6	Momordica saponin I	[7]
7	Momordica saponin II	[8]
8	3-O-α-L-rhamnopyranosyl(1→3)-6'-O-methyl-β-D-glucuronopyranosyl-gypsogenin	[9]
9	Arjunolic acid	[10]
10	Gypsogenic acid	[10]
11	Gypsogenin	[10]
12	Hederagenin	[10]
13	Oleanolic acid	[10]
14	Oleragenin	[10]
15	α-D-galacturopyranosyl-gypsogenin	[10]
16	3-O-6'-O-methyl-β-D-glucuronopyranosyl-28-O-methyl-gypsogenin	[10]
17	3-O-6'-O-methyl-β-D-glucuronopyranosyl-gypsogenin	[10]
18	3-O-β-D-galactopyranosyl-(1→2)-[α-L-rhamnopyranosyl(1→3)]-6'-O-methyl-β-D-glucuronopyranosyl-gypsogenin	[10]
19	3-O-β-D-galactopyranosyl-(1→2)-6'-O-methyl-β-D-glucurono-pyranosyl-28-O-β-D-galactopyranosyl-gypsogenin	[10]
20	3-O-β-D-galactopyranosyl-(1→2)-6'-O-methyl-β-D-glucuronopyranosyl-gypsogenin	[10]
21	3-O-β-D-glucuronopyranosyl-gypsogenin	[11]
22	Gypsogenin 3-O-β-D-galactopyranosyl (1→2)-[α-L-rhamnopyranosyl(1→3)]-β-D-glucuronopyranoside	[12]
23	3-O-6'-O-methyl-β-D-glucuronopyranosyl-quilliac acid	[10]
24	3-O-β-D-galactopyranosyl(1→2)-[α-L-rhamnopyranosyl(1→3)]-6'-O-methyl-β-D-glucuronopyranosyl-quilliac acid	[10]
25	3-O-β-D-galactopyranosyl-(1→2)-6'-O-methyl-β-D-glucuronopyranosyl-quilliac acid	[10]
26	3-O-β-D-galactopyranosyl-(1→2)-β-D-galactopyranosyl-(1→3)]-β-D-glucuronopyranosyl-quilliac acid	[9]
27	Quillaic acid 3-O-β-D-galactopyranosyl(1→2)-[α-L-rhamnopyranosyl(1→3)]-β-D-glucuronopyranoside	[12]
28	3-O-β-D-glucofuranosidurono-6,3-lactone-gypsogenin	[13]
29	5-dehydrokarounidiol	[13]
30	7-oxodihydrokarounidiol	[14]
31	Isokarounidiol	[14]

(*Continued*)

Table 1 (Continued).

NO.	Compound Name	Ref.
32	Karounidiol	[14]
33	Momordic acid	[2]
34	Ursolic acid	[15]
35	α-amyrin	[16]
36	Momordin III	[9]
37	3α-[(*E*)-feruloyloxy]-D:C-friedooleana-7,9(11)-dien-29-oic acid	[9]
38	Lupeol	[9]
39	Momordicoside F2	[9]
40	Goyaglycoside g	[9]
41	Karaviloside I	[9]
42	Karaviloside III	[9]
43	Kuguacin F	[9]
44	Momordicoside Q	[9]
45	Neokuguaglucoside	[9]
46	(3β,7β)-3,7,22,23-tetrahydroxy-cucurbita-5,24-dien-19-al	[11]
47	Cucurbitacin B	[17]
48	Cucurbitacin E	[17]
49	Ganoderic acid A	[13]

Volatile Oils and Fatty Acids

MS is characterized by a distinct greasy odor, attributed to its high oil content (>50% dry weight). The oil consists primarily of volatile compounds and fatty acids, including olefins, aldehydes, esters, and alcohols, with linoleic and oleic acids as the major constituents. While the crude oil exhibits irritant and purgative properties, pharmacological studies have shown that specific fatty acid components display a range of biological activities, including anti-infective, antitumor, and immunomodulatory effects.[18] The specific compounds are detailed in Table 2, and their chemical structures are illustrated in Figure 3.

Lignans

Lignans constitute a major class of bioactive constituents in MS, primarily exhibiting antitumor and anti-inflammatory pharmacological activities.[24,25] These compounds are listed in Figure 4 and Table 3.

Phenolic Acid and Glycosides

Phenolic acids, the prominent secondary metabolites in MS, demonstrate potent antioxidant activity, owing to their polyhydroxylated structures. The chemical compositions and structures of these phenolic acids isolated from MS are detailed in Table 4 and illustrated in Figure 5.

Flavonoids

MS contains a relatively high level of flavonoids [(18.1 ± 2.3) mg/100 g DW], which may explain its observed anti-inflammatory and antioxidant effects.[29] The chemical compounds and structures of the flavonoids isolated from MS are listed in Table 5 and illustrated in Figure 6.

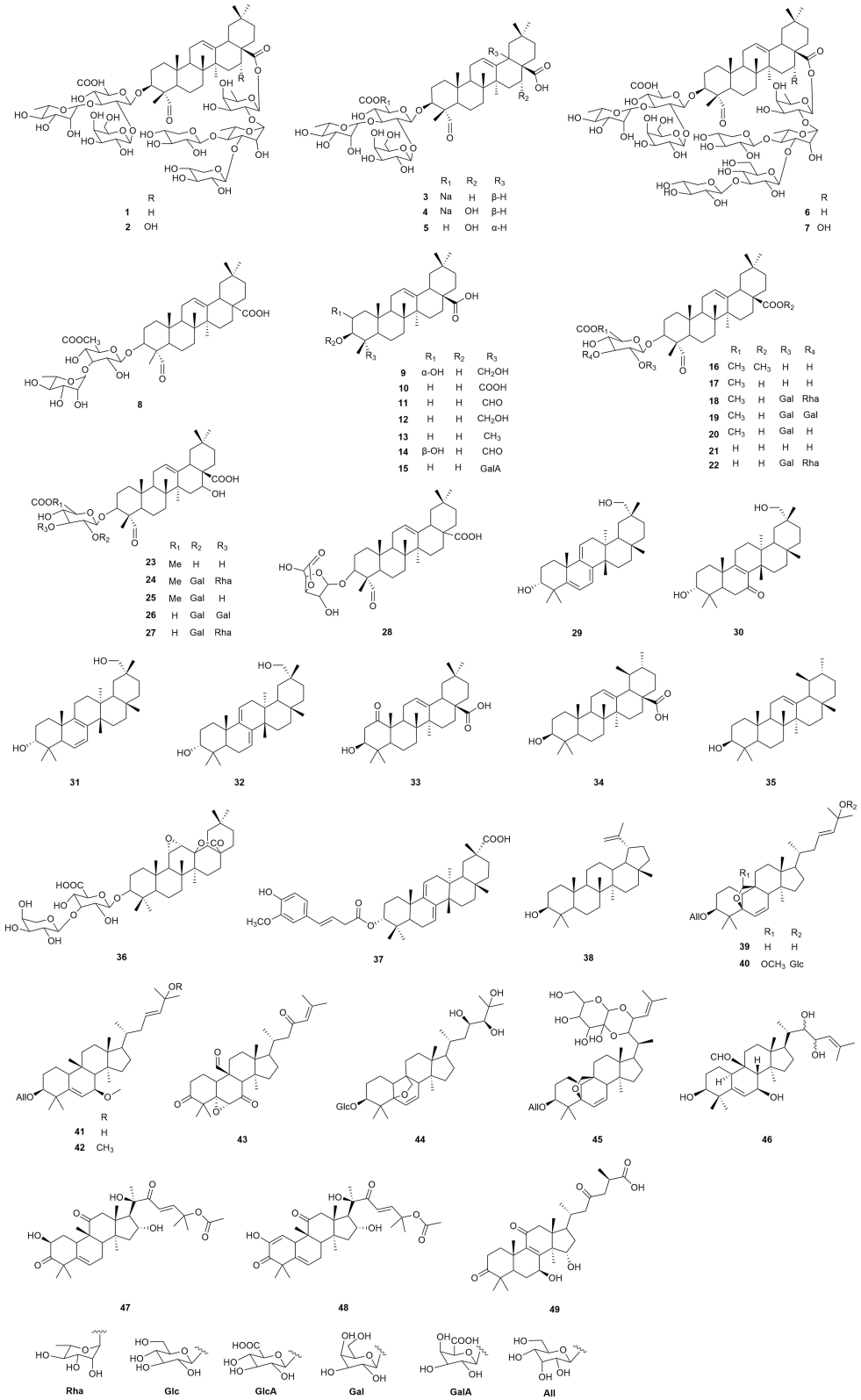


Figure 2 Chemical structures of triterpenoids and their saponins in MS (1–49).

Table 2 Volatile Oils and Fatty Acids in MS (50–215)

NO.	Compound Name	Ref.	NO.	Compound Name	Ref.
50	(*Z*)-icos-11-enoic acid	[19]	**133**	Heptanal	[20]
51	Docosanoic acid	[19]	**134**	Hexanal	[20]
52	Heptadecanoic acid	[19]	**135**	Pentanal	[20]
53	Hexadecanoic acid	[19]	**136**	2-heptenal	[21]
54	Icosanoic acid	[19]	**137**	(*E*) −2-octenal	[19]
55	Nonadec-10-enoic acid	[19]	**138**	(*E, E*)-2,4-nonadienal	[19]
56	Nonadecanoic acid	[19]	**139**	(*R*)-(+)-3-methyl cyclopentanone	[19]
57	Octadec-6-enoic acid	[19]	**140**	2-butyl-2-octenal	[19]
58	Octadeca-10,13-dienoic acid	[19]	**141**	2-ethylhexenal	[19]
59	Pentadecanoic acid	[19]	**142**	2-hexanone	[19]
60	9,12-octadecadienoic acid (*Z, Z*)	[15]	**143**	2-isopropyl-5-methylhex-2-enal	[19]
61	Cis-13-octadecenoic acid	[15]	**144**	2-propyl-2-heptenal	[19]
62	Nonanedioic acid, monomethyl ester	[15]	**145**	3-ethyl cyclopentanone	[19]
63	Palmitic acid	[20]	**146**	4-octanone	[19]
64	Hexanoic acid	[21]	**147**	5-decanone	[19]
65	Octadecanoic acid	[21]	**148**	5-nonanone	[19]
66	Arachidic acid	[22]	**149**	5-undecanone	[19]
67	Cis-vaccenic acid	[22]	**150**	Hexyl formate	[19]
68	Linolenic acid	[18]	**151**	Nonanal	[19]
69	Myristic acid	[18]	**152**	1-(1-methylethoxy)-2-propanol	[20]
70	Oleic acid	[18]	**153**	1,3-dioxan-5-ol	[20]
71	Palmitoleic acid	[18]	**154**	2,4-dimethyloctan-4-ol	[20]
72	Stearic acid	[18]	**155**	2-methylpentan-1-ol	[20]

(*Continued*)

Table 2 (Continued).

NO.	Compound Name	Ref.	NO.	Compound Name	Ref.
73	(9*Z*,11*Z*,13*E*)-octadeca-9,11,13-trienoic acid	[9]	**156**	3-methoxypropane-1,2-diol	[20]
74	Eleostearic acid	[18]	**157**	5-ethylheptan-2-ol	[20]
75	11-hexadecenoic acid	[9]	**158**	5-methylnonan-5-ol	[20]
76	9-oxononanoic acid	[9]	**159**	Butan-1-ol	[20]
77	Arachic acid	[9]	**160**	Butane-1,3-diol	[20]
78	Daturic acid	[9]	**161**	Heptan-2-ol	[20]
79	Linoleic acid	[9]	**162**	Pentan-1-ol	[20]
80	Nonadecylic acid	[9]	**163**	Pentan-2-ol	[20]
81	Nonanedioic acid	[9]	**164**	2,5-dimethyl-3-hexanol	[19]
82	Pentacosanoic acid	[9]	**165**	5-nonanol	[19]
83	Pentadecylic acid	[9]	**166**	5,5-dimethyl-cyclohex-3-en-1-ol	[21]
84	Tetracosanoic acid	[9]	**167**	1-(1-ethoxyethoxy) butane	[20]
85	Trans-gondoic acid	[9]	**168**	1-(1-ethoxyethoxy) pentane	[20]
86	2-hexycyclopropaneoctanoic acid	[23]	**169**	1,1-diethoxyethane	[20]
87	2-ethylbutanoic acid	[20]	**170**	1,1-diethoxypentane	[20]
88	2-hydroxypropanoic acid	[20]	**171**	1,3-dioxolane	[20]
89	Heptanoic acid	[19]	**172**	1-ethenoxybutane	[20]
90	Pentanoic acid	[19]	**173**	2,3-dimethyloxirane	[20]
91	2-ethylbutyric acid	[20]	**174**	2-ethoxybutane	[20]
92	Butanedioic acid, monomethyl ester	[20]	**175**	2-ethoxypropane	[20]
93	1-acetyloxyethyl acetate	[20]	**176**	2-methoxy-1,3-dioxolane	[20]
94	1-methoxypropan-2-yl acetate	[20]	**177**	4-methyl-1,3-dioxane	[20]
95	Ethyl acetate	[20]	**178**	2,6,10-trimethyl dodecane	[19]
96	Ethyl pentanoate	[20]	**179**	2,6,10-trimethylpentadecane	[19]

97	Pentyl acetate	[20]	**180**	2-methylhexadecane	[19]
98	Pentyl formate	[19]	**181**	3,8-dimethyl decane	[19]
99	(2-dodecen-1-yl) succinic anhydride	[19]	**182**	4-tridecene	[19]
100	2-methylbutyl ester pentanoic acid	[19]	**183**	Hexadecane	[19]
101	3,3-dimethylglutaric anhydride	[19]	**184**	Octacosane	[19]
102	3-methylbutyl-2-ethylhexanoate	[19]	**185**	Pentadecane	[19]
103	Amyl caproate	[19]	**186**	Tetradecane	[19]
104	Amyl valerate	[19]	**187**	Tridecane	[19]
105	Heptyl butyrate	[19]	**188**	(*E,E*)-7,11,15-trimethyl-3-methylene-1,6,10,14-tetraene	[21]
106	Heptyl ester-2-methyl butanoic acid	[19]	**189**	1,1,2-trimethyl-3-methylenecyclopropane	[21]
107	Octano-1,4-lactone	[19]	**190**	2,3-dihydro-3,5-dihydroxy-6-methyl-4(H)-pyran-4-one	[20]
108	1-acetoxypentane	[20]	**191**	1,2,4-triethenyl cyclohexane	[19]
109	2-butanol,3-methyl-, acetate	[20]	**192**	1-methyl cycloundecene	[19]
110	Ethyl valerate	[20]	**193**	1-methyl-3-isopropyl-1-cyclohexene	[19]
111	Butanedioic acid, phenyl-, dimethyl ester	[20]	**194**	2,6-dichloro-3-nitropyridine	[19]
112	9,12-octadecadienoic acid (*Z, Z*), methyl ester	[20]	**195**	2-fluoro-4-methoxy benzyl alcohol	[19]
113	9-octadecenoic acid (*Z*), methyl ester	[15]	**196**	2-furfuryl thiol	[19]
114	Methyl stearate	[15]	**197**	2-hexanoylfuran	[19]
115	6,9,12-octadecatrienoic acid, methyl ester	[15]	**198**	2-isopropyl-3-methoxy pyrazine	[19]
116	Methyl 9-oxononanoate	[15]	**199**	3-ethyl-thiophene	[19]
117	Dimethyl azelate	[15]	**200**	4-allyloxy-2-chloroquinazoline	[19]
118	Methyl myristate	[15]	**201**	4-propylresorcinol	[19]
119	Methyl hexadecanoate	[18]	**202**	5-methyl-2-ethyl furan	[19]
120	Methyl heptadecanoate	[18]	**203**	6-(5-methyl-furan-2-yl)-hexan-2-one	[19]

(*Continued*)

Table 2 (Continued).

