Research Progress on Purification Process, Content Determination and Pharmacological Action of Atractylodin

Xin SUN[1], Jingwen WANG[1], Yang XI[1]*, Chenghao JIN[2]*

1. College of Science, Heilongjiang Bayi Agricultural University, Daqing 163319, China; 2. College of Life Science and Biotechnology, Heilongjiang Bayi Agricultural University, Daqing 163319, China

Abstract Atractylodis Rhizoma comes from the dry rhizome of *Atractylis lancea* or *Atractylodes chinensis* in the Compositae family, and it is suitable for preventing and treating diseases such as cold, edema, night blindness and rheumatic arthralgia. Atractylodin is the main active component extracted and isolated from Atractylodis Rhizoma. A large number of studies have found that atractylodin has excellent drug activity in improving gastrointestinal emptying, anti-inflammation, inhibiting malignant tumor and reducing blood lipid. In this paper, the purification process and pharmacological activity of Atractylodin were summarized to provide a theoretical basis for basic research, clinical application and further development and utilization of atractylodin.

Key words Atractylodin, Pharmacological action, Purification process, Content determination

1 Introduction

Atractylodis Rhizoma is a plant in the Compositae family derived from the dry rhizome of *Atractylis lancea* or *Atractylodes chinensis*. In the 2020 edition of *Chinese Pharmacopoeia*, *A. lancea* and *A. chinensis* are listed as Chinese herbal medicines[1], which are often used to treat diseases such as cold, adrenalitis, night blindness and rheumatic arthralgia. The main active component of Atractylodis Rhizoma is volatile oil (generally 5% - 9%), and atractylodin, atractylol, β-eduesmol, atractylone, hinesol are important components of volatile oil[2].

Atractylodin, the main active component extracted and separated from Atractylodis Rhizoma, is polyacetylene compound and presents light yellow needle-like crystal. Its molecular formula is $C_{13}H_{10}O$ and its molecular weight is 182.22. A large number of studies have found that atractylodin has excellent drug activity in improving gastrointestinal emptying, anti-inflammation, inhibiting malignant tumor and reducing blood lipid. In this paper, the purification process and pharmacological activity of atractylodin were reviewed to provide a theoretical basis for the basic research, clinical application and further development and utilization of atractylodin.

2 Physical and chemical characteristics, purification process and content determination of atractylodin

Due to the existence of unsaturated bonds in the chemical molecules of atractylodin, the molecular structure of atractylodin is unstable to some extent. Yang Dongli *et al.*[3] found that there were significant differences in the stability of atractylodin in different media. Although the stability of atractylodin can be maintained in low temperature environment, it is necessary to control the storage time and the storage time should not be too long. The experimental results of Xie Xiaoling *et al.*[4] also showed that atractylodin was easier to decompose or transform under strong light and high heat conditions. In addition, the stability of atractylodin in the fine powder and volatile oil of medicinal materials was more stable than that in other substances. It can be seen that low temperature environment is beneficial to maintaining the stability of atractylodin.

Atractylodin is an important characteristic substance of Atractylodis Rhizoma, and has a relatively high content. The extraction methods of atractylodin mainly include steam distillation, Soxhlet extraction, ultrasonic extraction and supercritical CO_2 fluid extraction[5-6]. Gao Ying *et al.*[7] first used molecular distillation technology to refine Atractylodis Rhizoma oil extracted by supercritical fluid, and then used thermal uniformity analysis technology to design testing methods with two factors of temperature and vacuum and five levels, so that volatile atractylodin could be directly enriched in a lower temperature and higher vacuum environment. By comparing traditional water extraction, reflux extraction and microwave-assisted extraction, Wang Daowu *et al.*[6] found that microwave-assisted extraction could effectively extract a large number of volatile oil components from Atractylodis Rhizoma. Ge Zhenkai *et al.*[8-9] optimized the extraction process by orthogonal test, and finally screened out the microwave extraction method with the advantages of simple operation, high effectiveness, short duration, low consumption and safety.

