

Traditional Chinese Medicine Treatment for Acute Pancreatitis Research Progress

Shijie Yu, Ting Lei*

Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

*Correspondence Author

Abstract: *Acute pancreatitis (AP) is one of the common clinical acute abdominal diseases due to various causes of excessive activation of pancreatic enzymes and excessive inflammatory reaction of the pancreas as the main pathologic mechanism. Nowadays, the clinical treatment of AP is mainly based on the combination of Western medicine and traditional Chinese medicine, and a large number of studies have confirmed that traditional Chinese medicine (TCM) compound as an effective means for the treatment of clinical AP has significant effects. In this paper, the mechanism of Chinese medicine compound treatment of AP is reviewed, aiming to provide ideas and methods for clinical Chinese medicine treatment of AP.*

Keywords: Traditional Chinese medicine, Acute pancreatitis, Traditional Chinese medicine prescription, Mechanism of action.

1. Introduction

Acute pancreatitis (AP) is one of the most common critical acute abdominal diseases in clinical practice, characterized by high incidence, high treatment costs, high mortality, and numerous complications [1]. The "Revised Atlanta Classification" and the "Guidelines for the Diagnosis and Treatment of Acute Pancreatitis in China (2014)" classify AP into mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP). Among the three classifications, MAP is mainly characterized by blood biochemical indicators and clinical manifestations, without complications or local functional impairment, with a recovery time usually within 1-2 weeks and a low mortality rate. The main difference between MSAP and SAP lies in the duration of organ dysfunction: compared with SAP, the dysfunction in MSAP generally lasts ≤ 48 hours, with or without local or systemic complications [2]. Common pathogenic factors for SAP include drug abuse, alcohol abuse, overeating, ischemic injury to the body, and pancreaticobiliary diseases, all of which can cause SAP. The pathogenesis of SAP is still unclear, with different academic viewpoints proposed in related studies, such as excessive activation of pancreatic proteases leading to autodigestion of pancreatic tissue, calcium ion overload, damage to the intestinal mucosal barrier, excessive activation of inflammatory cytokines leading to self-digestion of pancreatic tissue, apoptosis and necrosis of pancreatic acinar cells, oxidative stress, etc [3]. Currently, there is no specific and effective drug or treatment method for the disease, and clinical practice advocates the use of a multidisciplinary collaborative treatment team (MDT) model. Early treatment mainly includes fluid infusion, antispasmodic and analgesic therapy, nutritional support, fasting, gastric and intestinal decompression, and symptomatic treatment for the etiology and complications in the early stage [4]. With the advantages of traditional Chinese medicine (TCM) in targeting specific effects and related clinical pharmacological research in recent years, TCM prescriptions have gradually become a commonly used treatment for SAP. The proficient use of TCM theory and the syndrome differentiation and treatment have made TCM prescriptions play an extremely important role in the clinical treatment of SAP. This article reviews the basic and clinical research progress of TCM prescriptions in the

treatment of SAP in recent years.

2. Traditional Chinese Medicine's Understanding of SAP

Pancreatitis was not extensively documented in ancient texts, but it was referred to as "Cui" and "San Gao" in ancient times, as mentioned in the "Nanjing" and "Compendium of Materia Medica" by Li Shizhen in the Ming Dynasty, respectively. Traditional Chinese Medicine (TCM) believes that the onset of acute pancreatitis (AP) is primarily caused by the misuse of "San Gao," manifesting mainly as severe abdominal pain, bloating, nausea, and vomiting [5]. There is no specific TCM term for AP; based on its clinical manifestations and characteristics, AP is generally classified under the same type of diseases as "Jie Xiong" (chest congestion), "Wei Tong" (gastric pain), "Fu Tong" (abdominal pain), "Pi Xintong" (splenic pain), and "Pi Shi" (spleen excess) [6].

