Phytochemical and Pharmacological Properties of Radix Codonopsis: A Review

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***Abstract*-Radix Codonopsis (RC) was a well-known Chinese traditional medicine. In clinical practice, RC was usually used to cure poor appetite, fatigue, psychoneurosis, inflammatory diseases, etc. Recently, many studies focused on its antitumor, antioxidant, anti-ulter, and antibacterial properties. This paper was a review of the phyto-chemical and pharmacological properties of RC. Moreover, the application prospect of RC was also discussed.**

Keywords-Radix Codonopsis (RC); Chinese Traditional Medicine; Clinical Practice; Phytochemistry; Pharmacology

I. INTRODUCTION

Radix Codonopsis (RC) has been considered as a traditional herbal medicine for a long history in China. According to the Chinese pharmacopoeia, 2005 [1], RC was the root of Codonopsis pilosula (Franch.) Nannf., C. pilosula Nannf. var. modesta (Nannf.) L. T. Shen, and C. tangshen Oliv. These three species belong to the family Campanulaceae, genera Codonopsis, and distribute in Gansu, Sichuan, Shanxi, Shaanxi province, China [2].

Recently, more and more pharmacological actions of RC have been reported. These researches showed that RC could not only regulate the blood glucose level, improve the immune, digestive, hematopoietic and coagulation functions, but also stimulate the appetite. In clinical practice, RC was usually used to cure poor appetite, dyspepsia, fatigue, psychoneurosis, inflammatory diseases etc [3-7]. It was considered as a safe herbal medicine with only insignificant side-effect and sometimes used as an invigorant substitute of Panax ginseng [8, 9]. Recently, many studies focused on its antitumor, antioxidant, anti-aging, anti-ulter and antibacterial properties [10-17]. Other species of the same genera Codonopsis were also used as the new medicine resources, for instance, C. tubulosa Kom, C. subglobosa Smith, C. canescens Nannf., C. clematidea (Schrenk) Clarke., C. xundianensis Wang ZT ex Xu GJ, and C. lanceolata (Sieb. et Zucc.) Trautv[18].

The chemical components of RC were very complex, such as sterol, monosaccharide, polysaccharide, glycoside, alkaloid, volatile oil, triterpene, amino acid and inorganic elements. These chemical components became the material bases for the pharmacological activities of the crude drug. In this paper, the phytochemical and pharmacological properties of RC were reviewed. Moreover, the application prospect of RC was also discussed.

II. PHYTOCHEMISTRY

In recent years, there were many further studies on the chemistry compositions of RC. The results showed that these chemistry compositions acted different efficiency to improve human health.

A. Carbohydrates and Glycosides

The traditional medication experience held that the sweeter the taste, the better the quality of RC [19]. And the studies considered the sweet of RC as main basis for the levulose content. Lu studied and compared five samples of RC from different places and pointed out that the content of levulose in C. pilosula (Franch.) Nannf. from Shanxi was the highest [20].

Besides monosaccharide, the carbohydrates in RC also include oligosaccharide and polysaccharide. The oligosaccharide mainly was inulin. Polysaccharides were the main component of RC carbohydrates, and many of them were heteropolysaccharide. There were some codonopsis acidic polysaccharides and four heteropolysaccharide CP-1, CP-2, CP-3, and CP-4 which include levulose. Zhang purified three polysaccharide fractions CPPS1, CPPS2, and CPPS3 from C. pilosula (Franch.) Nannf. [21]. And Han separated polysaccharide fractions COP-Ⅰ and COP-Ⅱ from C. tangshen Oliv. [22].

There were more than ten kinds of glycosides separated from RC. He separated syringin, hexyl-β-D-glucopyranoside, and butyl-β-D-fructofumanoside from C. pilosula (Franch.) Nannf. [23]; Cai summarized a lot of literatures about RC and pointed out that there were ethyl-α-D-frucofuranoside, (E)-2-hexenyl-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside, (E)-2-hexenyl-α-L-arabinopyranosyl-(1→6)-β-D-glucopyranoside, hexyl-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside, exyl-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside, (E)-3-hexenyl-β-L-glucopyranodide, and (E)-2-hexenyl-β-L-glucopyranodide in RC[24]; Wang separated (6R,7R)-trans, -trans,-trans-tetradeca-4,12-diane-8,10-digne-1,6,7-triol-O-β-D- glucopyranoside from C. tangshen Oliv. and K. Mizutani separated five lignan glycosides from C. tangshen Oliv., including Radix Codonopsisoside Ⅰ, Radix Codonopsisoside Ⅱ, Radix Codonopsisoside Ⅲ, Radix Codonopsisoside Ⅳ and syringing [25]. The Radix Codonopsisoside Ⅰ, Ⅱ, Ⅲ, and Ⅳ were the special compositions of Codonopsis [26, 27].

B. Steroids

The steroids of RC included sterol，steroidal glycoside and sterone. Wang examined α-spinasterol, α-stigmasta-7, 22-diene-3-one, and α-spinasterol-β-D-glucoside in C. tangshen Oliv.. There also stigmasterol, δ-spinasterol, stigmasterol, stigmasterone, stigmasterol-β-D-glucoside, Δ7-stigmastenone, Δ7-stigmasterol and Δ7-stigmasterol-β-D-glucopyranoside were separated [25].

C. Alkaloids and the Nitrogen Components

The alkaloids and nitrogen components of RC included codonopsine, 5-hydroxy-2-hydroxymethyl pyridine, n-butyl-

allophanate, codopiloic acid and choline, etc [28].

