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Research progress of Mu Xiang in the treatment of ulcerative colitis

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Abstract: *Ulcerative colitis is an inflammatory bowel disease characterized by recurrent episodes of intestinal mucosal inflammation, with three major clinical manifestations: abdominal pain, diarrhea, and posterior urgency. The pathogenesis is still unclear, therefore, treatment is also based on anti-inflammatory and other symptomatic support. With the rapid development of Traditional Chinese medicine, Chinese herbal medicine plays an important role in the treatment of ulcerative colitis. This paper presents a review of Mu Xiang, a Chinese herbal medicine, in the treatment of ulcerative colitis.*

Keywords: *ulcerative colitis, pathogenesis, immune regulation, anti-inflammatory, antioxidant*

Ulcerative colitis (UC) is a chronic inflammatory bowel disease (IBD) mediated by nonspecific immunity[1]and is characterized by recurrent episodes of intestinal mucosal inflammation, which mostly starts in the rectum and tends to progress proximally along the colon. Initially, it may present as spasmodic abdominal pain, diarrhea, and mucus (blood) stools, with the risk of colorectal cancer if it continues to develop or is improperly treated [2].The incidence of UC is increasing year by year, especially in Asia and Africa[3], and its peak age of onset is concentrated in the 20s and 40s[4]. Western medicine has studied UC for many years, but its pathogenesis is still not completely clear, and the treatment is also based on the application of aminosalicylic acid preparations and immunosuppressive agents, which inhibit the development of UC and also bring a certain degree of adverse effects[5]. With the development of Traditional Chinese medicine, the understanding of UC has been deepened, and now it is believed that UC involves the category of Traditional Chinese medicine diseases "diarrhea and dysentery", the pathogenesis of which is caused by damp-heat evil injury to the intestinal organs. The treatment is mostly based on the combination of Huang Lian, Mu Xiang, Paeonia and Amaranthus[6]. Among them, mullein and its extracts, which are effective in promoting the healing of damaged mucous membranes and preventing cancer, are widely used in clinical practice.

1. Ulcerative colitis pathogenesis

1.1 Traditional Chinese medicine pathogenesis

The clinical manifestations of UC belong to dysentery, due to deficiency of the spleen and stomach, diet, emotions, external evil, etc., invasion of the body by the evil, Qi elevation and lowering inappropriate, intestinal conduction of the internal organs is not proper, long time Qi stagnation, dampness, blood stasis, heat and toxicity, etc., each other in the intestinal tract, especially the evil of dampness and heat, dysfunction of the intestinal tract and clear turbidity is not distinguished, the barrier is damaged and injury to the lipid complex, the onset of Qi and blood corruption. The pathological basis is the weakness and dysfunction of the spleen and stomach, and the key to the pathogenesis is the interaction of qi, fire, dampness and toxicity affecting the conduction of the intestinal organs, and the important stage is the damage of the lipid membrane and the corruption of qi and blood. Clinical symptoms include abdominal pain, diarrhea, urgency, and mucus-pus-blood stool, which are distinguished from other diseases.

1.2 Western medical pathogenesis

Western medicine has studied UC for many years and failed to clearly explain its pathogenesis,

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suggesting that it is related to genetic susceptibility, dysbiosis, barrier damage and immune stimulation, and that the occurrence of UC is caused by an inflammatory response in the intestinal mucosa of genetically susceptible people due to dysbiosis of intestinal microorganisms[7].

Studies have shown that the occurrence of inflammatory bowel disease is largely associated with family inheritance, with 8%-14% of UC patients having a family history of the disease[8].A meta-analysis of genome-wide association study (GWAS) data for IBD revealed that 23 of 163 loci were classified as UC-specific loci[9]. These involved several genes such as IL23/Th17 signaling, HLA, IL10, IL1R2, REL, PRDM1, SMAD3, and ORMDL, and some of these loci are in turn involved in the human immune response [10][11].