There were great differences in the content of atractylodin in Atractylodis Rhizoma of various raw materials and producing are-

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* Corresponding author. Yang XI, master's degree, lecturer, research fields: numerical calculation and statistical analysis of data; Chenghao JIN, PhD., professor, research fields: preparation technology and pharmacological activity of anticancer drugs.

as. Chen Jia *et al.* [10] used the application software of "Similarity Evaluation System of Chromatographic Fingerprints of Traditional Chinese Medicine" to determine the content of atractylodin in *A. lancea*, which confirmed that the fingerprints of *A. lancea* from different producing areas were quite different. Sun Jikai *et al.* [11] used HPLC to determine the content of atractylodin in *A. chinensis* from different producing areas and different growing years, and calculated that the content of atractylodin in *A. chinensis* from different producing areas was 0.323 2% – 0.595 9%, and the decoction pieces of *A. chinensis* produced in Arong Banner had the highest content of atractylodin. Among the three-year-old, four-year-old and five-year-old Atractylodis Rhizoma, the four-year-old *A. chinensis* had the highest content of atractylodin, and the best cultivation time of *A. chinensis* was four years. In addition, Bi Jiayao *et al.* [12] studied varieties from different producing areas under the same cultivation techniques, and found that there were still great differences in the content of atractylodin in *A. chinensis*, *Atractylodes lyrata S. et. Z. f.* ternata Nak. and *A. lancea* in the same growth period, among which *A. lancea* had the highest content of atractylodin while *Atractylodes lyrata S. et. Z. f.* ternata Nak. had the lowest content of atractylodin.

3 Anti-inflammatory effect of atractylodin

Inflammation is the defense response of living tissues with vascular system to injury factors. Many diseases are associated with inflammation, such as cardiovascular disease and diabetes. Yu *et al.* [13] found that atractylodin could effectively improve jejunal epithelial inflammation in constipation and diarrhea model rats by inhibiting pro-inflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), interleukin-6 (IL-6), inflammatory mediators inducible nitric oxide synthase (iNOS) and nuclear transcription factor (NF-κB). Qiu Weijian *et al.* [14] found that atractylodin could effectively slow down the inflammatory response of chondrocytes by inhibiting the activation of NF-κB mediated by IL-1β, and could inhibit the inflammatory response of chondrocytes mediated by IL-1β by activating the activity of nuclear receptor (LXRα) ($P < 0.05$). Tang *et al.* [15] found that atractylodin could down-regulate the content of nucleotide binding domain-like receptor protein 3 (NLRP3) inflammatory corpuscles and inhibit Toll-like candidates. Bailly *et al.* [16] found that atractylodin could play an anti-inflammatory role by regulating the signaling pathway of central regulators TLR4, NF-κB and Nrf2.

4 Gastric emptying effect of atractylodin

Gastric emptying refers to the process that food is discharged to duodenum through stomach. The influence of food quantity in stomach on emptying rate and the influence of gastrin production on gastric emptying are two factors to promote gastric emptying. Zhang Mingfa *et al.* [17] found that atractylodin had a good effect on promoting gastric emptying, and its mechanism of action was mainly to inhibit the production of central corticotropin secretion and stimulate vagus nerve, promote the release of gastrointestinal hormones gastrin and motilin, inhibit the release of vasoactive intestinal peptide and increase the number of interstitial cells in gastrointestinal tissues. Bai *et al.* [18] found that atractylodin could promote myosin light chain (MLC) phosphorylation through growth hormone secretagogue receptor, and then promote gastric emptying in mice. In addition, Liu Fen *et al.* [19] found that Atractylodis Rhizoma extract (containing 46.97% atractylodin) could reduce gastric mucosal damage caused by spleen deficiency and inhibit gastrointestinal dysfunction caused by spleen deficiency.

5 Anticancer effect of atractylodin

Cancer cell is a kind of malignant cell mutated by normal cells, and has strong infinite proliferation ability and can destroy normal cell tissues. Therefore, inhibiting the expansion of cancer cells is one of the main means to treat cancer at present. It has been reported that atractylodin can inhibit the growth of many tumor cells, including cholangiocarcinoma, colon cancer and lung cancer.

