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## Review

# Research Progress on Chemical Constituents of *Cistanches Herba* and their Pharmacological Effects

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### ABSTRACT

*Cistanches Herba*, a famous traditional Chinese materia medica, has a laudatory title "desert ginseng". According to *Chinese Pharmacopoeia 2000*, *Cistanches Herba* is the dry fleshy stem with scale-like leaves of *Cistanche deserticola*. In order to expand the drug source, *Chinese Pharmacopoeia 2005* increased the plants in *Cistanche* Hoffmg. et Link (Orobanchaceae), *C. tubulosa*, and dry scaly leaf succulent stems were as genuine *Cistanches Herba* and still in use. In order to have more comprehensive understanding on *Cistanches Herba*, this paper focuses the reviews on the biological characteristics, chemical constituents, and pharmacological activities of *Cistanches Herba*, and its development prospects are looked forward. It provides the relative theoretical basis for the subsequent research work of *Cistanches Herba* and can be conducive to the development and utilization of *Cistanches Herba*.

#### Key words

chemical constituents; *Cistanches Herba*; pharmacological effects

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## 1. Introduction

*Cistanches Herba* (CH), a herb with scaly leaves and fleshy stems, belongs to *Cistanche* Hoffmg. Et Link in Orobanchaceae family, which includes *Cistanche deserticola* Y. C. Ma and *C. tubulosa* (Schrenk) Wight, and is a well known Chinese materia medica (CMM) for the treatment of kidney deficiency, female infertility, and constipation (Pharmacopoeia Committee of P. R. China, 2010). CH was first described in *Shen Nong's Herbal Classic* as a top grade. The later classical works, such as *Bencao Jingshu*, *Bencao Huiyan*, and *Yue Hua Zi Bencao*, also had many records on it. CH has a medical history of more than 2000 years, and it occupies a prominent position on the list of Chinese drugs for invigoration in ancient Chinese medicine prescription.

Moreover, it is also used for anti-aging in clinic, only listed later to the ginseng. The taste and nature of CH is sweet, salty, and warm, and has the function of invigorating kidney and strengthening *Yang*, replenishing essence and marrow, enriching blood, moistening dryness, and so on. It is used to treat men impotence, women infertility, vaginal discharge, vaginal bleeding, waist and knee crymodynia, and constipation induced by blood exhaustion.

Original plant of CH is a parasitic plant in genus *Cistanche* Hoffmg. et Link, within around 20 species in the world and widely distributed in warm drily regions of Europe and Asia, from Iberian Peninsula to northern Africa, Arabia, Iran, Afghanistan, Pakistan, northern India, ex-Soviet Central Asian state, Mongolia, and northwest of China. There are four species, including *C. deserticola* Y. C. Ma (Inner Mongolia,

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Gansu province, and northern Xinjiang Uygur Autonomous Region), *C. salsa* (C. A. Mey.) G. Beck (Inner Mongolia, Gansu, Qinghai, Ningxia provinces, and Xinjiang Uygur Autonomous Region), *C. tubulosa* (Schrenk) Wight (southern Xinjiang Uygur Autonomous Region), and *C. sinensis* G. Beck (Inner Mongolia, Gansu, Qinghai, and Ningxia provinces), and a variant species *C. salsa* var. *albiflor* P. F. Tu et Z. C. Lou (Ningxia and Xinjiang provinces). CH has certain hardness and drought resistance, and mainly distributes in north latitude of 36°–37°. There is also a small amount of the distribution in the region from east to west across Inner Mongolia, Shaanxi, Gansu, Ningxia, Qinghai provinces, and Xinjiang Uygur Autonomous Region (Chen et al, 2005).

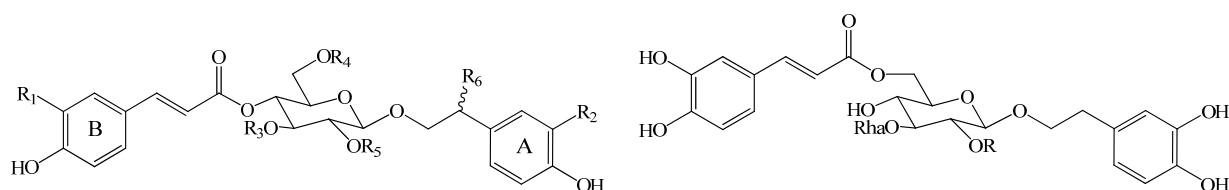
In this review, the useful information on the chemical composition, pharmacological effects, and other aspects of the latest research are provided, and also a method to conduct further study on CH to identify its potential effects is suggested.