The human gastrointestinal tract is a huge microbial tribe, and the gastrointestinal mucosa is in direct contact with millions of microorganisms in the intestinal environment[12], and the outermost layer of the mucosa is covered with a layer of mucin that, under normal physiology, can defend the intestinal mucosa from various microorganisms and has an antibacterial effect. When UC occurs, mucin synthesis and secretion are impaired, the intestinal mucosal barrier is weakened, permeability is increased, antigen uptake is increased[13], and sustained stimulation of intestinal immune cells causes secretion of cytokines and chemokines (e.g., Toll-like receptors and NOD proteins), which signals activation of multiple transcription factors that trigger an inflammatory cascade response[14], which produces tumor necrosis factor (TNF)-a, interleukin (IL)-17, interferon-c, chemokines, and other pro-inflammatory cytokines that activate the innate immune response. At this time, activation and sensitivity of mature dendritic cells are also increased[15], and intestinal dendritic cells metastasize to the mesenteric lymph nodes and cause an imbalance between effector T helper (Th)2 cells by activating antigen-specific primitive T lymphocytes.Th2 responses activate natural killer T cells in the colon, which secrete a variety of cytokines, including IL-13, after stimulation, inducing epithelial cell apoptosis and interrupt tight junctions[16]. Circulating leukocytes are also recruited into the inflamed mucosa, further enhancing the inflammatory response. Initiating and eliciting an intestinal immune response dominated by adaptive immunity, this effect is mainly mediated by cytokines, which stimulate the expression of adhesion molecules on the vascular endothelium, thus promoting leukocyte adhesion and infiltration into the tissue, manifesting as an intestinal inflammatory response[17].

2. Mu Xiang for ulcerative colitis

Muxiang, the dried root of the woody plant of the Asteraceae family. Remove the sediment and whisker roots, cut into sections, cut the large ones longitudinally into lobes, and after drying, knock off the coarse skin[18].The sexual warmth and taste are hard, attributed to the spleen, stomach, large intestine, three jiao, and bile meridian,which has the effect of relieving pain, strengthening the spleen and eliminating food, used for chest and flank, abdominal distension and pain, diarrhea after heaviness, food accumulation, Not thinking about eating or drinking.Simmering Muxiang sausage to stop diarrhea.,can be used to relieve diarrhea abdominal pain. Mu Xiang first appeared in the Shennong Materia Medica[19]: "Spicy, warm. The Lord evil qi, the evil spirit to avoid the poisonous epidemic, the strong will, the Lord to drench..."; The new cultivation of Materia Medica" contains "This is Aoki Kaya, now all imported from foreign countries to cure poison and swelling and eliminate evil qi"; "Compendium of Materia Medica says:"All stagnant qi of the henchman." and stomach qi, lung qi, liver qi. Those who are depressed and uncomfortable, should use it." The "elimination of evil qi" recorded "in the new cultivation of Materia Medica " is consistent with the effect of "Xingqi" in the Chinese Pharmacopoeia. Therefore, the Mu Xiang recorded " in the new cultivation of Materia Medica " is the Mu Xiang used in the Chinese Pharmacopoeia today.Up to now, about 250 kinds of chemical components have been isolated and identified from Mu Xiang, which can be divided into terpenes, anthraquinones, flavonoids, lignosides and other types according to their structure[20].Many studies at home and abroad have shown that it is widely used in anti-inflammatory[21][23], antibacterial[24][26], anti-tumor[27] and other aspects.In recent years, the frequency of application of Mu Xiang in digestive diseases has gradually increased.Mainly in promoting gastrointestinal motility, antidiarrheal, protecting gastric mucosa, anti-ulcer and choleretic, etc[20], especially in the treatment of ulcerative colitis, it has repeatedly achieved miraculous results.

2.1 Treatment of combination and group of Mu Xiang

Muxiang is often used in combination with various Chinese medicines in the treatment of UC to maximize its effectiveness. Zhang Lin[28] et al. treated UC with Xianglian Pills,Muxiang is good at promoting qi, relieving pain, strengthening spleen and digestion, and stomach. Coptis chinensis is good

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at clearing heat, drying dampness, purging fire and detoxification. The combination of the two is mainly used in the treatment of damp heat dysentery, tenesmus, abdominal pain and diarrhea;The data mining results show that[29] the combination of Mu Xiang and Bai Shao is used to treat UC. Bai Shao nourishes blood and liver, relieves pain in the Spleen and stomach, Mu Xiang promotes qi to relieve pain, and relieves digestion and stomach. The combination of the two drugs reflects the method of "blood circulation leads to spontaneous healing of pus, while regulating qi leads to spontaneous removal";An Yuqiu [6] et al. used data mining to study the traditional Chinese medicine in the UC activity period, and found that the combination of Mu Xiang and Gan Cao had a good effect. The Gan Cao flavor is sweet, into the heart, lung, spleen and other meridians, which had the effect of tonifying the spleen and invigorating qi, relieving toxin in an urgent manner, and harmonizing various drugs. The combination of Mu Xiang and Gan Cao could not only promote qi and stop dysentery, but also relieve pain in an urgent manner;When Yang Shanshan[30] studied the national patent compound of traditional Chinese medicine to treat UC, who found that Mu Xiang is used with Bai Zhu, Bai Zhu strengthens the spleen and qi, dry moisture and water, and Mu Xiang can treat dysentery for a long time, diarrhea is thin, Mu Xiang is used to dispel evil spirits, and Bai Zhu replenishes qi to solidify the spleen and stomach, so it is commonly used in the treatment of chronic dysenter. It can be seen from the above that the ancient people used to treat dysentery mainly by supplementing spleen and qi, clearing away heat and dampness, promoting qi and blood. They not only used powerful products such as Mu Xiang and Huang Lian, but also not forgetting to use sweet and mild products such as Bai Shao, Bai Zhu and Gan Cao and other sweet and light slow of goods to defend righteousness.