Regarding the pathogenesis of SAP, its fundamental pathology is the obstruction of abdominal qi, leading to a complex and difficult-to-treat condition characterized by the internal accumulation of stagnant toxins. In the initial stages, SAP is often caused by food stagnation, qi stagnation, or the accumulation of heat in the liver, gallbladder, spleen, or stomach, leading to damp-heat accumulation and subsequent interplay of stasis and toxins. This condition obstructs blood vessels, infiltrates the pericardium, and affects the lungs, making the disease progression intricate. The pathological factors of this disease mainly involve heat, stasis, dampness, and toxins gathering in the middle burner, resulting in dysfunction of spleen and stomach's transportation and transformation, as well as irregular movement of qi within liver and gallbladder. The key to the transformation of the disease lies in the internal accumulation of stagnant toxins.

Based on the nature of the pathogenic factors and the balance between pathogenic and healthy factors, AP can be divided into acute and recovery phases. The acute phase is characterized by food stagnation, qi stagnation, predominance of pathogenic factors, and a mixture of heat, toxins, dampness, and stasis. The recovery phase is marked by deficiency of vital energy, insufficient qi and blood, yin-yang deficiency,

and a mixture of deficiency and excess. The corresponding patterns include liver depression and spleen deficiency, qi and yin deficiency, among others [7].

3. Traditional Chinese Medicine Compound's Effectiveness in Treating SAP

3.1 Chaihu Shugan Powder

Chaihu Shugan Powder, originating from the Ming Dynasty's Zhang Jiebin's "Complete Works of Jingyue" Volume 25 on Rib Pain, is composed of Chaihu, Xiangfu, Chuanxiong, Zhike, Baishao, Gancao, and Chenpi. It is a commonly used prescription in clinical practice for soothing the liver, promoting qi circulation, activating blood, and relieving pain. With the research on the pharmacological effects of Chaihu Shugan Powder, it has been found to have unique efficacy in digestive and gastrointestinal diseases [8]. Chaihu Shugan Powder can control pancreatic inflammation and reduce pancreatic fibrosis, thereby achieving the effect of treating pancreatitis [9]. Studies have shown that tumor necrosis factor-alpha (TNF- α), interleukin-1 beta (IL-1 β), and immune indicators (CD4+, CD8+, CD4+/CD8+) are closely related to the pathogenesis of pancreatitis. Chaihu Shugan Powder can reduce local circulatory inflammation by lowering TNF- α levels in the body. It can also enhance the host's resistance to inflammation substances by increasing IL-1 β levels and increase CD4+/CD8+ to enhance the body's immune function [10]. Chaihu in Chaihu Shugan Powder contains saikosaponins, which can effectively inhibit pancreatic protease secretion to reduce pancreatic infection. Saikosaponin a and saikosaponin b can effectively inhibit pancreatic infection. Shaoyao glycoside in Baishao and glycyrrhizic acid and glycyrrhetic acid in Gancao combine to have the effect of relieving urgency and pain. Jupi glycoside in Chenpi can effectively relieve gastrointestinal smooth muscle spasms, thereby achieving the effect of pain relief. The volatile oil of Xiangfu can inhibit inflammatory reactions, thereby relieving pain during SAP attacks. Chuanxiong can improve gastrointestinal microcirculation, and its mechanism of action has a significant antagonistic effect on mesenteric vessels. The volatile oil extract of Zhike achieves the effect of relieving pain by bidirectionally regulating the function of gastrointestinal smooth muscles [11]. In summary, Chaihu Shugan Powder has significant efficacy in treating SAP and is worthy of clinical promotion.

3.2 Da Cheng Qi Tang

Da Cheng Qi Tang originated from the classic Chinese medicine book "Shanghan Lun" by the medical expert Zhang Zhongjing at the end of the Eastern Han Dynasty. This prescription is a routine purgative decoction, mainly used to treat Yangming bowel syndrome, composed of rhubarb, mirabilite, citrus aurantium, and magnolia bark. Through the compilation of related research literature, it was found that Da Cheng Qi Tang can treat severe acute pancreatitis (SAP) through multiple aspects, and its mechanism of action may be related to improving intestinal function, initiating enteral nutrition early, regulating immune inflammatory responses, improving pancreatic microcirculation and coagulation function [12]. Inflammatory factors are important factors affecting the prognosis of AP. With the development of the

disease, patients generally experience an increase in inflammatory factor levels, leading to a cascade reaction of inflammation, and eventually progressing to multiple organ dysfunction. Therefore, controlling inflammatory factor indicators is the key to treating SAP.

