

Advancements in the Investigation of Chemical Components of Codonopsis Radix: A Review

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Abstract: Codonopsis Radix, as a traditional Chinese medicinal (TCM) herb, not only holds a place in the dietary therapy culture but also represents a highly potential natural medicine. Codonopsis Radix has the effects of strengthening the spleen and tonifying the lung, as well as nourishing blood and engendering liquid. Modern research has shown that Codonopsis Radix not only contains abundant nutrients but also possesses various active components, such as alkaloids, phenylpropanoids, flavonoids, and terpenoids. These components confer protective effects on the nervous system, protection of the gastrointestinal tract, antioxidation, anti-inflammation, and immune regulation on Codonopsis Radix, making it one of the potential TCM with enhanced immune capacity. Codonopsis Radix is often used as a medicinal dish and health supplement, and is widely applied in medicine. Codonopsis Radix is often used as a medicinal dish and health supplement, and is also widely applied in medicine. It has high medicinal value and economic value. This article will provide an overview of the current research status of the chemical components and pharmacological activities of plants belonging to the genus Codonopsis over the past 20 years. This lays a theoretical foundation for the sustainable development, food and medicine integration development, and comprehensive utilization of Codonopsis Radix. It also provides a reference for the systematic and rational development of other natural drug resources.

1. Introduction

Codonopsis Radix is a TCM with a very long history of medicinal use in China. It is one of the Chinese medicinal materials that are both food and medicine. Codonopsis Radix is derived from the dried roots of the plant *Codonopsis pilosula* (Franch.) Nannf, *C. pilosula* Nannf.var. *modesta* (Nannf.) L. T. Shen or *Codonopsis tangshen* Oliv.in the genus *Codonopsis* of *Platycodonaceae*. *Codonopsis Radix* has a mild nature and enters the spleen and lung meridians [1]. It has the functions of tonifying the spleen and lungs, promoting the production of body fluids and quenching thirst, as well as tonifying qi and promoting the production of body fluids. It has a similar effect to ginseng, but its medicinal power is milder and it can replenish blood. *Codonopsis Radix* is one of the most commonly used medicinal materials in traditional Chinese medicine clinical practice, and its efficacy has been recorded in famous books throughout history [2]. Studies have shown that the

whole plant of *Codonopsis Radix* is rich in nutrients and various bioactive substances, and has high nutritional value [3]. The chemical components contained in *Codonopsis Radix* are quite diverse, mainly including flavonoids, alkaloids, polysaccharides, saponins, steroids, etc. It has multiple pharmacological effects such as enhancing immunity, protecting the heart, nerves, gastrointestinal tract, regulating blood sugar, antioxidation, anti-fatigue, antibacterial, antiviral and anti-tumor [2,4-5]. More than 300 compounds have been isolated and identified from plants of the *Codonopsis* genus so far, including alkaloids, saccharides, flavonoids, phenylpropanoids, terpenoids, steroids, etc. [6-7]. TCM represented by plants of the *Codonopsis* genus have mild effects and excellent therapeutic effects. *Codonopsis Radix* can replace most precious medicinal materials and has now become a hot spot in new product development. This article reviewed the research progress on the chemical composition of *Codonopsis Radix*, laying a theoretical foundation for its sustainable development, the development of food and medicine sharing the same origin, and comprehensive utilization.

2. Chemical composition

The genus *Codonopsis* has a wide variety of species, which can be classified into *Codonopsis nervosa*, *Codonopsis tangshen* Oliv, *Codonopsis pilosula* (Franch) Nannf, *C. pilosula* (Franch.) Nannf, *C. lanceolata* Benth. et. Hook. f, *C. tubulosa* Kom, *C. subglobosa* W. W. Sm, and *C. tsinlingensis* Pax & K. Hofim. etc. At present, more than 300 compounds have been extracted and separated from *Codonopsis pilosula*, mainly including flavonoids, alkaloids, phenylpropanoids, steroids, and polysaccharides, as shown in Fig 1. Among them, alkaloids, flavonoids and polysaccharides are considered to be the main active components. Clinically, it is mainly used for gastritis or gastric ulcers, gastric cancer, type 2 diabetes, hyperlipidemia, hematopoietic dysfunction or anemia caused by chemotherapy [2].