NO.	Compound Name	Ref.	NO.	Compound Name	Ref.
121	Methyl oleate	[18]	**204**	Benzothiazole	[19]
122	Methyl-9,11-octadecadienoate	[18]	**205**	Butylated hydroxytoluene	[19]
123	Methyl ester 10,12-octadecadienoate	[18]	**206**	Isothiocyanato cyclohexane	[19]
124	Methyl nonadecanoate	[18]	**207**	Selinane	[19]
125	Methyl eleostearate	[18]	**208**	Thujone	[19]
126	Octadecyl-6,9-diene-12-alkynate methyl ester	[18]	**209**	Trimethyl amine	[19]
127	10,13-eisosadienoic acid methyl ester	[18]	**210**	2,3 dihydro-3,5-dihydroxy-6-methyl-4H-Pyran-4-one	[20]
128	Palmitin	[21]	**211**	2-chlorobenzal chloride	[20]
129	Octadecanoic acid 2,3-dihydroxypropyl ester	[21]	**212**	10,11-dihydro-10-hydroxy- 2,3-dimethoxydibenz(b,f)ox epin	[15]
130	2,6-dimethylheptane-3,5-dione	[20]	**213**	α-cadinol	[15]
131	2-oxopropanal	[20]	**214**	1-oxaspiro [4,4]nonan-4-one	[21]
132	3-hydroxybutanal	[20]	**215**	1-(+)-ascorbic acid 2,6-dihexadecanoate	[21]

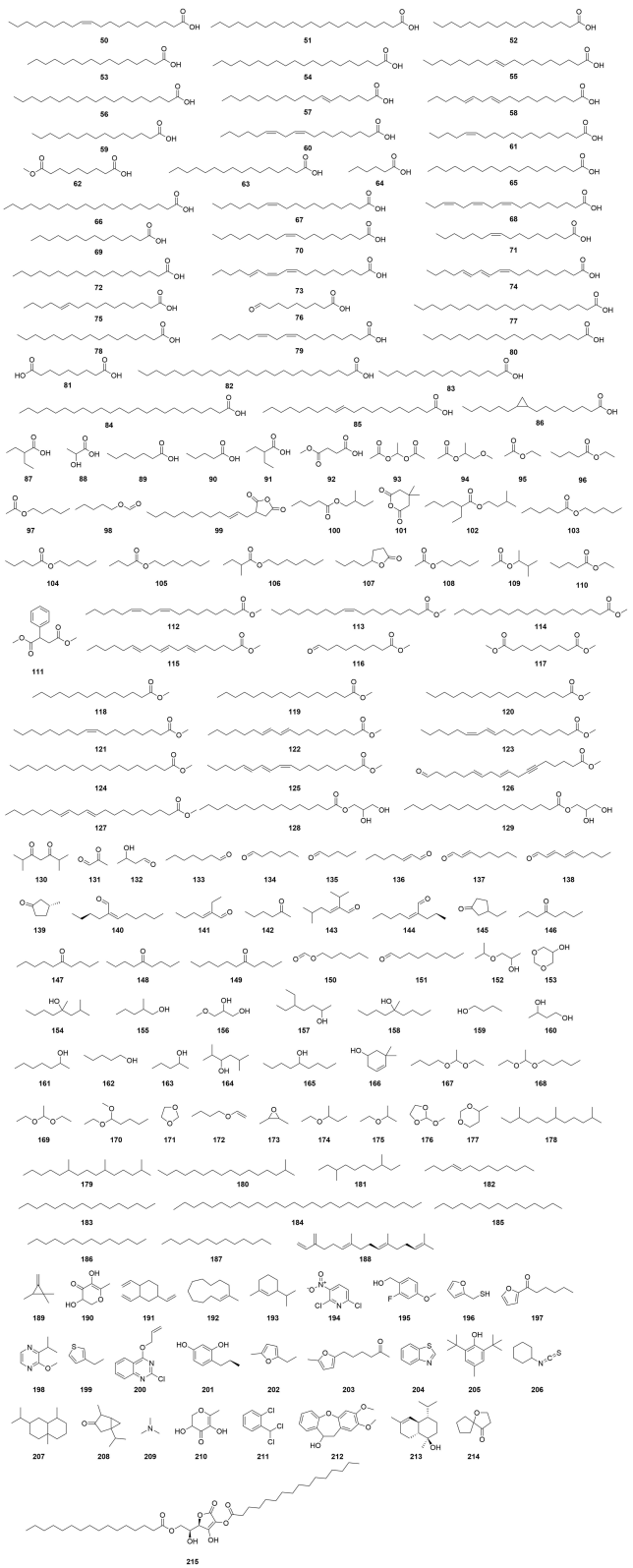


Figure 3 Chemical structures of volatile oils and fatty acids in MS (50–215).

https://doi.org/10.2147/DDDT.S555032

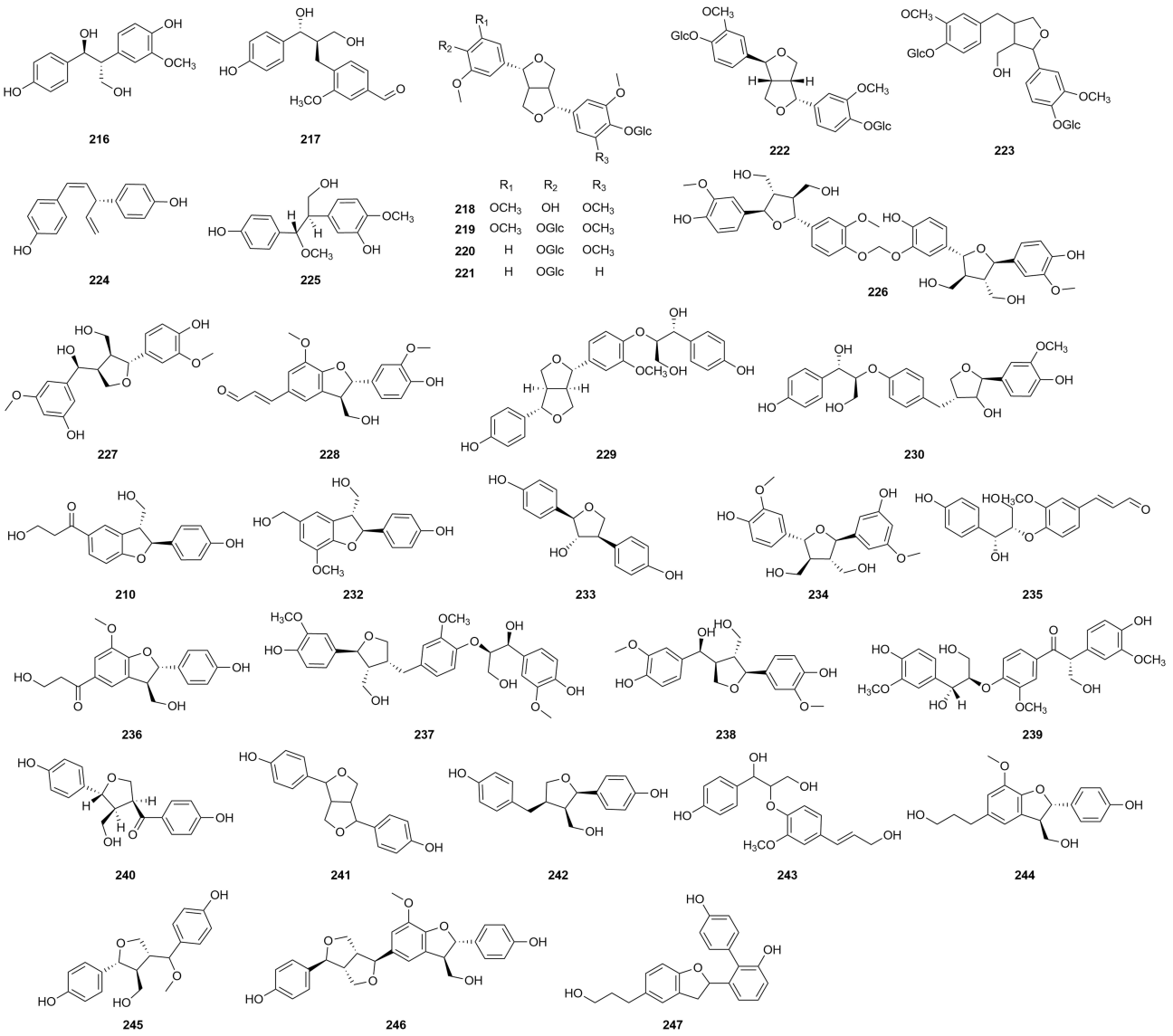


Figure 4 Chemical structures of lignans in MS (216–247).

Steroids

Steroids are also important components in MS, classified into two types: 3-hydroxyl steroids, and 3-glycosides steroids. The steroid compounds found in MS are detailed in Table 6 and depicted in Figure 7.

Proteins and Peptides

MS is a seed herb containing a significant amount of proteins and peptides, such as ribosome-inactivating proteins (RIPs), trypsin inhibitors (TIs), and inhibitor cystine knot (ICK) peptides. Table 7 lists the identified proteins and peptides isolated from MS. Notably, specific RIPs and TIs isolated from MS have demonstrated significant antitumor activity in preclinical studies.[31,32] However, current research on MS proteins and their enzymatically derived bioactive products remains limited.

Nitrogenous Compounds

Based on structural diversity, nitrogenous compounds in MS are categorized into amide alkaloids, amino acids, and organic amines. However, pharmacological studies on these compounds remain limited, and their role as primary

Table 3 Lignans in MS (216–247)

NO.	Compound Name	Ref.
216	Mubezhisol	[11]
217	Mubezhisal	[11]
218	Episyringaresinol-4-O-β-D-glucopyranoside	[11]
219	Liriodendrin	[11]
220	Medioresinol-4,4'-di-O-β-D-glucopyranoside	[11]
221	Episyringaresinol-4,4'-di-O-β-D-glucopyranoside	[11]
222	Epipinoresinol-4,4'-di-O-β-D-glucopyranoside	[11]
223	Lariciresinol-4,4'-di-O-β-D-glucopyranoside	[11]
224	Nyasol	[11]
225	Carayensin C	[11]
226	Neoolivil	[11]
227	Dysosmarol	[11]
228	Balanophonin	[11]
229	Mubiesin A	[24]
230	Mubiesin B	[24]
231	Mubiesin C	[24]
232	Mubiesin D	[24]
233	Mubiesin E	[24]
234	Laxanol	[24]
235	Threo-1-(4hydroxyphenyl)-2-{4-[2-formyl-(*E*)-vinyl]-2-methoxyphenoxyl}-propane-1,3-diol	[24]
236	Chushizisin F	[24]
237	Ehletianol C	[24]
238	Tanegool	[24]
239	(7*R*,8*R*,8'*R*)-4'-guaiacylglyceryl-evofolin B	[24]
240	Ligballinone	[24]
241	Ligballinol	[26]
242	(7*R*,8*S*,8'*R*)-4,4',9-trihydroxy-7,9'-epoxy-8,8'-lignan	[24]
243	Chushizisin A	[24]
244	Chushizisin E	[24]
245	Chushizisin G	[24]
246	Chushizisin I	[24]
247	3-[2-(4-hydroxyphenyl)-3-hydroxyphenyl-2, 3-dihydro-1-benzofuran-5-yl] propane-1-ol	[24]

https://doi.org/10.2147/DDDT.S555032

Table 4 Phenolic Acid and Glycosides in MS (248–270)

NO.	Compound Name	Ref.
248	p-hydroxybenzoic acid	[24]
249	Vanillin	[15]
250	Benzaldehyde, 4-hydroxy-3,5-dimethoxy	[15]
251	Phenol,2,2'-methylenebis [6-(1,1-dimethylethyl)-4-methy	[15]
252	(*E*)-4-(3-hydroxyprop-1-en-1-yl)-2-methoxyphenol	[15]
253	Ferulic acid	[13]
254	Sinapinic acid	[13]
255	(threo)-1-(4-hydroxyphenyl)-1-ethoxy-2,3-propanediol	[11]
256	Juglanin D	[11]
257	p-hydroxybenzaldehyde	[11]
258	Gallic acid	[27]
259	Protocatechuic acid	[27]
260	Chlorogenic acid	[27]
261	Vanillic acid	[27]
262	Caffeic acid	[27]
263	Syringic acid	[27]
264	p-coumaric acid	[27]
265	p-coumaraldehyde	[27]
266	Coniferylaldehyde	[26]
267	Mubeside A	[28]
268	Mubeside B	[28]
269	Mubeside C	[28]
270	Mubeside D	[28]

bioactive components requires further validation. The nitrogenous compounds identified from MS are systematically cataloged in Table 8, with their structural configurations elucidated in Figure 8.

Other Compounds

In addition to the previously mentioned compounds, eight additional constituents have been isolated from MS. Notably, MS contains carotenoids with high concentrations, particularly lycopene and β-carotene, which are important natural antioxidants.[29,37] Their chemical information is presented in Figure 9 and Table 9.

Pharmacological Activities

Pharmacological studies have demonstrated that the extracts and pure compounds from MS possess multiple therapeutic properties, including antitumor, anti-ulcer, anti-inflammatory, antimicrobial, antiviral, antioxidant, immunomodulatory, hypolipidemic, hypotensive, and neuroprotective effects. This review synthesizes current evidence on the therapeutic effects and molecular mechanisms of MS based on recent studies.

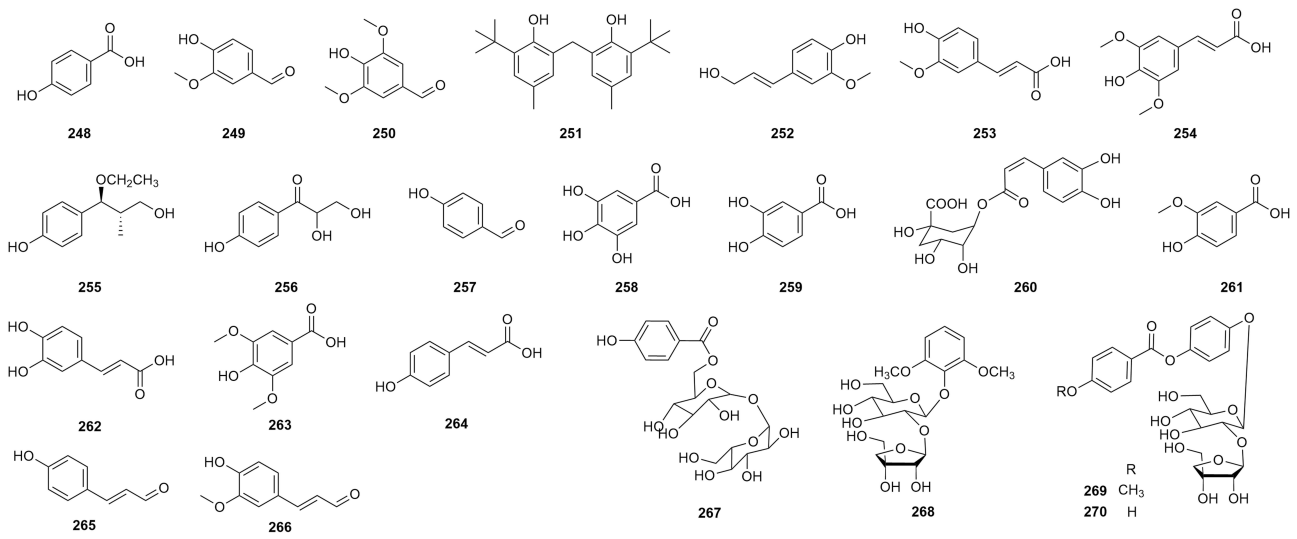


Figure 5 Chemical structures of phenolic acid and glycosides in MS (248–270).

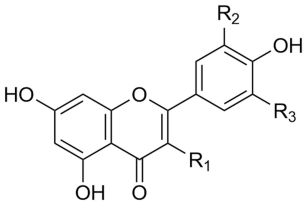
Antitumor Activity

MS exhibits broad-spectrum antitumor activity across multiple cancer types, as evidenced by preclinical studies utilizing diverse cell lines and animal models. Table 10 and Figure 10 summarize the key molecular mechanisms by which active ingredients derived from MS exert their antitumor effects. These mechanisms include the induction of apoptosis, cell cycle arrest, suppression of proliferation, inhibition of angiogenesis, and synergistic interactions with chemotherapeutic agents. While most investigations into these activities of MS have focused on its crude extracts, limited research has been conducted on its bioactive constituents, including saponins, phenolic compounds (p-hydroxycinnamaldehyde), and proteins (cochinin B). Preclinical studies have further validated the synergistic antitumor potential of MS in combination with other herbs. Muyin extract (MSE), a combination of MS and *Epimedii Folium* extract, has exhibited potent antitumor activity. Compared to Xiaojinwan, MSE showed a higher tumor inhibition rate and effectively inhibits the Akt/mTOR-mediated autophagy and apoptosis signaling pathways.[38,39]

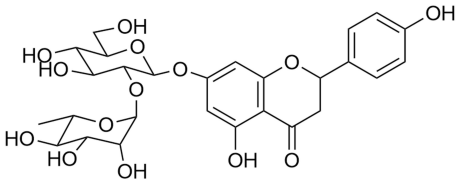
Table 5 Flavonoids in MS (271–280)

NO.	Compound Name	Ref.
271	Quercetin	[13]
272	Luteolin	[13]
273	Myricetin	[27]
274	Apigenin	[27]
275	Kaempferol	[27]
276	Hyperin	[13]
277	Naringin	[13]
278	Rutin	[13]
279	Violanthin	[28]
280	Kaempferitrin	[28]

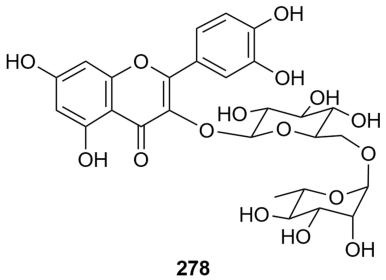
https://doi.org/10.2147/DDDT.S555032



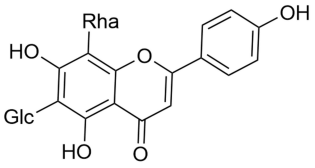
	R_1	R_2	R_3
271	OH	H	OH
272	H	H	OH
273	OH	OH	OH
274	H	H	H
275	OH	H	H
276	OGal	OH	H



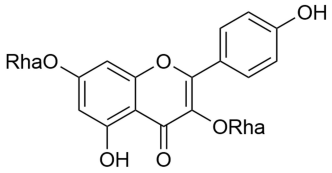
277



278



279



280

Figure 6 Chemical structures of flavonoids in MS (271–280).

