/ Review

Herba *Cistanche* (Rou Cong Rong): A Review of Its Phytochemistry and Pharmacology

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Herba *Cistanche*, known as Rou Cong Rong in Chinese, is a very valuable Chinese herbal medicine that has been recorded in the Chinese Pharmacopoeia. Rou Cong Rong has been extensively used in clinical practice in traditional herbal formulations and has also been widely used as a health food supplement for a long time in Asian countries such as China and Japan. There are many bioactive compounds in Rou Cong Rong, the most important of which are phenylethanoid glycosides. This article summarizes the up-to-date information regarding the phytochemistry, pharmacology, processing, toxicity and safety of Rou Cong Rong to reveal its pharmacodynamic basis and potential therapeutic effects, which could be of great value for its use in future research.

Key words Herba *Cistanche*; phytochemistry; pharmacology; phenylethanoid glycoside; review

1. Introduction

Herba *Cistanche* comprises 22 species all over the world and is distributed mainly in arid lands and even deserts across Eurasia and North Africa, such as in China, Japan, Iran, India, and Mongolia.[1)] Among all these plants, four main species and a variant species are found in China according to the Taxonomical Index of Chinese Higher Plants; all of these species are called Rou Cong Rong in Chinese.[2)] These species include *Cistanche deserticola* Y.C. Ma, *C. tubulosa* (Schenk) R. Wight, *C. sinensis* G. Beck, *C. salsa* (C.A. Mey.) G. Beck, and *C. salsa* var. albiflora P.F. Tu et Z.C. Lou.[3)] The dried succulent stems of the genus *Cistanche* Hoffmg. Et Link belong to the Orobanchaceae family.[4)] Among these four *Cistanche* plants, only *C. deserticola* and *C. tubulosa* have been authenticated as officinal plants in the Chinese Pharmacopoeia (2015 edition), though *C. salsa* and *C. sinensis* are commonly used in the regions of Ningxia and Xinjiang due to their remarkable medicinal effects and the source shortage of *C. deserticola* and *C. tubulosa*. As for the Japanese Pharmacopoeia, the dried stems of *C. salsa*, *C. deserticola*, and *C. tubulosa* are authorized as a crude drug "Nikujuyou."[5)] Besides, three species including *C. tubulosa*, which mainly distributed in the Central Sahara (Tassili N'Ajjer); *C. tinctoria*, which is locally known as danoun to treat diabetes, diarrhea and abdominal pains in Saharo-Mediterranean region, *C. violacea*, which is a holoparasitic plant on Chenopodiaceae and Limoniastrum in the Northern Africa are the reperesented *Cistanche* in the Algerian sahara.[6)] *Cistanche* was first recorded in *Shen Nong's Herbal Classic* and has had a very long medical history in China.[7)] *C. tubulosa* (Kanka-nikujuyou in Japanese) has traditionally been used to promote blood circulation.[8)] In Korea, *Cistanche* also has a long medicinal history and *C. salsa* has been reported to be efficacious in the treatment of sexual dysfunction diseases in Korean medicine book called the DonguiBogam.[9)] Currently, it is generally used to treat chronic renal disease, female infertility, morbid leucorrhea, profuse metrorrhagia, and constipation in the elderly.[10)] It has also been used since ancient times as an herbal drug to treat kidney deficiency.[11)] Among the tonics in traditional Chinese medicine (TCM), this medicine is widely accepted as superior and has been honored as the "Ginseng of the desert." Besides the remarkable uses in China, Herba *Cistanche* is also used as a healthy food supplement in Japan and Southeast Asia and scholars in many countries like Japan, Korea, Germany, Russian, Australia, Greece, Algérie and Italy have made a lot of modern scientific researches on this plant since 1980s.[12)] Chemical research has indicated that phenylethanoid glycosides (PhGs), iridoids, lignans, and polysaccharides are the major constituents of these species,[13,14)] and Herba *Cistanche* extracts have been proved to have a range of pharmacologically active functions that include improving chronic renal disease and constipation in the elderly, increasing learning or memorization abilities, treating Alzheimer's disease (AD), and improving immunity by researchers all over the world.[1,15–18)]

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This paper mainly updates the available information about the phytochemical constituents, pharmacological activities and safety of *Cistanches* Herba to provide useful information for the development of plant-derived drugs and Chinese medicine preparations from this medicinal plant.

2. Phytochemistry

As the oriental medicinal tonic in Japan, *C. salsa* have

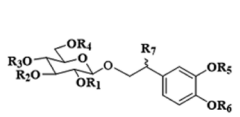
Table 1. PhGs from *Cistanche* Species

No.	Compound	Source	References
1	2′-Acetylacteoside	*Cd*, *Ct*, *Cp*, *Csi*, *Csa*	19–24)
2	Acteoside	*Cd*, *Ct. Cp Csa*, *Csi*	19–22, 24–26)
3	Cistanoside A	*Cd*, *Ct*, *Csa*	21, 26–28)
4	Cistanoside B	*Cd*	28, 29)
5	Cistanoside C	*Cd*, *Csa*	19, 29)
6	Cistanoside D	*Cd*, *Csa*	19)
7	Cistanoside E	*Cd*	19)
8	Cistanoside G	*Cd*, *Ct*	30, 31)
9	Cistanoside H	*Cd*	29, 32)
10	Decaffeoylacteoside	*Cd*, *Ct*	25, 32)
11	Echinacoside	*Cd*, *Ct*, *Cp*, *Csa*, *Csi*	20–25, 33)
12	Isoacteoside	*Cd*, *Ct*, *Csa*, *Csi*	20, 24, 25, 33, 34)
13	Isosyringalide 3′-*α*-L-rhamnopyranoside	*Cd*, *Ct*	35, 36)
14	Osmanthuside B	*Cd*, *Ct*, *Csa*	19, 36)
15	Salidroside	*Cd*, *Ct*	25, 30, 37, 38)
16	Syringalide A 3′-*α*-L-rhamnopyranoside	*Cd*, *Ct*, *Cp*	25, 34, 35, 37)
17	Tubuloside A	*Cd*, *Ct*, *Cp*	20, 25, 34, 39)
18	Tubuloside B	*Cd*, *Ct*, *Cp*, *Csi*, *Csa*	20, 21, 33, 37)
19	Tubuloside C	*Ct*	20)
20	*E*-Tubuloside D	*Ct*	20)
21	*Z*-Tubuloside D	*Ct*	20)
22	*E*-Tubuloside E	*Cd*, *Ct*, *Cp*	35, 39, 40)
23	*Z*-Tubuloside E	*Cd*, *Ct*, *Cp*	35, 39, 40)
24	Cistantubuloside A	*Ct*	41)
25	Cistantubuloside B1	*Ct*	41)
26	Cistantubuloside B2	*Ct*	41)
27	Cistansinenside A	*Csi*	42)
28	Jionoside D	*Csi*	42)
29	Poliumoside	*Csi*	42)
30	Kankanoside F	*Ct*	31)
31	Kankanoside G	*Ct*	31)
32	Eutigoside A	*Csa*	33)
33	Cistantubuloside C1	*Ct*	41)
34	Cistantubuloside C2	*Ct*	41)
35	2′-Acetylcistanoside C	*Csa*	43)
36	Cistansinenside B	*Csi*	24)
37	Campneoside II	*Ct*, *Csi*	24, 37)
38	Brandioside	*Csi*	24)
39	Cistanoside K	*Cd*	44)
40	Isocistanoside C	*Cd*	44)
41	2′-Acetyl osmanthuside	*Csa*	43)
42	Kankanoside H1	*Ct*	37)
43	Kankanoside H2	*Ct*	37)
44	Kankanoside I	*Ct*	37)
45	Kankanosides J1	*Ct*	45)
46	Kankanosides J2	*Ct*	45)
47	Kankanosides K1	*Ct*	45)
48	Kankanosides K2	*Ct*	45)
49	Isocampneoside I	*Ct*	45)
50	Campneoside I	*Ct*	37, 41)
51	*cis*-Acteoside	*Ct*	37)
52	Arenarioside	*Ct*	37)
53	Wiedemannioside C	*Ct*	37)
54	*E*-Osmanthuside B6	*Cd*	40)

Table 1. Continued

No.	Compound	Source	References
55	*Z*-Osmanthuside B6	*Cd*	40)
56	Cistanoside M	*Cd*	44)
57	Pheliposide	*Cp*	46)
58	Salsaside D	*Cd*, *Csa*	40, 47)
59	Salsaside E	*Cd*, *Csa*	40, 47)
60	Salsaside F	*Csa*	47)
61	Cistanoside J	*Cd*	44)
62	Cistanoside L	*Cd*	44)
63	Cistanoside N	*Cd*	44)
64	Epimeridinoside A	*Cd*	44)
65	Plantainoside C	*Cd*	40)
66	6'-Acetylsalidroside	*Cd*	44)
67	Acetylacteoside	*Cd*, *Ct*	48)
68	Calceolarioside A	*Cd*, *Ct*	49)
69	*cis*-Cistanoside J	*Cd*	50)
70	*cis*-Cistanoside K	*Cd*	50)
71	*cis*-Isocistanoside C	*Cd*	50)
72	Cistansalside A	*Csa*	51)
73	Cistansalside D	*Csa*	51)
74	Cistansalside E	*Csa*	51)
75	Cistubuloside B	*Cd*	50)
76	Cistubuloside D	*Cd*, *Ct*	52)
77	*cis*-Verbascoside	*Cd*, *Ct*	52)
78	Isocistanoside J	*Cd*, *Ct*	52)
79	Isocistanoside K	*Cd*, *Ct*	52)
80	Isomartynoside	*Cd*, *Ct*	50)
81	Isopoliumoside	*Cd*, *Ct*	53)
82	Jionoside C	*Csa*	51)
83	Phenylethyl-glucopyranoside	*Cd*	50)
84	*β*-D-Glucopyranoside,2-(4-hydroxyphenyl)ethyl,6-acetate	*Cd*	44, 54)
85	Crenatoside	*Cd*, *Ct*	25)

Cd, *C. deserticola*; Ct, *C. tubulosa*; Cp, *C. phelypaea*; Csa, *C. salsa*; Csi, *C. sinensis*.