Studies have found that the combination of Da Cheng Qi Tang and octreotide in the treatment of SAP patients is significantly more effective than using octreotide alone. The levels of immune-related indicators such as CD4+, CD8+, IgG, IgM, as well as inflammatory factors such as TNF- α , IL-6, and hs-CRP in the Da Cheng Qi Tang group patients significantly increased before and after treatment, while the levels of TNF- α , IL-6, and hs-CRP decreased significantly [13]. Research has found that the NLRP3 inflammasome is a large molecular complex closely related to the pathogenesis of SAP, playing an important role in host immune mediation, and also serving as activation platforms for IL-1 β and IL-18. IL-18 is the main activation factor, which can activate more inflammatory factors, exacerbate inflammatory reactions, and compared with healthy individuals, the level of IL-18 in SAP patients is significantly increased. Da Cheng Qi Tang can reduce the activation of NLRP3 inflammasome by lowering the IL-18 in the patient's serum, thereby reducing the level of inflammation in SAP patients [14].

It has been found that the severity of SAP in patients is positively correlated with the level of IL-6 in the serum, and the mechanism of Da Cheng Qi Tang in treating SAP may be related to its ability to reduce IL-6 release. Intestinal dysfunction is a common complication of SAP, and intestinal dysfunction may be related to the increased release of 5-HT in the intestine during SAP and the expression of 5-HT7 receptors. The level of 5-HT in the intestine of SAP patients increases, leading to the activation of the corresponding receptor reflex pathway of the vagus nerve and increased intestinal peristalsis. Studies have shown that 5-HT7 located in the myenteric plexus of the gastrointestinal tract can activate downward neurons, ultimately leading to relaxation of gastrointestinal smooth muscles, indirectly causing gastrointestinal dysfunction in SAP patients [15]. Shen Yanping [16] and others applied Da Cheng Qi Tang to SAP animal models for experiments and found that Da Cheng Qi Tang can reduce the effect of SAP on intestinal peristalsis by reducing the 5-HT content in the bodies of SAP rats. At the same time, Da Cheng Qi Tang, as a 5-HT7 antagonist, has an antagonistic effect on 5-HT7 or reduces the generation of 5-HT itself, making it unable to activate 5-HT7, thereby relieving the excessive relaxation of intestinal circular muscles and restoring intestinal function. The above research and clinical observations confirm that Da Cheng Qi Tang is worth being widely used in the clinical treatment of SAP.

3.3 Clearing Pancreatic Soup

The prescription of Clearing Pancreatic Soup comes from the modification of Da Cheng Qi Tang in Zhang Zhongjing's "Treatise on Cold Pathogenic Diseases." According to the medication composition of "Tianjin Nankai Hospital," the herbs include Bupleuri Radix, Scutellariae Radix, Coptidis Rhizoma, Paeoniae Radix Alba, Agastachis Herba, Corydalis Rhizoma, Rheum Palmatum, and Natrii Sulfas, eight herbs in total [18]. It has the effects of soothing the liver and