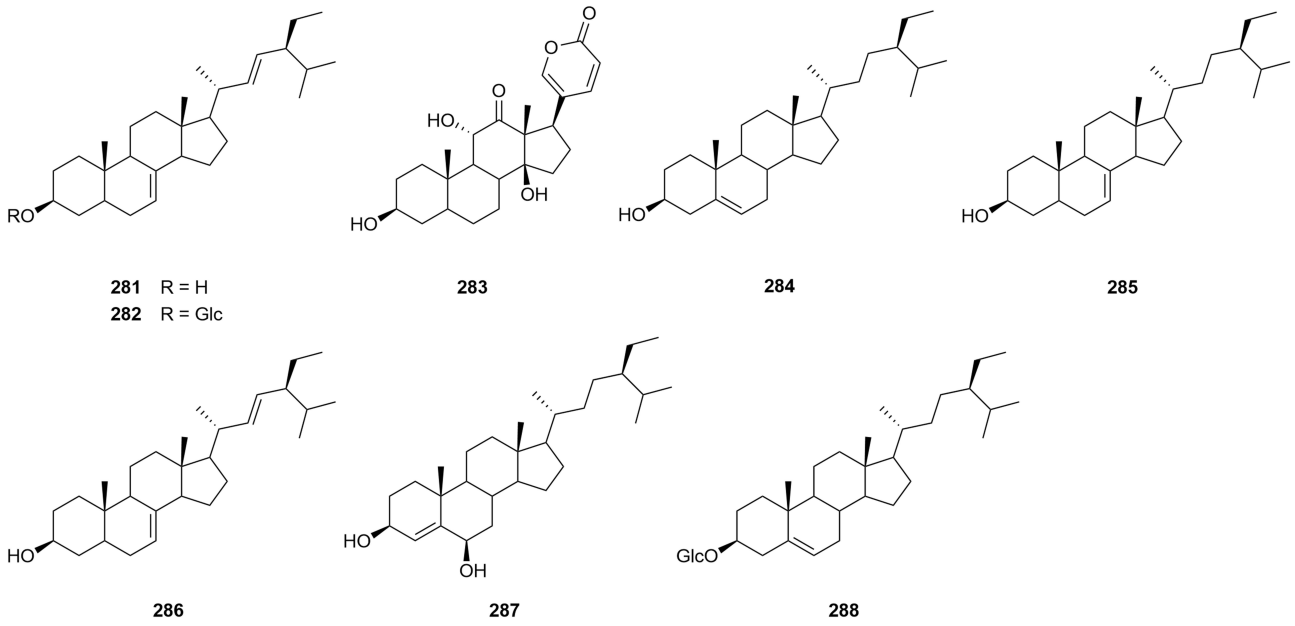
Anti-Ulcer Activity

SK-MS10, an MS extract predominantly composed of momordica saponins, has demonstrated potent gastroprotective properties. Experimental evidence shows that SK-MS10 effectively attenuates acute gastric damage induced by ethanol and nonsteroidal anti-inflammatory drugs (NSAIDs) in rats, as well as chronic gastritis models triggered by acetic acid and *Helicobacter pylori*.[57–59] Notably, the protective mechanisms of SK-MS10 differ in experimental models. In the ethanol-induced model, SK-MS10 suppresses proinflammatory cytokines and downregulates the cytosolic phospholipase A2/5-lipoxygenase (cPLA2/5-LOX) pathway, mediating anti-inflammatory effects.[60] In the acetic acid-induced model, SK-MS10 accelerates healing by upregulating vascular endothelial growth factor (VEGF) and promoting angiogenesis.[59] Furthermore, SK-MS10 has been shown to protect against cysteamine-induced duodenal ulcers via cPLA2 inhibition and glutathione preservation.[61] The major active component of MS, momordica saponin I, is a glycoside triterpenoid saponin containing a disaccharide chain. Studies have confirmed that it inhibits gastric mucosal lesions induced by ethanol or indomethacin in rats.[58]

Collectively, these findings highlight MS as a promising gastroprotective herbal medicine, with momordica saponin I serving as a potential Q-marker for MS-based therapeutics.

Table 6 Steroids in MS (281–288)

NO.	Compound Name	Ref.
281	α-spinasterol	[24]
282	α-spinasterol-3-O-β-D-glucoside	[24]
283	Arenobufagin	[13]
284	β-sitosterol	[14]
285	Stigmast-7-en-3β-ol	[14]
286	Stigmast-7,22-dien-3β-ol	[14]
287	Stigmast-4-ene-(3β,6α)-diol	[16]
288	Daucosterol	[30]



281 R = H
282 R = Glc

283 **284** **285**

286 **287** **288**

Figure 7 Chemical structures of steroids in MS (281–288).

Anti-Inflammatory Activity

Various saponins and lignans isolated from MS have exhibited significant anti-inflammatory activities. In LPS-induced RAW 264.7 macrophages, these compounds significantly suppress pro-inflammatory mediators including nitric oxide (NO), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α). The anti-inflammatory activity of saponins is enhanced by glycosylation, with increased sugar chain number correlating to stronger inhibition.[24,62] Momordica saponin I has

Table 7 Proteins and Peptides in MS (289–301)

NO.	Compound Name	Ref.
289	MCo-I	[33,34]
290	MCo-2	[33,34]
291	MCo-3	[33]
292	MCo-4	[33]
293	MCo-5	[33]
294	MCo-6	[33]
295	MCoTI-I	[33]
296	MCoTI-II	[33]
297	Cochinin B	[31]
298	Cochinchinin	[35]
299	Viscumamide	[25]
300	Clavatustide C	[25]
301	McPAL1	[36]

Table 8 Nitrogenous Compounds in MS (302–315)

NO.	Compound Name	Ref.
302	Adenosine	[13]
303	Guanosine	[13]
304	Glutamic acid	[13]
305	L-carnitine	[13]
306	L(+)-arginine	[13]
307	Pipecolinic acid	[13]
308	Leucine	[13]
309	Phenylalanine	[13]
310	2-pyrrolidinone, 4-phenyl	[15]
311	3,4,5-trimethoxybenzhydra zide	[15]
312	2-oxo-4-phenyl-pyrrolidin e-3-carboxylic acid ethyl ester	[15]
313	1,1'-carbonyldiimidazole	[21]
314	9-octadecenamide, (*Z*)	[15]
315	13-docosenamide, (*Z*)	[15]

shown potent anti-inflammatory activity by suppressing the NF-κB signaling pathway. This inhibition is mediated through the downregulation of key inflammatory signaling proteins, including IκBα, Src, and Syk, all of which participate in NF-κB activation.[63]

Antimicrobial and Antiviral Activity

Both crude and "frost-like powder method" processed MS have shown significant inhibition of *Candida albicans* growth while demonstrating no antibacterial activity against *Escherichia coli* or *Pseudomonas aeruginosa*.[64] Subsequent research has identified several purified triterpenoid saponins from MS kernels with strong antifungal activity against *C.albicans, C. parapsilosis*, and *C. tropicalis*.[6] Additionally, MS extracts have been found to reduce the infectivity of the influenza A virus H3N8 in vitro, particularly at high concentrations (0.5–1%).[65]

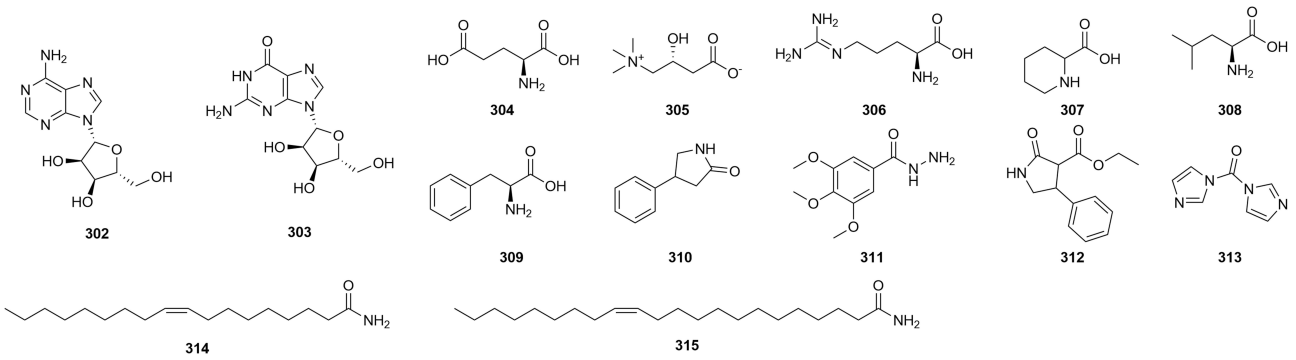


Figure 8 Chemical structures of nitrogenous compounds in MS (302–315).

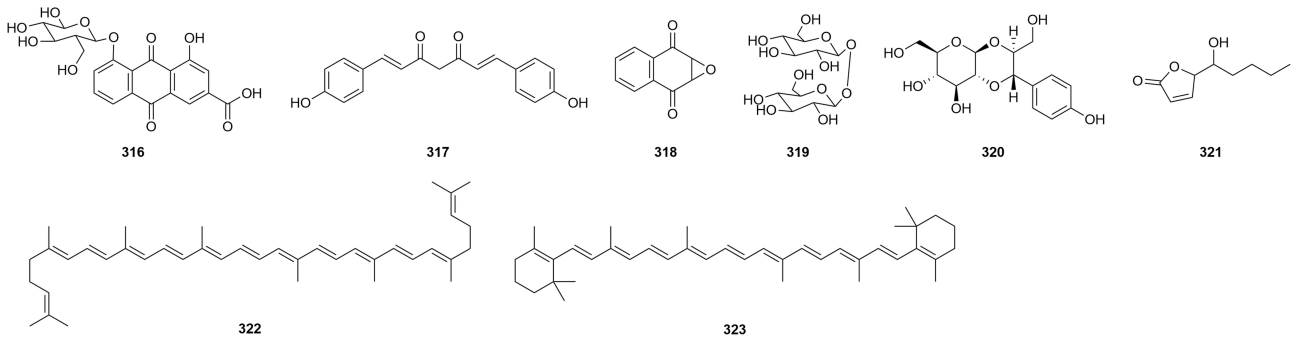


Figure 9 Chemical structures of other components in MS (316–323).

Antioxidant Activity

Chemical analyses have revealed that MS contains substantial amounts of total flavonoids and phenols, which exhibit strong antioxidant activity against DPPH and ABTS free radicals and provide protective effects against LPS-induced oxidative damage in BV2 cells.[66] HPLC analysis further confirms that MS effectively scavenges hydroxyl radicals, underscoring its potential as a natural antioxidant.[67] MCoCI, a chymotrypsin-specific potato type I inhibitor derived from MS, significantly reverses t-BHP-induced oxidative damage in hepatocytes by mitigating glutathione depletion and lipid peroxidation. Moreover, MCoCI treatment enhances the activities of glutathione-S-transferase and superoxide dismutase.[68] These findings collectively emphasize the antioxidant potential of MS and its bioactive components.

Immunomodulatory Activity

Recent studies have established that the ethanol extract of MS (ECMS) enhances immune responses.[69] For instance, the addition of ECMS extract to a foot-and-mouth disease vaccine has been shown to increase immune responses in pigs, guinea pigs, and mice.[69–71] Similarly, subcutaneous administration of ECMS has been shown to boost the immune response to ovalbumin (OVA) in mice.[72] Further studies have revealed that ECMS can enhance immune responses to both influenza vaccination (H5N1) and Newcastle disease (ND) in chickens.[73,74] Furthermore, when used as an adjuvant with influenza vaccines, MS significantly increases IgG antibody levels in chickens.[73] MCoCI has been found to stimulate the proliferation of various immune cells, including splenocytes, splenic lymphocytes, bone marrow cells, and macrophages, akin to the effects of Concanavalin A. Additionally, MCoCI suppresses hydrogen peroxide formation in neutrophils and macrophages.[75]

Table 9 Other Components in MS (316–323)

NO.	Compound Name	Ref.
316	Rhein-8-O-β-D-glucopyranoside	[13]
317	Bisdemethoxycurcumin	[13]
318	2,3-epoxy-2,3-dihydro-1,4-naphthoquinone	[11]
319	α, α-trehalose	[11]
320	Meliadanoside B	[11]
321	5-(1'-hydroxypentyl)-5H-furan-2-one	[25]
322	Lycopene	[29]
323	β-carotene	[29]

https://doi.org/10.2147/DDDT.S555032

Table 10 Anticancer Effects and Mechanisms of MS

Cancer Type	Animal/Cell Line	Extract/Compound	Mechanism/Results	Ref.
Pancreatic cancer				
	Capan-2, MIA PaCa-2 cells	Methanol extract	Inhibited migration and induced apoptotic cell death by regulating c-Myc and CNOT2; enhanced the sensitivity of 5-FU in pancreatic cancer.	[40]
Melanoma cancer				
	D24, C1 cells	Aqueous extract	Induced apoptosis and necrosis, upregulated TNFR1, downregulated NF-kB, BRAF/MEK, and Nrf2 pathways.	[41]
	MM418C1, D24 cells	Water extract	Reduced cell viability by 75.5% (MM418C1) and 66.9% (D24); linked to trypsin inhibitors.	[42]
	B16 cells, C57BL/6 mice	p-hydroxycinnamaldehyde	Inhibited tumor growth and metastasis by suppressing Wnt/β-catenin pathway, upregulating E-cadherin, and downregulating vimentin, MMP-2 and MMP-9; activated MAPK pathways (p38 and JNK).	[43–45]
Chronic Myeloid Leukemia				
	KBM5, KBM5-T315I cells	Chloroform extract	Blocked Bcr-Abl and downregulated Mcl-1, inducing apoptosis.	[15]
	Nude mice (KBM5/KBM5-T315I xenograft)	Chloroform extract	Suppressed tumor growth in vivo without significant toxicity.	[15]
Esophageal cancer				
	Kyse 30, TE-13 cells	p-hydroxylcinnamaldehyde	Inhibited proliferation (dose-dependent), downregulated CEA/SCC mRNA and C-myc/N-myc protein expression	[46]
	BALB/c nude mice (Kyse30 xenograft)	p-hydroxylcinnamaldehyde	Reduced tumor volume/weight, decreased C-myc/N-myc protein in tumor tissues	[46]
	Kyse 30, TE-13, Eca109 and Kyse180	p-hydroxylcinnamaldehyde	Induced the differentiation of Kyse30 and TE-13 cells through mediating the cAMP-Rho-AMAPK axis; inhibits proliferation via G0/G1 phase arrest; reduced migration/invasion; downregulated CEA, SCC, IL-6, MIC-1, C-myc, N-myc; suppressed RhoA-MAPK pathway (↓GTP-RhoA, ↓p-ERK1/2, ↓p-JNK, ↑p-p38)	[47,48]
Gastric cancer				
	SGC7901, MKN-28 cells	Ethanol extract	Induced apoptosis via caspase-3, −8, −9 activation, PARP cleavage, and p53 upregulation.	[49]

(*Continued*)

Table 10 (Continued).

Cancer Type	Animal/Cell Line	Extract/Compound	Mechanism/Results	Ref.
Lung cancer				
	A549, H1264, H1299, Calu-6 cells	Gypsogenin 3-O-D-galactopyranosyl(1→2)-[α-L-rhamnopyranosyl(1→3)]-D-glucuronopyranoside; quillaic acid 3-O-β-D-galactopyranosyl(1→2)-[α-L-rhamnopyranosyl(1→3)]-β-D-glucuronopyranoside (20, 60 μg/mL)	Decreased cell proliferation in a dose-dependent manner.	[50]
	NCI-H187 cells	Cochinin B	Exhibited anti-proliferative activity through ribosome inactivation.	[31]
	A549, H1299 cells	Ethanol extract	Induced apoptosis via ↑p53, ↑Bax/Bcl-2 ratio, ↓PI3K/Akt/NF-κB pathways; inhibited migration and invasion by ↓MMP-2 activity	[51]
Breast cancer				
	MDA-MB-231 Cells	Ethanol extract	Induced G2/M Arrest and Apoptosis by Modulating the PI3K/Akt Pathway	[21,52]
	ZR-75-30 cells	Water extract	Inhibited cell migration and invasion dose-dependently; downregulates MMP-2 and MMP-9 expression and enzymatic activity; promoted autophagy: ↑BECN1, ↑LC3II/LC3I ratio	[53,54]
	MCF-7 cells	Ethanol extract	Induced apoptosis via ↑caspase-3, ↑cytochrome c, ↑p21; ↓cyclin D1, ↓MVA pathway, ↓Rac1/RhoA; inhibited migration via ↓MMP-2, ↓MMP-9, ↓VEGFA.	[55]
Liver cancer				
	MHCC97-H cells	MS extract	Inhibited proliferation, migration, invasion; downregulated MMP-2, MMP-9, p-PI3K, p-Akt, and circRNA_002178 expression.	[56]
Cervical cancer				
	HeLa cells	Cochinin B	Inhibited protein synthesis via N-glycosidase activity, leading to cell death.	[31]
Kidney cancer				
	HEK293 cells	Cochinin B	Induced cytotoxicity by ribosome inactivation, reducing cell viability.	[31]

Notes: ↑, elevation/upregulation/activation; ↓, reduction/downregulation/inhibition.