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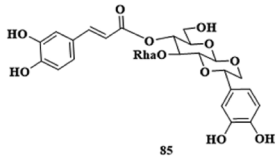

85

1 R_1 = Ac, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = OH, R_6 = OH, R_7 = H
2 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = OH, R_6 = OH, R_7 = H
3 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Glc, R_5 = OMe, R_6 = OH, R_7 = H
4 R_1 = H, R_2 = Rha, R_3 = Fr, R_4 = Glc, R_5 = OMe, R_6 = OH, R_7 = H
5 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = OMe, R_6 = OH, R_7 = H
6 R_1 = H, R_2 = Rha, R_3 = Fr, R_4 = H, R_5 = OMe, R_6 = OH, R_7 = H
7 R_1 = H, R_2 = Rha, R_3 = H, R_4 = H, R_5 = OMe, R_6 = OH, R_7 = H
8 R_1 = H, R_2 = Rha, R_3 = H, R_4 = H, R_5 = H, R_6 = OH, R_7 = H
9 R_1 = Ac, R_2 = Rha, R_3 = H, R_4 = H, R_5 = OH, R_6 = OH, R_7 = H
10 R_1 = H, R_2 = Rha, R_3 = H, R_4 = H, R_5 = OH, R_6 = OH, R_7 = H
11 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
12 R_1 = H, R_2 = Rha, R_3 = H, R_4 = Cf, R_5 = OH, R_6 = OH, R_7 = H
13 R_1 = H, R_2 = Rha, R_3 = Cm, R_4 = H, R_5 = OH, R_6 = OH, R_7 = H
14 R_1 = H, R_2 = Rha, R_3 = Cm, R_4 = H, R_5 = H, R_6 = OH, R_7 = H
15 R_1 = H, R_2 = H, R_3 = H, R_4 = H, R_5 = H, R_6 = OH, R_7 = H
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19 R_1 = Ac, R_2 = TA-Rha, R_3 = Cf, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
20 R_1 = Ac, R_2 = TA-Rha, R_3 = Cm, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
21 R_1 = Ac, R_2 = TA-Rha, R_3 = *c*-Cm, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
22 R_1 = Ac, R_2 = TA-Rha, R_3 = Cm, R_4 = H, R_5 = OH, R_6 = OH, R_7 = H
23 R_1 = Ac, R_2 = TA-Rha, R_3 = *c*-Cm, R_4 = H, R_5 = OH, R_6 = OH, R_7 = H
24 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Glc, R_5 = H, R_6 = OH, R_7 = H
25 R_1 = H, R_2 = Rha, R_3 = Cm, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
26 R_1 = H, R_2 = Rha, R_3 = *c*-Cm, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
27 R_1 = Ac, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = OH, R_6 = OMe, R_7 = H
28 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = OH, R_6 = OMe, R_7 = H
29 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Rha, R_5 = OH, R_6 = OH, R_7 = H
30 R_1 = H, R_2 = Rha, R_3 = H, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
31 R_1 = H, R_2 = Rha, R_3 = H, R_4 = Cf, R_5 = H, R_6 = OH, R_7 = H
32 R_1 = H, R_2 = H, R_3 = H, R_4 = Cm, R_5 = H, R_6 = OH, R_7 = H
33 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = OH(*R*)
34 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = OH(*S*)
35 R_1 = Ac, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = OMe, R_6 = OH, R_7 = H
36 R_1 = Ac, R_2 = Rha, R_3 = Cf, R_4 = Rha, R_5 = OH, R_6 = OMe, R_7 = H
37 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = OH, R_6 = OH, R_7 = OH
38 R_1 = Ac, R_2 = Rha, R_3 = Cf, R_4 = Rha, R_5 = OH, R_6 = OH, R_7 = H
39 R_1 = Ac, R_2 = Rha, R_3 = H, R_4 = Cf, R_5 = OMe, R_6 = OH, R_7 = H
40 R_1 = H, R_2 = Rha, R_3 = H, R_4 = Cf, R_5 = OMe, R_6 = OH, R_7 = H
41 R_1 = Ac, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = H, R_6 = OH, R_7 = H
42 R_1 = Ac, R_2 = Rha, R_3 = Cm, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
43 R_1 = Ac, R_2 = Rha, R_3 = *c*-Cm, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = H
44 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Glc, R_5 = H, R_6 = H, R_7 = H
45 R_1 = Ac, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = OH, R_6 = OH, R_7 = OMe(*R*)
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47 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = OMe(*R*)
48 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = Glc, R_5 = OH, R_6 = OH, R_7 = OMe(*S*)
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82 R_1 = H, R_2 = Rha, R_3 = Cf, R_4 = H, R_5 = H, R_6 = H, R_7 = H
83 R_1 = H, R_2 = H, R_3 = H, R_4 = H, R_5 = H, R_6 = H, R_7 = H
84 R_1 = H, R_2 = H, R_3 = H, R_4 = Ac, R_5 = H, R_6 = H, R_7 = H

Fig. 1. Structures of PhGs from *Cistanche* Species

Ac, acetyl; OMe, methoxyl; Cm, *trans*-coumaroyl; *c*-Cm, *cis*-coumaroyl; Cf, *trans*-caffeoyl; *c*-Cf, *cis*-caffeoyl; Fr, *trans*-feruloyl; *c*-Fr, *cis*-feruloyl; Glc, *β*-D-glucopyranosyl; Rha, *α*-L-rhamnopyranosyl; Xyl, *β*-D-xylopyranosyl; TA-Rha, 2‴,3‴,4‴-triacetyl-*α*-L-rhamnopyranosyl.

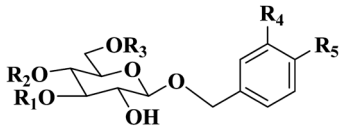
been reported to have the constituents, such as monoterpene glucoside, iridoid glucoside, phenylpropanoid glycoside and lignan glycoside early in 1983–1986 by Kobayashi, which may be the earliest modern research report on the chemical constituents of *Cistanche*. Until now, 213 compounds, including PhGs, benzyl glycosides, phenylacylated oligosugars, iridoids, monoterpenoids, lignans, sterols, alkaloids, polysaccharides and other compounds, have been obtained from *Cistanche* plants. Among them, PhGs account for the largest proportion relative to the other types of compounds. Chemical structures that have previously been reported from *Cistanche* plants are shown in Figs. 1–9.

2.1. PhGs PhGs have been thought to be the primary active components in the *Cistanche* species. They are a type of phenolic compound characterized by a *β*-glucopyranoside structure bearing a hydroxy phenylethyl moiety as the aglycone. This kind of compound commonly includes a number of acyl groups, such as cinnamic acid, *p*-coumaric acid, caffeic acid, ferulic acid, and isoferulic acid, and various sugars, such as rhamnose and xylose, that are attached to the glucose residue through ester or glycosidic linkages, respectively. In the past few decades, 85 PhGs including 6 monosaccharide glycosides, 52 disaccharide glycosides, and 27 trisaccharide glycosides (Table 1) have been reported in *Cistanche* plants. The structures of PhG compounds are presented in Fig. 1. Generally, monosaccharide glycosides only contain a glucosyl linked at the C-8 position of the phenylethanol. The disaccharide glycosides generally contain a Rha (1→3) Glc linkage. In the trisaccharide glycosides, there is another glucose or rhamnose at the C-6 position of the inside glucose.

2.2. Benzyl Glycosides Lei *et al.* obtained four benzyl glycosides from *C. salsa* for the first time in 2007.[47] Then, in 2013, another three benzyl glycosides were isolated and identified from *C. deserticola*.[44] The structures of the benzyl glycosides are similar to those of the PhGs. The glucosyl often links directly to the benzyl alcohol aglycone, and a coumaroyl or caffeoyl group is usually located at the glucosyl C-4 or C-6 position (Fig. 2; Table 2).

2.3. Phenylacylated Oligosugars To date, nine phenylacylated oligosugars have been obtained from the genus *Cistanche* (Fig. 3; Table 3). In these phenylacylated oligosugars, the sugar moiety consists of glucose and rhamnose connected by a Rha (1→3) Glc linkage, and there is generally a coumaroyl or caffeoyl group linked at the glucosyl C-4 position. Occasionally, an additional glucosyl moiety is linked at the glucosyl C-6 position.

2.4. Iridoids Iridoids are a type of monoterpenoid



86 R_1 = Rha, R_2 = H, R_3 = Cf, R_4 = H, R_5 = H
87 R_1 = Rha, R_2 = Cf, R_3 = H, R_4 = H, R_5 = H
88 R_1 = Rha, R_2 = Cm, R_3 = H, R_4 = H, R_5 = H
89 R_1 = Rha, R_2 = *c*-Cm, R_3 = H, R_4 = H, R_5 = H
90 R_1 = H, R_2 = H, R_3 = H, R_4 = OMe, R_5 = OMe
91 R_1 = H, R_2 = H, R_3 = H, R_4 = H, R_5 = OH
92 R_1 = H, R_2 = H, R_3 = H, R_4 = H, R_5 = H

Fig. 2. Benzyl Glycosides from *Cistanche* Species

Table 2. Benzyl Glycosides from *Cistanche* Species

No.	Compound	Source	References
86	Salsaside A	*Csa*	47)
87	Salsaside B	*Cd*, *Csa*	44, 47)
88	Salsaside C1	*Csa*	47)
89	Salsaside C2	*Csa*	47)
90	3,4-Dimethoxybenzyl-*β*-D-glucoside	*Cd*	44)
91	4-Hydroxybenzyl-*β*-D-glucoside	*Cd*	44)
92	Benzyl-glucopyranoside	*Cd*	44)

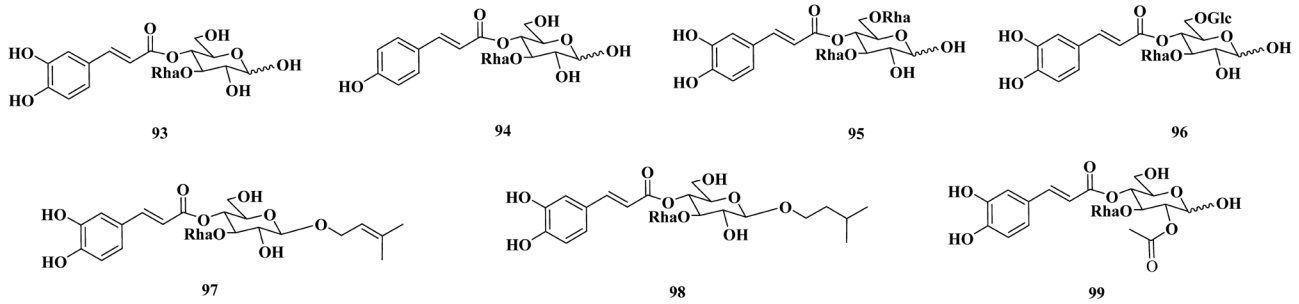


Fig. 3. Phenylacylated Oligosugars from *Cistanche* Species

Table 3. Phenylacylated Oligosugars from *Cistanche* Species

No.	Compound	Source	References
93	Cistanoside F	*Cd*, *Ct*	31, 34, 36, 37, 41, 55, 56)
94	Cistanoside I	*Cd*	32)
95	Cistansinensose A1/A2	*Csi*	42)
96	Kankanose (Cistantubulose A1/A2)	*Ct*	31, 37, 41)
97	Cistansalside B	*Csa*	51)
98	Cistansalside C	*Csa*	51)
99	*α*-L-Rhamnopyranosyl-(1→3)-2-*O*-acetyl-(4-*O*-caffeoyl)-*O*-*β*-glucopyranoside	*Cd*	57)