5.1 Inhibitory effect of atractylodin on proliferation of cancer cells After treating colorectal cancer cells with different concentrations (20, 40, 80 mg/L) of atractylodin for 24 h, Shao Chen *et al.* [20] used MTT method to detect cell survival rate and found that atractylodin could significantly reduce the viability of colorectal cancer cell LS174T, and then inhibit the proliferation of colorectal cancer cell LS174T in a time-and concentration-dependent manner. Through flow cytometry, it was found that the percentage of G_0/G_1 cells in cycle of colorectal cancer cell LS174T increased significantly after being treated with atractylodin. Furthermore, it was found that atractylodin could inhibit the secretion of IL-6 and IL-7 by colorectal cancer cell LS174T by liquid chip detection. These results suggest that atractylodin can inhibit the proliferation of LS174T cells by regulating the release of cytokines (CK) and blocking the cell cycle of colorectal cancer.

5.2 Apoptosis induced by atractylodin Apoptosis is a kind of programmed cell death, which is mainly realized by exogenous pathway mediated by cell death receptor caused by apoptosis receptor and endogenous pathway mediated by mitochondria. At present, inducing apoptosis of malignant tumor cells has become one of the main technical means to treat cancer. Zhang Tong *et al.* [21] used Western blot analysis to find that atractylodin could regulate mitogen-activated protein kinase (MAPK), transcription activator signal transducer 3 (STAT3) and nuclear factor (NF-κB) signaling pathway, up-regulate the expression of p-JNK, p-p38 and p-IκBα, Bad, cytochrome c, cle-caspase-3 and cle-PARP protein, and down-regulate the expression of p-ERK, p-STAT3, NF-κB-p65 and Bcl-2 protein, thus inducing apoptosis of lung cancer cell A549. Kotawong *et al.* [22] found that atractylodin could also induce apoptosis of cholangiocarcinoma CCA cells by regulating caspase-level pathway.

5.3 Inhibitory effect of atractylodin on metastasis of cancer cells Metastasis of cancer cells means that cancer cells invade

other organs or lymphoid tissues of the body through blood metastasis, lymphatic metastasis and implantation metastasis from the primary site, and continue to grow in other places, which can form malignant tumors with the same pathological types as the primary tumors. Qu *et al.* [23-24] found that atractylodin inhibited the migration and invasion of HuCCT1 cells and Huh7 cells in a concentration-dependent manner. Zhang Tong *et al.* [20] used Western blot analysis to find that the expression level of N-cadherin protein decreased significantly and the expression level of E-cadherin protein increased significantly after being treated with atractylodin, indicating that atractylodin could effectively inhibit the migration of lung cancer cell A549.

6 Preventive and therapeutic effect of atractylodin on cardiovascular diseases

Cardiovascular and cerebrovascular diseases are a serious threat to human beings. The number of people who die from cardiovascular and cerebrovascular diseases in the world is as high as 15 million every year, ranking first among all causes of death, with the characteristics of high morbidity rate, high disability rate and high mortality rate. Gao Li *et al.* [25] found that atractylodin could increase the amplitude of calcium release from myocardial cells by regulating PKA-SERCA2a pathway, exert positive inotropic effect, and dilate peripheral blood vessels to reduce diastolic blood pressure. Zhu Huijing *et al.* [26] found that atractylodin could alleviate arrhythmia caused by myocardial ischemia and ischemia-reperfusion in rats, and could reduce SOD activity and MDA concentration in plasma after ischemia and ischemia-reperfusion, thus reducing the scope of myocardial infarction.

7 Prospects

Atractylodin is a natural active substance extracted from Chinese herbal medicine Atractylodis Rhizoma, having many pharmacological effects such as anti-inflammation, anti-tumor, promoting gastric emptying, preventing and treating cardiovascular diseases. It has broad market and development prospects in the optimization of purification process of atractylodin, the basic research and clinical application of pharmacological effects, *etc.* With the national policy support for the revitalization and development of traditional Chinese medicine, it is still necessary to optimize and improve the preparation technology of atractylodin, and at the same time, carry out more scientific and in-depth research on the pharmacological activity of atractylodin, so as to provide a theoretical basis for the further development and utilization of atractylodin.

References

[1] State Pharmacopoeia Commission. Pharmacopoeia of the People's Republic of China[M]. Beijing: China Pharmaceutical Science and Technology Press, 2015. (in Chinese).

[2] ZHANG MF, SHEN YQ. Research progress on anti-inflammatory, anti-tumor and immunomodulatory effects of Atractylodis Rhizoma[J]. Drug Evaluation and Research, 2016, 39(5): 885-890. (in Chinese).

