Anti-cancer, Anti-inflammatory, Antioxidant and Other Pharmacological Effects of Wedelactone and Their Molecular Mechanisms

Mingxinzhi WANG, Jingchao WANG, Xichun HUANG, Xinyu LIU, Quan QUAN, Chenghao JIN*

College of Life Science and Biotechnology, Heilongjiang Bayi Agricultural University, Daqing 163319, China

Abstract Wedelolide is a coumarin-like active substance extracted from Ecliptae Herba. It not only has pharmacological effects of anti-pulmonary fibrosis, anti-arthritis, blood vessel protection and liver protection, but also effectively inhibits the proliferation of cancer cells and induces apoptosis of cancer cells, thereby delaying the further development of malignant tumors. In this paper, the pharmacological effects and mechanisms of wedelactone were reviewed to lay a foundation for further study and clinical application of wedelactone.

Key words Wedelactone, Anti-tumor, Anti-pulmonary fibrosis, Protection of blood vessels, Liver protection

1 Introduction

Ecliptae Herba, which is the dry terrestrial part of *Eclipta prostrata.*, has pharmacological effects pf hemostasis, kidney tonifying, annealing and swelling reducing. It is widely distributed in Liaoning, Hebei, Shandong and other provinces of China. Wedelolactone (WEL) is a small molecule active substance of coumarin extracted from Ecliptae Herba, and is chemically named 7-methoxy-5,11, 12-trihydroxy-coumarin, with molecular formula $C_{16}H_{10}O_7$. It is white crystalline and soluble in solvents such as methanol and DMSO. WEL has a variety of biological activities, including anti-inflammation, anti-oxidation, anti-tumor and liver protection. In this paper, the pharmacological effects and molecular mechanisms of WEL in recent years will be reviewed to provide a theoretical basis for its clinical application and research.

2 Anticancer, anti-inflammatory, antioxidant and other pharmacological effects and their molecular mechanisms

2.1 Anti-cancer The occurrence and development of tumors are closely related to the expression and regulation of intracellular proteins, cytokines and signaling pathways. For example, overexpression of apoptosis-promoting protein Bax and Caspase can increase the apoptosis rate of cancer cells, and abnormal activation of JAK2/STAT3 and PI3K/Akt signaling pathways can promote the proliferation and migration of cancer cells. Therefore, the regulation of related signaling pathways in cancer cells has become one of the hot spots in anti-tumor research. Studies have showed that WEL, as an active component of Chinese herbal extracts, can reduce the survival rate of cancer cells and induce their apoptosis by regulating cancer cell signaling pathways.

2.1.1 Anti-lung cancer. Lung cancer is one of the most common malignant tumors in the world, and has a certain genetic susceptibility. Through MTT method and flow cytometry, Jiang Shan *et al.*[1] found that WEL can effectively reduce the viability of lung cancer A549 cells, and induce cell cycle arrest and apoptosis. The IC_{50} values after 24 and 48 h were 21.12 and 16.24 μmol/L, and the retarded and apoptotic rates were 47% and 30%, respectively. In order to explore the mechanism of apoptosis of A549 cells, Western Blot experiment was further conducted, and it is found that after A549 cells were treated with WEL (20 μmol/L), the expression level of anti-apoptotic protein Bcl-2 significantly decreased, and the expression level of proapoptotic protein Bax and Caspase-3 significantly increased. In addition, WEL can reduce the phosphorylation level of JAK2 and STAT3 in cancer cells, regulate the JAK2/STAT3 signaling pathway, and then improve the apoptosis-inducing effect on A549 cells, ultimately delaying and improving the development process of lung cancer.

2.1.2 Anti-renal cell carcinoma. Renal cell carcinoma (RCC) originates from epithelial cells of kidney tubules, has a high metastasis rate and mortality, and is one of the main causes of neurological and digestive complications. Xian Shuli *et al.*[2] detected the cycle, apoptosis and expression level of related proteins in ACHN and 786-O cells of renal cancer by MTT method, flow cytometry and Western Blot experiment, and found that compared with the control group, WEL can effectively reduce the viability of ACHN and 786-O cells and induce the arrest of cancer cells in G1 phase. The retardation rates were 54.14% ± 1.91% and 60.01% ± 2.61%, respectively. WEL can also down-regulate the expression level of anti-apoptotic protein Bcl-2 and its family member Bcl-xL, and up-regulate the expression level of Bax, thereby activating the mitochondrial signaling pathway of Caspase cascade, and finally inducing apoptosis of ACHN and 786-O cells.