Table 4. Iridoids from *Cistanche* Species

No.	Compound	Source	References
100	Bartsioside	*Cd*, *Ct*	58, 59)
101	6-Incatalpol	*Cd*, *Ct*, *Cp*	11, 35, 39, 59, 60)
102	Catalpol	*Cd*, *Ct*	38)
103	8-Epideoxyloganic acid	*Cd*, *Ct*, *Csi*	24, 59, 61)
104	8-Epiloganic acid	*Cd*, *Ct*, *Csa*, *Csi*	11, 24, 27, 35, 60, 62–65)
105	8-Epiloganin	*Ct*	24, 42)
106	Geniposide	*Cd*, *Csi*	24, 42, 66)
107	Geniposidic acid	*Cd*, *Ct*, *Csi*, *Csa*	58, 59, 61, 64)
108	Gluroside	*Cd*, *Ct*, *Cp*	39, 58, 59, 61)
109	Leonuride	*Cd*, *Ct*, *Cp*, *Csi*, *Csa*	24, 39, 58, 59, 65)
110	Mussaenosidic acid	*Cd*, *Ct*	58, 59, 61, 64)
111	Adoxosidic acid	*Ct*	64)
112	Kankanoside A	*Cd*, *Ct*	50, 58, 61)
113	Kankanoside B	*Ct*	58)
114	Phelypaeside	*Cp*	39)
115	Kankanoside C	*Ct*	58)
116	Kankanoside D	*Ct*	58)
117	Antirrhide	*Ct*	58)
118	Kankanoside L	*Ct*	61)
119	Kankanoside M	*Ct*	61)
120	Kankanoside N	*Ct*	61)
121	Mussaenoside	*Csi*	24)
122	Cistadesertoside A	*Cd*	67)
123	Cistachlorin	*Cd*, *Ct*	58, 66)
124	Cistanin	*Cd*, *Ct*	38, 58, 66)
125	Kankanol	*Ct*	58)
126	Argyol	*Ct*	58)

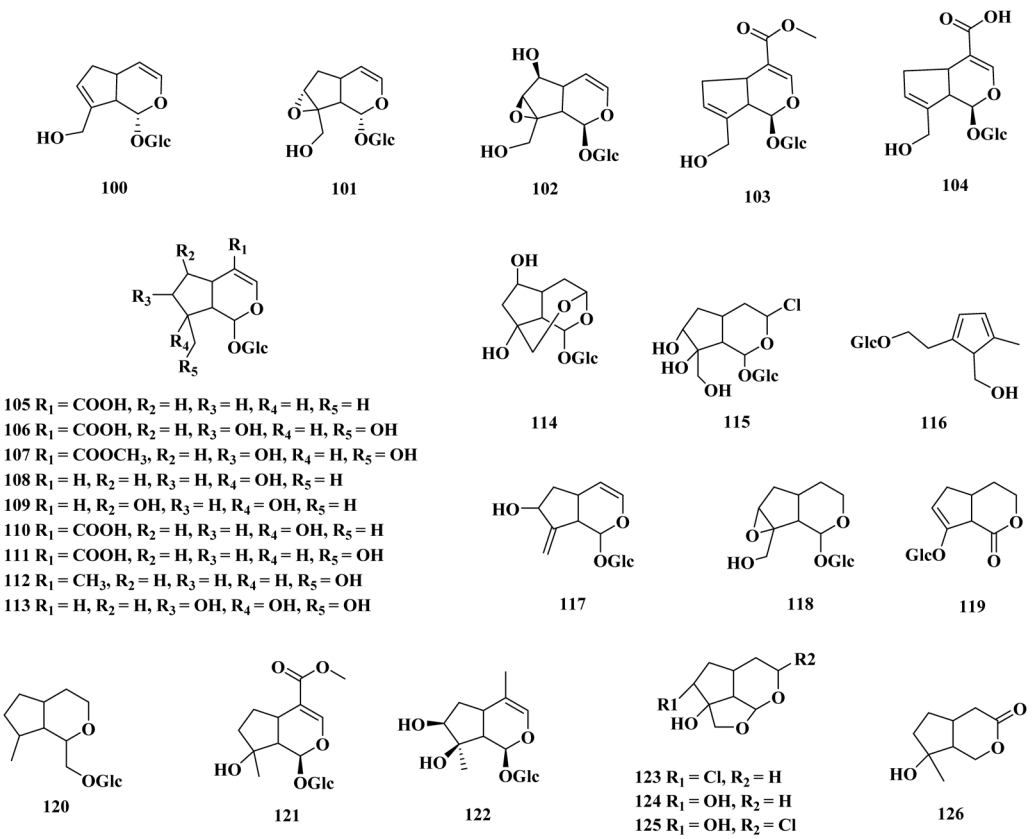


Fig. 4. Iridoids from *Cistanche* Species

constructed from a 10-carbon skeleton of isoprene building units with a cyclopentanopyran ring system. During structure identification and elucidation studies of iridoid constituents from the *Cistanche* species, 4 iridoid aglycones and 23 iridoid glycosides were isolated (Table 4; Fig. 4). Their structural features can be summarized as follows. A glucosyl is generally linked at the aglycone C-1 position, a carboxyl is usually linked at the aglycone C-4 position and H-5 and H-9 are *β*-oriented. Hydrogenation accidentally appears at C-3 and C-4 whereas hydroxylation often occurs at C-6, C-7, C-8 and C-10. Sometimes, dehydration may occur between the C-10 hydroxyl and that at C-1 or C-3 to form an epoxy substructure.

2.5. Monoterpenoids To date, 14 monoterpenoids have been isolated from *Cistanche* plants, among which 4 are monoterpenes and 10 belong to monoterpene glycosides (Table 5; Fig. 5). Their structural characteristics can be summarized as follows: a methyl is generally linked at the aglycone C-2 or C-6 position and a double bond occurs between C-2 and C-3. The positions between C-6 and C-7 or between C-7 and C-8 also often have a double bond. Hydroxyl or carboxyl groups

Table 5. Monoterpenoids from *Cistanche* Species

No.	Compound	Source	References
127	(*2E*)-2,6-Dimethyl-2,7-octadiene-1,6-diol	*Cd*	62)
128	(*2E,6R*)-8-Hydroxy-2,6-dimethyl-2-octenoic acid	*Ct*, *Csa*	68)
129	(*2Z*)-2,6-Dimethyl-2,7-octadiene-1,6-diol	*Cd*	62)
130	8-Hydroxygeraniol	*Ct*	64)
131	(*2E,6E*)-8-Hydroxy-2,6-dimethyl-2,6-octadien-1-yl-*O*-*β*-D-glucopyranoside	*Ct*	61)
132	(*2E,6Z*)-8-*O*-*β*-D-Glucopyranosyloxy-2,6-dimethyl-2,6-octadienoic acid	*Ct*	58, 61)
133	8-Hydroxygeraniol-8-*O*-*β*-D-glucopyranoside	*Ct*, *Csa*	61, 69)
134	8-Hydroxygeraniol 1-*β*-D-glucopyranoside	*Cd*, *Ct*, *Csa*	35, 62, 69)
135	Betulalbuside A	*Ct*	61)
136	Kankanoside E	*Ct*	58, 61)
137	Kankanosides O	*Ct*	61)
138	Kankanosides P	*Ct*	61)
139	2,6-Dimethyloctan-1,8-diol diglucoside	*Cd*	57)
140	(*2E,6E*)-3,7-Dimethyl-8-hydroxyoctadien-1-yl-*O*-*β*-D-glucopyranoside	*Ct*	61)