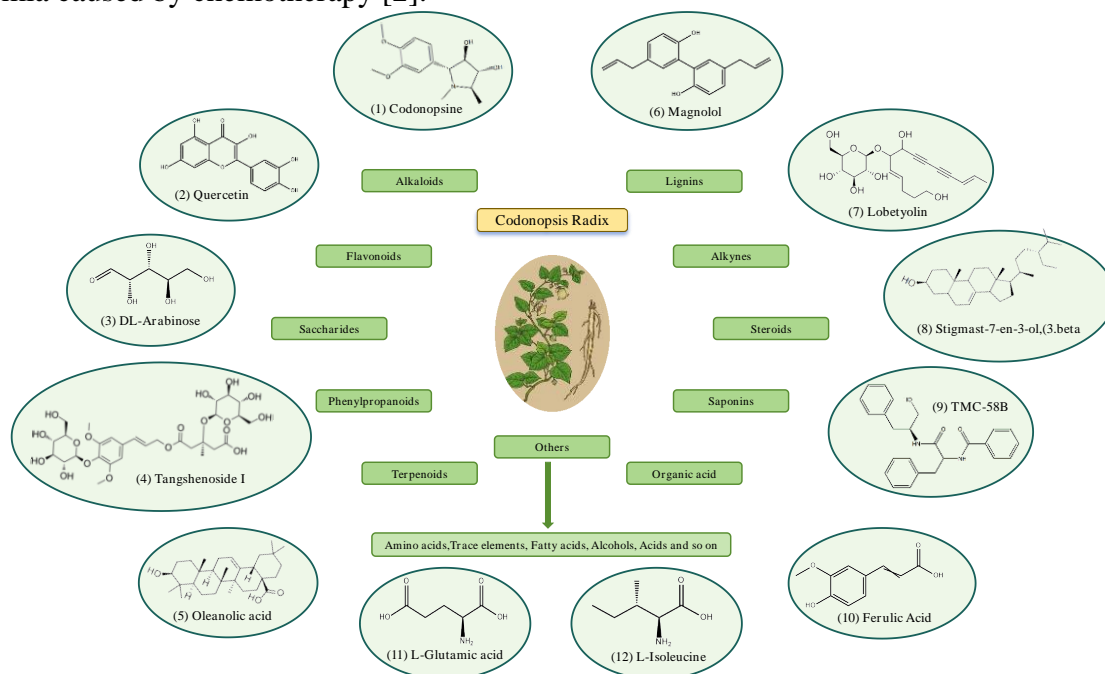


Figure 1 The classification of chemical components in *Codonopsis Radix*.

2.1 Alkaloids

Alkaloid components are a class of nitrogen-containing basic compounds with numerous

biological activities, including anti-tumor, neural regulation, anti-aging and the like [4]. *Codonopsis Radix* contains many alkaloid substances, including codonopsine(1), choline hydroxide, choline chloride, codotubulosine A~B, 6-methoxyquinoline-4-carbaldehyde, 6-hydroxypurine, harmane, uracil, nicotine, 1,2,3,4-tetrahydro- β -carboline-3-carboxylic acid, N-[(tert-butoxy)carbonyl] -D-tryptophan, 1-carbomethoxy- β -carboline, 6-methoxyquinoline-formylquinoline and the like [8-13]. Codonopsinol is a pyrrolidine alkaloid isolated from the roots of *Codonopsis Radix* [2].

2.2 Flavonoids

Flavonoid components possess antioxidant properties. They can effectively eliminate free radicals and alleviate oxidative damage. The ability to eliminate hydroxyl free radicals increases with the increase in content. In addition, the antioxidant, microcirculation improvement and cell migration promotion effects are possessed by *Codonopsis Radix* flavonoids [14]. Among the plants belonging to the *Codonopsis Radix* genus, there are relatively more flavonoid compounds isolated. The flavonoid components in *Codonopsis Radix* mainly include codonopilate A~C, 24-methylenecycloartanyllinolate, Luteolin, Quercetin(2), hesperidin, emodin, kaempferol, atractylenolide II~III, atractylenolide I~III, neokurarinol, apigenin, 7-glucoside, lupeol, taraxerol, dandelion terpene ketone, taraxerol acetate, wogonin, friedelin, oleanolic acid, luteolin-7-O- β -D-gentiobioside, cynaroside, cynaroside and so on [15-16].

2.3 Saccharides

Codonopsis Radix is rich in Saccharides, and sugar is one of the important active ingredients of *Codonopsis Radix*. It mainly covers monosaccharides, oligosaccharides and polysaccharides, etc. Due to the sugar components it contains, the sweeter the *Codonopsis Radix* tastes, the better. Among them, *Codonopsis Radix* polysaccharides are one of the main active substances in *Codonopsis Radix*. Polysaccharides mainly include inulin-type fructans and other heteropolysaccharides. *Codonopsis* polysaccharides have various pharmacological effects such as immune regulation, antioxidant activity, anti-aging, anti-inflammation, anti-tumor, improvement of cognitive impairment, and regulation of intestinal flora and so on [17].