2.1.3 Anti-prostate cancer. Prostate cancer, which is the most common malignant tumour of urinary system in men, is caused by malignant hyperplasia of prostate epithelial cells. Oncogene C-myc can induce infinite proliferation of cancer cells and participate in the occurrence and metastasis of tumors. Sivalokanathan *et al.*[3-4] found that WEL can significantly reduce the expression level of C-myc mRNA in LNCaP, PC-3 and DU145 cells of pros-

Received: June 12, 2023 Accepted: November 25, 2023
Supported by the Talent Training Program for the Reform and Development of Local Colleges and Universities of the Central Government (2020GSP16); Innovation and Entrepreneurship Training Planning Project for University Students in Heilongjiang Province (202310223173).

* Corresponding author. E-mail: jinchenghao3727@qq.com

tate cancer, as well as the binding activity of related enzymes and DNA during transcription, and inhibit the survival rate and migration ability of cancer cells. WEL can also regulate the JNK signaling pathway in cancer cells, down-regulate the expression level of protein kinase Cε (PKCε), survivin, cyclin D1, aurora kinase and cell cycle dependent kinase 4 (CDK4), up-regulate the expression level of ATF3 gene, and then induce cycle arrest and apoptosis of cancer cells. In addition, the combination of WEL and enzalutamide can reduce the growth rate, weight and volume of transplanted tumor in nude mice.

2.1.4 Anti-colon cancer. Colon cancer (CRC) is the most common malignant tumor of digestive tract, and its recurrence and metastasis is the main reason leading to the failure of resection. Li Yanxi *et al.* [5] found that WEL can effectively reduce the viability of HCT116 cells in colon cancer, and block cell cycle and induce cell apoptosis. Western Blot and real-time quantitative PCR (RT-qPCR) showed that WEL can inhibit the proliferation of colon cancer cells and promote the apoptosis of colon cancer cells by inhibiting the expression level of β-catenin. In order to explore the effect of WEL on tumor growth *in vivo*, after further treatment of WEL (100 mg/kg) in transplanted nude mice, it was found that the expression level of cell-related proteins Ki67, Bcl-2, C-myc and survivin in transplanted tumor tissues significantly reduced, while the apoptosis rate of colon cancer cells significantly increased. However, WEL had no effect on normal colonic epithelial cells and vital organs such as heart and kidney in nude mice.

2.1.5 Anti-retinoblastoma. Retinoblastoma (RB) is an intraocular malignancy caused by RB1 gene mutation or deletion. Jiang *et al.* [6] found that WEL can block RB cell cycle and induce pyroptosis and apoptosis by up-regulating the expression level of Caspase-1, Caspase-3, porin-forming proteins GSDME, GSDMD and ROS in RB cells. In order to explore the anti-tumor activity of WEL *in vivo*, RB cells were further used to construct a nude mouse model of transplanted tumor, and it was found that WEL can effectively inhibit the growth rate, volume and weight of tumor in mice, but had no obvious toxic and side effects on normal organs and tissues. Harkin *et al.* [7] found that WEL can down-regulate the expression level of AIM2 mRNA in the retinal inflammasome, effectively protect the retinal neurodegeneration caused by the DNA alkylating agent N-methyl-n-nitrosourea (NMU), and improve the thickness of retina and photosensitive layer, thereby preventing the occurrence of diseases caused by retinal neurodegeneration.

2.2 Anti-inflammation and antioxidation Inflammation is a dynamic expression of damage and repair of human organism, and is closely related to the occurrence of many diseases. Abnormal proliferation and apoptosis of keratinocytes (HaCaT) are the main causes of psoriasis. Xu Jing *et al.* [8] constructed an inflammatory injury model of HaCaT, and found that WEL can inhibit the proliferation and autophagy of HaCaT cells by down-regulating the expression level of p-mTOR protein in HaCaT after LPS stimulation, thus slowing down the development of inflammation. Lin Yuqing *et al.* [9] found that WEL can promote NLRP3 phosphorylation and inhibit the activation of NLRP3 inflammatorites and pyroptosis by enhancing PKA signal transduction in the G protein-coupled system, thus playing an anti-inflammatory role. Cheng Min *et al.* [10] used Aspergillus fumigatus spores to construct a mouse model of fungal keratitis, and through immunofluorescence, myeloperoxidase (MPO) method and Western Blot, it was found that WEL can inhibit the expression level of Caspase-1 and the secretion of interleukin IL-1β, reduce the aggregation of neutrophils in the keratitis area, and then effectively reduce the degree of inflammation of keratitis in mice. Fan *et al.* [11] found that WEL can up-regulate the expression level of glutathione peroxidase 4 (GPX4), down-regulate the expression level of Caspase-1 and 11, and the content of pancreatic digestive enzyme and pro-inflammatory cytokine (ferroptosis) in serum, thus inhibiting pyroptosis and ferroptosis, and ultimately slow the development of acute pancreatitis (AP).