Wang Zhibin et al. [31] compared mild to moderate UC with mesalazine by clearing intestines and warming Chinese herbs (Huang Lian, Pao Jiang, Ku Shen, Qing Dai, San Qi, Mu Xiang, Zhi Gancao, Di Yutan), and found that this method can improve clinical symptoms and reduce disease activity.Chen Jieling[32] clinical research has proved that the prescription for Yi Qijieduhuayu (Dang Shen, Chao Baizhu, Chi Shao, Bai Shao, Wei Muxiang, Ma Chixian, Chao Yiyiren, Bai Ji,San Qi ,Chao Guya, Huang Lian and Huang Bai) combined with conventional western medicine can improve the oxidative stress state, reduce cell iron death and alleviate clinical symptoms.

2.2 Treatment of effective components of Mu Xiang

A number of western medical studies on UC and Aucklandia odora have shown that sesquiterpenoids, the active components in Mu Xiang, play a key role in the treatment of UC. As one of the earliest sesquiterpenoids found in the extract of Mu Xiang, its hydroxylactone has anti-inflammatory, antioxidant, immune regulation and other activities[6].

2.2.1 Regulate immune imbalance

Since the imbalance of Thl/Th2 cell subsets in CD4+ T lymphocytes is a key factor in the occurrence of UC, in turn, the intestinal flora disorder exacerbates the Thl/Th2 imbalance and promotes the progression of UC[33].Costunolide can block the phosphorylation of extracellular signal regulated kinase (ERK) and p38MAPK, reduce the level of CD4+T cell activation marker CD69, and reduce T cell proliferation[34].Song Jie and other experimental studies have shown that Costunolide can improve the imbalance of Thl/Th2 in UC mice, and reduce the inflammatory damage caused by the dominance of Thl over Th2.The downregulation of TNF-α and IL-6 levels inhibited the activation of TLR-4/NF-κB inflammatory pathway, thereby blocking the positive feedback regulation of TLR-4/NF-κB on Thl-type cytokines[35].

2.2.2 Anti inflammation and anti-oxidation

The expression of the transcription factor nuclear factor κB (NF-κB) is a key link in pro-inflammatory genes. Costunolide can block lipopolysaccharide (LPS) stimulation of IκBα phosphorylation, thereby inhibiting NF-κB activation and reducing the expression of pro-inflammatory markers[36].Costunolide can also inhibit the expression of inflammatory factors such as inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2), and tumor necrosis factor α (TNF-α)[37].At the same time, Costunolide reduced interleukin-22 (IL-22) or γ-interferon (IFN-γ) to induce STAT1 and STAT3 phosphorylation[38].Costunolide inhibits phosphorylation of mitogen-activating protein kinase (MAPK), which blocks the transcriptional activity of activating protein (AP-1), thereby inhibiting the expression of interleukin (IL)-1β protein and mRNA[39].

When UC occurs, oxidative stress damages membrane phospholipids on the intestinal mucosa, producing peroxides such as malondialdehyde (MDA) and hydroxynonanal (HNE), thereby causing oxidative tissue damage. Costunolide also decreased the level of lipid peroxidation in MCF-7 and MDA

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MB-231 cells, and increased the activities of SOD, catalase and GPx[40].It has also been reported abroad that the treatment of LPS-stimulated mouse monocytic macrophage leukemia (RAW264.7) cells with Costunolide can reduce the production of TNF-α and IL-6, enhance the nuclear accumulation of erythrocyte-associated factor-2 (Nrf2), thereby increasing the activity of heme oxidase (HO-1). The use of HO-1 inhibitors inhibits LPS-induced production of TNF-α and IL-6[41].