The main components of monosaccharides include fructose, glucose, galactose, α -L-rhamnopyranose monohydrate, etc, while oligosaccharides are composed of monosaccharides and their derivatives. BAI et al. extracted codonopsis radix oligosaccharides (*Codonopsis Radix* Oligosaccharides, CPO) from *Codonopsis Radix* at an extraction rate of 14.3% by water extraction and alcohol precipitation combined column chromatography, which indicates that CPO is also one of the important components in *Codonopsis Radix* [18]. By using analytical methods such as gas chromatography-mass spectrometry and magnetic resonance imaging, it can be concluded that the main monosaccharide components of CPO are glucose and fructose.

Polysaccharides are the main components of the Saccharide substances in *Codonopsis Radix*. Polysaccharides of *Codonopsis Radix* refer to compounds with polysaccharide structures extracted from *Codonopsis Radix*. So far, various polysaccharides have been isolated from different parts of *Codonopsis Radix*, and the main type is heteropoly saccharides [16]. It includes various polysaccharide molecules such as α -glucan, B-glucan, DL-Arabinose(3), etc. These polysaccharide molecules can significantly enhance the immune function of the body, improve antioxidant capacity, and also have a significant effect in anti-tumor, having a positive impact on human health [19]. In addition, *Codonopsis Radix* polysaccharides can also regulate inflammatory responses and have certain therapeutic effects on inflammation-related diseases.

2.4 Phenylpropanoids

Codonopsis Radix phenylpropyl has excellent anti-inflammatory and antidepressant activities, and the content of phenylpropyl varies among different varieties of Codonopsis Radix. Studies have shown that Codonopsis tangshen Oliv. contains tangshenoside I(4)~IV[20-23]. Codonopsis cordifolia P. C. Tsong contains cordifoliketone A, cordifoliketone B, coniferaldehyde, sinapinaldehyde, etc [24].

2.5 Terpenoids

Terpenoids have anti-inflammatory, anti-cancer, analgesic, antibacterial, antioxidant, expectorant and antiasthmatic effects [25]. The research has found that triterpenoids, sesquiterpenoids and monoterpenoids are the main terpenoid compounds isolated from Codonopsis Radix. Among them, the triterpenoid compounds were the most abundant [16]. The terpene components in Codonopsis Radix mainly include tangshenoside I(4)~III, echinocystic acid, codonopilate A~G, luteolin, quercetin, 24-methylenecycloartanylinate, hesperidin, atractylenolide II~III, lupeol, taraxerol, aster, taraxerol acetate, saponin Hb, dandelion terpene ketone, friedelin, oleanolic acid(5) [15-16].

2.6 Lignins

Lignins have antioxidant, anti-cancer and anti-hypoxic activities and have a significant effect on improving cardiovascular health. The lignin components in Codonopsis Radix mainly include Tangshenoside I to VI, Tangshenoside VIII, Syringin, syringaresinol, Methylsyringin, Tetrahydro-2-(4-hydroxy-3-methoxyphenyl)-4-((4-hydroxy-3-methoxyphenyl)methyl)-3-furanemethanol, dehydridiconiferyl alcohol. Yan Meng et al. [26] isolated and purified 10 lignan compounds from Codonopsis Radix. Ten compounds were classified as schisandrin A, gomisin A, gomisin N, schisandrol A, angylolyl gomisin Q, angylolyl gomisin H, benzoylgomisin Q, honokiol, magnolol (6), codonopiloneolignanin A. Of these 10 compounds, except for Codonopiloneolignanin A, the other 9 were isolated from the genus of Codonopsis Radix for the first time.

2.7 Alkynes

The polyacetylenes in TCM have various pharmacological effects such as anti-tumor, anti-depression, neuroprotection, anti-inflammation, regulation of blood lipid, antioxidation, anti-fatigue, promotion of estradiol secretion, and anti-uric acid [27]. They also have good metabolic performance. The alkyne components of Codonopsis Radix have good anti-tumor activity, among which Codonopsis Radix has a better effect [17]. The enyne compounds in Codonopsis ginseng mainly include lobetyolin, Lobetyolinin, lobetyol, and so on. Among them, the ethinyl side is one of the index components of Codonopsis ginseng quality evaluation, but the content of ethinyl in different varieties of Codonopsis ginseng in different regions is quite different. Studies have shown that puerarin can promote the synthesis and secretion of estradiol(E2) by ovarian cells, without affecting cell proliferation and normal differentiation [28]. A certain amount of puerarin can significantly enhance the activity of xanthine oxidase(XO) in the liver of rats and inhibit uric acid production [29].