gallbladder, relieving urgency and pain, and clearing the intestines to reduce heat. It is currently a commonly used prescription for treating acute pancreatitis (AP) clinically. Wu Zhishui [19] and others found through clinical studies that Clearing Pancreatic Soup can effectively improve the symptoms of severe acute pancreatitis (SAP) patients, reduce the levels of white blood cells (WBC), C-reactive protein (CRP), and amylase (AMS), and increase the total effective rate of treatment. This may be related to the regulation of inflammatory factors in the body by the chemical components contained in it. Bupleuri Radix contains a large amount of saponins and flavonoids, which have anti-inflammatory, antipyretic, and hepatoprotective effects; Scutellariae Radix contains baicalin and baicalein, which can relax intestinal smooth muscles, alleviate the hypoxia and ischemia caused by inflammatory factors in SAP intestines, and reduce the level of vasoactive intestinal peptide (VIP) in the body; Paeoniae Radix Alba contains paeoniflorin and paeonol, which can promote the secretion of anti-inflammatory factors, thus exerting an anti-inflammatory effect. Intestinal barrier damage caused by SAP is the main cause of death in SAP patients. When intestinal damage occurs, the levels of serum diamine oxidase (DAO), serum D-lactic acid, and endotoxin in the patient's body increase significantly. These contents are important indicators for evaluating the intestinal barrier function before and after treatment. Research has found that the levels of DAO, D-lactic acid, and endotoxin in the bodies of SAP patients treated with Clearing Pancreatic Soup are all lower than those in the control group, significantly improving the intestinal barrier function of SAP patients [20]. Studies have found that Clearing Pancreatic Soup can inhibit the c-Jun N-terminal kinase (JNK) signaling pathway, prevent the activation of p-JNK, reduce the further expression of inflammatory cells, alleviate lung injury and pulmonary edema caused by SAP, and thus relieve the lung injury complications of SAP. At the same time, once the JNK signaling pathway is activated to produce p-JNK, JNK can quickly transfer from the cytoplasm to the nucleus of cells, participate in cell apoptosis and inflammatory reactions in the body, and aggravate pancreatic injury. Lung injury accompanies SAP in the early stage, which will activate the JNK signaling pathway, so Clearing Pancreatic Soup should be used in the early stage of the disease course to alleviate the progression of lung injury caused by SAP [21]. Serum amylase (AMS) is secreted by the pancreas and is commonly used clinically as an indicator of the severity of pancreatitis. Tumor necrosis factor- α (TNF- α) can not only aggravate pancreatic injury but also promote the release of pro-inflammatory factors such as interleukin-6 (IL-6), further worsening the condition of pancreatitis. Triggering receptor expressed on myeloid cells-1 (TREM-1) is an inflammatory activation receptor that significantly increases in the serum of AP patients, exacerbating disease progression. The reason may be that it induces downstream cells to infiltrate and damage pancreatic tissue, promote the release of IL-6, and then promote pancreatic injury. Microtubule-associated protein 1 light chain 3 (MAP1-LC3) is an autophagy-related gene closely related to inflammatory reactions [22]. Vasoactive intestinal peptide (VIP) and gastric inhibitory polypeptide (GIP) participate in regulating pancreatic secretion of pancreatic juice. Lüan Xiaofeng and others used Clearing Pancreatic Soup with modifications to assist in the treatment of SAP patients and found that the levels of TNF- α ,

IL-6, TREM-1, MAP1-LC3, VIP, and GIP in their bodies were significantly lower than those in the Western medicine treatment group. The mechanism may be that Clearing Pancreatic Soup can reduce TNF- α in the body, thereby reducing inflammation, inhibit the abnormal secretion of VIP and GIP in the serum, thereby inhibiting pancreatic juice secretion, and thus slowing down the progression of SAP [23]. Hu Wei [24] and others found through animal experiments that Clearing Pancreatic Soup combined with curcumin can significantly reduce the degree of intestinal mucosal and pancreatic injury in SAP rats. This may be related to its ability to reduce bacterial translocation in the intestine, reduce the levels of intestinal pathogens (genus *Clostridium*, order Clostridiales, and genus *Bacillus*), increase the levels of beneficial bacteria in the intestine (order Bacteroidales, genus *Bacteroides*, and genus *Lactobacillus*), inhibit the absorption of endotoxin in the intestine, and thus alleviate a series of mechanisms related to pancreatic tissue injury.