D. Terpenes

K. Ogihara reported the isolation of taraxerol, taraxerylacetate, friedelin, vanillic acid, and 5-hydroxymethyl-2 -furaldehyde from C. tangshen Oliv. [29]. Wang examined atractylenolide Ⅱ and atractylenolide Ⅲ in C. pilosula (Franch.) Nannf., which was the first report about Campanulaceae. Besides these components, the terpenes of RC also included stearic acid, 5-methoxymethyl-2-furaldehyde, 5-hydroxymethylfurfural, phthalic anhydride-Bis-(2-ethyl)-hexyl ester, 2-furfural sodium, and syringaldehyde [30].

E. Volatile Components

The volatile components of RC contained two kinds: neutral and acidic, and the total number was over hundreds of kinds. Xie extracted 268 volatile components by using cold leaching in diethyl ether-reflux extraction-distillation with vapour from C. pilosula (Franch) Nannf., and sixty-four of them were identified. Involving Alkanes: tetradecane, pentadecane, hexadecane etc.; Fatty acids: hexanoic acid, heptanoic acid, decanoic acid; Fatty acid esters: methyl octanoate, tricrotylorthoformate, methy tetradecanoate, and so on. In addition, there were also aldehydes, alcohols, olefins, and nitrogen components [31]. Recently, Yang analyzed volatile components of C. tangshen Oliv. by GC-MS and identified seventy-three species volatile compounds. The results showed that the main volatile components of C. tangshen Oliv were aliphatic hydrocarbon, fatty acid, phenols, terpenes. Among them, palmitic acid occupies 36.89%, and (E, E)-9, 12-Octadecadienoic acid, and methyl ester 34.25% [32].

F. Amino Acids

Twenty amino acids were isolated from RC. They were: asp, thr, ser, glu, gly, ala, cys, val, met, ile, tyr, phe, lys, his, arg, pro, leu, asp-NH2 and glu-NH2. It was firstly found trp from C. pilosula (Franch) Nannf [23].

G. Inorganic Elements

Zhang analyzed the inorganic elements of C. pilosula (Franch) Nannf. by using ICP-AES and AAS, and he found thirty-three inorganic elements, such as Fe, Cu, Zn, Mn, Cr, Mg, Ca, Se, Al, P, B, Sr, Hg, Pb, Ba, As, Ce, Be, Ni, Nb, V, Ti, Co, Ge, Mo, Cd, Li, Te, W, Ag, Si, Bi and Sn. Furthermore, the results showed that the contents of nutrient elements for human body such as P, Ca, Mg, Si, Mn, Sr, Zn and Cu were higher, but the contents of pollution elements such as Pb, Cd, As, Hg and Be were lower [33].

H. Others

Zhu isolated and identified angelicin, succinic acid and psoralen from C. pilosula firstly [28]. Meng determined the content of ferulic acid by HPLC in 2003 [34]. He analyzed eleven different RC samples from different places, concluded that lobetyolin was one of the active components of Codonopsis, which could be used to control the quality of RC [35]. Later, He separated lobetyolin, lobetyolinin, 3', 4', 5, 9, 9'-pentaydroxy-5-4, 7'- epoxylignan, uracil and emodin from C. pilosula (Franch.) Nannf, and the latter three compounds were isolated from genus Codonopsis for the first time [19].

III. PHARMACOLOGY

According the traditional medical, RC could invigorate spleen to replenish qi, promote the production of body fluid to quench thirst, activating blood and dissolving stasis, regulating spleen and stomach. The modern pharmacology researches showed that the chemical components of RC discussed above constituted the material basis for being invigorator. RC could strengthen physical fitness, improve human immunity, improve memory and it has the effects of anti-aging, antioxidation, anti-hypoxia, anti-fatigue, antitumor, and so on.

A. Effect on Central Nervous System

Wang reported that the injection of RC extractions could inhibit central nervous system significantly. The extractions could cooperate with the anesthetic action of aether, enhance the sleeping caused by sodium amobarbital, and antagonize convulsion caused by electricity, pentylenetetrazol and strychnine nitrate [36]. Xu studied the mice freedom movement after intraperitoneal administration and found that Codonopsis polysaccharide (CPP) had inhibition effect on central nervous system, which could obviously decreased mice freedom movement, increased sleeping effect induced by pentobarbital sodium and chloral hydrate. At the same time, CPP could decrease the body temperature. Therefore, CPP had the analgesic and antipyretic activities and implied that it was the central inhibitory components of RC [37].

RC could act on both side of cerebrum to facilitate the memory of young and elder man. Zhang found that RC could prolong the sleeping time induced by pentobarbital sodium and ether by the method of water maze performance. In addition, RC could also improve the study and memory disturbance of mice induced by scopolamine [38].

B. Effect on Immunoregulation

Many studies proved that RC could enhance the organic immune activity. Song observed the efficiency of the mixture of RC, Atractylodes and Poria cocos extracts treating on fifteen cases cystic acne patients and five cases psoriasis vulgaris. The result showed that it could enhance the E-rossette formation, IgG content and rate of lymphocyte transformation induced by phytohemagglutinin [39].

And CPP had a potentiation of mitogenic responses stimulated by concanavalin A (ConA) or lipopolysaccharide (LPS) [40]. There were preliminary immunological tests in vitro showed that CPP could stimulate ConA or LPS induced lymphocyte proliferation in a dose-dependent manner [41]. B.E. Shan found that RC extract had a stimulating activity on human lymphocytes and it could be used clinically for the treatment of diseases such as cancer [42].

Jia studied the murine macrophage J 774 cell treated with RC aqueous extract in different concentrations, and measured the phagocytic activity directly using a computerized microplate fluorometer. The result showed that the phagocytosis of macrophage J 774 was enhanced significantly by RC solution in the concentration 500μg/mL to 3000μg/mL ($P<0.05$), and the maximum rate of increase was 170% when compared with the control group. The results suggested that the mechanism of the enhancing immunocompetence of RC could be probably accomplished through the augment of macrophage function [43].