Cellular oxidative damage can seriously affect the normal life activities of the human body. Xu Jing *et al.* [12] found that WEL can up-regulate the expression level of DJ-1 protein, superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) in human coronary endothelial cells (HCAECs), and down-regulate the content of malondialdehyde (MDA), thereby protecting HCAECs oxidative stress damage induced by hydrogen peroxide.

2.3 Induction of osteocyte differentiation Cartilage injury is one of the common orthopedic diseases. Its surgical treatment is relatively difficult, and has a long recovery period. Yang Lin *et al.* [13] found that WEL can induce cartilage differentiation of bone marrow mesenchymal stem cells (BMSCs) through targeted binding and regulation of RNA methyltransferase 4 (Nsun4) expression. Further analysis of RT-qPCR and transcriptomics shows that WEL can improve the translation ability of Sox9, the core transcription factor of differentiation, and promote the complete chondrogenic differentiation of BMSCs. Zhu *et al.* [14] found that by regulating the signaling pathway of c-Jun amino terminal kinase (JNK) and external regulatory protein kinase (ERK), WEL (2 μg/mL) can up-regulate the expression level of bone cell markers (Runx2, Bglap and Sp7) and bone morph protein-2 (BMP-2) in BMSCs, and enhance bone mineralization and Smad1/5/8 phosphorylation level of BMSCs, thereby promoting the differentiation of BMSCs into osteoblasts.

2.4 Liver and blood vessel protection The liver plays an important role in the circulation of Qi, blood and water, and is one of the important organs of the human body. Excessive intake of antipyretic and analgesic acetaminophen (APAP) can lead to acute liver failure and even death[15]. Sun Xiaoming *et al.* [16] used APAP to construct a liver injury model for mice, and found that the degree of liver disease and the necrotic area of liver cells in the mice with liver injury in WEL treatment groups could be effectively improved. Further studies have shown that WEL can down-regulate the expression level of liver injury markers (ALT, AST), MDA and GSH in liver tissue homogenate and pro-inflammatory

cytokines (TNF-α, IL-6) in serum of mice with liver injury, and up-regulate the expression level of SOD and GSH-PX in liver tissue homogenate, and inhibit the inflammatory response, thereby reducing the degree of liver damage and protecting the liver. Xu Jing *et al.* [17] found that WEL can reduce the degree of lipid peroxidation of hepatocytes by inhibiting free radical activity, thus stabilizing the biofilm structure of hepatocytes and protecting the liver from ischemia reperfusion injury. Ping Ping *et al.* [18] found that WEL can effectively protect liver from being damaged by carbon tetrachloride, and reduce the degree of liver tissue degeneration.

Blood vessels are important transportation channels to maintain normal life activities of the human body. Huang Chuanfeng *et al.* [19] combined WEL with earthworm plasminase to treat the rats with hyperhomocysteinemia (HHcy), and found that it can effectively reduce the expression level of homocysteine (Hcy), interleukin 1-α and 1-β, serum cholesterol (TC), triglyceride (TG) and low density lipoprotein (LDL-C) in plasma of HHcy rats, and up-regulate the expression level of high-density lipoprotein (HDL-C), thus reducing the incidence of cardiovascular diseases, and protecting blood vessels.

2.5 Anti-rheumatoid arthritis Rheumatoid arthritis (RA) is an autoimmune disease. The main symptom is joint swelling and pain, and it can induce patients to develop lung, cardiovascular, liver and kidney tissue lesions. Cao *et al.* [20] constructed a mouse model of arthritis (CIA) by subcutaneous injection of type II collagen, and found that compared with the control group, the expression level of pro-inflammatory factors IL-1β, IL-6, TNF-α, IL-18 and RANKL, MMP-3 and NF-κB in synovium of CIA significantly decreased after WEL treatment, and the volume of the swelling ankle joint decreased. In addition, WEL can also up-regulate the expression level of cadherin E and reduce the incidence of cardiac tissue complications caused by RA.