Hypolipidemic and Hypotensive Activity

Animal studies have demonstrated that dietary administration of ECMS in rats significantly lowers serum triacylglycerol and total cholesterol levels.[76] Triterpenoid saponins isolated from MS, especially gypsogenin 3-O-β-D-galactopyranosyl (1→2)-[α-L-rhamnopyranosyl (1→3)]-β-D-glucuronopyranoside, have been found to inhibit adipocyte differentiation by suppressing the gene and protein expression of adipogenic transcription factors *C/EBPα* and *PPARγ*. This inhibition not only reduces lipid accumulation but also exhibits anti-obesity effects by targeting adipogenesis, inflammation, and lipolysis in mature adipocytes.[12] Furthermore, the protein hydrolysate of MS has exhibited angiotensin-converting enzyme (ACE) inhibitory activity, indicating its potential for lowering blood pressure.[32]

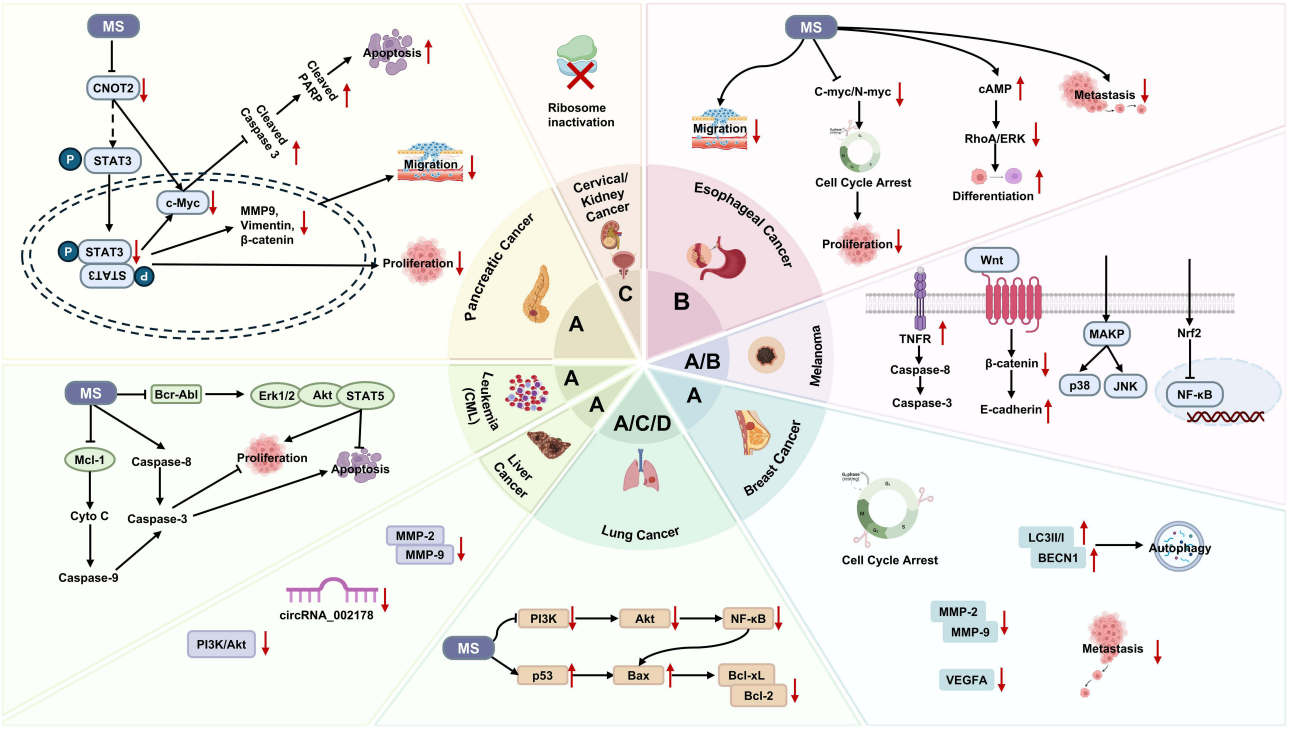


Figure 10 Mechanism of antitumor effect of MS. The figure illustrates MS's anticancer effects through three concentric layers: outer layer (Mechanisms); middle layer (Cancer Types); inner layer (Components). Symbol Legend: Solid black arrow (→): Promotion or activation of proteins/pathways; Solid T-bar (⊣): Inhibition of proteins/pathways; Dashed black arrow (– →): Interactions with uncertain mechanisms; Red upward arrow (↑): Upregulation of proteins/pathways; Red downward arrow (↓): Downregulation of proteins/pathways. Component Legend: (**A**) MS Extract; (**B**) p-hydroxycinnamaldehyde; (**C**) Cochinin B; (**D**) Gypsogenin derivatives.

Neuroprotection Activity

Emerging evidence indicates that MS possesses moderate neuroprotective activity in vitro experiments. E. Mazzio et al employed a high-throughput screening of over 1100 nutraceuticals (vitamins, herbal plant parts, polyphenolics, teas, fruits, and vegetables) to identify a neurogenic factor using a PC-12 cell model. Subsequent investigations resulted in the isolation of a stable protein with a mass of 17 kDa from MS, which have been confirmed to possess neurotrophic and neuroprotective functions.[77,78] The ethanol extract of MS exerts neuroprotective effects by activating Nrf2/Keap1 signaling pathway, increasing antioxidant enzyme activity, inhibiting oxidative stress damage, and regulating Bcl-2/Bax pathway to suppress cell apoptosis.[79] Additionally, MS has demonstrated potent antioxidant and anti-inflammatory effects, as evidenced by its ability to significantly reducing oxidative stress markers (ROS) and inflammatory cytokines (NO, TNF-α, IL-6) in LPS-stimulated BV2 microglial cells. These findings strongly support its potential as a natural therapeutic agent for neurotoxicity-related diseases.[66]

Other Effects

Current research has revealed that MS downregulates the MAPK pathway, thereby providing protection against cisplatin-induced acute kidney injury.[80] Moreover, MS extracts have been shown to inhibit pathological angiogenesis and exhibit therapeutic potential for proliferative diabetic retinopathy.[81] However, further in vivo validation remains necessary to confirm these findings.

Toxicity

Despite its broad spectrum of biological activities, the potential toxicity of MS must be considered. *The Chinese Pharmacopoeia* recommends a daily oral dosage of 0.9–1.2 g.[82] Nevertheless, clinical research findings reveal that decoctions of MS administered within the therapeutic dose range (8–12 g) have a favorable safety profile. A small number of patients have reported only mild and transient adverse effects, specifically nausea, diarrhea, and headache.[83]

Acute toxicity studies have determined an LD_{50} of 146.17 mg/kg for aqueous extracts and 16.777 g/kg for ethanol extracts (ECMS) in mice via intraperitoneal administration.[9,84] Chronic toxicity studies have demonstrated that long-term MS administration significantly increases heart, liver, and spleen indices in rats, suggesting potential toxicity in these organs. However, the observed organ index changes may be confounded by significant body weight loss induced by MS.[85] Zebrafish studies have further revealed that MS extract induces cardiotoxicity, characterized by pericardial edema, cardiac apoptosis, and reduced blood flow, mediated through inflammation, oxidative stress, and apoptosis pathways.[13] Recent research has identified that the toxicity of MS is primarily concentrated in the seed kernel, while the seed shell is non-toxic.[76] Additionally, some researchers have proposed that saponins and cochinchinin may represent the primary toxic constituents of MS.

In summary, elucidating the mechanism and material basis of MS's toxicity is crucial for effectively managing its toxicity and ensuring clinical safety, thereby warranting further investigation.

Medica Processing

In clinical applications, MS is typically used in processed products to attenuate toxicity and enhance efficacy. Historically, various processing methods were employed, such as simmering, heating with vinegar, making frost-like powder, and stir-baking with bran.[86] While most traditional methods have been discontinued, two processed forms remain officially recognized in the *Chinese Pharmacopoeia*: Momordicae Semen and Momordicae Semen Pulveratum. The processing of Momordicae Semen involves removing the shell and breaking the kernel into pieces, while Momordicae Semen Pulveratum (MSP) requires stir-baking the clean kernels, triturating them, wrapping them in paper, and pressing to remove the oil. Research indicates that the optimal frosting conditions include a pressing temperature of 80 °C, a pressing time of 30 minutes, and a particle size of 60 mesh.[87,88]

Processing induces significant compositional changes in MS, which fundamentally underpin the reduction in toxicity and modulation of efficacy. These changes include the disappearance of some components, the emergence of new components, and the transformation of existing ingredients. For instance, nine previously undetected terpenoids/saponins emerge after processing, while total saponins increase due to fat removal and enhanced thermal solubility.[9] Studies have shown that the content of components changes before and after processing. For example, the content of effective components in the fat oil increases significantly, with linoleic acid increasing by 6.97% and oleic acid by 15.85% after processing. These changes in fatty oils, proteins, and triterpenoid saponins may constitute the material basis for the pharmacological and toxicological differences between crude MS and MSP.[89]

Toxicological evaluations have shown that MSP exhibits significantly lower acute toxicity than crude MS, with murine LD_{50} values of 28.56 g/kg and 16.48 g/kg, respectively. Furthermore, the injury of liver and kidney by MSP was much weaker than that by raw MS. Frost-like powder processing not only significantly reduces toxicity but also enhances the therapeutic efficacy of MS. MSP may increase levels of IL-2, IL-6, and TNF-α, regulate apoptotic genes (*Bcl-2* and *Bax*), and enhance antitumor effects.[9] These transformative effects of processing on the composition, efficacy, and safety profile of MS are summarized in Figure 11.

These findings indicate that the alterations in the chemical compositions of MS during processing significantly influence its pharmacological effects and safety profile.

Clinical Application

The earliest documented medicinal application of MS appears in *Kai Bao Ben Cao*, where it was prescribed for treating fractures, swollen sores, back pain, acne, breast carbuncles in women, and anal swelling and pain.

In clinical applications, raw MS is frequently combined with other blood-activating and stasis-removing medications, such as Olibanum, Myrrh, and Trogopteri Faeces, for external applications in treating burns, scalds, rheumatoid arthritis, carbuncles, edema, sore throat, and breast hyperplasia. Notably, MS is typically processed in oral formulas to reduce potential toxicity. Commonly used formulations include Xiaojin Wan/Jiaonang/Pian, which are listed in the National Essential Drugs List and serves as the first-line Chinese patent medicine for the clinical treatment of mammary gland hyperplasia in modern Chinese medicine.

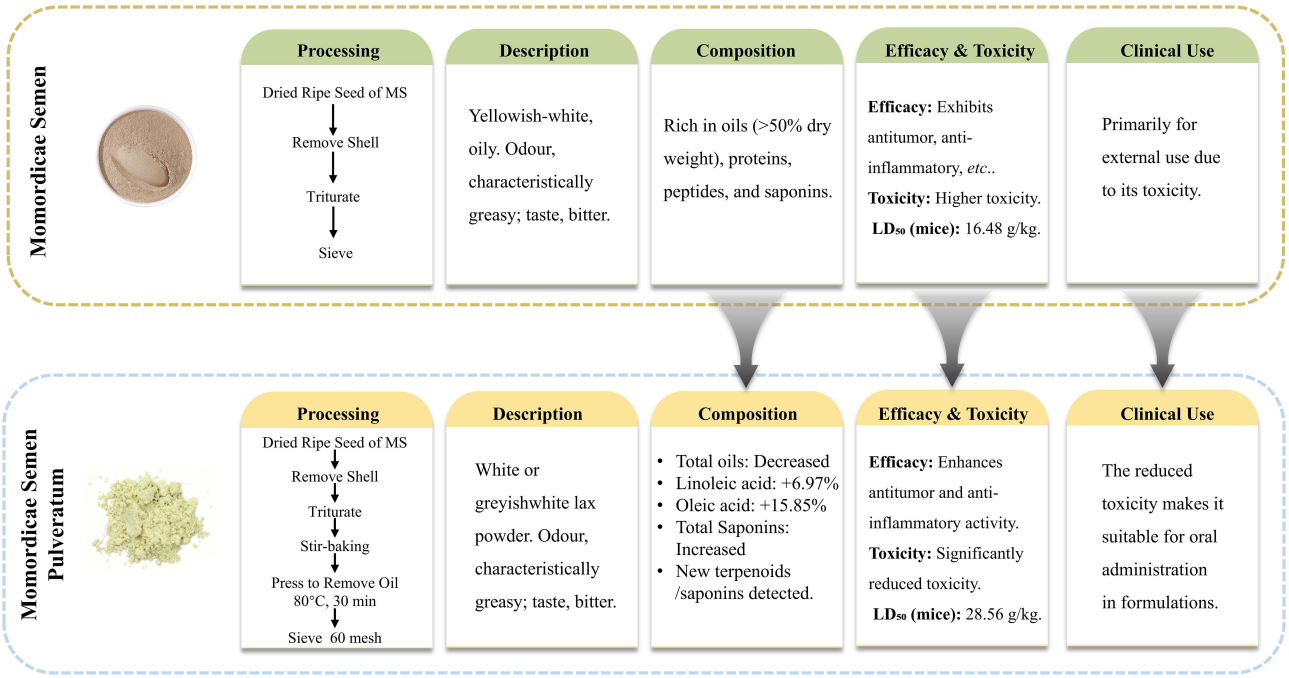


Figure 11 The processing procedure, compositional changes, and corresponding efficacy-toxicity alterations of MS before and after being processed into MSP.

As a Mongolian medicinal herb, MS has been traditionally used clear xiere (Mongolian: pathogenic heat) and detoxify. It is often synergistically combined with TCMs in formulations like Alatan Wuwei Pills,[90] Sirixi Powder,[91] and Qinggan Jiuwei Powder[92] to treat gastrointestinal heat, jaundice, abdominal distension, and liver-gallbladder-spleen heat. Representative Chinese patent medicines are summarized in Table 11.

Predictive Analytics for Q-Markers

As a toxic TCM, MS requires rigorous quality evaluation to ensure both therapeutic effects and clinical safety. However, relying on a single index for quality assessment is insufficient and hinders the clinical application.

The Q-markers theory of TCMs, first proposed by Academician Changxiao Liu, establishes a framework for identifying and regulating key quality substances to guarantee their safety and efficacy. This approach provides a

Table 11 The Traditional and Clinical Uses of MS in China

Prescription Name	Ingredients	Indications	Ref.
Topical application			
Awei Huapi Gao	Cyperi Rhizoma; Magnoliae Officinalis Cortex; Sparganii Rhizoma; Curcumae Rhizoma; Angelicae Sinensis Radix; Aconiti Kusnezoffii Radix (not prepared); Aconiti Radix (not prepared); Allii Bulbus; Quisqualis Fructus; Angelicae Dahuricae Radix; Manis Squama; **Momordicae Semen**; Catharsius; Picrorhizae Rhizoma; Rhei Radix et Rhizoma; Ricini Semen; Olibanum; Myrrha; Aloe; Draconis Sanguis; Realgar; Cinnamomi Cortex; Camphora; Ferulae Resina	Qi stagnation and blood congealing, abdominal masses, pain in the epigastrium and abdomen, distension and fullness in the chest and the hypochondrium.	[93]

(*Continued*)

Table 11 (Continued).