[3] YANG DL, WANG CM, LIU JL, *et al.* Determination of atractylodin in volatile oil of Jingfukang preparation and its stability in different media [J]. Chinese Journal of Traditional Chinese Medicine Information, 2013, 20(7): 55-57. (in Chinese).

[4] XIE XL, GUO JX, YE BH, *et al.* Study on the influencing factors of the stability of atractylla in different existing states[J]. Pharmacy Today, 2013, 23(9): 596-599. (in Chinese).

[5] FU MH, ZHU DH, FANG J, *et al.* Research progress of chemistry, molecular pharmacognosy and pharmacology of Atractylodis Rhizoma[J]. Chinese Journal of Traditional Chinese Medicine, 2009, 34(20): 2669-2672. (in Chinese).

[6] WANG DW, YU WW, CHEN ZM, *et al.* Microwave-assisted extraction and GC-MS analysis of volatile oil from Atractylodis Rhizoma[J]. Shi Zhen Chinese Medicine, 2010, 21(11): 3020-3024. (in Chinese).

[7] GAO Y, LI WM, NI C, *et al.* Application of molecular distillation technology in separation of effective parts of Atractylodis Rhizoma oil[J]. Journal of Guangzhou University of Traditional Chinese Medicine, 2004 (6): 476-478. (in Chinese).

[8] GE ZK, YANG CX, ZHAO YH, *et al.* Orthogonal optimization of microwave extraction process of atractylodin from Atractylodis Rhizoma[J]. Journal of Hubei Medical College, 2016, 35(5): 458-460, 464. (in Chinese).

[9] GE ZK, ZHAO YH, YANG CX, *et al.* Ultrasonic-microwave synergistic extraction of atractylodin from Atractylodis Rhizoma[J]. Medical Herald, 2018, 37(4): 470-472. (in Chinese).

[10] CHEN J, XIE XX, LIU HG. Study on fingerprint of Atractylodis Rhizoma and determination of atractyloin content in several authentic producing areas[J]. Chinese Journal of Experimental Prescription, 2013, 19 (10): 125-127. (in Chinese).

[11] SUN JK, ZHANG MJ, ZHANG HL, *et al.* Determination of Atractylodin in Atractylodis Rhizoma from different sources by HPLC[J]. Journal of Xinjiang Medical University, 2021, 44(1): 102-104. (in Chinese).

[12] BI JY, YIN HB, DENG C, *et al.* Comparative analysis of the contents of three Atractylodes lancestrin and chlorophyll in Liaoning[J]. Guangdong Chemical Industry, 2019, 46(9): 45-47, 69. (in Chinese).

[13] YU C, XIONG Y, CHEN D, *et al.* Ameliorative effects of atractylodin on initial injection and coocccurring dysmotility in both constipation and diarrhea prominent rats[J]. Korean Journal of Physiology & Pharmacology, 2017, 21(1): 1-9.

[14] QIU WJ, XIAO P, WU XJ. Atractylodin inhibits interleukin-1β-induced chondrocyte inflammation of human osteoarthritis[J]. Chinese Journal of Experimental Surgery, 2019(8): 1442-1444. (in Chinese).

[15] TANG F, FAN K, WANG K, *et al.* Atractylodin attenuates lipopolysaccharide-induced acute lung injection by inhibiting NLRP3 inflammasome and TLR4 pathways[J]. Journal of Pharmacological Sciences, 2018, 136 (4): 203-211.

[16] BAILLY, C. Atractylenolides, essential components of At-ractylodes-based traditional herbal medicines: antioxidant, anti-infammatory and anticancer properties[J]. European Journal of Pharmacology, 2021 (891): 173735.

[17] ZHANG MF, SHEN YQ. Research progress on pharmacological effects of Atractylodis Rhizoma and its effective components in digestive system [J]. Drug Evaluation Research, 2017, 40(3): 411-419. (in Chinese).

[18] BAI Y, ZHAO YH, XU JY, *et al.* Atractylodin induces myosin chain phophorylation and promotes gastric emptying through grelin receptor [J]. Evidence-based Complementary and Alternative Medicine, 2017: 2186798.

[19] LIU F, TIAN CM. Effect of atractylodin on gastric mucosal ultrastructure and gastrointestinal function in rats with spleen deficiency syndrome [J]. Chinese Journal of Traditional Chinese Medicine, 2016, 31(3): 1002-1005. (in Chinese).