2.6 Anti-pulmonary fibrosis and anti-pneumonia Pulmonary fibrosis is one of the end-stage manifestations of many interstitial lung diseases, and its clinical symptoms are mostly dry cough, dizziness, dyspnea, *etc.* Yang *et al.* [21] used bleomycin (BLM) to construct a lung fiber ICR mouse model, and found that the expression levels of pro-inflammatory factors, fibrosis marker α-SMA and type I collagen in the lung tissue significantly reduced, and the degree of lung tissue injury, pulmonary fibrosis and alveolar wall thickness were effectively improved. Besides, WEL can also reduce the expression level of transforming growth factor β1 (TGF-β1) and the phosphorylation level of Smad2/3 in mouse lung tissue, and induce AMPK activation, thereby inhibiting the transformation of lung tissue cells into fibrocytes.

Pneumonia is a disease of the lungs caused by bacteria and viruses. Through RT-qPCR and Western blot experiments, Zheng Dawei *et al.* [22] found that WEL can effectively inhibit the cellular inflammation mediated by Streptococcus pneumoniae by up-regulating the expression level of miR-142-3p, IL-10 and Bax in alveolar epithelial cells and down-regulating the expression level of IL-6 and Bcl-2.

2.7 Antineurotic disease Central nervous system degenerative diseases mainly include Parkinson's disease (PD), Alzheimer's disease (AD), *etc.*, and are caused by the degeneration of central nervous system tissue. Studies have shown that inhibition of phosphodiesterase (PDEs) activity can effectively delay the pathological progression of neurological diseases[23]. Mao Mingqiang *et al.* [24] used cortisone stimulation to construct a hippocampal mouse neuron HT-22 cell injury model, and found that the viability of damaged neurons could be effectively improved in the wedelide treatment group. Sharma *et al.* [25] found that WEL can effectively inhibit α-synuclein (α-syn) aggregation, improve oxidative stress and mitochondrial dysfunction, and alleviate PD pathology.

2.8 Other pharmacological effects Diabetes is a common metabolic disease with a high incidence, and can lead to complications of the human foot, blood vessel and nerve tissue. Shahab *et al.* [26] found that WEL can delay the further development of diabetes by effectively reducing the fasting blood glucose level and the expression level of glycated serum protein in mice. In addition, WEL derivative 3-butoxy-1, 8, 9-trihydroxy-6h-benzofuran [3, 2-C] benzopyrane-6-one (BTB) can play a good anti-tumor role in the treatment of breast cancer, endometrial cancer and ovarian cancer[27].

3 Outlook

WEL, an active substance isolated and purified from Ecliptae Herba, has good chemical properties, biological activity and pharmacological effects, and plays a valuable role in medical development and industrial application. Although WEL has good anti-tumor activity, the specific mechanisms and signaling pathway of its effects on tumor cells are still in the initial stage, and researchers need to conduct more comprehensive and deeper studies on WEL from the molecular, cellular and animal levels, so as to lay a foundation for accelerating the development and utilization of WEL.

References

[1] JIANG S, LIU M, ZHANG L, *et al.* Wedelolactone induces apoptosis of human lung adenocarcinoma A549 cells via inhibiting JAK2/STAT3 pathway[J]. Acta Medicinae Universitatis Scientiae et Technologiae Huazhong, 2021, 50(4): 488-492. (in Chinese).

[2] XIAN SL, LUO QQ. Inhibition of wedelolactone on the growth of human renal cancer cells in vitro[J]. Anti-tumor Pharmacy, 2019, 9(5): 726-730. (in Chinese).

[3] SARVESWARAN S, GHOSH R, PARIKH R, *et al.* Wedelolactone, an anti-inflammatory botanical, interrupts c-Myc oncogenic signaling and synergizes with enzalutamide to induce apoptosis in prostate cancer cells [J]. Molecular Cancer Therapeutics, 2016, 15(11): 2791-2801.

[4] SARVESWARAN S, GAUTAM SC, GHOSH J. Wedelolactone, a medicinal plant-derived coumestan, induces caspase-dependent apoptosis in prostate cancer cells via downregulation of PKCε without inhibiting Akt [J]. International Journal of Oncology, 2012, 41(6): 2191-2199.