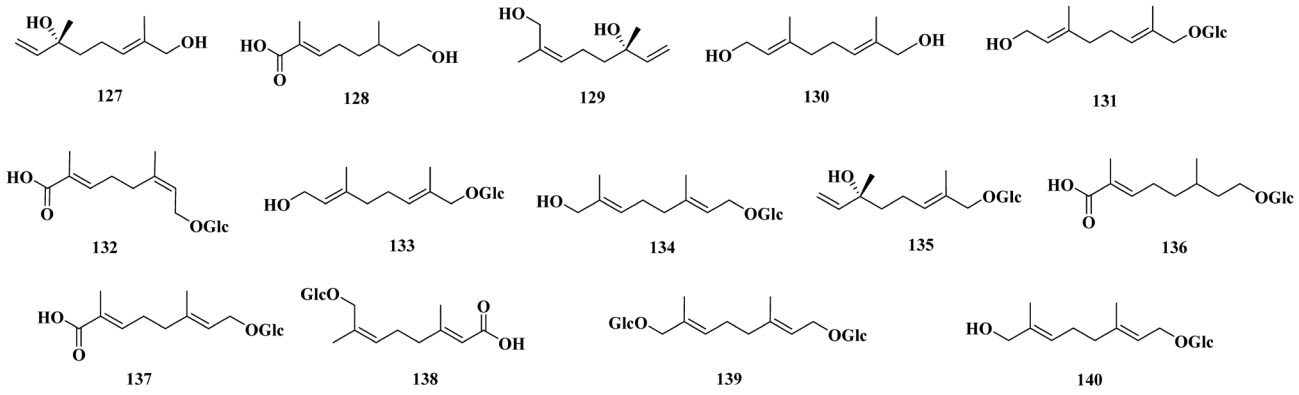


Fig. 5. Monoterpenoids from *Cistanche* Species

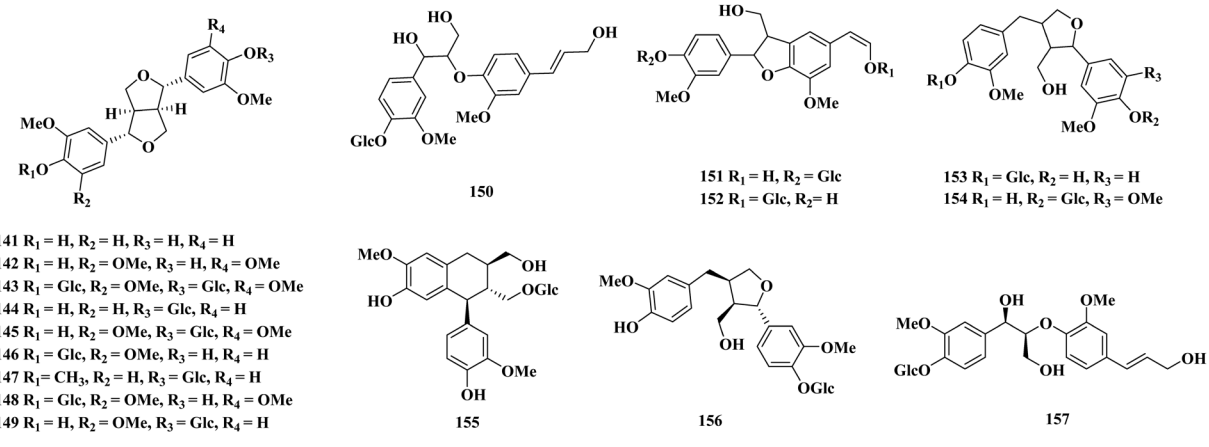


Fig. 6. Lignans from *Cistanche* Species

Table 6. Lignans from *Cistanche* Species

No.	Compound	Source	References
141	(+)-Pinoresinol	*Cd*, *Ct*	30)
142	(+)-Syringaresinol	*Cd*	50)
143	Liriodendrin	*Cd*, *Ct*	11, 29, 35, 55, 60)
144	(+)-Pinoresinol-*O*-*β*-D-glucopyranoside	*Ct*	35)
145	(+)-Syringaresinol-*O*-*β*-D-glucopyranoside	*Cd*, *Ct*	35, 50, 55, 64)
146	Eucommin A	*Cd*, *Ct*	50, 61)
147	(+)-Pinoresinol-monomethylether-*β*-D-glucoside	*Cd*	50)
148	(+)-Syringaresinol-4′-*O*-*β*-D-glucoside	*Cd*	70)
149	Isoeucommin A	*Cd*, *Ct*	50, 61)
150	Citrusin A	*Cd*	50)
151	Dehydrodiconiferyl alcohol 4-*O*-*β*-D-glucopyranoside	*Cd*, *Ct*	35, 50)
152	Dehydrodiconiferyl alcohol *γ*′-*O*-*β*-D-glucopyranoside	*Cd*, *Ct*	35, 50)
153	Lariciresinol-4′-*O*-*β*-D-glucopyranoside	*Cd*	50)
154	Conicaoside	*Cd*	50)
155	Isolariciresinol-9′-*O*-*β*-D-glucopyranoside	*Csi*	24)
156	Lariciresinol-4-*O*-*β*-D-glucopyranoside	*Cd*	50)
157	Alaschanioside A	*Cd*	50)

Table 7. Sterols from *Cistanche* Species

No.	Compound	Source	References
158	*β*-Daucosterol	*Cd*, *Csa*, *Ct*	27, 38, 60, 63, 66, 69)
159	*β*-Sitosterol 3-*O*-*β*-D-xylopyranoside	*Cd*	50)
160	*β*-Sitosterol	*Cd*, *Cp*, *Csa*, *Ct*	27, 38, 39, 66)
161	*β*-Sitosteryl glucoside 3′-*O*-heptadecoicate	*Cd*, *Csa*	60, 69)
162	20-Hydroxyecdysone	*Ct*	35)

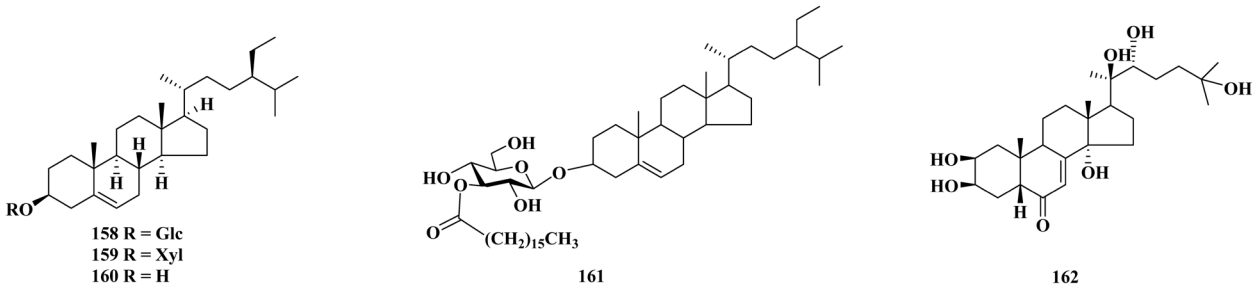


Fig. 7. Sterols from *Cistanche* Species

are often linked at the C-1 position and a hydroxyl is usually linked at C-8 in monoterpenes. Monoterpene glycosides are all monoglycosides that only contain a glucosyl linked at the aglycone C-1 or C-8 position.

2.6. Lignans Until now, there have been 2 lignan aglycones and 15 lignan glycosides purified from *Cistanche* plants (Table 6; Fig. 6).

2.7. Sterols Sterols are relatively rare in *Cistanche* plants, and only five such compounds have been reported in this genus (Table 7). The structures of the sterol compounds are presented in Fig. 7.

2.8. Alkaloids *Cistanche* plants also contain alkaloids, and approximately 19 compounds have been found and elucidated (Fig. 8; Table 8).

2.9. Other Types of Compounds Some other compounds, such as phenolic glycosides, flavonoids, and long-chain fatty acid derivatives, have been isolated from *Cistanche* plants (Table 9; Fig. 9). A considerable proportion of polysaccharides have also been reported in *Cistanche* species.[75] A large number of studies have shown that the polysaccharides are regarded as active constituents to advance body immunity and show antiaging and anticancer activities in Herba *Cistanche*.[76–78]

3. Pharmacology

Cistanches Herba has wide medicinal uses as a kind of TCM. Many researchers have investigated its pharmacological actions in traditional records and have validated its therapeutic potential in modern methods. Biological activity studies have shown that *Cistanches* Herba exhibits a wide spectrum of pharmacological activities such as antioxidation, antisenile dementia, anti-Parkinson's disease, immunoregulation, antiaging, hepatoprotection, and antimyocardial ischemia effects, which may mainly be attributed to its bioactive components, including PhGs, polysaccharides and so on. As the major active components in *Cistanche* plants, components **2** and **11** were selected as reference substances for quality control in

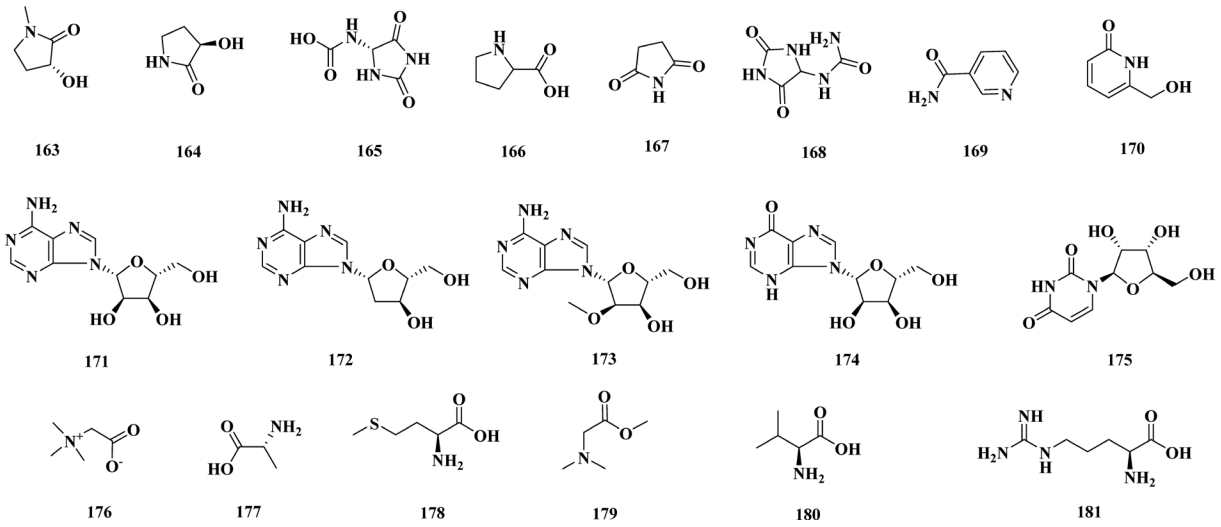


Fig. 8. Alkaloids from *Cistanche* Species

Table 8. Alkaloids from *Cistanche* Species

No.	Compound	Source	References
163	(*3R*)-3-Hydroxy-1-methyl-2-pyrrolidinone	*Ct*	58)
164	(*3R*)-3-Hydroxy-2-pyrrolidinone	*Ct*	58)
165	2,5-Dioxo-4-imidazolidinyl-carbamic acid	*Cd*, *Csa*	13, 38)
166	DL-Proline	*Cd*	71)
167	Succinimide	*Csa*	13)
168	Allantoin	*Cd*	40, 72)
169	Nicotinamide	*Cd*	50)
170	2-Methanol-5-hydroxy-pyridine	*Csa*	69)
171	Adenosine	*Cd*	50, 72)
172	2'-Deoxyadenosine	*Cd*	55)
173	2′-*O*-Methyladenosine	*Cd*	55)
174	Inosine	*Cd*	55)
175	Uridine	*Ct*	58)
176	Betaine	*Cd*, *Csa*	38, 69, 73, 74)
177	D-Alanine	*Cd*, *Ct*	72)
178	L-Methioinicnine	*Cd*, *Ct*	72)
179	*N*,*N*-Dimethylglycine methyl ester	*Ct*	56)
180	Valine	*Cd*, *Ct*	72)
181	L(+)-Arginine	*Cd*, *Ct*	72)

Chinese Pharmacopoeia. And it is stipulated that the total content of these two compounds should not less than 0.30 and 1.5% in *C. deserticola*, *C. tubulosa*, respectively, which may indicate the varying pharmacological reactions that based on PhGs.[86] Nevertheless, it is insufficient to evaluate the quality of *Cistanche* herbs only based on these two PhGs compounds due to they could not represent the other effective PhGs ingredients. Until now, dozens of bioactive PhGs have been used as reference substances for quality evaluation of *Cistanche* herbs even their corresponding formulations.[87] A method of RPLC-hydrophilic interaction chromatography (HILIC)-MS/MS for the 23 analytes, including three organic acids, four nucleosides, two sugars, one amino acids, one benzylglucoside, two lignans, seven PhGs and three iridoids, was conducted in *C. tubulosa* by Yan *et al.* in 2017, and the results showed that those 23 components exhibited wide content ranges and significant variations among 20 batches of *C. tubulosa*, of which compounds **2**, **11**, and **202** were abundant in content, whereas ferulic acid showed trace distributions in these 20 batches.[88] In 2018, Dong *et al.* conducted a comparison of the seven PhGs including compounds **1**, **2**, **3**, **5**, **11**, **12** and **67** between *C. deserticola* and *C. tubulosa* by only one marker using a new calculate method of relative correction factor. The analysis results showed that chemical compositions and content of these 7 PhGs were quite different.[89] In 2019, Zhang *et al.*[90] analyzed the changes of the total PhGs, total polysaccharides and four PhGs content in raw product of *C. deserticola* and its processed product by using UV spectrophotometry method, the phenol-sulfuric acid method and HPLC method, respectively. The results exhibited that the processed *C. deserticola* has higher amounts of total polysaccharides, total PhGs, compounds **12** and **14** than raw *C. deserticola*, while the content of compounds **1** and **2** decreased after processing. Moreover, there are also many other research on the quantitative analysis of *Cistanche* Herba due to their obvious and remarkable pharmacological activity.[91–97] It should be affirmed that the related