Cao found that CPP could promote lymphocyte proliferate reaction and IL-2 production obviously, and this preference was potentiated by increasing dose in chickens [44].

Yang injected the sheep red blood cells (SRBC) and

ovalbumin into mice in vivo, and then detected their corresponding antibodies after gaveling with CPP, they found that the immune response increased by gaveling CPP. This result may indicate that polysaccharides macromolecules could exert immunoregulatory activities with receptor of intestinal mucosal immune system, but the mechanism need to be further studied [45]. There were also researches indicating that, after subcutaneous administration of RC liquor and RC polysaccharide, the phagocytic index and phagocytic percentage of intraperitoneal macrophages significantly increased, so did the weight of immune organs [46].

C. Effect on Cardiovascular System

There were many studies focused on the effect of RC on cardiovascular system. Wang treated twenty-four angina pectoris patients with RC oral liquor for seven days, and another ten cases were treated by aspirin as the control group. After treatment, cyclooxygenase, TXA2 synthase and PGI2 synthase were inhibited by RC in a dose-dependent (3-300mg/ml), and TXA2 synthase was distinctly inhibited with a dose of 100 mg/ml, which suggested that RC might be an inhibitor of TXA2 synthase to prevent thrombus formation at that dose. And at the dose of 300mg/ml, TXA2 synthase and PGI2 synthase were inhibited simultaneously, so the balance of PGI2/ TXA2 was disturbed. Then RC showed procoagulant effect. These results indicated that RC possessed a biphasic effect on thrombus formation under different dosage [47, 48].

Wang researched about the effect of RC on improving cardiac function and activating circulation and removing stasis in coronary heart disease. The results indicated that the maximum velocity of E-wave and gradient of twenty patients were increased obviously after taking medicine for fourteen days, but acceleration time, acceleration time addition deceleration time were significantly reduced as diastole earlier period, and cardiac output were increased while heart rate showed no significant change. Wang also found that different extraction solvents corresponded different effects. The water extraction of RC were able to reduce the blood stickiness of rats while the ether extraction could increase the activity of fibrimolysis and reduce the platelet aggregation, the plasma level of TXB2 and 6-keto-PGF1α in rats [49].

Lin adopted the cytochemical qualitative and quantitative analysis to detect the quantity and activity of the glycogen and succinate dehydrogenase (SDH) in peripheral blood cells of the coronary heart patients after continuous administration of RC oral liquor for four weeks. The results indicated that the quantity and activity of glycogen and SDH of the coronary heart patients were significantly increased [50].

D. Effect on Digestive System

The antiulcer action, effect on gastrointestinal motility and endocrine of RC had been confirmed by several studies. Liu conducted a series of studies to examine the effect of RC on resisting gastric mucosa lesion. The results indicated that RC could protect gastric mucosal damage significantly. It could resist gastric mucosa injury caused by alcohol, 0.6N HCl and 0.2N NaOH, increase the content of conjugated mucus markedly on gastric mucosal wall of the normal rats, decrease the content of gastric juice, gastric acidity, total acid output and clearance neutral red from blood to gastric juice in ligated pylorus rats. Liu held that the effects of RC on preventing gastric mucosal damage were related to the enhancement of cytoprotective effect on gastric mucosa and these pharmacological effects were in a dose dependent manner. RC also could markedly antagonize the spasmodic constriction of isolated ileum segments of rabbits induced by acetylcholine [51-56].

Han reported that the neutral butanol extract of RC (NBEC) had obvious prevention and protection effects on gastric ulcer in rat models induced by stress, pyloric ligation, indomethacin and aspirin. NBEC could raise the content of PGE2, hexosamine and cAMP which had been decreased by indomethacin and aspirin in rats gastric glandular mucosa, it also could inhibit the gastric secretion and prevent the back diffusion of H+ and Na+ induced by aspirin damaged gastric mucosal barrier. This could be concluded that the antiulcer effect of NBEC was related to the inhibitation of gastric acid and the strengthening of gastric mucosal barrier [57].

Wang obtained the same conclusion as Han by using RC extract onto five animal models of gastric ulcer and he found that the extract was capable of reducing gastric acid pepsin secretion. Hence, Wang believed that one of the mechanisms underlying the antiulcer effect of RC could be attributed to the inhibition of gastrointestinal movement and propulsion [58].

Song studied the protective effect of lobetyolin on gastric mucosa of experimental gastric ulcer rats induced by ethanol. The results showed that the index of ulcer was markedly decreased; the level of gastrin was decreased while the level of 6-K-PGF1α was increased, in degree, and the level of epidermal growth factor (EGF) was increased in lobetyolin small dose group. This indicated that lobetyolin could play a protective role in gastric mucosa injury, and the mechanism may be relate to the increase of the level of 6-K-PGF1α, and the inhibition effect of the excretion of gastric acid, then stimulated gastric mucosa to synthesize and release EGF [59].

Kong reported that RC extracts could promote ornithine decarboxylase (ODC) protein expression better than single medicine. And this phenomenon may indicate that the extract could promote cell proliferation by activating ODC and repair mucosa [60].

It was reported that magnetized RC solution could increase the activity of stomach protease [61]. Ning reported that magnetized RC solution had remarkable effects on small intestines smooth muscle. While the magnetization concentration increased, so did the inhibition on contractive activity. Magnetized medicine liquid could also release spasmodic and automatic contraction of isolated rabbit intestines induced by BaCl2 [62]. Li held that the magnetized RC solution could increase the small intestinal propulsion movement remarkably [63].