## 2. Chemical constituents

Reports indicated the presence of a number of different chemical constituents in the stems of the plants in *Cistanche Hoffmg. et Link*, including phenylethanoid glycosides (PhGs), polysaccharides, oligosaccharides, galactitol, volatile components, iridoids, lignin and its glycosides, flavonoids, alkaloids, etc (Table 1).

**Table 1** Numbers of compounds currently isolated from plants in *Cistanche Hoffmg. et Link*

Species	PhGs	Iridoids	Lignins	Others	Total
<i>C. deserticola</i>	17	10	3	39	69
<i>C. tubulosa</i> (China)	9	4	1	7	21
<i>C. tubulosa</i> (Pakistan)	11	2	5	3	21
<i>C. sala</i>	11	–	–	18	29
<i>C. sinensis</i>	4	2	–	5	11



No.	Compounds	R	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	R <sub>5</sub>	R <sub>6</sub>
1	campneoside II <sup>a</sup>	–	OH	OH	Rha	H	H	(S or R) OH
2	isomer of campneoside I <sup>a</sup>	–	OH	OH	Rha	H	H	(S or R) OH
3	echinacoside	–	OH	OH	Rha	Glc	H	H
4	cistanoside A	–	OH	OCH <sub>3</sub>	Rha	Glc	H	H
5	acteoside	–	OH	OH	Rha	H	H	H
6	isoacteoside	H	–	–	–	–	–	–
7	cistanoside C	–	OH	OCH <sub>3</sub>	Rha	H	H	H
8	2'-acetylacteoside	–	OH	OH	Rha	H	AC	H
9	osmanthuside B	–	H	H	Rha	H	H	H
10	tubuloside B	AC	–	–	–	–	–	–

**Figure 1** Elucidated chemical structures of identified PhGs from CH

### 2.1 Phenylethanoid glycosides

Sugar chain of PhGs is only composed of glucose and rhamnose, and the center glucose is directly connected with aglycone. In addition to single glucoside, all center of glucose is connected with rhamnose glycoside in C-3; In the C-4 or C-6 position of center glucose there often exists coffee group, such as ferulic acid or coumaroyl benzene acryloyl group (Tu et al, 1997). The PhGs were echinacoside (ECH), acteoside, isoacteoside, 2'-acetylacteoside, decaffeoylacteoside, cistanosides A, B, C, D, E, G, and H, 2'-acetylcistanoside C, isocistanoside C, tubuloside A, B, C, D, tubuloside E, isotubuloside E, cistantubuloside A, cistantubuloside B1, B2, cistantubuloside C1 and C2, salsaside D, E and F, kankanoside F and G, osmanthuside B, 2'-acetyl-osmanthuside, cistansinenside A, syringalide A, 3'- $\alpha$ -L-rhamnopyranoside, isosyringalide A 3'- $\alpha$ -L-rhamnopyranoside, salidoside, crenatoside I, jionoside D, poliumoside, eutigoside, pheliposide, and campneosides I and II (Figure 1).

### 2.2 Polysaccharides

The carbohydrate component of CH, monosaccharide composition, was mainly as follows: glucose, galactose, rhamnose, arabinose, and fructose. The monosaccharide composition ratio of polysaccharide molecular weight range, the connection point in the form of monosaccharides and monosaccharides-glycosidic bond types, and the repeat units were the current research focus with priority. The polysaccharides were cistan A, CDA-1A, CDA-3B, CDP-4, ACDP-2 (Figure 2), and SPA (Figure 3).

### 2.3 Oligosaccharides

Oligosaccharide is 2 to 10 monosaccharides by glycosidic bond to form a straight-chain or branched-chain polymer of low sugar.



Gao et al (2005) found that CH glycosides (with 44.3% ECH) could improve the learning and memory in focal cerebral ischemia-reperfusion model of vascular dementia mice.