2.8 Steroids

Steroid compounds have excellent anti-inflammatory, antibacterial and anti-tumor activities. At present, the steroid compounds isolated from Codonopsis Radix mainly include stigmasterols and

brassanols [16]. The steroid compounds in *Codonopsis Radix* mainly include β -sitosterol, eleutheroside A, delta(7)-stigmastenone-3, α -spinasterol, 7-dehydrostigmasterol, $\Delta^5,25$ -stigmasterol, Stigmast-7-en-3-ol, (3. β (8), α -spinasteryl-3-O- β -D-glucoside, stigmasterol, etc. [30-31].

2.9 Saponins

Saponin components play a crucial role in anti-inflammation and neuroprotection. Besides this, saponins possess various pharmacological activities such as anti-oxidation and anti-aging, and also have great potential in the treatment of cardiovascular and cerebrovascular diseases. 1,3-dilinolein, aurantiamide(TMC-58B)(9), taraxerol, atractylenolide I, codonolaside I-III, codonolapolin, codonolaside, echinocystic acid 3-O- β -D-glucuronic acid, ziyu glycosideI, eclalbasaponinXIII, echinocystic acid, lobetyolin, etc. are the main saponins in *Codonopsis Radix* [31-33].

2.10 Organic acid

The main organic acid components in *Codonopsis Radix* include aliphatic acids, aliphatic alcohols, and phenolic acids [2]. These compounds have the ability to regulate the immune system. The leaves of *Codonopsis Radix* contain organic acid components such as shikimic acid and maleic acid. The Chinese yam contains two organic acid components, namely codonopyrrolidiums A and B. In other plants belonging to the genus *Codonopsis Radix*, the following compounds were also discovered, including succinic acid, cyclohexanecarboxylic acid, ferulic acid(10), and vanillic acid [2].

2.11 Others

Codonopsis Radix is rich in 17 kinds of amino acids needed by the human body, among which the contents of L(+)-arginine, L-glutamic acid(11) and L-aspartic acid are relatively high, accounting for about half of the total [34]. In addition, *Codonopsis Radix* also contains essential amino acids for the human body such as valine, L-isoleucine(12), L-methionine, L-threonine and L-lysine. *Codonopsis Radix* is also rich in trace elements, among which there are many nutrients beneficial to the human body. These trace elements include Mg, P, Ca, Fe, Mn, Zn, Cu, etc, among which the contents of Na, K, Mg, Ca and Fe are relatively high [35]. In addition, among the plants belonging to the *Codonopsis* genus, there are over 30 kinds of inorganic elements including heavy metals, including Cr, Ca, Se, P, B, Be, Hg, Ag, Ce, Pb, Ba, As, Ni and so on. Some harmful elements, such as As, Cd, Pb, and Hg [33], when they accumulate in the human body to a certain concentration, will damage the immune system and impair various physiological functions. In addition, *Codonopsis Radix* is rich in volatile components, mainly including fatty acids, alcohols, acids, fatty acid esters, alkanes, aldehydes and alcohols, etc.

3. Conclusion

Codonopsis Radix is a TCM that is used to tonify the qi. It is also one of the Chinese medicinal materials that have both medicinal and edible properties. This article systematically reviews the chemical components and key compounds of *Codonopsis Radix*. The research has found that the effective active components of *Codonopsis Radix* that have been discovered both domestically and internationally so far mainly include polysaccharides, alkaloids, phenylpropanoids, triterpenoids, flavonoids, organic acids, etc.

In recent years, with the development of the *Codonopsis Radix* health industry, the research and development of *Codonopsis Radix* functional foods have become a hot topic in today's society.

Codonopsis Radix can be used as the main raw material to produce snack foods. Codonopsis Radix is rich in nutrition, low in fat and contains the digestive aid and stomach nourishment factor Lobetyolin, making it an ideal accompaniment food, leisure health food. The pharmacological effects of Codonopsis Radix, such as regulating blood glucoser, promoting hematopoietic function, lowering blood pressure, anti-oxygen deficiency, resisting fatigue, enhancing the body's immunity, delaying aging, regulating gastric contraction and anti-ulcer, have been increasingly applied in health products. In the development of health products, the main functions of Codonopsis Radix are to enhance immunity and improve nutritional anemia.

It is easy to see that Codonopsis Radix is a natural medicinal plant with great potential. Its various extracts all have significant pharmacological effects, and no obvious adverse reactions have been observed. It is believed that Codonopsis Radix has the ability to play a more important role in preventing and treating various diseases that widely trouble people. In addition, as one of the precious raw materials for both medicine and food, Codonopsis Radix has abundant resources and high usability value, which has opened up broad prospects for the in-depth development of Codonopsis Radix. This article conducts a review of the chemical components of Codonopsis Radix, aiming to provide a reference for the subsequent clinical application and development of Codonopsis Radix.

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