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tion. In the future, we will prepare recombinant Hcp protein of *A. hydrophila* to further study its immunogenicity.

4.2 Conclusions In this study, the *hcp* gene was successfully cloned from *A. hydrophila* and its bioinformatics analysis was performed. The results showed that the hcp gene had a total length of 1 650 bp and encoded 549 amino acids, with molecular formula $C_{2\,681}H_{4\,196}N_{696}O_{783}S_{24}$, theoretical molecular weight 59 476.44 kDa, and theoretical pI 5.00. The instability coefficient was 20.50, indicating the protein was stable. Neither obvious signal peptide cleavage site nor signal peptide was found, and the protein had no transmembrane region. It might have close genetic relationship with *A. veronii* due to high homology. In the secondary structure, the α-helix, β-sheet, random coil and extended strand accounted for 45.36%, 6.01%, 37.52% and 11.11%, respectively. The tertiary structure model consisted of 18 α-helix and 22 β-sheet. Through the above bioinformatics prediction results, the basic information of *hcp* gene of *A. hydrophila* is preliminarily understood, and the possible function of this protein is predicted, in order to provide guidance for subsequent vaccine research.

References

[1] WANG NN. Functional characteristics of the type VI secretion system effector Hcp in *Aeromonas hydrophila*[D]. Nanjing: Nanjing Agricultural University, 2018. (in Chinese).

[2] BLEVES S, VIARRE V, SALACHA R, *et al.* Protein secretion systems in *Pseudomonas aeruginosa*: A wealth of pathogenic weapons. Journal of Medical Microbiology, 2010(300): 534-543.

[3] LUO GD. Cloning and bioinformatics analysis of T6SS chaperone protein ClpV from *Aeromonas hydrophila*[D]. Ji'nan: Shandong Agricultural University, 2018. (in Chinese).

[4] RUSSELL AB, PETERSON SB, MOUGOUS JD. Type VI secretion system effectors: Poisons with a purpose[J]. Nature Reviews Microbiology, 2014, 12(2): 137-148.

[5] ASCHTGEN MS, BERNARD CS, DE SB, *et al.* SciN is an outer membrane lipoprotein required for type VI secretion in enteroaggregative *Escherichia coli*[J]. Journal of Bacteriology, 2008, 190(22): 7523-7531.

[6] FELISBERTORODRIGUES C, DURAND E, ASCHTGEN MS, *et al.* Towards a structural comprehension of bacterial type VI secretion systems: Characterization of the TssJ-TssM complex of an *Escherichia coli* pathovar[J]. PLoS Pathogens, 2011, 7(11): e1002386.

[7] MA LS, LIN JS, LAI EM. An IcmF family protein, Imp LM, is an integral inner membrane proteirinteracting with ImpKL, and its Walker A motif is required for type VI secretionsystem-mediated Hcp secretion in *Agrobacterium tumefaciens*[J]. Journal of Bacteriology, 2009, 191(13): 4316-4329.

[8] LEROUX M, LEON JA D, KUWADA N J, *et al.* Quantitative singlecell characterization of bacterialinteractions reveals type VI secretion is a double-edged sword[J]. Proceedings of the National Academy of Sciences of the United States of America, 2012, 109(48): 19804-19809.

[9] RUSSELL AB, SINGH P, BRITTNACHER M, *et al.* A widespread bacterial type VI secretion effectorsuperfamily identified using a heuristic approach[J]. Cell Host & Microbe, 2012, 11(5): 538-549.

[10] WANG P. Advances in hemolysin co-regulated protein of bacterial type VI secretion system[J]. Progress In Microbiology and Immunology, 2018, 46(3): 67-71. (in Chinese).

[11] HO BT, DONG TG, MEKALANOS JJ. A view to a kill: The bacterial type VI secretion system[J]. Cell Host & Microbe, 2014, 15(1): 9-21.

[12] WHITNEY JC, BECK CM, GOO YA, *et al.* Genetically distinct pathways guide effector export through the type VI secretion system[J]. Molecular Microbiology, 2014, 92(3): 529-542.