Table 9. Other Types of Compounds from *Cistanche* Species

No.	Compound	Source	References
182	*E*-Coniferin	*Cd*, *Ct*	50, 61)
183	Syringin	*Cd*, *Ct*, *Cp*	30, 35, 38, 39, 61)
184	Demethyl syringing	*Cd*	50)
185	Sinapic aldehyde 4-*O*-*β*-D-glucopyranoside	*Ct*	61)
186	Sinapaldehyde glucoside	*Ct*	46)
187	Vanillic acid	*Csa*	43)
188	P-Hydroxybenzoic acid	*Cd*	50)
189	P-Coummaric acid	*Cd*	57)
190	3-(2′-*β*-*O*-Pyranoglaucoside)-phenyl-2-transpropenoic acid	*Csa*	79)
191	Androsin	*Cd*	50, 72)
192	4-Hydroxy-benzeneethanol	*Cd*	50)
193	4-Hydroxybenzyl-*β*-D-glucoside	*Cd*	80)
194	Ononin	*Cd*	40)
195	1-*O*-Hexadecanoyl-3-*O*-*β*-D-galactopyranosyl glycerol	*Cd*	50)
196	Triacontanoic acid	*Cd*	72, 81)
197	Stearic acid	*Cd*	38)
198	1-Triacontanol	*Cd*	73, 81, 82)
199	Panaxytriol	*Cd*	50)
200	2-Nonacosanone	*Cd*	81)
201	*2S,3S,4S*-Trihydroxypentanoic acid	*Cd*	80)
202	D-Mannitol	*Cd*, *Ct*, *Csa*	27, 38, 63, 66, 83)
203	Galactitol	*Cd*, *Ct*, *Csi*, *Csa*	11, 40, 42, 60)
204	3-Methyl-but-2-en-1-yl-*β*-D-giucopyranoside	*Cd*	50)
205	3-Methylbutanol *β*-D-glucopyranoside	*Ct*	31)
206	Ethyl *β*-D-glucopyranoside	*Ct*	31)
207	D(−)-Fructose	*Ct*	84)
208	D(+)-Glucose	*Cd*, *Ct*, *Csa*	29, 60, 84, 85)
209	Succinic acid	*Cd*, *Ct*, *Csa*	66, 73, 82, 84, 85)
210	D(+)-Sucrose	*Cd*	29, 60)
211	*n*-Butyl-*α*-D-fructofuranoside	*Cd*	50)
212	(±)-*γ*-Valerolactone	*Cd*	60)
213	Phelypaeside	*Cp*	39)

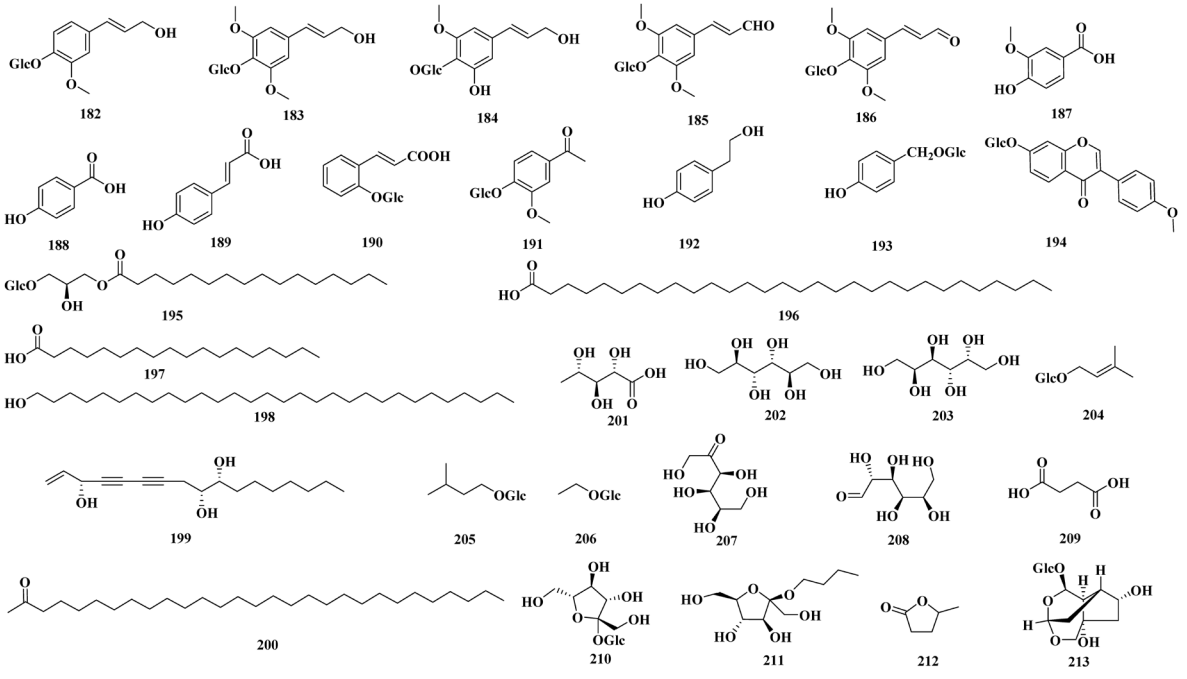


Fig. 9. Other Types of Compounds from *Cistanche* Species

quantitative research on the active ingredients of *Cistanche* has laid a solid foundation for its related research on pharmacological activities.

3.1. Antioxidation Antioxidation activity is against free radicals. Antioxidant drugs can reduce the damage of oxygen free radicals to the blood vessel wall, thus playing an antiarterial sclerosis role. Shi *et al.*[98] first found that extracts from *Cistanche* species had a lipid peroxidation suppression-effect and an immunological enhancement effect. The PhGs from *Cistanches* Herba could obviously lower the levels of lipid hydroperoxide in humans, which was regarded as effective for antioxidative activity.[99,100] The phenolic hydroxyl group in PhGs is necessary for the antioxidant activity. A study found that because of the phenolic hydroxy structure, PhGs can combine with free radicals and activate antioxidant defense systems, and by increasing the number of phenolic hydroxyl groups, the antioxidant activity is increased.[34] In another study, Cistanche glycosides showed inhibitory effects on lipid hydroperoxide and thromboxane production in rabbit blood, revealing that these glycosides had protective effects against hemorrhagic shock and reperfusion injury.[101] Wu *et al.*[102] found that PhGs from *C. salsa* possessed very high antioxidant activities. Other studies found that PhGs from *C. deserticola* dramatically increased super oxide dismutase activities, which decreased malondialdehyde levels in mouse hearts, livers, and brains; thus, the authors believed that PhGs could protect skeletal muscles from oxidative injury by eliminating the over-accumulation of free radicals.[103] Researchers focused attention on natural antioxidants to combat diabetic-nephropathy disease, and study results have indicated that PhGs from *C. deserticola* could inhibit reactive oxygen free radicals *in vitro* and repair free radical damage related to diabetic nephropathy.[104] Liang *et al.*[105] pointed out that PhGs extracted from Herba *Cistanche* had protective effects on human sperm DNA with oxidative damage in 2015. Compound **18** obtained from *Cistanche* plants could increase pheochromocytoma cell (PC12 cell) viability against H_2O_2-induced cytotoxicity and decrease the apoptotic rate at the same time.[106] Wang and Zhao[107] established the antioxidant activity of *C. deserticola* polysaccharides *in vitro* and found that polysaccharides could obviously scavenge free radicals including the hydroxyl radical, superoxide anion radical, singlet oxygen and diphenyl acyl. In 2016, an efficient ultrasonic-cellulase-assisted extraction of *C. tubulosa* polysaccharides was established, and its polysaccharides showed appreciable antioxidant activity.[108] Another study pointed out that polysaccharides from *C. tubulosa* also had great antioxidant activities when evaluated for diphenyl acyl and hydroxyl radicals as well as the scavenging ability of copper ions *in vitro*.[109] In summary, PhGs and polysaccharides in *Cistanche* plants are the main antioxidants.

3.2. Anti-Alzheimer's Disease AD is one of the most harmful neurological diseases facing elderly individuals and is the focus of much research. As a TCM, studies have proven that water and alcohol extracts of *Cistanches* Herba have good anti-Alzheimer's effects. The Consumer Price Index database of China announced that glycosides in Cistanche and Cistanche Yizhi capsules are authorized for the treatment of AD.[110] Nerve growth factor (NGF) can enhance memory function, and Korea scholars[111] found that *Cistanches* Herba could stimulate NGF secretion, improving cognitive behaviors related to memory abilities. An intracisternal infusion of amyloid β peptide 1–42 ($A\beta_{1-42}$) into rats was primarily deposited in the frontal cortex and hippocampus, causing memory deficits in behavioral tasks and inducing an AD-like pathology. The extracts from *C. tubulosa* have been proven to reduce cognitive impairment caused by $A\beta_{1-42}$ by reversing cholinergic neuronal function and blocking amyloid deposition.[112] Amyloid β peptide 25–35 ($A\beta_{25-35}$) neurotoxicity can lead to cholinergic system damage, which is an important determinant of cognitive dysfunction. AD. Luo[113] explained the effects and mechanism of Cistanche glycosides in a rat model of AD induced by $A\beta_{25-35}$, proposing that PhGs could decrease acetylcholinesterase activities and Ca^{2+} contents in the hippocampus in AD model rats, which would promote normal acetylcholine levels and improve the learning and memory capabilities of AD rats.[114] Additionally, *C. tubulosa* extract, which contains PhGs, similar to compounds **2** and **11**, could ameliorate the cognitive dysfunction caused by $A\beta_{1-42}$ *via* blocking amyloid deposition and reversing cholinergic and hippocampal dopaminergic neuronal function.[115] Li *et al.*[116] evaluated the neuroprotective effects of *Cistanches* Herba on AD patients and found that the levels of total tau protein, tumor necrosis factor-α, and interleukin-1β were decreased in the *Cistanches* Herba capsule group, which proved that this plant has potential neuroprotective effects for AD. PhGs have protective effects on cognitive dysfunction by improving synaptic plasticity in an AD rat model. Jia *et al.*[117] revealed that this AD protective mechanism may inhibit cytotoxicity mediated by $A\beta_{1-42}$ administration and reduce oxidant stress. Another experiment also found that PhGs protect neurons by lowering the expression of $A\beta_{1-42}$ and $A\beta_{1-40}$ protein in the mouse hippocampus. All of these results provide theoretical support for the further development of new drugs against AD.[118]