E. Effect on Blood and Hemopoietic System

It was reported that RC could improve microcirculation and organism hemorheology, and decrease erythrocyte sclerosis index [64].

Song found that RC had inhibition and depolymerization functions on the aggregated platelets induced by ADP in rabbits, and the action intensity related to dosage [65].

Zhang reported that RC polysaccharides could elevate the hemoglobin content of the hemolysis-induced bloodideficiency mice and increase the formation of endogenous spleen colony, but have less effect on DNA synthesis in the bone marrow of blood-deficiency mice caused by 60Co-γ ray. In conclusion, RC polysaccharides could

improve the compensatory hematopoiesis of spleen [66].

Wang held that RC could increase leukocyte count of all cancer patients who treated with radiotherapy and the effect was better when combining with the leukocyte increasing drug [67]. Gao found that RC could significantly decrease red blood cell count and hemoglobin concentration ($p<0.01$), and increase the platelet count. And the effect of magnetized medicinal solution was better than non-magnetized one [68].

F. Organism-Protecting Actions

Recently, some studies showed that RC had protective effects on body injury. It was reported that RC could increase the concentrations of blood gastrin and motilin, also lower blood tumor necrosis factor markedly. Therefore, it was beneficial to ameliorate gastrointestinal functional disturbance and prevent gut-derived infection [69].

Yan and Zhang observed the preventive effect of the RC saponin on the lesion of cultured primary atrocities in rats induced by hypoxia and hypoglycemia reoxygenation. The results showed that RC saponin had a remarkable inhibitory effect on the necrosis of astrocytes after hypoxia and hypoglycemia reoxygenation lesion but no preventive effect on apoptosis, which indicated saponin is the main active principle in RC for treatment of acute stroke [70, 71].

It was reported that RC polysaccharides could inhibit the production of linear DNA and make DNA keep at nature state without damage; it could also reduce neural stem cells death rate and lactate dehydrogenase (LDH) leakage which induced by Na2S2O3 [72].

G. Anti-Aging and Anti-Oxidation

At present, many studies focused on the anti-aging and anti-oxidation effects of RC, and provided scientific basis for making RC as a new health product or drug.

Wang showed that RC could improve IL-2 level and repair immune senescence of senescence organism, so as to delay senile immunity [73].

T. B. Ng compared the aqueous extracts of Panax quinquefolium, Panax notoginseng, Codonopsis pilosula, Pseudostellaria heterophylla and Glehnia littoralis, and found that Glehnia littoralis and Codonopsis pilosula were the most potent in inhibiting erythrocyte hemolysis [74].

Xu found that RC polysaccharide could notably enhance thymus index and spleen index, decrease malondialdehyde while enhance superoxide dismutase in serums and livers, decrease lipofuscin in brains while enhance activities of glutathione peroxidase and nitric oxide synthase in kidneys of senile model rats. So that, it was thought that the postpone senility mechanism of RC polysaccharide probably connected with its ability of rising immunity, eliminating free radicals and anti-lipid peroxidation [75].

Chan studied the antihyperglycemic and antioxidative effects of a herbal formulation (SR10) of Radix Astragali, Radix Codonopsis and Cortex Lycii in a mouse model of type Ⅱ diabetes mellitus, and concluded that SR10 was effective in decreasing the blood glucose level in chronic treatment by improving β-cell function. The activities and expression of antioxidant enzymes, catalyses and superoxide dismutase, were up-regulated when treated with SR10. Moreover, SR10 treatment did not exhibit any toxic effect to the host [76, 77].

H. Others

Besides the functions above-mentioned, RC also had antibacterial, anti-tumor [17], anti-stress [78], anti-anoxia and anti-fatigue [79, 80] activities.

IV. CONCLUSIONS

In recent years, RC was more and more in people's graces as a security Chinese traditional medicine. And because of the abundant amino acid, inorganic elements and vitamin, the edibility of RC has gotten more and more attention, and its health products also has been accessed to market.

With the further attention and more application of RC, it was imperative to develop new resources. For a long time, people just used its root, and the aerial part was deserted. But later, many studies indicated that the content of amino acid, trace element, choline and carbohydrate were abundant in the aerial part [81, 82]. Therefore, further study and utilization should focus on the aerial part as the food plant and health product.

Recently, many studies reported that there were other species in Codonopsis also have similar chemical constituents and medicinal function. Just like C. lanceolata, C. clematidea (Schrenk) Clarke., C. xundianensis Wang ZT et Xu GJ [83]. For example, there were six flavonoids, four alkaloids, twelve triterpenes and sterols, ten volatile oils, twelve trace elements and seventeen amino acids isolated from C. lanceolata [84, 85]. It could prevent and protect hepatic against alcoholic injury [86, 87], and have the effects on anti-mutation, antioxidation, anti-aging, improving immunity, anti-fatigue, sedation, analgesic, lowering blood pressure, and so on [88].

The mechanism of traditional chinese medicine was very complicated, it did not just react by single chemical constituent or single medicine, but was the comprehensive action of many chemical constituents and medicines. The current researches mainly concentrated on the chemical constituent and pharmacological action, but the study on the pharmacological mechanism was seldom. Moreover, the combined application of the compound codonopsis preparation and western medicine could increase the efficacy and release the toxic and side effects of western medicine. So, more and more studies were needed in these aspects to support the tangible proof for clinical application.

REFERENCES

[1] Chinese Pharmacopoeia Commission. China Pharmacopoeia, Vol.1, Chemical Industry Press, Beijing, pp. 199, 2005.

[2] Editorial committee of flora of China. Flora of China, vol. 73. Science Press, Beijing, pp. 2-77, 1983.