Prescription Name	Ingredients	Indications	Ref.
Anyang Jingzhi Gao	Aconiti Radix; Aconiti Kusnezoffii Radix; Linderae Radix; Ampelopsis Radix; Angelicae Dahuricae Radix; Bletillae Rhizoma; **Momordicae Semen**; Akebiae Caulis; Chaenomelis Fructus; Sparganii Rhizoma; Curcumae Rhizoma; Angelicae Sinensis Radix; Paeoniae Radix Rubra; Cinnamomi Cortex; Rhei Radix et Rhizoma; Forsythiae Fructus; Draconis Sanguis; Ferulae Resina; Olibanum; Myrrha; Catechu; Mentholum; Methyl Salicylate; Borneolum Syntheticum	Abdominal masses, *bi* syndrome due to wind, cold and dampness, fear of cold, and numbness of the extremities.	
Badu Gao	Lonicerae Japonicae Flos; Forsythiae Fructus; Rhei Radix et Rhizoma; Platycodonis Radix; Rehmanniae Radix; Gardeniae Fructus; Phellodendri Chinensis Cortex; Scutellariae Radix; Paeoniae Radix Rubra; Angelicae Sinensis Radix; Chuanxiong Rhizoma; Angelicae Dahuricae Radix; Ampelopsis Radix; **Momordicae Semen**; Ricini Semen; Scrophulariae Radix; Atractylodis Rhizoma; Scolopendra; Camphore; Manis Squama; Myrrha; Catechu; Olibanum; Hydrargyri Oxydum Rubrum; Draconis Sanguis; Calomelas	Sore and ulcer due to heat toxin stagnating in the skin, manifested as redness, swelling, heat, pain, or even pus in the skin.	[93]
Jintongxiao Ding	Olibanum (processed); Myrrha (processed); Rhei Radix et Rhizoma; Carthami Flos; Pyritum (calcined); Notoginseng Radix et Rhizoma; Draconis Sanguis; Chuanxiong Rhizoma; Curcumae Radix; Angelicae Radix; Gardeniae Fructus; Siphonostegiae Herba; Lagerstroemiae Cortex; Catechu; Angelicae Dahuricae Radix; Cinnamomi Cortex; Saposhnikoviae Radix; Aucklandiae Radix; Cyperi Rhizoma; Magnoliae Officinalis Cortex; Foeniculi Fructus; Aconiti Radix Cocta; Aconiti Kusnezoffii Radix Cocta; Fritillariae Thunbergii Bulbus; Arisaematis Rhizoma (processed); Chaenomelis Fructus; Camphor; Borneolum Syntheticum; **Momordicae Semen**; Notopterygii Rhizoma et Radix; Citri Pericarpium Reticulatae	Acute closed soft tissue injury.	[93]
Sanjierupi Gao	Curcumae Rhizoma; Curcumae Longae Rhizoma; Impatientis Semen; Semiaquilegiae Radix; **Momordicae Semen**; Angelicae Dahuricae Radix	Hyperplasia of mammary glands due to qi stagnation and blood stasis, manifested as pain and swelling in the breasts, breast lump, restlessness, vexation, agitation, chest distension, and fullness.	[94]
Shujin Dieda Gao	Rehmanniae Radix; Angelicae Sinensis Radix; Scrophulariae Radix; Rhei Radix et Rhizoma; Paeoniae Radix Rubra; **Momordicae Semen**; Angelicae Dahuricae Radix; Crinis Carbonisatus; Scolopendra; Cinnamomi Cortex; Ferulae Resina; Olibanum; Myrrha	Traumatic injuries, sprain of the lower back, abdominal cramp, externally contracted wind-cold, extremities numbness, lumbago, leg pain, accumulation, and glomus.	[94]

(*Continued*)

https://doi.org/10.2147/DDDT.S555032

Table 11 (Continued).

Prescription Name	Ingredients	Indications	Ref.
Wanling Jinggu Gao	Aconiti Radix; Aconiti Kusnezoffii Radix; Angelicae Pubescentis Radix; Notopterygii Rhizoma et Radix; Saposhnikoviae Radix; Angelicae Sinensis Radix; Curcumae Rhizoma; Sparganii Rhizoma; Cyperi Rhizoma; Eupolyphaga Steleophaga; **Momordicae Semen**; Ricini Semen; Rhei Radix et Rhizoma; Galla Chinensis; Pharbitidis Semen; Knoxiae Radix; Genkwa Flos; Kansui Radix; Crotonis Fructus; Gleditsiae Fructus Abnormalis; Salicis Folium et *Ramulus*; Cinnamomi Cortex	Wind-cold-dampness obstruction, injuring the muscles and bones, manifested as joint pain, numbness of the limbs, and difficulty in movement.	[94]
Gong Ying detoxification lotion	Taraxaci Herba; Sophorae Flavescentis Radix; Phellodendri Chinensis Cortex; Forsythiae Fructus; **Momordicae Semen**; Lonicerae Japonicae Flos; Angelicae Dahuricae Radix; Paeoniae Radix Rubra; Moutan Cortex; Glycyrrhizae Radix et Rhizoma	Diabetes foot ulcer, venous leg ulcer.	[95]
Runfei Huahe Gao	Rehmanniae Radix; Scrophulariae Radix; Phellodendri Chinensis Cortex; Stemonae Radix; Euphorbiae Ebracteolatae Radix; Isatidis Radix; Scutellariae Radix; Pinelliae Rhizoma Praeparatum; **Momordicae Semen**; Typhonii Rhizoma; Bufo Siccus; Salviae Miltiorrhizae; Radix et Rhizoma; Paeoniae Radix Rubra; Olibanum (Processed); Myrrha(Processed); Persicae Semen; Sparganii Rhizoma; Curcumae Rhizoma; Angelicae Sinensis Radix; Astragali Radix; Angelicae Dahuricae Radix; Borneolum Syntheticum; Moschus; Draconis Sanguis; Rosin	Adjuvant therapy of infiltrative pulmonary tuberculosis and tuberculous pleurisy with yin deficiency and fire effulgence, blood deficiency, and blood stasis.	[94]
Liutiao Gao	Strychni Semen; Scolopendra; **Momordicae Semen**; Aconiti Radix; Aconiti Kusnezoffii Radix; Olibanum; Myrrha; Serpentis Periostracum; Salicis Folium et Ramulus; Sophorae Ramulus; Mori Ramulus	Carbuncles, sores and boils, frostbite.	[94]
Jingwanhong Ruangao	Sanguisorbae Radix; Rehmanniae Radix; Angelicae Sinensis Radix; Persicae Semen; Coptidis Rhizoma; **Momordicae Semen**; Papaveris Pericarpium; Crinis Carbonisatus; Trachycarpi Petiolus; Lobeliae Chinensis Herba; Eupolyphaga seu Steleophaga; Ampelopsis Radix; Phellodendrl Chinensis Cortex; Arnebiae Radix; Lonicerae Japonicae Flos; Carthami Flos; Rhei Radix et Rhizoma; Sophorae Flavescentis Radix; Galla Chinensis; Sophorae Flos; Chaenomelis Fructus; Atractylodis Rhizoma; Angelicae Dahuricae Radix; Paeoniae Radix Rubra; Scutellariae Radix; Picrorhizae Rhizoma; Chuanxiong Rhizoma; Gardeniae Fructus; Mume Fructus; Borneolum Syntheticum; Draconis Sanguis; Olibanum; Myrrha.	Scalds and burns by boiling water, fire or electricity, painful swelling of sore and ulcer, skin damage, and wound ulceration.	[93]

(*Continued*)

Table 11 (Continued).

Prescription Name	Ingredients	Indications	Ref.
Oral administration			
Dabaidu Jiaonang	Rhei Radix et Rhizoma; Taraxaci Herba; Citri Reticulatae Pericarpium; **Momordicae Semen**; Angelicae Dahuricae Radix; Trichosanthis Radix; Lonicerae Japonicae Flos; Phellodendri Chinensis Cortex; Olibanum; Angelicae Sinensis Radix; Paeoniae Radix Rubra; Glycyrrhizae Radix et Rhizoma; Serpentis Periostracum; Bufo Siccus; Scolopendra; Scorpio; Natrii Sulfas	Syphilis, blood strangury, white turbid, stabbing pain in the urethra, constipation, scabies, abscesses and cellulitis, sore and ulcer, redness and swelling, and pain.	[94]
Yujin Yinxie Pian	Gentianae Macrophyllae Radix; Angelicae Sinensis Radix; Acori Tatarinowii Rhizoma; Phellodendri Amurensis Cortex; Cyperi Rhizoma (stir-backed with wine); Curcumae Radix (stir-backed with vinegar); Curcumae Rhizoma (processed with vinegar); Realgar; Strychni Semen Pulveratum; Gleditsiae Spina; Persicae Semen; Carthami Flos; Olibanum (stir-backed with vinegar); Sal Ammoniaci; Natrii Sulfas Exsiccatus; Rhei Radix et Rhizorma; Eupolyphaga; Indigo Naturalis; **Momordicae Semen**	Psoriasis.	[93]
Zhonghua Dieda Wan	Hedyotidis Herba; Piperis Sarmentosi Herba; Hyperici Japonici Herba; Smilacis Ripariae Herba; Centipedae Herba; Achyranthis Bidentatae Radix; Linderae Radix; Parabarii seu Ecdysantherae Cortex; Breyniae Herba; Glycosmis Parviflorae Folium; Inulae Herba; Artemisiae anomalae Herba; Entadae Caulis; Hyptis Suaveolentis Herba; Cudraniae Radix; Zanthoxyli Radix; Spatholobi Caulis; Claoxyli Cacumen; Ilicis Asprellae Radix; **Momordicae Semen**; Solani Radix et Caulis; Begoniae Rhizoma; Angelicae Pubescentis Radix; Atractylodis Rhizoma; Impatientis Semen; Gardeniae Grandiflorae Fructus; Aconiti Radix Cocta; Caryophylli Flos; Cyperi Rhizoma; Kadsurae Radix seu Caulis; Cinnamomi Ramulus; Camphor	Sinew and bone sprain and contusion, acute and persistent pain due to blood stasis, injury and bleeding, wind-dampness stasis, and pain.	[93]
Xiaojin Jiaonang/Xiaojin Pian	Moschus Artifactus; **Momordicae Semen** (removed from shell and oil); Aconiti Kusnezoffii Radix Cocta; Liquidambaris Resina; Olibanum (processed with vinegar); Myrrha (processed with vinegar); Trogopteri Faeces (processed with vinegar); Angelicae Sinensis Radix (stir-baked with wine); Pheretima; Sumi Sinensis	Early onset of yin flat-abscesses, painful swollen bones and joints with normal skin color, multiple abscesses, goiter tumor, scrofula, rocky mass in the breast (breast cancer), and mammary hyperplasia.	[93]

(*Continued*)

https://doi.org/10.2147/DDDT.S555032

Table 11 (Continued).

Prescription Name	Ingredients	Indications	Ref.
Xiaojin Wan	Moschus or Moschus Artifactus; **Momordicae Semen** (removed from shell and oil); Aconiti Kusnezoffii Radix Cocta; Liquidambaris Resina; Olibanum (processed); Myrrha (processed); Trogopteri Faeces (stir-baked with vinegar); Angelicae Sinensis Radix (stir-baked with wine); Pheretima; Sumi Sinensis	Scrofula, goiter, tumor, rocky mass in the breast (breast cancer), and mammary hyperplasia due to stagnation of phlegm and qi, manifested as one or more than one palpable movable mass under the skin, or hard, painful, swollen bones and joints with normal skin color.	[93]
Sanjieling Jiaonang	Olibanum; Myrrha; Trogopterus Xanthipes; Pheretima; **Momordicae Semen**; Angelicae Sinensis Radix; Acori Tatarinowii Rhizoma; Aconiti Kusnezoffii Radix; Liquidambaris Resina; Sumi Sinensis	Early onset of yin flat-abscesses, painful swollen bones and joints with normal skin color, scrofula.	[94]
Alatan Wuwei Pills	Chebulae Fructus; Har Gabur; Pomegranate; **Momordicae Semen**/Herpetospermum Semen; Trogopterus Xanthipes	Pattern of stomach and intestinal heat, liver-gallbladder fever, and jaundice.	[90]
Bawei Zhixue Honghua San	Carthami Flos; Fellis Ursi Pulvis; Flos Pisi; **Momordicae Semen** (processed); Euphorbiae Humifusae Herba; Belamcandae Rhizoma; Lignum Pterocarpi	Tuberculosis, bronchial dilatation, gastric ulcer, colonic ulcer, functional uterine bleeding and other internal bleeding disorders.	[96]
Sirixi San	Chebulae Fructns; **Momordicae Semen**; Trogopteri Faeces; Trona Venenum; Punicae Granati Fructus; Har Gabur; Calcitum; Rhizoma Rhei et Radix; Inulae Radix; Kaempferiae Rhizoma,	Pattern of stomach and intestinal heat, dyspepsia, acid reflux, abdominal distension, and constipation.	[91]
Lidan Bawei San	Corydalis Bungeanae Herba; **Momordicae Semen**; Ophiopogonis Radix; Aucklandiae Radix; Gentianae Radix et Rhizoma; Coptidis Rhizoma; Anisi Stellati Fructus; Phellodendri Chinensis Cortex	Clearing heat, eliminating heat in liver, gallbladder, blood, stomach and intestine.	[97,98]
Xiaobaidu Gao	Taraxaci Herba; Lonicerae Japonicae Flos; Trichosanthis Radix; Phellodendri Chinensis Cortex; Rhei Radix et Rhizoma; Angelicae Dahuricae Radix; Citri Reticulatae Pericarpium; Olibanum (processed); Angelicae Sinensis Radix; Paeoniae Radix Rubra; **Momordicae Semen**; Glycyrrhizae Radix et Rhizoma	Sore and ulcer due to accumulated heat toxin in skin, manifested as redness, swelling, heat, and pain.	[94]
Xiaoshi Shiwei Wan	Har Gabur; Amomi Fructus Rotundus; Powder of Bovis Bile; Forsythiae Fructus; Piperis Longi Fructus; Punicae Granati Fructus; **Momordicae Semen** (processed); Halite; Chebulae Fructus; Cinnamomi Cortex	Indigestion, gastric pain, cold stuffiness, belching and acid reflux.	[99]
Gei Wang-9 Powder	Corydalis Bungeanae Herba; Carthami Flos; Scabiosae Flos; Aristolochiae Manshuriensis Caulis; Aucklandiae Radix; Dianthi Herba; **Momordicae Semen**	Clearing liver, cooling blood, eliminating heat in liver and gallbladder, curing jaundice.	[100]

novel perspective for advancing quality control in TCMs.[101] Therefore, a systematic literature review was conducted to predict the Q-markers of MS, facilitating the establishment of a scientific foundation for quality control.

Q-Markers Based on Kinship and Chemical Composition Specificity

The genus *Momordica* comprises approximately 80 species globally, including four documented in China: *M. charantia* L., *M. cochinchinensis* (Lour.) Spreng., *M. subangulata* Blume, and *M. dioica* Roxb. Current research identifies triterpenes and their glycosides as the principal secondary metabolites in this genus, demonstrating diverse biological activities. Momordica saponins I and II, the main saponins in MS, serve as unique biomarkers specific to this species. In addition, *Momordica* plants are rich in peptide-based protease inhibitors, particularly the squash family of trypsin inhibitors. MCoTI-I and II are cyclotides identified exclusively in MS, featuring stable cyclic disulfide-rich structures with potent trypsin-inhibitory activity.

Therefore, based on kinship and chemical composition specificity, momordica saponin I/II and MCoTI-I/II may serve as Q-markers for MS.

Q-Markers Predictive Analysis by Chemical Composition Measurability

The measurable quantification of chemical constituents serves as a primary criterion for selecting Q-markers. The *Chinese Pharmacopoeia* (2025) identifies gypsogenin 3-O-β-D-glucuronopyranoside as the quality control marker for MS, with a minimum required content of 0.25%.[93] This secondary glycoside, formed through saponin degradation in MS, is abundant and serves as a practical indicator compound.[102] Yao et al established a UPLC fingerprint for MS and developed a method to simultaneously quantify linoleic acid and oleic acid.[89] Similarly, Xing et al developed a rapid and sensitive method for detecting p-hydroxybenzoic acid in MS.[103] Furthermore, Lin et al established an HPLC-UV method for assaying TI activity, identifying MCoTI-I and MCoTI-II as cyclic peptides with cystine-knot motifs. Their distinct molecular weights (3478 and 3449) and chromatographic profiles enable specific and reproducible quantification, fulfilling core Q-marker requirements.[104]

In summary, six compounds of gypsogenin 3-O-β-D-glucuronopyranoside, p-hydroxybenzoic acid, linoleic acid, oleic acid, and MCoTI-I/II qualify as potential Q-markers for MS.

Q-Markers Based on the Correlation Between Ingredients and Efficacy

For TCMs with complex ingredients, efficacy depends not on all constituents but on key ingredients with optimal "drug-like properties". These efficacy-determining components form the basis for determining the Q-markers.

As discussed above, MS exhibits a wide range of pharmacological activities, including antitumor, anti-inflammatory, antioxidant, immunomodulatory, hypolipidemic, hypotensive, and neuroprotective, and anti-ulcer effects. These activities are attributed to its diverse bioactive constituents, such as saponins, phenolic compounds, flavonoids, and trypsin inhibitors. For instance, p-hydroxycinnamaldehyde and momordica saponins I and II have been identified as key components responsible for antitumor and anti-inflammatory effects, respectively. Notably, momordica saponin I can be considered as a critical Q-marker for gastric mucosal lesions in SK-MS10, a momordica saponin-rich extract of MS. It exerts synergistic effects by inhibiting cPLA2/5-LOX-mediated inflammation and activating VEGF-dependent mucosal repair. Moreover, MS's antioxidant and immunomodulatory properties are linked to its high flavonoid and phenolic content.[105]

Based on the component-efficacy correlation, saponins (eg, momordica saponins I/ II), flavonoids, and phenolic acids (eg, p-hydroxycinnamaldehyde) can be selected as critical Q-markers to characterize the efficacy of MS.