3.3. Anti-Parkinson's Disease PD is a chronic neurodegenerative disorder characterized by the progressive loss of dopaminergic neurons in the substantia nigra, and its main clinical manifestations include dyskinesia, muscle stiffness, postural instability and resting tremors.[119] To date, the etiology of PD has not been fully revealed. However, previous studies consider oxidative stress due to the cellular dysfunction between the production and scavenging of free radicals as the primary mechanism associated with neuronal death.[110] Echinacoside (**11**), a PhG compound, has been proven by many studies to have anti-PD effects. This compound showed neuroprotection in PD mice induced with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP).[120] Geng *et al.*[121] found that compound **11** could improve the behavioral and neurochemical outcomes in a MPTP mouse model of PD, which suggested that it can be used as a therapeutic compound for PD. Moreover, Chen *et al.*[122] also concluded that compound **11** could protect striatal dopaminergic neurons by increasing the levels of monoamine neurotransmitters including dopamine, 3,4-dihydroxyphenylacetic acid, and homovanillic acid in 6-hydroxydopamine (6-OHDA) lesion rats and may be useful in the prevention and treatment of PD. Compound **11** also protected PC12 cells against 6-OHDA by increasing the mitochondrial membrane potential while decreasing the mitochondria-mediated apoptosis rate, which reduced cytotoxicity and produced a significant neuroprotective effect.[123] Furthermore, acteoside (**2**), an isomer of compound **11**, is another important active PhG compound from *Cistanche* species that showed

anti-PD potential by inhibiting 1-methyl-4-phenylpyridinium ion (MPP^+)-induced SH-SY5Y cell apoptosis; the mechanism of action was also elucidated.[124] Additionally, compound **2** also had a significant protective effect on MPP^+-induced cerebellar granule neurons, which may be due to the inhibition of active caspase-3 and proteolytic poly polymerase fragment expression.[125] Compounds **18** and **37**, which are bioactive compounds from *Cistanche* plants, have also been indicated to possess effective neuroprotective effects against PD.[126,127]

3.4. Endocrine Regulation Activities Androgen play a key role in the development of male reproductive tissues, and its imbalance can cause kinds of symptoms, including kidney-yang deficiency. As we all know, *Cistanches* Herba is one of the most frequently used tonic drugs in the prescription for invigorating the kidney-yang. Research has confirmed that there are two main ways to replenish the kidney-yang. One is by enhancing the function of the hypothalamus–pituitary–adrenal axis and promoting the release of related neurotransmitters and hormones in body, the other is by fighting fatigue and improving physical function.[128] *Cistanche* can increase the number of pituitary cells, promote the secretion of ovarian progesterone, enhance the expression of estrogen receptor and progesterone receptor of gonadal axis, and inhibit the expression of interleukin-2 receptor in ovaries and interstitial. At the same time, it also can stimulate the production of androgen due to the result of one test that the index of prostate and testis increased significantly in the castrated mice group compared with healthy group.[129–132] PhGs in *Cistanche* have some intervention on lipid peroxidation damage of sperm membrane in test rats, and they also play a protective role in the structure and function of sperm membrane.[133] Studies have shown that PhGs has obvious therapeutic effect on spermatogenic disorders induced by cyclophosphamide in mice, and its mechanism may be related to the improvement of testosterone level in testis.[134] PhGs have the function of inhibiting the disorder of sexual hormones in perimenopausal model rats and mice, adjusting the imbalance of androgen receptor and estrogen receptor and improving the pathological changes of uterus, thymus, spleen and pituitary.[135] In addition, decoction of *Cistanche* can improve the anti-fatigue effect of yang deficiency mice.[136] In 2004, Pan and Min[137] found that the alcohol extracts from *Cistanche* could prevent atrophy of the adrenal cortex in mice with kidney-yang deficiency, and also had a certain protective effects on renal function. Wu *et al.*[138] thought that *C. deserticola* and *C. tubulosa* both had certain tonic effect on kidney-yang, and their decoction could significantly increase the weight and obviously prolong the cold tolerance time of kidney yang deficiency model mice. *C. deserticola* decoction was reported to be able to increase the content of serum testosterone and the weight of seminal vesicles and the prostate gland in male rats.[139] In another research, *C. deserticola* decoction eased the reproductive toxicity in male rats caused by Leigongteng glycoside.[140] Jiang *et al.*[141] pointed out that a 70% ethanol extract of *C. tubulosa* could reverse testicular and sperm damage in Sprague-Dawley (SD) rats by upregulating steroidogenesis enzymes in the gonad axis, and compound **11** was one of the active constituents. Moreover, Wang *et al.*[142] found that *C. tubulosa* extracts could improve SD rat progesterone and testosterone levels. In 1996, Zong *et al.*[143] researched the androgen-like action on male rats and the effect on phagocytosis of peritoneal macrophages in female mice using *C. deserticola*, *C. tubulosa* and *C. deserticola* that soaked in water for 2 d in order to compare their pharmacological effects. The results showed that *C. tubulosa* could significantly increase the weight of the anterior space of spermatic sac in castrated rats compared with the other two plants. As for the function on phagocytosis of peritoneal macrophages, *C. deserticola* and *C. tubulosa* were similar which both could obviously increase the phagocytic activity. The results of this study may highly be related to the water-soluble compounds with androgen-like effects in these plants. In the same year, a comparison of pharmacological effects of tonifying kidney yang on mice model of yang deficiency caused by hydrocortisone was conducted. The results showed that *C. salsa* decoction had the best effect, *C. deserticola* decoction took the second place, and *C. tubulosa* decoction had the worst effect, which was related to the difference in the content of the three plant medicinal ingredients.[144] Wu *et al.*[145] studied the pharmacological effects of *C. deserticola* and *C. tubulosa* on defecation and invigorating yang, and found that the water extracts of them both had certain laxative effects, and could significantly shorten the defecation time of animals. For the kidney-yang deficiency mice, the cold tolerance time of the mice were both prolonged. So they drew a conclusion that *C. tubulosa* can be used instead of *C. deserticola* when the current resources of *C. deserticola* are rapidly reduced. Studies have shown that the ethanol extracts of *Cistanche* can significantly increase the weight of testis and seminal vesicle prostate of castrated young mice and rats, the water decoction can improve the phagocytic function of peritoneal macrophages of mice. So the hormonal-like effect, androgen-like effects and non-specific immune function of *C. deserticola* were confirmed.[146]

3.5. Antidepressant A large amount of evidence suggests that depression, a neuropsychiatric disorder, is linked with the gut microbiome through the gut-brain axis. Iridoids from Herba *Cistanche*, such as Catalpol (**102**) and Geniposide (**106**), have been found to ameliorate chronic unpredictable stress-induced depression-like behaviors, while compound **102** can also upregulate brain-derived neurotrophic factor expression.[147,148] Through experiments, Wang *et al.*[149] found that decoctions of *C. deserticola* and *C. tubulosa* exhibited antidepressant effects and improved spatial learning and memory abilities in a mouse model, which strongly suggests that *Cistanche* species possess potential antidepressant-like qualities. Moreover, extracts from *C. tubulosa* can restore brain levels of 5-hydroxytryptamine and brain-derived neurotrophic factor expression in a rat depression model induced by chronic unpredictable stress, and significantly improved depression-like behaviors.[53] Li *et al.*[150] investigated the metabolism of a *C. tubulosa* extract in normal and chronic unpredictable stress-induced depressive rats, and the results contributed to understanding the therapeutic mechanism of antidepressant properties.

3.6. Anti-osteoporosis Activities Osteoporosis is a very common chronic disease. This disease is often characterized by low bone mass, which is most commonly seen in middle aged and elderly people, especially women; for example, the loss of estrogen is thought to be the major reason for bone loss in postmenopausal woman. A previous research indicated that *Cistanches* Herba can guide bone mesenchymal stem cells to differentiate into osteoblasts, which leads to good prospects for

the treatment of osteoporosis and bone fracture disunion.[151] Liang *et al.*[152] reported that a water extract of *Cistanches* Herba could reverse bone loss and prevent the occurrence of osteoporosis in female rats. Chen *et al.*[153] pointed out that *Cistanches* Herba polysaccharides may accelerate the bone marrow cell cycle transition, promote the recovery of hematopoietic function in bone marrow-depressed anemic mice, and expedite hematogenesis in rubrum and macronucleus strains. By combining the *in vivo* and *in vitro* experimental data, compound **11** isolated from *C. tubulosa* has remarkable activity against osteoporosis.[154,155] Li *et al.*[156] used Western blotting to investigate the mechanism of action of *C. deserticola* extract and concluded that *C. deserticola* may be a novel bone formation agent for the treatment of osteoporosis. In 2013, another researcher aimed to elucidate the molecular mechanism of *Cistanches* Herba aqueous extracts on postmenopausal osteoporosis in an ovariectomized rat model and concluded that *Cistanches* Herba has a protective effect against bone degeneration by partially regulating some bone metabolism-related genes.[157] Xu *et al.*[158] focused their attention on Cistanoside A (**3**), a compound from *C. deserticola*, for osteoporosis treatment. Their study revealed that compound **3** could promote bone formation by downregulating TNF-receptor-associated factor 6 and coordinating the inhibition of nuclear factor kappa-light chain enhancer in activated B cells and stimulation of the phosphatidylinositol 3-kinase/Akt pathway.

3.7. Hepatoprotective Activities The liver plays a key role in detoxifying the body and synthesizing useful substances. Hepatic fibrosis is a pathophysiological process considered as the wound-healing response of the liver to various toxic stimuli, such as hepatitis, alcohol and immunostimulant compounds, and the long-term development of fibrosis may lead to serious disease consequences. However, despite the high incidence of liver fibrosis worldwide, there is no generally accepted anti-fibrosis therapy to date. Previous studies focused on the preventive and therapeutic effects of PhGs on bovine serum albumin-induced hepatic fibrosis in rats have provided a direction for the treatment of this disease. An experiment on the hepatoprotective effects of four PhGs, namely, compounds **1, 2, 12**, and **18**, on both carbon tetrachloride- and D-galactosamine-induced hepatotoxicity *in vitro*, as well as the effects of compound **2** against carbon tetrachloride-intoxication *in vivo*, showed that these four PhGs all possessed hepatoprotective activities.[159] Morikawa *et al.* from Japan found that acylated phenylethanoid oligoglycosides from fresh stems of *C. tubulosa* showed hepatoprotective effects in 2010.[37] The ability to block carbon tetrachloride bioactivation and free radical scavenging effects may be the mechanisms of compound **2** against carbon tetrachloride-induced hepatotoxicity, which was confirmed by the scholars of South Korea.[160] In another study, free radical damage of the liver caused by carbon tetrachloride in rats was tested with compound **11**, and the results showed that serum alanine aminotransferase and aspartate aminotransferase levels, hepatic malondialdehyde contents, and reactive oxygen species production were reduced dramatically. Additionally, histopathological damage to the liver and the number of apoptotic hepatocytes were all distinctly ameliorated.[161] By increasing free radical-clearing activities, alleviating lipid-overoxidation damage, and improving respiratory chain function in the mitochondria, compound **3** could protect the liver from carbon tetrachloride-induced hepatotoxicity in mice.[162] Moreover, Luo *et al.*[163] also demonstrated that compound **3** could enhance the survival rate of primary cultured hepatocytes and alleviate apoptosis and necrosis. By inhibiting apoptosis and inflammation, compound **11** could provide a pronounced protection against D-galactosamine-induced acute liver injury in mice.[164] You *et al.*[165] demonstrated that compounds **2** and **11** can block transforming growth factor-β1 signaling pathways and inactivate hepatic stellate cells, indicating that *C. tubulosa* may be a potential herbal medicine for the treatment of liver fibrosis. Guo *et al.*[166] discovered that polysaccharides from *C. deserticola* possessed hepatoprotective activities against chronic hepatic injury induced by alcohol, and the underlying mechanism was also proposed. Recent studies have proven that PhGs possess hepatoprotective properties against alcohol-induced chronic hepatic disease[167] and induced apoptosis in hepatocellular carcinoma cells through both the intrinsic and extrinsic signaling pathways.[168]