### 3.1.3 Protection on brain cells and anti-apoptotic effect

Apoptosis is a variety of pathogenic factors leading to programmed cell death in the developing nervous system. Neurodegenerative disease and injury in both excitatory neurons promote cell apoptosis. Deng et al (2005) found that ECH could inhibit apoptosis or animal brain particles decreased apoptosis rate.

### 3.1.4 Antitumor effect

Li et al (1995), Liu et al (2008), and studies by others have shown that ECH separated and extracted from the plants of *Pedicularis* Linn. had antitumor activity.

### 3.1.5 Hepatoprotective effect

Wu et al (2007) found that ip injection of ECH (50 mg/kg) could significantly weaken the hepatotoxicity induced by CCl<sub>4</sub> in rats. Xiong et al (1996) reported that four phenethyl alcohol glycosides (including ECH) were obtained from the plants of *Cistanche* Hoffing. et Link, and proved to have hepatoprotective activity.

### 3.1.6 Treatment of osteoporosis and fracture healing

In traditional Chinese medicine theory, the kidney generates marrow and dominates bone. Modern pharmacological studies have shown that the kidney-reinforcing drugs had the varying degrees of exciting the function of pituitary-adrenal-gonadal system, and bone metabolism was closely related. Estrogen can enhance osteogenesis-related androgens and promote protein synthesis and bone matrix to increase the role of calcium and phosphate deposition. PhGs, isoacteoside, and betaine in CH all have androgen-like effects, and can promote bone marrow mesenchymal stem cells (BMSCs) directed differentiation into osteoblasts. For the treatment of osteoporosis, fracture healing will have good prospects (Zeng and Liu, 2010).

### 3.1.7 Immunomodulatory effects

Li et al (1997) observed that PhGs could enhance SOD activity in erythrocyte, decrease MDA content in mice serum, increase DNA and RNA contents in liver and kidney tissues, enhance immunity and anti-aging, and also have some other effects.

### 3.1.8 Promoting wound healing and antiradiation

Speroni et al (2002) found that ECH had a protective effect on the skin and connective tissues, and promoted wound healing.

Li et al (1992) found ECH had protective and therapeutic effects on UVA/UVB radiation-induced skin damage. PhGs had a strong protective effect on irradiated mice.

### 3.1.9 Other effects

Pan and Min (2004) found that PhGs could enhance the

hypothalamic-pituitary adrenal function, promote *in vivo* release of related neurotransmitters and hormones, increase libido, and antifatigue, and improve physical skills.

Wu (2003) found that some CH glycosides had structural similarities with vitamin E, which had a phenolic hydroxyl group and a hydroxyl functional group.

## 3.2 Polysaccharides

### 3.2.1 Immunomodulatory effects

Zeng et al (1998; 2002) have shown that *Cistanche* polysaccharides (CPS) could increase the proliferative response of spleen and thymus lymphocyte and have a synergistic effect with concanavalin (ConA) and phytohemagglutinin. CPS can stimulate the proliferation of murine thymocytes and significantly improve murine splenic T lymphocytes to secrete interleukin-2 (IL-2).

Wang and Qi (2009) and other studies have shown that CPS could significantly promote the normal cell proliferation on mitogen (ConA and lipopolysaccharide)-activated and non-activated lymphocytes, and the secretion of IL-2. The ip administration with CPS can significantly improve the spleen indexes of both normal and immunocompromised mice.

Xu et al (1997) have shown that CPS had a recovery effect on spleen weight loss in mice with stagnation of liver *qi* induced by carbon tetrachloride (CCl<sub>4</sub>), and also could improve the immune cells and humoral immune function and enhance the ability of its occurrence allergy.

### 3.2.2 Anti-oxidative and anti-aging effects

Xue et al (1995) found that CPS could significantly delay the animal skin aging, enhance skin elasticity, increase hydroxyproline content in animal skin, increase the collagen fiber content and SOD activation, and reduce body ester lipofuscin accumulation.

Wu and Fu (2004) have reported that CPS showed significant anti-lipid peroxidation functions on subacute aging mice caused by *D*-galactose.

Xu et al (2008) reported that CPS could significantly improve the activity of Ca<sup>2+</sup>-ATP enzyme in liver of aging model rat, the membrane fluidity of liver mitochondrial, the activities of respiratory chain complexes I + III, and II + III.