[3] E. G. Han, S. Y. Cho. Effect of *Codonopsis lanceolata* water extract on the activities of antioxidative enzymes in carbon tetrachloride treated rats, Han'guk Sikp'um Yongyang Kwahak Heochi, 26(6): 1181-1186, 1997.

[4] Y. Li, P. Sun, X. Liu, J. M. Dan, et al. Extraction, content determinations and preliminary study on the immune function of polysaccharide of *Codonopsis clematidea* (schrenk) Clarke, Chinese Traditional Patent Medicine, 27(7): 839-840, 2005.

[5] T. Z. Zheng, W. Li, S. Y. Qu, Y. M. Ma, et al. Effects of Dangshen on isolated gastric muscle strips in rats, World Journal of Gastroenterology, 4(4): 354-356, 1998.

[6] X. D. Zhang, X. Tong, L. Liu, Y. S. Zhu. Comparison of *Radix Codonopsis* and *Radix Astragali* on ECG of experimental myocardial ischemia rats, Chinese Traditional and Herbal Drugs, 34(11): 1018-1020, 2003.

[7] X. D. Zhang, L. Liu, X. Tong. Comparison of effect of lanceolata and astragalus on electrocardiogram of rats with experimental myocardial

ischemia, Chinese Journal of Clinical Rehabilitation, 9(47): 142-143, 2005.

[8] Z. T. Wang, T. B. Ng, H. W. Yeung, G. J. Xu. Immunomodulatory effect of a polysaccharide-enriched preparation of *Codonopsis pilosula* roots, General Pharmacology: The Vascular System, 27(8): 1347-1350, 1996.

[9] C. Y. Li, H. X. Xu, Q. B. Han, T. S. Wu. Quality assessment of *Radix Codonopsis* by quantitative nuclear magnetic resonance, Journal of Chromatography A, 1216(11): 2124-2129, 2009.

[10] J. H. Peng, Y. J. YU. Advances in study of Codonopsis lanceolata, Special Wild Economic Animal and Plant Research, 31(1): 70-73, 2009.

[11] J. Q. Wang, W. X. Di, J. W. Yang, Y. Q. Liu. The effect of Radix Codonopsis essential on the mice transplant tumor Hep、E.C and the life span of drosophila, Journal of Traditional Chinese Veterinary Medicine, 5: 11-13, 1999.

[12] C. Q. Bai, X. Y. Di, G. J. Liu, N. X. Li, et al. Effect of Astragalus and Codonopsis extraction on toxicity relief of chemotherapy for lung cancer and survival quality, Chinese Journal of Rehabilitation Medicine, 21(8): 707-709, 2006.

[13] C. Q. Bai, Y. F. Song, D. T. Wang, H. L. Guo. Inhibitory effect of huangqi and dangshen extraction with pacilitaxel on metastasis and angiogenesis on mouse Lewis lung carcinoma model, Chinese Journal of Cellular and Molecular Immunology, 24(4): 375-377, 2008.

[14] C. Q. Bai, Y. F. Song, D. T. Wang, H. L. Guo. Inhibitory effect of Astragalus and Codonopsis extraction endothelial cell migration induced by lung cancer cell. Medical Journal of the Chinese People's Armed Police Forces, 19(6): 505-507, 2008.

[15] Z. Zhang, Y. F. Yan, Y. Wei, H. Lin, et al. Effect of total saponin of Radix Codonopsis on the apoptosis of nerve cell induced by hypoxia, hypoglycemia and reoxygenation in cortex of rats, Chinese Journal of Clinical Rehabilitation, 9(1): 131-133, 2005.

[16] X. Xu, Z. M. Zhang, B. Ge, J. F. Pu. Study effect and its mechanism on resisting senility of PCPN. Chinese Journal of Modern Applied Pharmacy, 26(8):729-731, 2006.

[17] J. Q. Wang, W. X. Di, G. L. Zhou, H. Y. Guo. Study on antitumor and antibacterial of Radix Codonopsis saponin and liposoluble constituent, Journal of Traditional Chinese Veterinary Medicine, 1: 11-12, 1999.

[18] H. Y. Bi, L. P. Zhang, Z. Chen, B. Wu. An overview of research on germplasm resources of Radix Codonopsis and their utilization, China Journal of Chinese Materia Medic, 33(5): 590-594, 2008.

[19] Y. L. He, X. E. Li, G. Z. Pan, W. J. Li. Study on quality variation of Codonopsis pilosula (Franch.) Nannf, Lishizhen Medicine and Materia Medica Research, 17(9): 1727-1728, 2006.

[20] Y. R. Lu, X. Y. Yang, D. Z. Sha. Determination of Δ7-stigmasterol and levulose of five Codonopsis, China Journal of Chinese Materia Medica, 14(8): 36-38, 1989.

[21] Y. J. Zhang, Z. Y. Liang, W. Zhao, X. Huo, et al. Separation, purification and compositional analysis of water soluble polysaccharide CPPS3 from Codonopsis pilosula, Chinese Pharmaceutical Journal, 40(14): 1107-1109, 2005.

[22] F. M. Han, L. L. Cheng, Y. Chen. Study on isolation and composition of Codonopsis tangshen polysaccharides, Chinese Pharmaceutical Journal, 40(18): 1381-1383, 2005.

[23] Q. He, E. Y. Zhu, Z. T. Wang, G. X. Yu, et al. Study on Chemical Constitutes of Codonopsis pilsula, Chinese Pharmaceutical Journal, 41(1): 10-12, 2006.

[24] D. G. Cai. Recent studies on the chemical constituents of Radix Codonopsis, China Journal of Chinese Materia Medica, 16(6): 376-377, 1991.