Q-Markers Based on Transfer and Traceability

The quality of TCM is highly variable, primarily influenced by origin, harvest season, species, and processing methods. These variations necessitate a quality control system that can track chemical transformations across the entire production chain, from raw material processing to in vivo absorption. An ideal Q-Marker should enable such traceability.

For MS, the chemical transformations that occur during processing provide a scientific foundation for quality traceability. For instance, the substantial increase in linoleic acid (6.97%) and oleic acid (15.85%) post-processing serves as a quantifiable indicator for verifying the completion of the "frost-like powder" procedure.[89] Similarly, tracking

the transformation of triterpenoid saponins can ensure the consistency of processed products. Furthermore, Ding's[106] study involving 14 origins across 8 provinces revealed that the content of gypsogenin 3-O-β-D-glucuronic acid methyl ester exhibits a positive correlation with altitude and negatively correlated with latitude and longitude.

Consequently, based on transfer and traceability, linoleic acid, oleic acid, relevant saponins, and gypsogenin 3-O-β-D-glucuronic acid methyl ester serve as critical Q-markers, effectively monitoring the quality transfer of MS from raw material to finished product and ensuring consistent efficacy.

Q-Markers Based on Traditional Medicinal Effects

The chemical composition of TCMs is closely linked to its medicinal properties. Incorporating drug properties and efficacy into the quality evaluation of TCMs reflects its holistic quality. MS possesses a cool medicinal property, a mildly sweet-bitter taste, and meridian tropism toward the liver, spleen, and stomach. Bitter-tasting TCMs primarily contain alkaloids, volatile oils, glycosides, flavonoids, and lignans. While few alkaloids have been reported in MS, substantial quantities of glycosides, flavonoids, and volatile oils have been identified. Contemporary research indicates that sweet-tasting TCMs primarily comprise sugars, glycosides, proteins, and amino acids. MS's distinctive sweet taste stems primarily from its glycoside content.

Therefore, saponins, flavonoids, volatile oils, lignans, and amino acids in MS likely constitute the material basis of its "nature and taste", making them suitable Q-markers candidates.

Prediction of Q-Markers Based on Network Pharmacology

Network pharmacology can establish a multidimensional network model of drug-body interactions. Its "multi-component, multi-target and multi-pathway" approach aligns with TCM theory. This paper employs network pharmacology to predict the Q-markers and establish a more comprehensive and scientific quality control system.

A preliminary screening of MS components was conducted using the TCMSP database (OB ≥ 0.30, DL ≥ 0.18) and the SwissADME platform (high GI absorption and at least two "Yes" in DL parameters), resulting in 10 candidate active components (Table 12) for subsequent network pharmacology analysis.

Network analysis identified 46 core targets through screening with betweenness, closeness, and degree centrality indices, all exceeding median thresholds. The top-ranked genes by degree value included *HSP90AA1, ESR1, PIK3CA, PIK3CB, PIK3CD, EGFR, HSP90AB1, PTPN11, MAPK1*, and *MAPK3* (Figure 12A).

Table 12 Candidate Active Components of MS for Network Pharmacology Analysis

NO.	Components
M1	2,3-epoxy-2,3-dihydro-1,4-naphthoquinone
M2	Chushizisin I
M3	Gypsogenin
M4	Momordic acid
M5	Monachosorin A
M6	Mubiesin A
M7	Mubiesin B
M8	Nyasol
M9	p-coumaraldehyde
M10	p-hydroxybenzoic acid

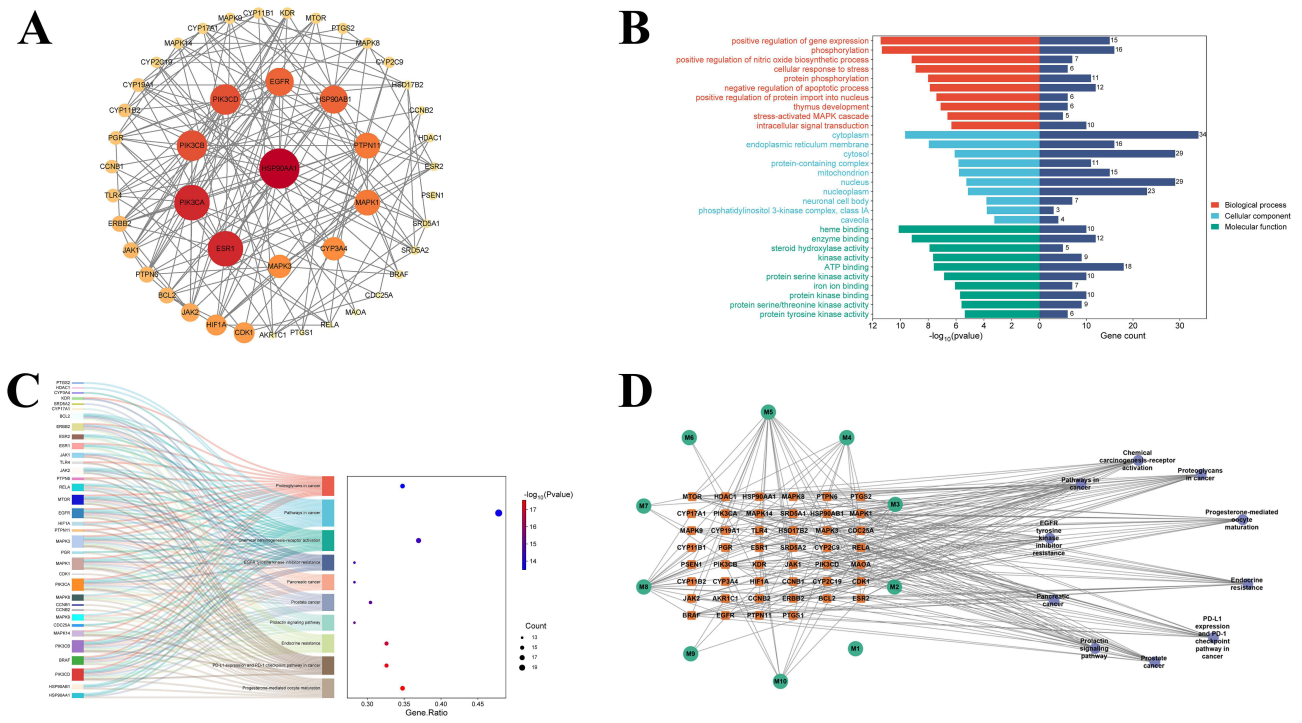


Figure 12 Network and functional enrichment analyses of MS-associated targets. (**A**) Core target interaction network. (**B**) GO enrichment analysis chart. (**C**) Bubble plot combined with a Sankey diagram of enriched KEGG pathways. (**D**) "Key active ingredient-core target-signaling pathway" network.

Functional enrichment analysis (GO and KEGG) of these targets revealed key biological processes, molecular functions, and cellular components (Figure 12B). KEGG pathways predominantly involved progesterone-mediated oocyte maturation, PD-L1/PD-1 tumor checkpoint signaling, and cancer-related pathways (including prostate/pancreatic cancer, EGFR tyrosine kinase inhibitor resistance, chemical carcinogenesis-receptor activation, and proteoglycans in cancer) (Figure 12C).

The component-target-pathway network (Figure 12D) highlighted connectivity degrees via node sizing. Monachosorin A, nyasol, gypsogenin, momordic acid, and p-hydroxybenzoic acid displayed high connectivity, suggesting them as key bioactive compounds mediating the therapeutic effects of MS. These compounds showed high connectivity to critical targets (*PIK3CB, PIK3CD, MAPK3, PIK3CA, mTOR, MAPK1, EGFR*) in oncogenic and inflammatory pathways.

A comprehensive evaluation system was established to assess ten candidate components as potential Q-markers for MS, based on six core criteria: component specificity, measurability, efficacy correlation, transfer and traceability, alignment with TCM properties, and network pharmacology analysis. Each criterion was scored on a scale of 1–3 (Table 13). The chemical structures of the candidate Q-markers, along with their classification, are summarized in Figure 13.Two components, momordica saponins I and II, were identified as core Q-markers due to their high specificity, definitive efficacy links, and alignment with TCM properties. Other candidates were designated as specialized markers: MCoTI-I and II for specificity, p-hydroxycinnamaldehyde for efficacy, linoleic and oleic acids for processing traceability, p-hydroxybenzoic acid for network pharmacology analysis, and gypsogenin 3-O-β-D-glucuronopyranoside as the official standard. This integrated panel of markers provides a multi-dimensional foundation for establishing a comprehensive quality standard for MS.

Conclusion and Perspectives

Momordicae Semen, a classic toxic TCM with centuries of clinical application in resolving stagnation, reducing swelling, and detoxification, faces significant challenges: its inherent toxicity restricts safe administration, and the current single-

https://doi.org/10.2147/DDDT.S555032

Table 13 Comprehensive Evaluation of Candidate Q-Markers for MS

Candidate Q-marker	Chemical Formula / Molecular Weight	Specificity	Measurability	Efficacy Correlation	Transfer & Traceability	Property Attribution	Network Pharmacology	Overall Evaluation & Rationale
Momordica Saponin I	$C_{76}H_{120}O_{40}$	★★★(Species-specific)[7]	★★(Quantitative method established)	★★★(Core anti-ulcer, anti-inflammatory)[63]	★★(Transforms during processing; key efficacy component)	★★★(Bitter; Cool; Liver; Spleen)	–(Not analyzed)	**Core Q-marker**. High specificity, definitive efficacy link, and aligns with TCM properties.
Momordica Saponin II	$C_{76}H_{120}O_{41}$	★★★(Species-specific)	★★(Quantitative method established)	★★(Antitumor activity)[8]	★★(Transforms during processing; key efficacy component)	★★★(Bitter; Cool; Liver; Spleen)	–(Not analyzed)	**Core Q-marker**. High specificity and strong link to TCM properties.
MCoTI-I	3478 Da	★★★(Unique to MS)	★★(HPLC-UV quantifiable)	★★(Antitumor, antioxidant, immunomodulatory)[68,75]	★(Unique species identifier)	★★(Attributed to sweet-tasting proteins/ glycosides)	–(Not analyzed)	**Specificity Q-marker**. Unique identifier for MS, with measurable bioactivity.
MCoTI-II	3449 Da	★★★(Unique to MS)	★★(HPLC-UV quantifiable)	★★(Antitumor, antioxidant)[68]	★(Unique species identifier)	★★(Attributed to sweet-tasting proteins/ glycosides)	–(Not analyzed)	**Specificity Q-marker**. Unique identifier for MS, with measurable bioactivity.
p-hydroxycinnamaldehyde	$C_9H_8O_3$	★★(Common in Cucurbitaceae)	★★(HPLC detectable)	★★★(Core antitumor component)[46,47]	★(Stable efficacy component)	★★(Bitter; heat-clearing)	★★★(Key network node)	**Efficacy Q-marker**. Pivotal role in antitumor efficacy and strong network support.

Linoleic Acid	$C_{18}H_{32}O_2$	–(Ubiquitous)	★★★(Easily measured by GC/UPLC)	★★(Immunomodulatory, increases after processing)	★★★(Increases by 6.97% post-processing)	★★(Slightly sweet; Oily)	–(Not analyzed)	**Traceability Q-marker**. Excellent analytical property and a key indicator for processing traceability.
Oleic Acid	$C_{18}H_{34}O_2$	–(Ubiquitous)	★★★(Easily measured by GC/UPLC)	★★(Immunomodulatory, increases after processing)	★★★(Increases by 15.85% post-processing)	★★(Slightly sweet; Oily)	–(Not analyzed)	**Traceability Q-marker**. Excellent analytical property and a key indicator for processing traceability.
p-Hydroxybenzoic Acid	$C_7H_6O_3$	–(Ubiquitous)	★★★(Established HPLC method)[103]	★(Contributes to antioxidant effect)[27]	–(No tracking data reported)	★(Bitter)	★★★(Key network node)	**Network Pharmacology Q-marker**. Highly measurable and a central node in the compound-target network.
Gypsogenin 3-O-β-D-Glucuronopyranoside	$C_{37}H_{56}O_{10}$	★(Common in Cucurbitaceae)	★★★(Pharmacopoeia standard, UPLC)[102]	★(Hypolipidemic activity)	★★(Content varies with geography and altitude; geographical traceability)	★★(Bitter; Saponin)	–(Not analyzed)	**Official Q-marker**. The official quality control standard, highly measurable with geographical traceability.

Notes: Candidate components were assessed based on six predefined criteria. Scores are defined as: ★★★ (High): strong evidence or unique property; ★★ (Medium): moderate evidence or established method; ★ (Low): limited or indirect evidence; – (None): criterion not met or data unavailable.

https://doi.org/10.2147/DDDT.S550532

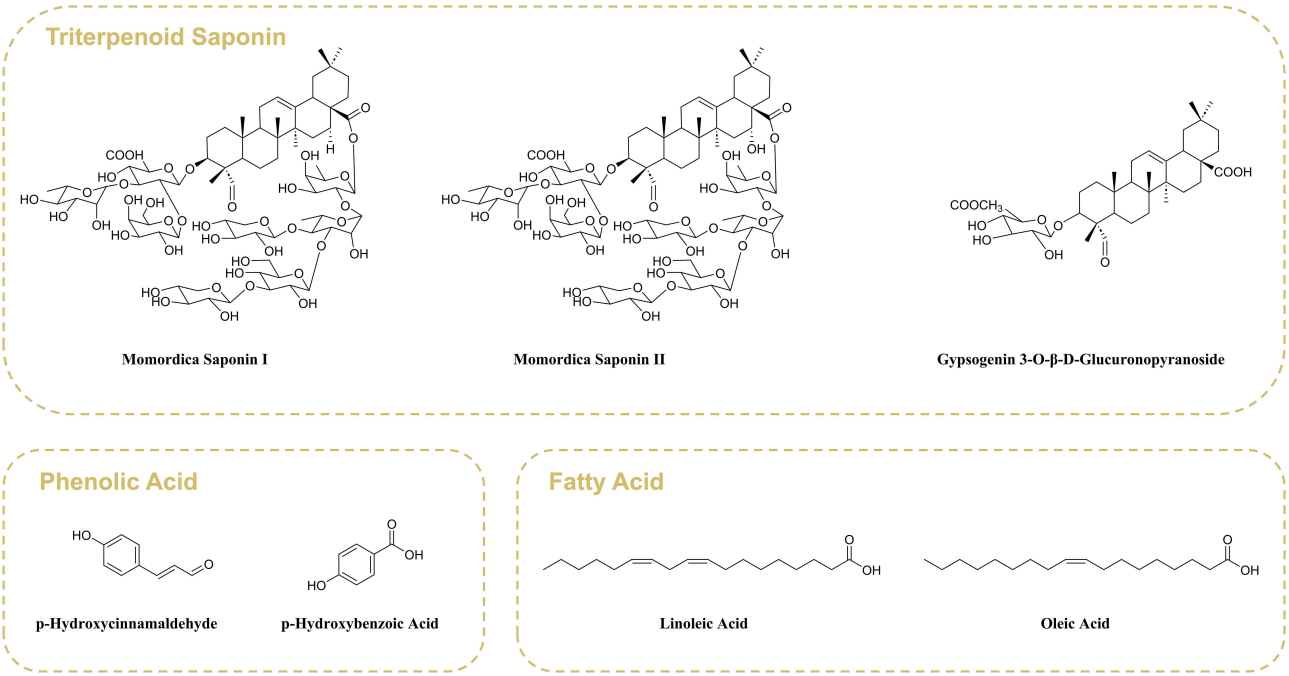


Figure 13 Chemical Structures and Classification of Candidate Q-markers for MS.
Note: Cyclotides MCoTI-I/II are not depicted due to their complex cyclic peptide structures.

compound quality standard in the *Chinese Pharmacopoeia* (2025) inadequately represents its multi-component therapeutic character.

This review synthesizes recent advances in the phytochemistry, pharmacology, toxicology, processing, and clinical applications of MS. Over 300 compounds have been isolated and identified from MS. Modern pharmacological studies confirm a spectrum of bioactivities, including antitumor, anti-inflammatory, and gastroprotective effects. Toxicity is primarily concentrated in the seed kernel, with saponins and cochinchinin implicated as key toxic constituents. Notably, the traditional "frost-like powder" processing method significantly mitigates hepatotoxicity and nephrotoxicity by altering the composition of both active and toxic components.

We propose nine compounds as potential Q-markers for MS: momordica saponins I/II, MCoTI-I/II, p-hydroxycinnamaldehyde, linoleic acid, oleic acid, p-hydroxybenzoic acid, and gypsogenin 3-O-β-D-glucuronopyranoside. These candidates were selected based on specificity, measurability, efficacy correlation, traditional property, transfer and traceability, and network pharmacology.