[13] CHEN Y, SHI H, XU WJ, *et al.* Preparation and characterization of single-chain antibodies against *Pseudomonas plecoglossicida* haemolysin co-regulatory protein[J]. Marine Fisheries, 2022, 44(6): 769-779. (in Chinese).

[14] HU YY. Hemolysin-coregulated protein and its related pathogenicity in *Acinetobacter baumannii*[D]. Wenzhou Medical University, 2018. (in Chinese).

[15] BEI L. *RbsB*, *vgrG*, *hcp* gene of type VI secretion system (T6SS) in *Vibrio harveyi*: Expression and functional analysis[D]. Shanghai: Shanghai Ocean University, 2018. (in Chinese).

[16] WANG XL, LI J, LI GY, *et al.* The effect of rpoS on Hcp expression and bactericidal activity in *Vibrio anguillarum* MHK3[J]. Progress in Fishery Sciences, 2021, 42(6): 125-134. (in Chinese).

[17] WANG YQ, WANG XY, ALI F, *et al.* Comparative extracellular proteomics of *Aeromonas hydrophila* reveals iron-regulated secreted proteins as potential vaccine candidates[J]. Frontiers in Immunology, 2019(10): 256.

[18] PAN HY, ZHOU ZJ, DING J, *et al.* Molecular cloning and bioinformatics analysis of T3SS chaperone escort protein VscO from *Vibrio alginolyticus*[J]. Biotechnology Bulletin, 2014(6): 155-61. (in Chinese).

[19] YUAN SB, ZHU AY. Progress on pathogenicity research on *Vibrio alginolyticus* to aquatic products[J]. Journal of Zhejiang Ocean University (Natural Science Edition), 2012, 31(3): 256-64. (in Chinese).

[20] WU NN, KANG C, RONG N, *et al.* Bioinformatics analysis of *Vibrio alginolyticus* TolB protein[J]. Journal of Henan Agricultural Sciences, 2018, 47(11): 134-141. (in Chinese).

[21] WEI C, LI H, YE SG, *et al.* Cloning and recombinant expression of pathogenic bacterium *Edwardsiella ictaluri hcp* gene[J]. Journal of Dalian Ocean University, 2013(5): 424-430. (in Chinese).

[22] SUAREZ G, SIERRA JC, SHA J, *et al.* Molecular characterization of a functional type VI secretion system from a clinical isolate of *Aeromonas hydrophila*[J]. Microbial Pathogenesis, 2008, 44(4): 344-361.

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[20] SHAO C, HU JP, YAN JC, *et al.* Effect of atractyl on proliferation of human colon cancer LS174T cells[J]. Journal of Jiangsu University (Medical Edition), 2016, 26(6): 480-483. (in Chinese).

[21] ZHANG T, LI SM, LI YN, *et al.* Atractylodin induces apoptosis and institutes the migration of A549 lung cancer cells by regulating ROS-mediated signaling pathways[J]. Molecules, 2022, 27(9): 2946.

[22] KOTAWONG K, CHAIJAROENKUL W, MUHAMAD P, *et al.* Cytotoxic activities and effects of atractylodin and β-eudesmol on the cell cycle arrest and apoptosis on cholangiocarcinoma cell line[J]. Journal of Pharmacological Sciences, 2018, 136(2): 51-56.

[23] QU L. LIN X. LIU C, *et al.* Atractylodin attenuates dextran sulfate sodium-induced colitisby alleviating gut microbiota dysbiosis and incubating influmatory response through the MAPK pathway. Frontiers in Pharmacology, 2021(12): 665376.

[24] LIU Z, JI X, CHEN G, *et al.* Atractylodin ameliorates lipopolysaccharide and d-galactosamine-induced acute liver failure via the support of propagation and oxidative stress. International Immunopharmacology, 2019(72): 348-357.

[25] GAO L, ZHANG WH, WANG YW, *et al.* Effect of atractyl on positive inotropic effect of rat heart and its mechanism[J]. Chinese Journal of Applied Physiology, 2020, 36(5): 408-413. (in Chinese).

[26] ZHU HJ, HONG Y, MA YL, *et al.* Protective effect of n-butanol extract of Atractylodis Rhizoma on myocardial ischemia and ischemia-reperfusion injury in rats[J]. Chinese Science and Technology of Traditional Chinese Medicine, 2000, 7(3): 173-174. (in Chinese).