3. Conclusion

With the increasingly clear understanding of UC, it is found that the pathogenesis of UC involves a wide range of factors, and its pathogenesis is extremely complex.According to current domestic and foreign research, it can only be roughly believed that its onset is related to family genetics, dietary preferences, living environment, bad habits such as smoking and drinking, intestinal microbiobia and long-term drug damage.The specific pathogenesis can be caused by the degree of expression of UC susceptibility gene in humans, the stress imbalance of Th cell population, and the transmission and expression of various inflammatory factors and signal pathways.

In terms of western medicine treatment, due to the uncertainty of its specific incidence, the main treatment purpose is to alleviate inflammation and provide symptomatic support. The commonly used drugs are mesalazine preparations. In recent years, various immunosuppressants are also widely respected in clinical application. However, the liver and kidney are toxic, and the incidence of gastrointestinal adverse reactions is high. Considering the patient's tolerance, the use is limited; Glucocorticoids can be used in severe patients during acute attack. Although glucocorticoids can improve clinical efficacy, they are prone to form hormone dependence; If the effect of drug treatment is not obvious or the range of lesions is too wide, even if there is a tendency to cancer, surgical treatment is also a method, and there are still risks of postoperative bleeding, postoperative infection, etc. A variety of western medicine treatments have their limitations to varying degrees, and the side effects suffered at the same time may deter patients.

Based on the continuous mastery of pharmacological knowledge such as the active ingredients of various Chinese medicines, the status of traditional Chinese medicine in the treatment of UC has been recognized.Such as Coptisine[42], Total glucosides of paeonia[43], Costunolide[35] and so on,It plays a role in blocking inflammatory pathways, regulating immune imbalance, oxidizing stress, and improving the intestinal environment.The Mu Xiang mentioned in the article has the function of activating qi and relieving pain, which can well relieve the symptoms of tenesmus and abdominal pain in UC; Because the chemical extract of Costunolide has the effect of anti inflammation, anti-oxidation and regulation of adaptive immune imbalance.When UC occurs, Costunolide maintains Thl/Th2 balance and blocks the activation of TNF-α, IL-6, TLR-4/NF-κB, etc., thus playing a key blocking and inhibiting role in UC progression.

The complexity of traditional Chinese medicine in treating diseases is determined by its multi molecule and multi target synergy. The effective ingredients of Mu Xiang found so far are not comprehensive, and its toxicity cannot be ruled out. It is also unknown whether the compatibility with other traditional Chinese medicines may cause new toxic and side effects. There are still concerns about its medical safety. It is expected that in the next phase of research, we can combine evidence-based and clinical tools to further study the safety of the effective ingredients of Mu Xiang and their molecular targets for the treatment of UC, provide more effective and direct evidence for the effectiveness of Mu Xiang in the treatment of UC, and have new exploration in reducing or reducing toxic and side effects.

References

[1] Eisenstein M. Ulcerative colitis: towards remission[J]. Nature, 2018, 563(7730): S33-S33.
[2] 2Kirsner J B. The local and systemic complications of inflammatory bowel disease[J]. Jama, 1979, 242(11): 1177-1183.
[3] Du L, Ha C. Epidemiology and pathogenesis of ulcerative colitis[J]. Gastroenterology Clinics, 2020, 49(4): 643-654.
[4] Cosnes J, Gower–Rousseau C, Seksik P, et al. Epidemiology and natural history of inflammatory bowel diseases[J]. Gastroenterology, 2011, 140(6): 1785-1794. e4.
[5] Yang Qianqian, Zhou Jianbo, Cai Sheng, et al.Feasibility analysis on the efficacy and adverse reactions of azathioprine in the treatment of ulcerative colitis and Crohn's disease [J]. Chinese Journal of Medicine and Clinical Medicine, 2018, 18 (10): 1739-1741

ISSN 2616-5791 Vol.4, Issue 1: 45-50, DOI: 10.25236/AJMHS.2023.040108

[6] An Yuqiu, Wang Huijuan. Research on the rule of drug use in active stage of ulcerative colitis based on data mining [J]. Shandong Journal of Traditional Chinese Medicine, 2022, 41 (07): 721-726. DOI: 10.16295/j.cnki.0257-358x.2022.07.005

[7] Xavier R J, Podolsky D K. Unravelling the pathogenesis of inflammatory bowel disease[J]. Nature, 2007, 448(7152): 427-434.

[8] Jewell D P, Sutherland L R, McDonald J W D, et al. Ulcerative colitis[J]. Evidence-based Gastroenterology and Hepatology, 2010: 232-247.