3.8. Antidiabetic Activities Diabetes can cause a variety of complications such as coronary heart disease, myocardial infarction, and cerebral infarction. In recent years, numerous investigations have demonstrated that PhGs, polysaccharides and polyphenols exert anti-hyperglycemic effects or have beneficial influences in type 2 diabetes mellitus through their cholesterol-lowering and free radical-scavenging effects and their modulation of glucose-induced oxidative stress by researchers from Japan, the United States and Australia.[169–172] These findings suggested that PhGs and polysaccharides are both main active ingredients in Herba *Cistanche*. For the first time, Xiong *et al.*[173] demonstrated that *C. tubulosa* could be used to fight diabetes by lowering blood sugar and lipid levels in type 2 diabetic male mice. The injection of compounds **2** and **11** lowered postprandial blood glucose levels, elevated glucose tolerance in starch-loaded mice and inhibited rat intestinal α-glucosidases, lens aldose reductase and human intestinal maltas activity *in vitro*.[174] Wong *et al.*[175] reported that a *Cistanches* Herba ethanol extract markedly reduced weight gain and improved the insulin sensitivity of diabetic mice, probably due to mitochondrial uncoupling and increased energy consumption.

3.9. Cardiovascular Protection Once cardiovascular disease appears, it does great harm to the human body and can even cause sudden death. Phenylethanoid oligoglycoside and acylated oligosugar compounds from the methanol extraction of *C. tubulosa* displayed vasorelaxant activities in isolated rat aortic strips.[31] Extracts from *C. deserticola* could stimulate ATP generation *via* enhancing oxidative phosphorylation in H9c2 cells; thus, rat hearts were protected against myocardial ischemia/reperfusion (I/R) injury.[176] To explain the role of the mitochondria in the cardioprotective actions of Herba *Cistanche*, Siu and Ko from Hong Kong, China[177] investigated the treatment of Herba *Cistanche* on mitochondrial glutathione status in rat hearts and observed enhanced mitochondrial glutathione status and functional ability as well as the putative induction of uncoupling proteins, which may be related to the cardioprotection by Herba *Cistanche*. Wong and Ko[178] revealed the mechanism underlying the cardioprotective actions of Herba *Cistanche via* mitochondrial respiration and glutathione antioxidant status in H9c2 cardiomyocytes. Combining *in vivo* and *in vitro* approaches, Yu and Cao [179] discussed the cardioprotective effects and mechanism of PhGs from *C.*

deserticola against I/R injury. The *in vitro* and *in vivo* effects of compound **2** on human platelet aggregation were examined by scholars from Italy, and it was found that long-term administration of compound **2** at a dose of 100 mg/kg significantly reduced platelet aggregation in subjects with cardiovascular risk factors.[180,181] The vasorelaxant activity of compound **11** was proven by its ability to improve endothelium-dependent relaxation through the NO-cGMP signal pathway in rat aortic rings.[182] Cai *et al.*[183] demonstrated that compound **11** suppressed noradrenaline-induced contraction of the rat pulmonary artery by reducing intracellular Ca^{2+} levels; compound **11** induced its relaxation and achieved its vasorelaxant effects through the NO-cGMP pathway and by opening K^+ channels.

3.10. Anti-inflammation Activities Inflammation is a common defensive response of the body to external stimuli that is characterized by redness, swelling, fever, pain, and dysfunction. As we all know, nitric oxide (NO) is a pro-inflammatory molecule that plays an important role in the lipopolysaccharide (LPS)-mediated inflammatory process. In 1997, Shimamura *et al.* in Japan found that the free fatty acids especially the *cis*-isomers from *C. Salsa* were the main components had the suppressive effect of the SOS-inducing activity of Trp-P-1(3-amino-l,4-dimethyl-*5H*-pyrido[4,3-*b*]indol) by GC and GC-MS method, which suggested they can be used as an anti-inflammatory substances.[184] Seven PhGs compounds, namely, compounds **1, 2, 3, 11, 12, 17** and **18** from the stems of *C. deserticola*, were investigated and proven to possess NO radical-scavenging activities by Japanese researchers, which may contribute to their anti-inflammatory effects.[185] Lin *et al.*[186] from China Taiwan found that the butanoic and aqueous layers from *C. deserticola* are the main active constituents with analgesic and anti-inflammatory effects. Nan *et al.*[44] found compounds **18** and **39** can potently inhibit NO production induced by LPS in mouse microglial cells (BV-2 cells). Acteoside (**2**) is a well-known PhG with antioxidant and anti-inflammatory activities, and many studies focused on its anti-inflammatory activities have been conducted. Systematic studies on the anti-inflammatories activity of compound **2** were carried out *in vitro* and *in vivo* by Hayashi and his co-workers from Japan.[187,188] Lee *et al.*[189] from South Korea discovered that compound **2** could inhibit NO synthase expression induced by LPS in the RAW264.7 macrophage cell line. In 2010, Japanese researchers Yamada[190] and his team investigated the effects of compound **2** extracted from *C. tubulosa* on the basophilic cell-mediated allergic reaction, and the results suggested that it could be a good candidate for the therapeutic treatment of various allergic diseases. Combination of the *C. tubulosa* extract with fucoidan inhibited NO and prostaglandin E_2 production in an air pouch inflammation mouse model caused by carrageenan.[191] Additionally, compound **2** also decreased lung inflammatory responses in an LPS-induced acute lung injury mouse model, the mechanism of which might be partially attributed to the inhibition of pro-inflammatory cytokine production and nuclear factor-kappaB (NF-κB) activation.[192] Moreover, a study on anti-inflammation found that compound **2** not only exhibits antinociceptive effects but also has antioxidant properties.[193] In 2015, Shin *et al.*[194] from Korea demonstrated that combination oral treatment of *Laminaria japonica* extract and *C. tubulosa* extract at appropriate doses and ratios can prevent hair loss and improve alopecia. Their conclusion is consistent with the results obtained by Seok from their own country in the same year.[195] *C. salsa* extracts also showed antiproliferative effects on benign prostatic hyperplasia rats by regulating inflammatory cytokines or depressing apoptosis-associated proteins, which was proven by Korean researchers.[196] In 2007, Hausmann *et al.* from Germany proved that PhGs could alleviate intestinal inflammation in dextran sulphate sodium-induced colitis.[197] Researchers from Australia and Greece found compound **2** could alleviate intestinal mucositis in mice by preventing inflammation in 2015.[198] In 2016, the chemical compounds in *C. violacea* and their anti-inflammatory activities were studied by scholars from Algérie and Italy.[6]

3.11. Gastrointestinal Tract Protection Activities *Cistanches* Herba has always been a good medicine for gastrointestinal diseases and constipation. Compound **2** not only ameliorated mucosal tissue damage in acute and chronic colitis mouse models and could be a therapeutic alternative for inflammatory bowel disease treatment but also alleviated mucosal layer damage in mice by potentially preventing inflammation.[197,198] A *C. deserticola* water extraction could increase gastrointestinal tract peristalsis and shorten the defecation time in a mouse model.[199] The water extract from *C. deserticola* reduced the number of mucosal hyperplasias and intestinal helicobacter infection in mice, indicating that this plant may prevent intestinal inflammation disorders including colorectal cancer.[200] Gao *et al.*[201] proved that the total oligosaccharides and galactitol were the main active laxative components in a mouse model. Compound **11** improved mucosal tissue repair and prevented dextran sulfate sodium-induced colitis in mice *via* cell and rat experiments, implying the potential of this compound to clinically treat inflammatory bowel disease.[202,203] Japanese scholars found that the medicinal extract from *C. tubulosa* could alter the route of intestinal absorption, which may lead to better management of human health.[204] A study of the chemical constituents and pharmacological effects of *C. salsa* and *C. deserticola* was conducted by Xu *et al.* early in 1995. Compared with *C. deserticola*, *C. salsa* not only contained similar chemical components, but also had the same functions of moistening intestines and defecating, nourishing yang, but the pharmacological effect of *C. salsa* was better than *C. deserticola* to a certain extent.[205] Also the cathartic action of *C. deserticola*, *C. salsa* and *C. tubulosa* was compared in another research and their effects were basically the same.[206]

3.12. Immunoregulatory Activities Many different types of polysaccharides with various immunomodulatory activities have been reported. Ebringerova *et al.*[207] from Slovakia reported that the isolated polysaccharide cistan A exhibited remarkable immunomodulatory activities that exceeded those of the commercial immunomodulator Zymosan. In an *in vitro* immune test on mitogen-induced lymphocyte proliferation, one crude polysaccharide fraction from *Cistanches* Herba showed significant stimulating activities towards both T- and B-cell proliferation, while another polysaccharide showed stimulating activities towards LPS-induced B-cell proliferation. These findings demonstrated that these two polysaccharides probably play an important role in the expression of immunological activity.[208] Japanese scholars Maruyama *et al.*[209] reported that a *C. salsa* extract could stimulate the production of immunoglobulin M (IgM) and immunoglobulin G (IgG) in human lymph node lymphocytes and speculated that the in-

crease in antibody production may be related to interleukin-6 receptor expression in B-cell activation. Both naive T and natural killer cells in blood and spleen cell populations in tested animals were significantly increased after the mice were orally administered a *C. deserticola* extract for 4 weeks. The results showed that *C. deserticola* possessed significant effects to extend life span, and this was probably achieved by antagonizing immunosenescence.[210] Li *et al.*[211] remarked that PhGs from *C. tubulosa* inhibited the growth of melanoma B16-F10 cells *in vitro* and *in vivo* probably through immunoregulatory functions. Polysaccharides from *C. deserticola* are a safe and effective vaccine adjuvant for eliciting both humoral and cellular immunity.[212] This has also been proven in seasonal influenza vaccines in young adult mice, in which polysaccharides enhanced the immunogenicity of the seasonal influenza vaccine by inducing hemagglutinin inhibition antibody generation. This study provided evidence for the induction of humoral and cellular responses, which were rapid immune responses in mice after intramuscular injection with aqueous extracts of a *C. deserticola*-adjuvanted vaccine.[213] Shi *et al.*[98] carried out immunopharmacological tests with ethyl acetate extracts in different species of Herba *Cistanche*, and the results showed that they all could activate lymphocytes to kill K562 cells at a certain concentration and *C. tubulosa* had the strongest medicinal effect to enhance the immunity among them. Taken together, we can conclude that polysaccharides are closely linked with immunoregulatory activities.