[25] J. Z. Wang, F. P. Wang. Studies on the chemical constituents of Codonopsis tangshen Oliv.. Natural product research and development, 8(2): 8-12, 1996.

[26] K. Mizutani, M. Yuda, O. Tanaka, Y.-I. Saruwatari, et al. Chemical studies on Chinese traditional medicine, Dangshen. I. : Isolation of (Z)-3- and (E)-2-Hexenyl β-D-Glucosids, Chemical & Pharmaceutical Bulletin, 36(7): 2689-2690, 1988.

[27] K. Mizutani, M. Yuda, O. Tanaka, Y.-I. Saruwatari, et al. Tanghenosides I and II from Chuan-Dangshen, the root of Codonopsis Tangshen Oliv., Chemical & Pharmaceutical Bulletin, 36(7): 2726-2729, 1988.

[28] E. Y. Zhu, Q. He, Z. T. Wang, L. S. et al. Chemical study on the root of Codonopsis pilsula, Journal of China Pharmaceutical University, 32(2): 94-95. , 2001.

[29] K. Ogihara, K. Munesada, T. Suga. Variations in leaf terpenoids with ploidy level in citrus cultivars and hybrids, Phytochemistry, 29(6): 1889-1891, 1990.

[30] Z. T. Wang, G. J. Xu, M. Hattori. Constituents of the roots of Codonopsis pilosula, Journal of China Pharmaceutical University, 42(4): 339-342, 1988.

[31] J. Xie, Y. Z. Zhang, Y. Z. Gu, C. Z. Dai. Analysis of volatile components in Radix Codonopsitis Pilosulae, Journal of Instrumental Analysis, 19(4): 54-56, 2000.

[32] R. P. Yang, B. H. Wang, N. Li，X. M. Zhang. Analysis of volatile components in Codonopsis tangshen Oliv. by GC-MG, China Practical Medicine, 2(25): 33-34, 2007.

[33] W. C. Zhang. An analysis on the inorganic elements of the Codonopsis pilosula, Journal of Sichuan Normal University (Natural Science), 18(2): 93-97, 1995.

[34] Y. B. Meng, S. Sun, Y. F. Su. Determination of ferulic acid content in Codonopsis pilsula with HPLC, Journal of Chengde Medical College, 20(2): 140-141, 2003.

[35] Q. He, E. Y. Zhu, Z. T. Wang, L. S. Xu, et al. Determination of lobetyolin in Radix Codonopsis by high-performance liquid chromatography, Chinese Pharmaceutical Journal. 40(1): 56-58, 2005.

[36] K. Z. Wang, H. X. Lu, F. C. Lu, G. Z. Ding, et al. The effect of Radix Codonopsis on central inhibitory, China Journal of Chinese Materia Medica, 11(3): 49-50, 1986.

[37] Q. P. Xu, J. N. Sun, C. X. Zhu, J. Y. Wu, et al. Dang Shen Fu Fang improve chemical-induced amnesia in mice, Pharmacology and Clinics of Chinese Materia Medica, 5(2): 25-28, 1989.

[38] X. D. Zhang, L. Liu, X. Tong. Comparison of Radix Codonopsis and Radix Astragali on central nervous system, Chinese Traditional and Herbal Drugs, 34(9): 822-823, 2003.

[39] F. J. Song, H. D. Chen, G. Y. Yue, J. C. Yang, et al. Study on the immune stimulation of Radix Codonopsis, atractylodes and poria cocos, New Medical Journal, 6: 60-61, 1979.

[40] Z. T. Wang, T. B. Ng, H. W. Yeung, G. J. Xu. Immunomodulatory effect of a polysaccharide-enriched preparation of Codonopsis pilosula roots, General Pharmacology: The Vascular System, 27(8): 1347-1350, 1996.

[41] Y. X. Sun, J. C. Liu. Structural characterization of a water-soluble polysaccharide from the Roots of Codonopsis pilosula and its immunity activity, International Journal of Biological Macromolecules, 43(3): 279-282, 2008.

[42] E. Shan, Y. Yoshida, T. Sugiura, U. Yamashita. Stimulating activity of Chinese medicinal herbs on human lymphocytes in vitro, International Journal of Immunopharmacology, 21(3): 149-159, 1999.

[43] T. Y. Jia, H. S. Lau Benjamin. The Enhancing Effect of Chinese Medicine Radix pilosulae on J774 Macrophage, Lishizhen Medicine and Materia Medica Research, 11(9): 769-770, 2000.

[44] L. Cao, C. N. Luo, Q. Y. Bian, J. M. Chen. Promotive effect of Codonopsis pilosula polysaccharide on IL-2 inductive activity and lymphocyte proliferative reaction in chickens, Journal of Traditional Chinese Veterinary Medicine, 1:3-4, 2004.

[45] G. Yang, F. S. Li, H. Liu, F. Xian. The effct of Codonopsis polysaccharide on immune function of mice, Pharmacology and Clinics of Chinese Materia Medica. 21(4):39-40, 2005.

[46] Q. X. Tang, G. Q. Cheng, X. W. Zhang. The effect of Codonopsis liquor and Codonopsis polysaccharide on immune function of C57BL/6 mice, Endemic Diseases Bulletin, 11: 1-3, 1996.

[47] S. R. Wang, G. Q. Zhu, X. Q. Qu, Z. Wang, et al. Effects of Codonopsis pilosulae on the synthesis of thromboxane A2 and prostacyclin, Chinese Journal of Integrated Traditional and Western Medicine, 10(7): 391-394, 1990.