Nevertheless, the clinical translation of these Q-markers continues to face several critical challenges. The primary research gaps can be summarized as follows: First, while "frost-like powder" processing reduces toxicity and enhances efficacy, the specific chemical transformations of Q-markers during processing and their subsequent impact on in vivo bioavailability remain unelucidated. This lack of clarity hinders the optimization of processing parameters (e.g., pressing temperature or time) to maximize efficacy while minimizing toxicity. Second, although saponins are known to exhibit dual therapeutic-toxic effects, the dose-response relationships between individual Q-markers and their molecular targets are undefined. For example, it remains unclear how momordica saponin I interacts with cPLA2/5-LOX (anti-inflammatory targets) at therapeutic doses versus inducing hepatocyte apoptosis at toxic doses, complicating the prediction of safe clinical dosages. Third, most biological activity studies have focused on crude extracts, lacking pharmacokinetic data for Q-markers. Additionally, the metabolic pathways of key active Q-markers are unknown. In the absence of such data, the link between Q-marker content in MS formulations and clinical efficacy cannot be definitively established.

Therefore, concerted research efforts should focus on the following directions. First, elucidating the dynamics of Q-markers during processing and absorption, distribution, metabolism, and excretion is essential. This can be achieved by employing UPLC-Q-TOF/MS to monitor structural transformations and establishing pharmacokinetic models in

relevant animal models, thereby guiding processing optimization and informing clinical dosing strategies. Second, defining the therapeutic window through efficacy-toxicity validation is critical. This requires concentration-response studies in vitro to map the safe effective range and subsequent in vivo validation to identify the key signaling pathways that mediate this balance. Finally, developing an integrated quality control system based on Q-markers is imperative. Such a system should combine candidate markers with chemical fingerprinting and bioactivity evaluation, and must be validated through clinical trials to ensure it accurately reflects real-world therapeutic performance.

In conclusion, this review highlights that Q-markers serve as a critical bridge linking the chemical composition of MS to its clinical value, offering a viable pathway to overcome challenges in toxicity and quality control. Addressing the identified research gaps will support the development of a robust, clinically relevant quality evaluation system, thereby advancing the safe, effective, and standardized application of this traditional medicine in modern practice.

Abbreviations

ABTS, 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); ACE, angiotensin-converting enzyme; Akt, protein kinase B; Bax, BCL2-associated X protein; Bcl-2, B-cell lymphoma 2; cPLA2, cytosolic phospholipase A2; CNKI, China National Knowledge Infrastructure; DL, drug-likeness; DPPH, 2,2-diphenyl-1-picrylhydrazyl; ECMS, ethanol extract of Momordicae Semen; EGFR, epidermal growth factor receptor; ESR1, estrogen receptor 1; GI, gastrointestinal; GO, Gene Ontology; HSP90, heat shock protein 90; IL-2, interleukin-2; IL-6, interleukin-6; KEGG, Kyoto Encyclopedia of Genes and Genomes; LD_{50}, median lethal dose; LPS, lipopolysaccharide; MAPK, mitogen-activated protein kinase; MC, Momordica cochinchinensis; MCoCI, Momordica cochinchinensis trypsin inhibitor I; MS, Momordicae Semen; MSE, Muyin extract; MSP, Momordicae Semen Pulveratum; mTOR, mammalian target of rapamycin; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; NO, nitric oxide; NSAIDs, nonsteroidal anti-inflammatory drugs; OB, oral bioavailability; OVA, ovalbumin; PD-1, programmed cell death protein 1; PD-L1, programmed death-ligand 1; PPI, protein-protein interaction; PPARγ, peroxisome proliferator-activated receptor gamma; PTPN11, protein tyrosine phosphatase non-receptor type 11; Q-markers, quality markers; RAW 264.7, murine macrophage cell line; Src, proto-oncogene tyrosine-protein kinase; Syk, spleen tyrosine kinase; TCM, traditional Chinese medicine; TNF-α, tumor necrosis factor-alpha; UPLC, ultra-performance liquid chromatography; VEGF, vascular endothelial growth factor; 5-LOX, 5-lipoxygenase.

Acknowledgments

This work was supported by the National Key Research and Development Program (2023YFC3504202), Natural Science Foundation of Anhui Provincial Colleges and Universities (KJ2021A0601, 2022AH050509 & 2023AH050779), Anhui Province Traditional Chinese Medicine Inheritance and Innovation Research Project (2024CCCX022), New Era Education Quality Project (Graduate Education, 2023dshwyx021), and the Zhejiang Provincial University Key Characteristic Discipline (Chinese Materia Medica, ZYAOXZD2019005).

Disclosure

The authors report no conflicts of interest in this work.

References

1. Huang HC, Chen CJ, Lai YH, et al. Momordica cochinchinensis aril ameliorates diet-induced metabolic dysfunction and non-alcoholic fatty liver by modulating gut microbiota. *Int J Mol Sci*. 2021;22(5):2640. doi:10.3390/ijms22052640
2. Zhao FH, Hao EW, Liang YF, Du ZC, Deng JG. Chemical constituents, toxicology and pharmacological effect of momordicae semen. *Chin J Exp Tradit Med Formulae*. 2020;26(3):222–235. doi:10.13422/j.cnki.syfjx.20192307
3. Gu HY, Zhong L, Zhang YX, Sun JH, Liu LP, Liu ZC. Exploring the mechanism of Jinlida granules against type 2 diabetes mellitus by an integrative pharmacology strategy. *Sci Rep*. 2024;14(1):10286. doi:10.1038/s41598-024-61011-8
4. Ma SB, Wang QR, Wang HQ, et al. Investigation of the mechanism of Bark of Ailanthus altissima in the treatment of ulcerative colitis based on network pharmacology and experimental verification. *J Ethnopharmacol*. 2025;337:118916. doi:10.1016/j.jep.2024.118916
5. Sławińska N, Olas B. Selected seeds as sources of bioactive compounds with diverse biological activities. *Nutrients*. 2022;15(1):187. doi:10.3390/nu15010187

6. Ding R, Wang JQ, Luo YY, Han YL, Li XB, Wang MY. Five new triterpenoid saponins from the kernels of *Momordica cochinchinensis*. *Acta Pharm Sin*. 2024;1–15. doi:10.16438/j.0513-4870.2024-1013
7. Wang JQ, Wu ZW, Shi XY, Li X, Wang MY. Study on NMR determination of momordica saponin I. *Acad J Shanghai Univ Tradit Chin Med*. 2023;37(3):42–47. doi:10.16306/j.1008-861x.2023.03.008
8. Wu ZW, Shi XY, Ma WQ, Luo YY, Li XB, Wang M. The biological activity, chemical structure, and purity determination of momordica saponin II. *Chem Life*. 2024;44(1):165–176. doi:10.13488/j.smhx.20230331
9. Song Y. *Preliminary Study on The Mechanism of* "Significant Attenuation and Synergistic Effect" *and Processing Technology of Momordicae Semen Cream*. MA thesis. Anhui University of Chinese Medicine; 2019. doi:10.26922/d.cnki.ganzc.2019.000037.
10. Fan R, Cheng RR, Zhu HT, et al. Two new oleanane-type triterpenoids from methanolyzed saponins of *Momordica cochinchinensis*. *Nat Prod Commun*. 2016;11(6):725–728.
11. Wang MY, Zhan ZB, Xiong Y, Zhang H, Li XB. New cytotoxic constituents in the water-soluble fraction from Momordicae Semen. *Nat Prod Res*. 2020;34(6):823–829. doi:10.1080/14786419.2018.1508146
12. Yu JS, Sahar NE, Bi YR, et al. The effects of triterpenoid saponins from the seeds of Momordica cochinchinensis on adipocyte differentiation and mature adipocyte inflammation. *Plants*. 2020;9(8):984. doi:10.3390/plants9080984
13. Du ZC, Xia ZS, Huang YF, et al. Cardiotoxicity induced by *Cochinchina momordica* seed extract in zebrafish. *J Appl Toxicol*. 2021;41(8):1222–1231. doi:10.1002/jat.4108
14. Kan LD, Hu Q, Chao ZM, Song X, Cao XL. Chemical constituents of unsaponifiable matter from seed oil of *Momordica cochinchinensis*. *China J Chin Mater Medica*. 2006;31(17):1441–1444.
15. Ai ZD, Ma C, Wan RM, et al. Anticancer activity and molecular mechanism of *Momordica cochinchinensis* seed extract in chronic myeloid leukemia cells. *Nutr Cancer*. 2022;74(7):2644–2656. doi:10.1080/01635581.2021.2014904
16. Liu T, Shi JF, Wu XZ. The chemical constituents study of Mongolian herb *Momordica cochinchinensis*. *Acta Acad Med Neimongol*. 2010;32(4):390–393. doi:10.16343/j.cnki.issn.2095-512x.2010.04.002
17. Tan ZM. Content determination and grey relational analysis of cucurbitaceaes in five varieties of cucurbitaceae plants. *China Pharm*. 2017;20(7):1201–1205.
18. Jiang Y, Yao MX, Zhang SS, et al. Fatty oil extraction process and analysis of gas chromatography-mass spectroscopy before and after processing of momordicae semen. *J Anhui Univ Chin Med*. 2020;39(6):68–72.
19. Lin J, Lu JQ, Jiang HM, et al. HS-SPME-GC-MS analysis of volatile components of momordicae semen. *J Chin Med Mater*. 2014;37(12):2231–2233. doi:10.13863/j.issn1001-4454.2014.12.029
20. Xing YH, Zhou R, Gao ZY. GC-MS analysis of the volatile oil constitutes of momordicae semen. *Tradit Chin Med J*. 2016;15(4):56–58. doi:10.14046/j.cnki.zyytb2002.2016.04.022
21. Zheng L, Zhang YM, Liu YP, Ou Yang XY, Zhan YZ. *Momordica cochinchinensis* Spreng. seed extract suppresses breast cancer growth by inducing cell cycle arrest and apoptosis. *Mol Med Rep*. 2015;12(4):6300–6310. doi:10.3892/mmr.2015.4186
22. Ishida BK, Turner C, Chapman MH, McKeon TA. Fatty acid and carotenoid composition of gac (*Momordica cochinchinensis* Spreng) fruit. *J Agric Food Chem*. 2004;52(2):274–279.
23. Ding XG, Zhang JL, Zheng J, Zhu YQ, Hou DY. Analysis of fatty acid in seed of *Momordica cochinchinensis* by GC/MS. *Lishizhen Med Mater Med Res*. 2005;2025(3):202–203.
24. Wang MY, Zhan ZB, Xiong Y, Zhang Y, Li XB. Cytotoxic and anti-inflammatory constituents from *Momordica cochinchinensis* seeds. *Fitoterapia*. 2019;139:104360. doi:10.1016/j.fitote.2019.104360
25. Wang MY, Zhan ZB, Xiong Y, Li XB. Studies on liposoluble constituents from Momordicae Semen. *China J Chin Mater Medica*. 2018;43(6):1175–1181. doi:10.19540/j.cnki.cjcmm.2018.0042
26. Geng YM, Zhao LM, Zhu XL, et al. Effect of p-hydroxylcinnamaldehyde on differentiation of melanoma cells and its mechanism. *Chin Tradit Herb Drugs*. 2013;44(14):1951–1956.
27. Kubola J, Siriamornpun S. Phytochemicals and antioxidant activity of different fruit fractions (peel, pulp, aril and seed) of Thai gac (*Momordica cochinchinensis* Spreng). *Food Chem*. 2011;127(3):1138–1145. doi:10.1016/j.foodchem.2011.01.115
28. Zhou CL, Li XB, Ju PJ, Ding R, Wang MY. Four new diglycosides from Momordicae Semen. *China J Chin Mater Medica*. 2024;1–6. doi:10.19540/j.cnki.cjcmm.20241213.202
29. Abdulqader A, Ali F, Ismail A, Esa NM. Antioxidant compounds and capacities of Gac (*Momordica cochinchinensis* Spreng) fruits. *Asian Pac J Trop Biomed*. 2019;9(4):158–167. doi:10.4103/2221-1691.256729
30. Fan R. *Chemical constituents and pharmacological activities of* Momordica cochinchinensis *(Lour.) Spreng. and* Camellia fengchengensis *Liang et Zhong*. MA thesis. Yunnan University of Chinese Medicine; 2015. https://kns.cnki.net/KCMS/detail/detail.aspx?dbcode=CMFD&dbname=CMFD201502&filename=1015331265.nh. Accessed November 15, 2024.
31. Chuethong J, Oda K, Sakurai H, Saiki I, Leelamanit W. Cochinin B, a novel ribosome-inactivating protein from the seeds of *Momordica cochinchinensis*. *Biol Pharm Bull*. 2007;30(3):428–432. doi:10.1248/bpb.30.428
32. Ngamsuk S, Huang TC, Hsu JL. ACE inhibitory activity and molecular docking of gac seed protein hydrolysate purified by HILIC and RP-HPLC. *Molecules*. 2020;25(20):4635. doi:10.3390/molecules25204635
33. Chan LY, He WJ, Tan N, Zeng GZ, Craik DJ, Daly NL. A new family of cystine knot peptides from the seeds of *Momordica cochinchinensis*. *Peptides*. 2013;39:29–35. doi:10.1016/j.peptides.2012.09.018
34. Chan LY, Wang CKL, Major JM, et al. Isolation and characterization of peptides from *Momordica cochinchinensis* seeds. *J Nat Prod*. 2009;72(8):1453–1458. doi:10.1021/np900174n
35. Wang XQ, Li T, Bai ZL, Jia TZ. Isolation and purification of cochinchinin. *Liaoning J Tradit Chin Med*. 2007;(1):78–79. doi:10.13192/j.ljtcm.2007.01.82.wangxq.055
36. Liew HT, To J, Zhang XH, et al. The legumain McPAL1 from *Momordica cochinchinensis* is a highly stable Asx-specific splicing enzyme. *J Biol Chem*. 2021;297(6):101325. doi:10.1016/j.jbc.2021.101325
37. Hanh PT, Wache Y. Isomerization and increase in the antioxidant properties of lycopene from *Momordica cochinchinensis* (gac) by moderate heat treatment with UV-Vis spectra as a marker. *Food Chem*. 2014;156:58–63. doi:10.1016/j.foodchem.2014.01.040