[9] Jostins L, Ripke S, Weersma R K, et al. Host–microbe interactions have shaped the genetic architecture of inflammatory bowel disease[J]. Nature, 2012, 491(7422): 119-124.

[10] Lees C W, Barrett J C, Parkes M, et al. New IBD genetics: common pathways with other diseases[J]. Gut, 2011, 60(12): 1739-1753.

[11] de Lange K M, Barrett J C. Understanding inflammatory bowel disease via immunogenetics[J]. Journal of autoimmunity, 2015, 64: 91-100.

[12] Sands BE, Kaplan GG. The role of TNFalpha in ulcerative colitis. J Clin Pharmacol 2007;47:930–41.

[13] Ordas I, Eckmann L, T alamini M, et al. Ulcerative colitis. Lancet 2012;380:1606–19.

[14] Zhang FX, Kirschning CJ, Mancinelli R, et al. Bacterial lipopolysaccharide acti-vates nuclear factor-kappaB through interleukin-1 signaling mediators in cultured human dermal endothelial cells and mononuclear phagocytes. J Biol Chem 1999; 274: 7611–4.

[15] Hart AL, Al-Hassi HO, Rigby RJ, et al. Characteristics of intestinal dendritic cells in inflammatory bowel diseases. Gastroenterology 2005;129:50–65

[16] Heller F, Fromm A, Gitter AH, et al. Epithelial apoptosis is a prominent feature of the epithelial barrier disturbance in intestinal inflammation: effect of pro-inflammatory interleukin-13 on epithelial cell function. Mucosal Immunol 2008;1(Suppl 1):S58–61

[17] Briskin M, Winsor-Hines D, Shyjan A, et al. Human mucosal addressin cell adhe-sion molecule-1 is preferentially expressed in intestinal tract and associated lymphoid tissue. Am J Pathol 1997; 151:97–110.

[18] National Pharmacopoeia Commission. Pharmacopoeia of the People's Republic of China: A [M] 2020 Edition. Beijing:China Medical Science and Technology Press.2020:266,63.

[19] ZHANG Nanping,YU Kunzi,KANG Shuai,LIAN Chaojie,CHEN Hong,MA Shuangcheng. Study of Muxiang Jiyuan in ancient Materia Medica[J].China Pharmaceutical Affairs,2019,33(02):172-176.DOI:10.16153/j.1002-7777.2019.02.009.)

[20] Zheng Jiamei, Shang Mingyue, Wang Jiale, et al.Chemical constituents, pharmacological effects, clinical application research progress and quality marker prediction of Aucklandia odora [J]. Chinese Herbal Medicine, 2022,53 (13): 4198-4213.

[21] Park E J, Park S W, Kim H J, et al. Dehydrocostuslactone inhibits LPS-induced inflammation by p38MAPKdependent induction of hemeoxygenase-1 in vitro and improves survival of mice in CLP-induced Sepsis in vivo [J]. Int Immunopharmacol, 2014, 22(2): 332-340.

[22] Lim H S, Ha H, Shin H K, et al. The genome-wide expression profile of Saussurea lappa extract on house dust mite-induced atopic dermatitis in nc/nga mice [J]. Mol Cells, 2015, 38(9): 765-772.

[23] Seo C S, Lim H S, Jeong S J, et al. Anti-allergic effects of sesquiterpene lactones from the root of Aucklandia lappa Decne [J]. Mol Med Rep, 2015, 12(5): 7789-7795.

[24] Mohamed A. Evaluation of antimicrobial activity of different solvent extracts of Saussurea lappa [J]. World J Pharm Pharm Sci, 2017: 12-18.

[25] Li Y, Xu C, Zhang Q, et al. In vitro anti-Helicobacter pylori action of 30 Chinese herbal medicines used to treat ulcer diseases [J]. J Ethnopharmacol, 2005, 98(3): 329- 333.

[26] Qiu J, Wang J, Luo H, et al. The effects of subinhibitory concentrations of Costus oil on virulence factor production in Staphylococcus aureus [J]. J Appl Microbiol, 2011, 110(1): 333-340.

[27] Wang Xuying, Jia Xiaobin, Chen Yan Research progress of woody incense [J]. Traditional Chinese Medicine, 2010, 33 (1): 153-157

[28] Zhang Lin, Xiao Yanying, Ma Baohua. Research progress on pharmacological effects of Xianglian Pills [J]. Shaanxi Journal of Traditional Chinese Medicine, 2015,36 (01): 127-128

[29] Qiu Kuan, Xiong Wenwen, Xu Song, et al. Study on the law of prescriptions for dysentery in ancient literature based on data mining [J]. Jiangxi Journal of Traditional Chinese Medicine, 2022,53 (09): 45-49.