3.13. Other Biological Activities Many other biological activities have been discovered during studies. A fatty acid from *C. sala* showed a suppressing effect on SOS-induced mutagenesis activity.[184] Lu[214] reported that *C. deserticola* extracts had sedative effects. Huang *et al.*[215] found that compound **2** could alleviate hyperuricemia in a potassium oxonate-induced hyperuricemic mouse model, and Cai *et al.*[216] found that a *C. deserticola* extract showed antifatigue effects. Compound **11** isolated from *C. salsa* had antisenescence activities by decreasing p53 expression and could improve the recovery of hematopoietic functions in a bone marrow depression mouse model by activating the granulocyte macrophage colony-stimulating factor (GM-CSF)/phosphatidylinositol 3-kinase (PI3K) pathway.[217,218] Wong *et al.*[175] conducted a study demonstrate that *Cistanches* Herba had obesity-suppressing activities through mitochondrial uncoupling. Wu *et al.*[219] found a new protective effect of *C. tubulosa* extract, whereby it can resist low-luminance blue light-induced degenerative retinopathy. Furthermore, water-soluble PhGs from *C. tubulosa* displayed effective anti-tumor effects in esophageal cancer by inducing apoptosis in Eca-109 cells through a mitochondrial-dependent pathway.[220]

4. Processing

As a tonic, Herba *Cistanche* has been used as medicine after multiple processing for a long time. “steaming or stewing with wine” is the processing methods of *Cistanche* in the 2015 Pharmacopoeia. Raw product of *Cistanche* can nourish the kidney, stop turbidity, and has a strong laxative effect. After processing according to method of Pharmacopoeia, it can strengthen the power of tonifying the kidney, and is mostly used for impotence, infertility. On the basis of the main chemical composition and pharmacological action of *Cistanche*, it is necessary to explain the processing principle of increasing efficiency about this plant, so as to provide necessary scientific basis for processing technology of Herba *Cistanche*. Cai *et al.* studied the processing technology of fresh *C. tubulosa* that was cut into 4 mm thick slices and killed enzyme at 70°C for 6 min. Compared with direct drying in traditional method, the compound content of **2** and **11** were greatly increased.[221] Wang *et al.*[222] researched the effect of different processing temperature on the chemical composition of *C. deserticola*. The content of PhGs was similar in natural temperature and drying at 40°C, but there was a downward trend when the processing temperatures exceed 40°C. The total amount of **2** and **11** was the highest in natural air-drying, while polysaccharide was the highest at 60°C. It is showed that the thickness, drying method, drying time and different enzyme inhibition methods of the decoction pieces could greatly affect the content changes of PhGs in *C. deserticola*.[223] Liu[224] optimized the three cutting processing technologies including moistening, softening, and steaming of *C. tubulosa*, the result showed that the steaming method had the highest recovery rate, and the content of ethanol extracts meets the requirements of the Pharmacopoeia, which can be used as the optimal cutting technology. Jiang *et al.*[225] examined the factors of the processing method of *C. deserticola* and considered that the slices were steamed for 2 h, softened, cut into 6 mm thick slices and dried at 70°C was the best processing technology. Based on the ancient and modern literature, according to the Pharmacopoeia and the national processing standards, through the experimental screening, combined with the appearance, color, odor, content of **176** and PhGs, Chen *et al.* determined that the best processing method of *C. deserticola* was adding 30% yellow wine and 25% water, steaming and stewing for 12 h.[226] Using high-pressure sterilization cabinet to steam *C. deserticola* could avoid the decrease in the content of active ingredients due to the loss of medicinal juice in traditional steaming method. Qian and He found that under the condition of 686 kpa and 120°C, steaming for 2 h is the best processing method of *C. deserticola*.[227] Yu *et al.*[228] found that the *Cistanche* processed by steam could increase the DNA synthesis rate and metal trace elements in yang deficiency animals, which indicated that the traditional processing method of Cistanche was significant. Duan *et al.*[229] studied the effects of processing of different concentrations of yellow wine on the laxative effect of *Cistanche deserticolata* and showed that within a certain range, the increase of the concentration of yellow wine would promote the laxative effect. In the study of modern processing of *Cistanche*, besides the processing method in the trueborn areas, more other studies are on the different technologies using yellow wine and its influence on the chemical compositions and pharmacological activities of *Cistanche*. It has been shown that the PhGs in Herba *Cistanche*, which have the function of tonifying kidney yang, will undergo hydrolysis reaction and isomerization reaction in the process of wine processing, but whether there will be further hydrolysis reaction and decaffeoyl reaction, and whether these components produced in the process of wine processing are the medicinal substance basis for the efficacy of *Cistanche* remains to be further studied. According to historical records, *C. deserticola* processed by wine can weaken its purgative effect, and modern research has also proved that the effect of raw products on defecation is better than that of wine products. Although wine products can also increase the

intestinal propulsion of mice, the laxative time is not significantly shortened. Duan *et al.*[230] also confirmed that when the concentration of rice wine was below 9.5%, the effect of Cistanche deserticola on the progress of intestinal push in mice increased with the increase of alcohol concentration. Further studies have shown that galactitol is one of the effective components of Cistanche deserticola for moistening intestines and defecating.[231,232] One study showed that there were no significant differences between the water decoction (for phagocytosis experiment) and the alcohol-soluble part (for aphrodisiac experiment) of *C. deserticae* and its processed product which was stewed with rice wine for 24 h, indicating that there was no significant difference between the two in kidney tonic and Yang tonic effects.[233] The appearance characters were softer, the powder color was brighter in steaming group than those of sun drying group. Except for cistanoside A (compound **3**), the contents of PhGs (compounds **1**, **2**, **11** and **12**), polysaccharides, soluble saccharides and ethanol-soluble extract in the steaming group were all higher than those in the sun drying group, and the antioxidant activity was significantly stronger, which indicated that steaming can be adopted in the large-scale post-harvest processing of *C. deserticola*.[234]

5. Toxicity and Safety Evaluation

Cistanches Herba has been regarded as an important tonic in traditional eastern medicine for centuries. Owing to its excellent nourishing functions, the stem of this herb has also been developed as a nourishing supplement and is popular in the health food market. Research data on the toxicity and safety evaluation of *Cistanches* Herba revealed that this medicine is truly safe. The acute, 90-d feeding test has been performed in rats, and genetic toxicities of Rou Cong Rong tea have been evaluated. The LD_{50} values of acute oral toxicity of Rou Cong Rong tea were greater than 60 g/kg. No severe genetic toxicity was observed in the experiments.[235] Studies focused on the acute toxicity, genetic toxicity and subchronic toxicity of *C. tubulosa* extract on Kunming mice and Wistar rats[236] as well as the subchronic toxicity of *C. tubulosa* extract on SD rats[237] have been conducted, and both experiments showed no apparent toxicity. In 2014, acute toxicity tests, including the bone marrow cell micronucleus test, mice sperm abnormality test, and Ames test, and a 90-d feeding study were conducted to toxicologically evaluate *C. deserticola*. The results showed that the acute oral maximum tolerated dose of *C. deserticola* to mice was greater than 20 g/kg body weight, which was over 600 times higher than the recommended human dose, indicating that *C. deserticola* was nontoxic.[238] The acute toxicity reaction of mice was observed after treatment with an ethanol extract from artificially planted *C. deserticola* for 14 successive days, and no acute toxicity was found.[239] In 2015, an acute oral toxicity test; mouse genetic toxicity tests, including the Ames test, mouse sperm abnormality test, and bone marrow cell micronucleus test; and a rat 30-d feeding test were conducted to evaluate the toxicological safety of Herba *Cistanche* granules. The results indicated that Herba *Cistanche* granules had no acute toxicity, genetic toxicity or subacute toxicity.[240] In 2016, a study of the acute toxicity and long-term feeding subchronic toxicity of *C. deserticola* was performed, and after 90 d of mixed feeding, animal indexes for food consumption, food utilization rate, blood, biochemistry, organ coefficients and tissue pathology were explored by using the maximum-tolerated dose (MTD) method, with no obvious toxicity observed.[241] The same year, Qiao[242] examined the acute toxicity of allantoin extract from Rou Cong Rong in mice fed the maximum concentration of 6.5 g crude drug/mL and the largest volume of 20 mL/kg twice a day for 14 d. The test results showed that allantoin extract from Herba *Cistanche* is safe. Herba *Cistanche* is also safe to maternal and fetal rats according to the results of a study testing the effect of *C. deserticola* on reproductive toxicity and teratogenicity in rats.[243] Acute toxicity test on rats and a 30-d feeding test were conducted to study the safety of *C. tubulosa* compound tablets. It showed that *C. tubulosa* compound tablets were safe to rats given a dose of 26.4 g/kg, and no poisoning symptoms were observed.[244] The potential toxicity of powdered *C. deserticola* as a novel food ingredient was examined in a subchronic toxicity study (90 d) in SD rats; this toxicological assessment included mortality, body and organ weight, food consumption, blood biochemistry, hematology, gross necropsy and histopathological examinations. The results showed no signs of toxicity or treatment-related changes in the rats treated with powdered *C. deserticola*.[245] *C. tubulosa* extract product Memoregain® was proved no genotoxicity based on the Ames test, chromosomal aberrations assay, and mammalian micronucleus test, and no observed adverse effect which was determined by both male and female rats.[246] Presently, no severe adverse drug events have been reported with Herba *Cistanche*, and Rou Cong Rong products are widely used in both the clinic and health food markets. More toxicity and safety data focused on Herba *Cistanche* and its products should be collected to ensure the safety and effectiveness of this medicine.

6. Discussion and Future Perspectives

Herba *Cistanche*, a folk herbal medicine, has been commonly used as a tonic herb in China for a thousand years and traditionally for tonifying kidneys and invigorating yang. PhGs are the most important active ingredients that have been proven to possess multiple medical functions, including those for the male reproductive system, bone metabolism, immune system, and neural system, through *in vivo* and *in vitro* studies and deserve to be studied more in the future. To date, most studies have mainly focused on compounds **2** and **11**; thus, other PhG compounds should be deeply investigated to better understand their pharmacological mechanisms.

In view of evident therapeutic efficiency, *Cistanches* Herba needs to be further developed into new pharmaceutical agents for the treatment of various diseases such as kidney yang deficiency and neurological and intestinal disorders. However, the difficulties associated with the development these agents are obvious, as most studies have only focused on phenotype analysis, such as morphocytology detection, immunohistochemistry and biochemical indicator analysis. Therefore, more bioactivity studies that investigate molecular biology, bioinformatics and chemical biology technologies should be carried out, as they may provide useful information and solid evidence for clinical applications. These may be important future challenges and opportunities for *Cistanches* Herba.

In this article, we reviewed the information available on *Cistanches* Herba, including its phytochemistry, pharmacology, toxicity and safety, to provide useful knowledge for future studies and for the commercial exploitation of *Cistanches*

Herba.

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Conflict of Interest The authors declare no conflict of interest.

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