[5] LI YX. The effect and mechanism of natural product wedelolactone inducing apoptosis of colorectal cancer cells by targeting β-catenin[D]. Shenyang: China Medical University, 2022. (in Chinese).

[6] JIANG H, NIU C, GUO Y, *et al.* Wedelolactone induces apoptosis and pyroptosis in retinoblastoma through promoting ROS generation[J]. International Immunopharmacology, 2022(111): 108855.
[7] HARKIN K, AUGUSTINE J, STITT AW, *et al.* Wedelolactone attenuates N-methyl-N-nitrosourea-Induced retinal neurodegeneration through suppression of the AIM2/CASP11 pathway[J]. Biomedicines, 2022, 10(2): 311.
[8] XU J, LIU D, XIE BX, *et al.* Effect of wedelitrilactone on autophagy induced by LPS in human keratinocytes[J]. Pharmacy Today, 2021, 31(7): 514 – 517. (in Chinese).
[9] LIN YQ. Study on the anti-inflammatory mechanism of wedelolactone by inhibiting NLRP3 inflammasome activation and pyroptosis[D]. Guangzhou: Guangzhou University of Chinese Medicine, 2021. (in Chinese).
[10] CHENG M. Effect and mechanism of wedelolatone on Aspergillus Fumigatus keratitis in mice[D]. Qingdao: Qingdao University, 2020. (in Chinese).
[11] FAN R, SUI J, DONG X, *et al.* Wedelolactone alleviates acute pancreatitis and associated lung injury via GPX4 mediated suppression of pyroptosis and ferroptosis[J]. Free Radical Biology and Medicine, 2021(173): 29 – 40.
[12] XU J, CHEN J, LUO ZL. Protective effects of wedelolactone on oxidative damage induced by hydrogen peroxide in human coronary artery endothelial cells[J]. The Chinese Journal of Clinical Pharmacology, 2019, 35(10): 1021 – 1024. (in Chinese).
[13] YANG L. Study on the mechanism of Wedelolactone regulating Nsun4 to promote chondrogenic differentiation of BMSCs[D]. Guangzhou: Guangzhou University of Chinese Medicine, 2021. (in Chinese).
[12] XU J, CHEN J, LUO ZL. Protective effect of wedelactone on oxidative injury of human coronary endothelial cells induced by hydrogen peroxide[J]. Chinese Journal of Clinical Pharmacology, 2019, 35(10): 1021 – 1024.
[13] YANG L. Mechanism of wedelactone targeting Nsun4 to promote chondrogenic differentiation of bone marrow mesenchymal stem cells[D]. Guangzhou: Guangzhou University of Chinese Medicine, 2021.
[14] ZHU D, DENG X, HAN XF, *et al.* Wedelolactone enhances osteoblastogenesis through ERK- and JNK-mediated BMP2 expression and Smad/1/5/8 phosphorylation[J]. Molecules, 2018, 23(3): 561.
[15] WANG Q, XU RJ, YANG J. Mechanisms of acetaminophen-induced hepatotoxicity and targets for drug intervention[J]. Pharmaceutical and Clinical Research, 2011, 19(3): 247 – 252. (in Chinese).
[16] SUN XM, ZUO XB, WANG CY, *et al.* Protective effect of wedelolactone against acetaminophen-induced liver injury in mice[J]. Chinese Journal of Comparative Medicine, 2019, 29(6): 86 – 91. (in Chinese).
[17] XU J, CHEN J, SUN PP, *et al.* Effects of wedelolactone on liver ischemia-reperfusion injury in rats[J]. Lishizhen Medicine and Materia Medica Research, 2014, 25(9): 2058 – 2059. (in Chinese).
[18] PING P, ZHANG TS, ZHANG XF, *et al.* Effects of wedelolactone on mice's acute hepatic injury induced by carbon tetrachloride[J]. Chinese Wild Plant Resources, 2012, 31(5): 41 – 43, 48. (in Chinese).
[19] HUANG CF, WEI Y, SHANG XY, *et al.* Protective effects of wedelolactone combined with earthworm fibrinolysin on the vessels of rats with hyperhomocysteinemia[J]. Clinical Journal of Chinese Medicine, 2021, 13(3): 47 – 49. (in Chinese).
[20] CAO J, NI Y, NING X, *et al.* Wedelolactone ameliorates synovial inflammation and cardiac complications in a murine model of collagen-induced arthritis by inhibiting NF-κB/ NLRP3 inflammasome activation[J]. Folia Histochem Cytobiol, 2022, 60(4): 301 – 310.
[21] YANG JY, TAO LJ, LIU B, *et al.* Wedelolactone attenuates pulmonary fibrosis partly through activating AMPK and regulating Raf-MAPKs signaling pathway[J]. Front Pharmacol, 2019(10): 151.
[22] ZHENG DW, DAI Y, GUO N, *et al.* The protective effect and mechanism of wedelolactone on alveolar epithelial cell injury infected by Streptococcus pneumoniae by regulating the expression of miR-142-3p[J]. Chinese Journal of Laboratory Diagnosis, 2021, 25(12): 1831 – 1836. (in Chinese).
[23] ZHENG G, ZHAO ZY, QIN JJ, *et al.* Research progress of phosphodiesterase inhibitors in the treatment of central nervous system diseases[J]. World Clinical Drugs, 2021, 42(3): 213 – 217. (in Chinese).
[24] MAO MQ, ZOU J, ZHENG J, *et al.* Protective effect of phosphodiesterase inhibitor DWEL on HT-22 cells damage[J]. Journal of Changzhou University(Natural Science Edition), 2019, 31(5): 87 – 92. (in Chinese).
[25] SHARMA S, TRIVEDI S, PANDEY T, *et al.* Wedelolactone mitigates parkinsonism via alleviating oxidative stress and mitochondrial dysfunction through NRF2/SKN-1[J]. Molecular neurobiology, 2021, 58(1): 65 – 77.
[26] SHAHAB U, FAISAL M, ALATAR AA, *et al.* Impact of wedelolactone in the anti-glycation and anti-diabetic activity in experimental diabetic animals[J]. IUBMB Life, 2018, 70(6): 547 – 552.
[27] XU D, LIN TH, YEH CR, *et al.* The wedelolactone derivative inhibits estrogen receptor-mediated breast, endometrial, and ovarian cancer cells growth[J]. Biomed Research International, 2014, 2014(17): 713263.