[30] Yang Shanshan, Hao Shaodong, Ye Hui, et al. Analysis of the medication law of national patent compound of traditional Chinese medicine for the treatment of peptic ulcer[J]. Shizhen Chinese Medicine and Chinese Medicine,2021,32(05):1269-1271.)

[31] Wang Zhibin, Chen Chen, Guo Yi, et al. Clinical study of Qingchang Wenzhong on mild to moderate ulcerative colitis [J]. Chinese Journal of Integrated Traditional and Western Medicine, 2018, 38 (01):

ISSN 2616-5791 Vol.4, Issue 1: 45-50, DOI: 10.25236/AJMHS.2023.040108

15-19
[32] Chen Jieling, Shen Jie, Liu Guozheng Clinical Study on 30 Cases of Ulcerative Colitis Treated by "Yiqi Jiedu Huayu Recipe" Combined with Conventional Western Medicine [J]. Jiangsu Traditional Chinese Medicine, 2021,53 (03): 34-37. DOI: 10.19,844/j.cnki.1X.2021.03.013
[33] Min Y Zhe S, Chao H Y' et a1. The therapeutic role of oral tolerance in dextran sulfate sodium. induced colitis via Thl-Th2 balance and V6 T cells [J]. Journal of Diges-tive Diseases, 2013, 14(10): 543-551.
[34] Park E, Song J H, Kim M S, et al. Costunolide, a sesquiterpene lactone, inhibits the differentiation of pro-inflammatory CD4+ T cells through the modulation of mitogenactivated protein kinases[J]. International Immunopharmacology, 2016, 40: 508-516.
[35] Song Jie, Guo Ruifang, Nie Hong, et al. The effect and mechanism of sasaki lactone on intestinal immune inflammation in mice with ulcerative colitis [J]. Journal of Guangxi Medical University, 2021,38 (12): 2300-2305. DOI: 10.16190/j.cnki.45-1211/r.2021.12.016
[36] Chen Y, Zheng H, Zhang J, et al. Reparative activity of costunolide and dehydrocostus in a mouse model of 5-fluorouracil-induced intestinal mucositis[J]. RSC advances, 2016, 6(7): 5249-5258.
[37] Koo T H, Lee J H, Park Y J, et al. A sesquiterpene lactone, costunolide, from Magnolia grandiflora inhibits NF-κB by targeting IκB phosphorylation[J]. Planta Medica, 2001, 67(02): 103-107.
[38] Scarponi, C., Butturini, E., Sestito, R. et al. Inhibition of inflammatory and proliferative responses of human keratinocytes exposed to the sesquiterpene lactones dehydrocostuslactone and costunolide. PLoS ONE 2014, 9, e107904.
[39] Kang J S, Yoon Y D, Lee K H, et al. Costunolide inhibits interleukin-1β expression by downregulation of AP-1 and MAPK activity in LPS-stimulated RAW 264.7 cells[J]. Biochemical and biophysical research communications, 2004, 313(1): 171-177.
[40] Rajalakshmi M, Anita R. In vitro and in silico evaluation of antioxidant activity of a sesquiterpene lactone, costunolide, isolated from costus specious rhizome on MCF-7 and MDA-MB-231 human breast cancer cell lines[J]. World J. Pharm. Pharm. Sci, 2014, 3: 1334- 1347.
[41] Pae, H.-O.; Jeong, G.-S.; Kim, H.-S. et al. Costunolide inhibits production of tumor necrosis factor-α and interleukin-6 by inducing heme oxygenase-1 in RAW264. 7 macrophages. Inflamm. Res. 2007, 56, 520–526.
[42] Xing Liying, Bai Xinglong, Shang Ke, et al. Exploring the mechanism of Huanglian Jiedu Decoction in treating ulcerative colitis based on network pharmacology [J]. China Pharmacoeconomics, 2022,17 (04): 78-82
[43] Wang Jing, Zhong Wei, Zhang Haihua, et al. Research progress on the role and mechanism of TGP in the treatment of ulcerative colitis [J/OL]. Chinese Materia Medica, 2022 (05): 1300-1304 [2022-11-27]. DOI: 10.13863/j.issn1001-4454.2022.05.045.