[48] S. R. Wang, Z. Q. Guo, J. Z. Liao. Experimental study on effeets of 18 kinds of Chinese herbal medicine for synthesis of TXA2 and PGI2, Chinese Journal of Integrated Traditional and Western Medicine, 13(3): 167-170, 1993.

[49] S. R. Wang, X. Xu, Q. Lin, H. Qin, et al. Study of Codonopsis pilosulae on effect of improving cardiac function and activating blood circulation and removing stasis, Pharmacology and Clinics of Chinese Materia Medica, 1: 32-37, 1994.

[50] Q. Lin, Y. H. Yu. Study on cytochemical quantitative analysis of the effect of Radix pilosulae on the peripheral blood cells of CHD patients and mice myocardium, Chinese Journal of Histochemistry and Cytochemistry, 3(4): 399-401, 1994.

[51] L. Liu. Studies on the pharmacologica effects and mechanisms of

Codonopsis pilosula (CP) and its efficacious chemical ingredients on preventing the gastric mucosal damage of rats Ⅰ. The effects of the decoction of CP, Pharmacology and Clinics of Chinese Materia Medica, 5(2): 11-14, 1989.

[52] L. Liu. Studies on the pharmacologica effects and mechanisms of Codonopsis pilosula (CP) and its efficacious chemical ingredients on preventing the gastric mucosal damage of ratsⅡ. The effects of the extracts of CP, Pharmacology and Clinics of Chinese Materia Medica, 5(3): 11-14, 1989.

[53] L. Liu. Studies on the pharmacologica effects and mechanisms of Codonopsis pilosula (CP) and its efficacious chemical ingredients on preventing the gastric mucosal damage of ratsⅢ. The effect of factions extracted from the section Ⅶ of CP, Pharmacology and Clinics of Chinese Materia Medica, 6(5): 20-23, 1990.

[54] L. Liu. Studies on the pharmacologica effects and mechanisms of Codonopsis pilosula (CP) and its efficacious chemical ingredients on preventing the gastric mucosal damage of rats Ⅳ. The effects of the fraction-2 of extract Ⅵ (Ⅵ-F2) of CP on gastric mucosal barrier, Pharmacology and Clinics of Chinese Materia Medica, 6(2): 11-14, 1990.

[55] L. Liu. Studies on the pharmacologica effects and mechanisms of Codonopsis pilosula (CP) and its efficacious chemical ingredients on preventing the gastric mucosal damage of rats Ⅴ. The effects of extract Ⅶ-F2 of CP on prostaglandins content in gastric mucosal of rats, Pharmacology and Clinics of Chinese Materia Medica, 6(3): 9-11, 1990.

[56] L. Liu. Studies on the pharmacologica effects and mechanisms of Codonopsis pilosula (CP) and its efficacious chemical ingredients on preventing the gastric mucosal damage of rats Ⅵ. The effects of extract Ⅶ-F2 of CP on gastric secretion, gastric mucosal blood flow and gastrointestinal motility, Pharmacology and Clinics of Chinese Materia Medica, 6(4): 20-23, 1990.

[57] P. S. Han, M. Y. Jiang, Q. P. Xu. Effects of extract of Codonopsis pilosula on experimental gastric ulcers and gastric mucosal barrier in rats, Pharmacology and Clinics of Chinese Materia Medica, 6(1): 19-23, 1990.

[58] Z. T. Wang, Q. Du, G. J. Xu, R. J. Wang, et al. Investigations on the protective action of condonopsis pilosula (CP) extract on experimentally-induced gastric ulcer in rats, General Pharmacology: The Vascular System, 28(3): 469-473, 1997.

[59] Song, Z. T. Wang, L. Y. Li, G. Y. Zhong. Protective effect of lobetyolin on gastric mucosa of experimental gastric ulcer in rats, Journal of Emergency in Traditional Chinese Medicine, 17(7): 963-964, 2008.

[60] X. Y. Kong, B. Wen, W. W. Chen. The effect on IEC-6 proliferation, the expression of ODC and hephaestin of Radix Codonopsis and Astragalus, Journal of Chinese Medicinal Materials, 32(3): 407-410, 2009.

[61] L. S. Gao, L. X. Ning, F. P. Zeng, H. Y. Zhou, et al. Researches on effects of magnetized Codonopsis pilosula (franch.) Nannf. or Atractylodes marocephala koidz medicinal solution on activity of stomach protease, Biomagnetism, 4(3): 3-5, 2004.

[62] L. X. Ning, F. P. Zeng, X. D. Wu, C. R. Li, et al. Studies on medicinal effects of magnetized Codonopsis pilosula Nannf. on contractive activity of small intestines smooth muscle, Biomagnetism, 4(3): 6-9, 2004.

[63] R. Li, L. X. Ning, S. J. Su, F. P. Zeng, et al. Researches on the effect of magnetized Codonopsis pilosula (franch.) Nannnf. solution on rat's small intestinal propulsion movement, Biomagnetism, 4(3): 9-11, 2004.

[64] K. Z. Wang, F. C. Lu, H. X. Lu, Z. X. Gao. The effect of Radix Codonopsis on hemorheology, Bulletin of Chinese Materia Medica, 13(12): 43-47, 1988.

[65] J. N. Song, F. Q. Li, P. L. Li, Y. S. Wu. The effect of some traditional Chinese medicine on platelet aggregation in rats, Bulletin of Chinese Materia Medica, 9(4): 38-40, 1984.

[66] X. J. Zhang, C. C. Zhu, L. Hu, X. P. Lai, et al. Pharmacological action of polysaccharides from Radix Codonopsis on immune function and hematopoiesis in mice, Traditional Chinese Drug Research & Clinical Pharmacology, 14(3): 174-176, 2003.