(From page 83)

[10] DU YC, ZHENG TX, SHI H, *et al.* Effect of aloin on proliferation, migration and invasion of hepatocellular carcinoma MHCC97H cells[J]. The Chinese Journal of Clinical Pharmacology, 2020, 36(12): 1669 – 1671. (in Chinese).
[11] CAI TY, CHEN XL, CHENG J, *et al.* Aloin inhibits lactate-induced proliferation and migration of gastric cancer cells by downregulating HMGB1 expression[J]. Journal of Southern Medical University, 2021, 41(11): 1700 – 1706. (in Chinese).
[12] LIU WB, GE MJ, YE SY, *et al.* Effect of aloin combined with cisplatin in non-small cell lung cancer cells[J]. The Chinese Journal of Clinical Pharmacology, 2020, 36(2): 150 – 153. (in Chinese).
[13] SHU KG, LAO FY, HUANG ZQ, *et al.* Anti-inflammation effects of aloin in rat osteoarthritis *in vivo* and *in vitro*[J]. Immunological Journal, 2021, 37(5): 425 – 432. (in Chinese).
[14] WEI LX, CUI Y, QIAN H. Intervention of aloin on the subchronic immune injury in rats induced by AFB_1[J]. Anhui Agricultural Science, 2015, 43(12): 10 – 14, 21. (in Chinese).
[15] ZHANG SN. Preliminary study on the therapeutic effect and mechanism of aloin on sepsis[D]. Fuzhou: Fujian Normal University, 2021. (in Chinese).
[16] BAI L, GONG TS, MU XH. Study on antimicrobial activity of aloin against main pathogens of foot[J]. Chinese-Foreign Footwear, 2017(8): 27 – 30. (in Chinese).
[17] WANG Y, DI Y, ZHU LQ, *et al.* Inhibitory effects of aloin on growth activity and hemolytic toxin expression of *Staphylococcus aureus*[J]. Journal of Clinical Laboratory, 2018, 36(4): 259 – 262. (in Chinese).
[18] ZHANG SS, WANG FS, SHI H, *et al.* Study on antibacterial and anti-inflammatory activities of *Aloe vera* extract[J]. Heilongjiang Science and Technology Information, 2014(23): 119. (in Chinese).