Sun et al (2001) and other researchers have reported that CPS could enhance lung tissue, erythrocyte SOD, and GSH-Px vitality of aging mouse, and be resistant to oxidative damage and senescence.

### 3.2.3 Antihepatitis

Zhang et al (1996) reported that CPS significantly inhibited the hepatic damage, while reduced the increase of serum alanine aminotransferase and aspartate aminotransferase due to liver and spleen functional impairment.

### 3.2.4 Effect on proliferation of fibroblasts

Gao et al (1998) observed the effect of CPS with different concentration on cultured human fibroblast cells, and proved that the drug could significantly promote the *in*

*vitro* growth of human fibroblasts.

### 3.2.5 Hematopoietic function

Chen et al (2007b) have reported that CPS could significantly promote bone marrow cells in G<sub>0</sub>/G<sub>1</sub> phase to S phase as well as cells in S phase to G<sub>2</sub>/M phase transformation. So cells in G<sub>2</sub>/M phase were significantly increased, and proliferation index (PI) was also significantly increased. CPS could promote the recovery of bone marrow function and growth of blood erythroid megakaryocytes through inducing the transformation of cell cycle in bone marrow of anemia mouse.

### 3.2.6 Inhibitory effect

CPS solution had a different degree of inhibiting the growth of *Colon bacillus*, *Bacillus subtilis*, *Saccharomyces cerevisiae*, and *Penicillium citrinum*. The research laid the foundation for the reasonable development and utilization of the plants in *Cistanche Hoffing.* et Link (Wang and Zhu, 2009).

### 3.3 Oligosaccharides

Functional oligosaccharide is difficult to be or not digested when absorbed by the body. So it is provided as a low or no energy value, and used as low energy food for the people with diabetes, obesity, or low blood sugar. At the same time, it can activate the intestinal bifidobacteria and promote their growth and reproduction. Since the functional oligosaccharides, as water-soluble dietary fiber, are not digested and absorbed by the body, they have some physiological functions of dietary fiber, such as lowering serum cholesterol and preventing colon cancer. Although they belong to small molecules, they do not change the original organization of food texture and physical properties when added to foods basically (Bai, 2006).

### 3.4 Galactitol

Tu et al (1997b) reported that the laxative active ingredients were galactitols in the plants of *Cistanche Hoffing.* et Link. The dose-effect relationship was studied and showed that 1.1% galactitols had a laxative effect, as the dose increasing gradually the laxative effect increased. However, the dose-response curve for the 10% galactitol went to flat. The laxative effect was not stronger with the dose increasing. (Zhang and Zhao, 2003a; 2003b; Tu and He, 1997; Pharmacopoeia Committee of P. R. China, 2010).

Ren (1987) proposed that drugs for the treatment of constipation were numerous but many had varying degrees of side effects or had the disadvantages of being hurt. CH was sweet, sour, salty, warm, and non-toxic, and nourished the essence and blood of liver and kidney. After taking the herb, liver and kidney functions of the patients were not aware of any injuries.

### 3.5 Pharmacological effects of other ingredients

Flavonoids, volatile components, and alkaloids in

addition to their traditional pharmacological effects have not been reported in the literature. In addition, CH flooding fluid, ethanol-water extract, and ethanol leaching solution can be used to anesthetize dogs, cats, and rabbits, and also have antihypertensive effect.

CH can stimulate saliva and palsy respiratory, some organic acid-like substances can stimulate saliva, glycosides can make respiratory paralysis.

## 4. Conclusion

*Cistanches Herba* (CH), a traditional valuable Chinese herbal medicine, has a laudatory title of “desert ginseng”. With the biological, chemical, and pharmacological activity updated in the literature, there is significant interest in CH as a invigoration, and anti-aging mainstream medicine. Furthermore, some literature and studies show that CH could promote the laxative and proliferation of fibroblasts, which suggest that CH may be used as a new potential medicine of development for the treatment of senile constipation and fractures. To date, studies show that some chemical constituents have the same similarities or cross synergies reflect of pharmacological activity, the results are according to the overall concept of the traditional Chinese medicine principles. In addition, the active ingredients and their unknown pharmacological effects are being studied.

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