[67] H. X. Wang, S. Y. Sui. The observation of curative effect of Radix Codonopsis and increased leukocyte drug, Modern Journal of Integrated Traditional Chinese and Western Medicine, 13(23): 3218, 2004.

[68] L. S. Gao, F. P. Zeng, L. X. Ning, H. Y. Zhou, et al. Researches on effects of magnetized Codonopsis Pilosula (Franch.) Nannf. Medicinal solution on blood function of small rats, Biomagnetism, 5(1): 14-16, 2005.

[69] S. G. Wang, H. Q. Xu, X. Y. Chen. Protective effect of Codonopsis pilosula on intestine in severe scalded guinea pigs, Chinese Journal of Integrated Traditional and Western Medicine in Intensive and Critical Care, 12(3): 144-145, 2005.

[70] Y. F. Yan, Z. Zhang, Y. Wei, F. L. Niu, et al. Prevective effect of total saponin of Radix Codonopsis on ast lesion induced by hypoxia and hypoglycemia reoxygenation in rats, Journal of Beijing University of Traditional Chinese Medicine, 29(12): 826-828, 2006.

[71] Z. Zhang, Y. Wei, N. Liu, Y. F. Yan, et al. Protective effect of saponin L1 of Radix Codonopsis on the damage of cultured astrocytes induced by hypoxia/hypoglycemia reoxygenation, Chinese Journal of Clinical Rehabilitation, 10(27): 28-31, 2006.

[72] B. F. Wu, J. Yang, H. Xie, X. S. Yang. Protective effect of polysaccharides from Codonopsis pilosula on neural stem cell injury induced by Na2S2O3, Lishizhen Medicine and Materia Medica Research, 19(2): 280-281, 2008.

[73] M. Wang, P. Wang, X. P. Hong, Y. M. Han. From IL-2 and its receptors expression to discuss deferring apolexis effect of Codonopsis pilosula, China Journal of Traditional Chinese Medicine and Pharmacy, 21(10): 620-630, 2006.

[74] T. B. Ng, F. Liu, H. X. Wang. The antioxidant effects of aqueous and organic extracts of Panax quinquefolium, Panax notoginseng, Codonopsis pilosula, Pseudostellaria heterophylla and Glehnia littoralis, Journal of Ethnopharmacology, 93(2-3): 285-288, 2004.

[75] X. Xu, Z. M. Zhang, B. Ge, J. F. Pu. Study effect and its mechanism on resisting senility of PCPN, Chinese Journal of Modern Applied Pharmacy, 23(8): 729-731, 2006.

[76] J. Y. W. Chan, P. C. Leung, C. T. Che, K. P. Fung. Protective effects of an herbal formulation of Radix Astragali, Radix Codonopsis and Cortex Lycii on streptozotocin-induced apoptosis in pancreatic β-cells: An implication for its treatment of diabetes mellitus, Phytotherapy Research, 22(2): 190-196, 2008.

[77] J. Y. W. Chan, F. C. Lam, P. C. Leung, C. T. Che, et al. Antihyperglycemic and Antioxidative Effects of a Herbal Formulation of Radix Astragali, Radix Codonopsis and Cortex Lycii in a Mouse Model of Type 2 Diabetes Mellitus, Phytotherapy Research, 23(5): 658-665. , 2009.

[78] X. Tong, X. D. Zhang, L. Liu, Y. S. Zhu, et al. Comparative study on Astragalus and Codonopsis on effect of anti-stress of mice, Journal of Harbin University of Commerce Natural Sciences Edition, 19 (5): 514-516, 2003.

[79] Z. T. Wang, G. J. Xu. Fatigue durabillty and anti-anoxia effeets of Radix Codonopsis, Journal of Plant Resources and Environment, 1(3): 10-14, 1992.

[80] K. Z. Wang, H. Xu, X. H. Liu, S. J. Jiang, et al. Preliminary study on anti-fatigue effect of Codonopsis pilosula mixture, Chinese Traditional Patent Medicine, 30(4): 599-600, 2008.

[81] P. F. Jiang, Y. H. Yan, Z. J. Zhao, W. Q. Jiang. Analysis of the nutritive constituents in the aerial parts of Codonopsis pilosula, Natural Product Research and Development, 4(3): 31-35, 1992.

[82] Y. H. Yan. The basic research on the aerial parts of Codonopsis pilosula, Journal of Jiangxi College of Traditional Chinese Medicine, 14(1): 30-31, 2002.

[83] Q. He, E. Y. Zhu, Z. T. Wang, L. S. Xu, et al. Flavones Isolated from Codonopsis xundianensis, Journal of Chinese Pharmaceutical Sciences, 13(3): 212-213, 2004.

[84] C. G. Fu, L. K. Wen, R. Dong. The research progress on chemical constituents and pharmacological activities of Codonopsis lanceolata, Journal of Chinese Medicinal Materials, 30(4): 497-499, 2007.

[85] Z. M. Liang, Z. Z. Lin, Z. Yuan. Studies on the chemical constituents of the Codonopsis lanceolata, China Journal of Chinese Materia Medic, 32(13): 1363-1364, 2007.

[86] L. Zhang, C. J. Han, L. J. Li, L. Tao, et al. The preventive effect of the compound Codonopsis lanceolata on alcoholic hepatic injury in mice, Journal of Toxicology, 21(4): 265-267, 2007.

[87] X. S. Bai, C. J. Han, J. Bao. Studys on the mechanism of the compound Codonopsis lanceolata on alcoholic hepatic injury, Journal of Toxicology, 22(1): 42-44, 2008.

[88] J. H. Peng, Y. J. Yu. Advances in study of Codonopsis lanceolata, Special Wild Economic Animal and Plant Research, 1: 70-73, 2009.

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