38. Kan YY, Song M, Cui XH, et al. Muyin extract inhibits non-small-cell lung cancer growth by inducing autophagy and apoptosis in vitro and in vivo. *Phytomedicine*. 2022;96:153834. doi:10.1016/j.phymed.2021.153834
39. Zang YL, Li J, Zeng R, et al. Screening effective sites of momordicae semen-epimedii folium and anti-lung cancer mechanism of its prescription. *Chin J Exp Tradit Med Formulae*. 2024;30(8):17–25. doi:10.13422/j.cnki.syfjx.20240303
40. Jee W, Ko HM, Park DI, et al. *Momordicae Semen* inhibits migration and induces apoptotic cell death by regulating c-Myc and *CNOT2* in human pancreatic cancer cells. *Sci Rep*. 2023;13(1):12800. doi:10.1038/s41598-023-39840-w
41. Nguyen D, Holien J, Dekiwadia C, Piva T, Huynh T, Thrimawithana T. *Momordica cochinchinensis* (Gấc) seed extracts induce apoptosis and necrosis in melanoma cells. *Pharmaceuticals*. 2023;16(1):100. doi:10.3390/ph16010100
42. Le AV, Huynh TT, Parks SE, Nguyen MH, Roach PD. Bioactive composition, antioxidant activity, and anticancer potential of freeze-dried extracts from Defatted Gac (*Momordica cochinchinensis* Spreng) seeds. *Medicines*. 2018;5(3):104. doi:10.3390/medicines5030104
43. Han LN, Zhang C, Wei SS, et al. Effects of p-hydroxycinnamaldehyde extract from the Cochinchina momordica seeds on growth and metastasis of melanoma transplanted tumors in mice and its mechanism. *Chin J Cancer Biother*. 2021;28(6):590–597.
44. Han LN, Zhao LM, Hu CX, et al. Effects of ethanol extract of cochinchina momordica seed on invasion and metastasis of mouse melanoma B16 cells in vitro and in vivo. *Tumor*. 2010;2010:1.
45. Zhao LM, Geng YM, Sun SP, Ren FZ, Han LN, Shan B. Effect and mechanisms of p-hydroxylcinnamaldehyde from cochinchina momordica seed on differentiation of mouse melanoma B16 cells *in vitro*. *Chin J Cancer Biother*. 2014;21(3):282–287.
46. Cui WX, Wu Y, Wei SS, et al. Inhibitory effects of p-hydroxylcinnamaldehyde on esophageal cancer xenograft tumor in vivo. *Chin J Cancer Biother*. 2017;24(2):145–150.
47. Dai S, Wu H, Zhao RY, et al. Study on mechanism of differentiation of esophageal carcinoma Kyse30 cells induced by p-hydroxylcinnamaldehyde. *Chin Tradit Herb Drugs*. 2018;2018:610–618.
48. Ma M, Zhao LM, Yang XX, et al. p-Hydroxylcinnamaldehyde induces the differentiation of oesophageal carcinoma cells via the cAMP-RhoA-MAPK signalling pathway. *Sci Rep*. 2016;6(1):31315. doi:10.1038/srep31315
49. Liu HR, Meng LY, Lin ZY, Shen Y, Yu YQ, Zhu YZ. Cochinchina momordica seed extract induces apoptosis and cell cycle arrest in human gastric cancer cells via PARP and p53 signal pathways. *Nutr Cancer*. 2012;64(7):1070–1077. doi:10.1080/01635581.2012.712737
50. Yu JS, Roh HS, Lee S, Jung K, Baek KH, Kim KH. Antiproliferative effect of *Momordica cochinchinensis* seeds on human lung cancer cells and isolation of the major constituents. *Rev Bras Farmacogn*. 2017;27(3):329–333. doi:10.1016/j.bjp.2017.02.002
51. Shen Y, Meng LY, Sun HJ, Zhu YZ, Liu HR. *Cochinchina Momordica* seed suppresses proliferation and metastasis in human lung cancer cells by regulating multiple molecular targets. *Am J Chin Med*. 2015;43(01):149–166. doi:10.1142/S0192415X1550010X
52. Meng LY, Liu HR, Shen Y, Yu YQ, Tao X. *Cochinchina momordica* seed extract induces G2/M arrest and apoptosis in human breast cancer MDA-MB-231 cells by modulating the PI3K/Akt pathway. *Asian Pac J Cancer Prev*. 2012;13:1.
53. Gao R, Li ZH, Ma JR, He T, Fang Y, Zheng L. The mechanisms of autophagy induced by *Momordica cochinchinensis*Seed on ZR-75-30 cells. *Biol Chem Eng*. 2019;5(3):99–101.
54. Zheng L, Zhang YM, Zhan YZ, Liu CX. *Momordica cochinchinensis* seed extracts suppress migration and invasion of human breast cancer ZR-75-30 cells via down-regulating MMP-2 and MMP-9. *Asian Pac J Cancer Prev*. 2014;15(3):1105–1110. doi:10.7314/APJCP.2014.15.3.1105
55. Buranrat B, Kraiklang R. *Momordica cochinchinensis* suppresses the human breast cancer cells growth and migration by inhibiting mevalonate pathway. *Pharmacogn Mag*. 2023;19(2):284–294. doi:10.1177/09731296231157982
56. Ou C, Zhang JJ, Zhong H, Song YQ. *Momordica cochinchinensis*regulates the expression of circRNA _002178 to inhibit the proliferation, migration, and invasion of liver cancer cells. *Chin J Integr Tradit West Med Liver Dis*. 2022;32(7):622–625.
57. Jung K, Chin YW, Chung YH, et al. Anti-gastritis and wound healing effects of Momordicae Semen extract and its active component. *Immunopharmacol Immunotoxicol*. 2013;35(1):126–132. doi:10.3109/08923973.2012.712139
58. Lim JH, Kim JH, Kim N, et al. Gastroprotective effect of *Cochinchina momordica* seed extract in nonsteroidal anti-inflammatory drug-induced acute gastric damage in a rat model. *Gut Liver*. 2014;8(1):49–57. doi:10.5009/gnl.2014.8.1.49
59. Kang JM, Kim N, Kim B, et al. Enhancement of gastric ulcer healing and angiogenesis by *cochinchina momordica* seed extract in rats. *J Korean Med Sci*. 2010;25(6):875. doi:10.3346/jkms.2010.25.6.875
60. Kang JM, Kim N, Kim B, et al. Gastroprotective action of cochinchina momordica seed extract is mediated by activation of CGRP and inhibition of cPLA2/5-LOX pathway. *Dig Dis Sci*. 2009;54(12):2549–2560. doi:10.1007/s10620-008-0671-6
61. Choi K, Kim E, Hong H, et al. Attenuation of cysteamine-induced duodenal ulcer with *Cochinchina momordica* seed extract through inhibiting cytoplasmic phospholipase A_2/5-lipoxygenase and activating γ-glutamylcysteine synthetase. *J Gastroenterol Hepatol*. 2012;27(s3):13–22. doi:10.1111/j.1440-1746.2012.07065.x
62. Jung K, Chin YW, Yoon KD, et al. Anti-inflammatory properties of a triterpenoidal glycoside from Momordica cochinchinensis in LPS-stimulated macrophages. *Immunopharmacol Immunotoxicol*. 2013;35(1):8–14. doi:10.3109/08923973.2012.715165
63. Yu JS, Kim JH, Lee S, Jung K, Kim KH, Cho JY. Src/Syk-targeted anti-inflammatory actions of triterpenoidal saponins from gac (*Momordica cochinchinensis*) seeds. *Am J Chin Med*. 2017;45(03):459–473. doi:10.1142/S0192415X17500288
64. Lu JX, Meng W, Chang CB, et al. Study on the bacteriostasis *in vitro* by pre- and post processed seed of *Momordica cochinchinensis*. *Res Pract Chin Med*. 2009;23(6):33–35.
65. Oyuntsetseg N, Khasnatinov MA, Molor-Erdene P, et al. Evaluation of direct antiviral activity of the Deva-5 herb formulation and extracts of five Asian plants against influenza A virus H3N8. *BMC Complement Altern Med*. 2014;14:235. doi:10.1186/1472-6882-14-235
66. Mairuae N, Buranrat B, Cheepsunthorn P. Crude extracts of *Momordica cochinchinensis* (Lour.) Spreng exerts antioxidant and anti-neuroinflammatory properties in LPS-stimulated BV2 microglia. *Trop J Pharm Res*. 2024;23(1):91–97. doi:10.4314/tjpr.v23i1.12
67. Zhang D, Pan L, Jiang Z, Hu YK, Chen ZZ, Yu YQ. Analysis of antioxidant property of the extract of *Momordica cochinchinensis* by HPLC. *Fudan Univ J Med Sci*. 2010;37(3):319–321,325.
68. Tsoi AYK, Ng TB, Fong WP. Antioxidative effect of a chymotrypsin inhibitor from *Momordica cochinchinensis* (Cucurbitaceae) seeds in a primary rat hepatocyte culture. *J Pept Sci*. 2005;11(10):665–668. doi:10.1002/psc.666
69. Sakwiwatkul K, Li RL, Song XM, Hu SH. Effect of the extract made from *Cochinchina momordica* seeds on the humoral immune responses of mice to a commercial foot-and-mouth disease vaccine (serotypes O and Asia 1). *Microbiol Immunol*. 2010;54(1):31–37. doi:10.1111/j.1348-0421.2009.00180.x

70. Chen WJ, Liu DW, Hu SH. Adjuvant effect of extract of *Cochinchina momordica* seed on foot-and-mouth disease vaccination against Asia-I and O type strain in Guinea pigs. *Chin J Vet Sci*. 2008;(1):51–54. doi:10.16303/j.cnki.1005-4545.2008.01.016
71. Xiao CW, Rajput ZI, Liu DW, Hu SH. Enhancement of serological immune responses to foot-and-mouth disease vaccine by a supplement made of extract of cochinchina momordica seeds. *Clin Vaccine Immunol*. 2007;14(12):1634–1639. doi:10.1128/CVI.00339-07
72. Xiao C, Hu S, Rajput ZI. Adjuvant effect of an extract from *Cochinchina momordica* seeds on the immune responses to ovalbumin in mice. *Front Agric China*. 2007;1(1):90–95. doi:10.1007/s11703-007-0017-8
73. Iqbal RZ, AA G, Mohammad SN. Improvement of the efficacy of influenza vaccination (H5N1) in chicken by using extract of Cochinchina momordica seed (ECMS). *J Zhejiang Univ BAn Int Biomed Biotechnol J*. 2007;2007(5):331–337.
74. Xiao C, Bao G, Hu S. Enhancement of immune responses to Newcastle disease vaccine by a supplement of extract of *Momordica cochinchinensis* (Lour.) Spreng. seeds. *Poult Sci*. 2009;88(11):2293–2297. doi:10.3382/ps.2009-00059
75. Tsoi AYK, Ng TB, Fong WP. Immunomodulatory activity of a chymotrypsin inhibitor from *Momordica cochinchinensis* seeds. *J Pept Sci*. 2006;12(9):605–611. doi:10.1002/psc.765
76. Zhao FH. *Study on toxicity, substance basis and target organs of* Momordica cochinchinensis *seed*. MA thesis. Guangxi University of Chinese Medicine; 2021. doi:10.27879/d.cnki.ggxzy.2021.000441.
77. Mazzio E, Badisa R, Eyunni S, Ablordeppey S, George B, Soliman KFA. Bioactivity-guided isolation of neuritogenic factor from the seeds of the Gac Plant (*Momordica cochinchinensis*). *Evid Based Complement Alternat Med*. 2018;2018:1–11. doi:10.1155/2018/8953958
78. Georges B. Nerve growth factor mimetic effects of momordica cochinchinensis in PC 12. *Cells*. 2015;2015:1.
79. Liang HM, Zhang LQ, Wan WR, et al. Ethanol extract of Momordica cochinchinensis alleviates hydrogen peroxideinduced oxidative damage in SH-SY5Y cells by regulating Nrf2/Keap1 signaling pathway. *Chin Tradit Herb Drugs*. 2025;56(16):5826–5836.
80. Jung K, Lee D, Yu JS, Namgung H, Kang KS, Kim KH. Protective effect and mechanism of action of saponins isolated from the seeds of gac (*Momordica cochinchinensis* Spreng.) against cisplatin-induced damage in LLC-PK1 kidney cells. *Bioorg Med Chem Lett*. 2016;26(5):1466–1470. doi:10.1016/j.bmcl.2016.01.056
81. Abdulqader A, Ali F, Ismail A, Esa N. Gac fruit extracts ameliorate proliferation and modulate angiogenic markers of human retinal pigment epithelial cells under high glucose conditions. *Asian Pac J Trop Biomed*. 2018;8(12):571. doi:10.4103/2221-1691.248093
82. Tang WJ, Bu BG, Gui WF. Analysis of emergency rescue in five cases of acute momordicae semen poisoning. *Chin Gen Pract*. 2009;12(22):2061–2062.
83. Wang YF, Li GD, Li XX, Yu MW, Wang XM. Analysis of Wang Xiaomin ‘s clinical experience in treating advanced malignant tumors from perspective of yang deficiency and toxin accumulation. *Shanghai J Tradit Chin Med*. 2020;54(6):72–74,86. doi:10.16305/j.1007-1334.2020.06.005
84. Zheng L, Yang RF, Yang F, Li MY. Experimental Study on Acute Toxicity of Momordica cochinchinensis in Mice. *China Pharm*. 2017;20(12):2242–2243,2290.
85. Xiang LH, Chen YP, Zhang Z, Shan ZY, Yu ZM, Lv AP. Influence of 24 traditional Chinese herbs to viscera index of rat in long term toxicity test. *Chin J Basic Med Tradit Chin Med*. 2006;2006(1):35–36,52.
86. Yao MX. Study on the Changes of Components and Network Pharmacology of Fatty Oil in the Treatment of Liver Cancer Before and After Processing of Momordicae Semen. MA thesis. Anhui University of Chinese Medicine; 2020. doi:10.26922/d.cnki.ganzc.2020.000069.
87. Han LL. The study on the Frost Process and Mechanism of Momoridica. MA thesis. Shandong University of Traditional Chinese Medicine; 2011. https://kns.cnki.net/KCMS/detail/detail.aspx?dbcode=CMFD&dbname=CMFD2012&filename=1011204910.nh. Accessed January 8, 2025.
88. Song Y, Ran S, Sun FF, Hong Y, Han YQ. Optimization of processing technology of Momordicae Semen cream by Box-Behnken design-response surface methodology. *Chin Tradit Herb Drugs*. 2019;50(2):382–387.
89. Yao MX, Wang XL, Pan LY, Zhang SS, Han YQ. Comparative study on the relative content of linoleic acid and oleic acid and fingerprint of Momordicae Semen before and after processing. *J Shanxi Univ Chin Med*. 2020;21(4):270–275. doi:10.19763/j.cnki.2096-7403.2020.04.11
90. He X, Tang GS, Shan D, Mo Xi YL, Wu SY. Mechanism of Alatan Wuwei Pills in treatment of chronic gastritis based on network pharmacology and molecular docking technology. *Drugs Clin*. 2024;39(5):1145–1154.
91. Aodengqimuge, Wang HR, Wuhanqimuge, Xilinqiqige, Tegexibaiyin, Alatengqimuge. Study of quality standard for mongolian medicine sirixi. *World Chin Med*. 2021;16(14):2082–2087.
92. Ge HY, Wang A, Gao L, Li YX. Effects and mechanisms of Qingganjiuwei powder on the liver fibrosis in rats. *Chin J Clin Pharmacol*. 2019;35(22):2859–2862. doi:10.13699/j.cnki.1001-6821.2019.22.023
93. Pharmacopoeia Commission of PRC. *Pharmacopoeia of the People's Republic of China*. First China Medical Science Press; 2025.
94. Song MX, Yang M. *Xin Bian Guo Jia Zhong Cheng Yao*. 3rd. Beijing: People's Medical Publishing House; 2020. https://book.douban.com/subject/36696133/. Accessed December 8, 2024.
95. Wang YR, Zheng L, Liu GY, Wang HJ, Liu Y, Wang BW. Network-based pharmacological analysis of the molecular mechanism of Gong Ying detoxification lotion with soaking agent in the treatment of diabetic foot ulcers. *Pharmacol Res - Mod Chin Med*. 2022;3:100084. doi:10.1016/j.prmcm.2022.100084
96. Wu XR. Progress in the study of the traditional therapeutic efficacy of Mongolian medicine Bawei Zhixue Honghua San. *J Med Pharm Chin Minor*. 2024;30(4):62–64. doi:10.16041/j.cnki.cn15-1175.2024.04.025
97. Guo MY, Jiang WJ, Yu JS, Pang XH. Investigating the authenticity of Ophiopogonis Radix and its Chinese patent medicines by using a nucleotide signature. *J Ethnopharmacol*. 2020;261:113134. doi:10.1016/j.jep.2020.113134
98. Yang DA, Wang FH, Qi ML. Determination of Corydalis bungeana and Ophiopogon japonicus from Lidan Bawei San by thin layer chromatography. *J Med Pharm Chin Minor*. 2008;(1):53–54. doi:10.16041/j.cnki.cn15-1175.2008.01.032
99. Bai CL, Li Z, Sarengerile, Wang Q. Quality standard for xiaoshi shiwei pills. *Chin Tradit Pat Med*. 2015;37(9):1951–1955.
100. Zhang L, Cui ZH, Mu YX, et al. Ethnopharmacological investigation and rapid authentication of mongolian patent medicines digeda. *Chin Herb Med*. 2015;7(3):223–237.
101. Liu CX. Construction of traceability system of Chinese materia medica product quality based on quality marker of Chinese materia medica. *Chin Tradit Herb Drugs*. 2017;2017:3669–3676.

102. Cheng ZQ, Han GL, Hong Y, et al. Determination of gypsoside 3-O-β-D-glucuronic acid methyl ester in *Momordica cochinchinensis* by UPLC. *J Shanxi Univ Chin Med*. 2017;18(2):25–27,38.
103. Xing YH, Qu QR, Gao WN. Content determination of p-hydroxybenzoic acid in *Momordica cochinchinensis* by HPLC. *Chem Bioeng*. 2020;37(3):62–64.
104. Lin ZY, Yu ZH, Chen C, Dong QX, Wang MZ, Yu YQ. An HPLC method for the assay of trypsin inhibitors and its application to the study of *Momordica cochinchinensis* extract. *J Chin Pharm Sci*. 2011;20(4):397–403.
105. Le AV, Parks SE, Nguyen MH, Roach PD. Effect of solvents and extraction methods on recovery of bioactive compounds from defatted Gac (*Momordica cochinchinensis* Spreng.) seeds. *Separations*. 2018;5(3):39. doi:10.3390/separations5030039
106. Ding YX, Lv WQ, Shen HW. Content comparison and correlation analysis of gypsogenin 3-O-β-D-glucuronic acid methyl ester in *Momordica cochinchinensis* from 14 production places of 8 provinces. *China Pharm*. 2017;28(34):4821–4825.

Drug Design, Development and Therapy

Dovepress
Taylor & Francis Group

Publish your work in this journal

Drug Design, Development and Therapy is an international, peer-reviewed open-access journal that spans the spectrum of drug design and development through to clinical applications. Clinical outcomes, patient safety, and programs for the development and effective, safe, and sustained use of medicines are a feature of the journal, which has also been accepted for indexing on PubMed Central. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit http://www.dovepress.com/testimonials.php to read real quotes from published authors.

Submit your manuscript here: https://www.dovepress.com/drug-design-development-and-therapy-journal