3.4 Da Chai Hu Tang

The formula Da Chaihu Tang comes from Zhang Zhongjing's "Treatise on Cold Damage" and consists of eight medicinal ingredients: chai hu, huang qin, shao yao, ban xia, da huang, zhi shi, sheng jiang, and da zao. It has the effects of harmonizing the shaoyang, clearing internal heat toxins, and is the basic formula for treating shaoyang-yangming combined diseases. Modern research has found that Da Chaihu Tang has hepatoprotective and choleric effects, enhances immunity, has anti-inflammatory and anti-tumor effects, lowers blood sugar and lipids, and is widely used clinically in the treatment of digestive system diseases, especially pancreatitis [25]. In severe acute pancreatitis (SAP), serum procalcitonin (PCT), C-reactive protein (CRP), and interleukin-6 (IL-6) gradually increase with disease progression, reflecting the severity of the disease. Clinical trials have shown that modified Da Chaihu Tang can significantly reduce the levels of these indicators, alleviate inflammation, and relieve clinical symptoms [26]. Feng Wentao [27] and others found through clinical trials that the use of Da Chaihu Tang can improve acute hyperlipidemic pancreatitis (AHL) by reducing serum amylase (AMS) levels and improving pancreatic injury. It can also reduce total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) levels, increase high-density lipoprotein cholesterol (HDL-C) levels, reduce blood viscosity, alleviate pancreatic microcirculation disorders, and reduce pancreatic injury. The main complications of SAP are gastrointestinal dysfunction, manifested as disorders in gastrointestinal hormone secretion such as excessive secretion of gastrin (GAS) leading to excessive secretion of gastric acid and pancreatic juice, decreased intestinal motility such as decreased serum motilin (MTL) levels, and decreased levels of beneficial bacteria in the intestine (*Lactobacillus*, *Bifidobacteria*). Da Chaihu Tang can improve gastrointestinal dysfunction symptoms in SAP patients, reduce serum GAS levels, increase MTL levels, increase *Lactobacillus* and *Bifidobacteria* content, improve SAP complications, and increase serum superoxide dismutase (SOD) and CD4+/CD8+ levels. It can also reduce serum tumor necrosis factor- α (TNF- α) levels, indicating that Da Chaihu Tang may improve SAP prognosis by enhancing antioxidant capacity, blocking the inflammatory response process, inhibiting inflammation,

and enhancing the body's immunity [28]. Gao Hua [29] and others found that Da Chaihu Tang can reduce intra-abdominal pressure, prevent compartment syndrome by promoting early defecation in SAP patients, stabilizing the intestinal environment, reducing intestinal mucosal edema, and reducing intestinal bacterial translocation.

3.5 Yin Chen Hao Tang

The formula Yinchenghao Tang originated from Zhang Zhongjing's "Treatise on Febrile Diseases". Zhang Zhongjing's Yinchenghao Tang consists of Yincheng, Zhizi, and Dahuang, which is commonly used to treat jaundice and malaria heat. Modern pharmacology indicates that the Yinchen in Yinchenghao Tang contains a compound called Yinchenin, which has antioxidant, anti-inflammatory, and anti-tumor properties. The main pharmacological components of Zhizi include flavonoids, terpenoids, esters, volatile oils, polysaccharides, and various trace elements. Among them, geniposide in terpenoids can reduce the release of inflammatory factors, achieving anti-inflammatory effects. Rhein in Dahuang can inhibit inflammation and bacteria, regulate immunity, and protect the pancreas. These all indicate that Yinchenghao Tang has a clear mechanism of action for treating pancreatitis [30]. Early apoptosis and autophagy of pancreatic acinar cells in patients with SAP are considered important factors affecting disease progression. Late apoptosis of pancreatic acinar cells can lead to cell necrosis and release of inflammatory factors, inducing inflammation. There is a mutual regulation between autophagy and apoptosis. Autophagy can slow down apoptosis, and excessive autophagy of pancreatic cells can also cause excessive accumulation of zymogen in pancreatic acini, aggravating pancreatic damage. Therefore, promoting early apoptosis of pancreatic cells and inhibiting autophagy are key to treating SAP. Yinchenghao Tang can regulate the expression level of miRNA-30a-5p in the mi-RNA family, increase it, prevent its upregulation of serine protease gene (HTRA1), induce inflammation, and increase its binding to the 3'-UTR region sequence of tumor cells, negatively regulating autophagy genes and apoptosis factors, to inhibit autophagy and accelerate apoptosis. In addition, it can also downregulate the level of endogenous competitive inhibitor of miRNA, lncRNA PVT1, to prevent autophagy and accelerate apoptosis of pancreatic acinar cells, improving SAP [31]. Ma Hui [32] and others used Yinchenghao Tang combined with Longdan Xiegan Tang to assist in the treatment of hepatobiliary damp-heat type SAP and achieved significant efficacy. The levels of serum high mobility group box 1 protein (HMGB1) and receptor for advanced glycation end products (RAGE) in the subjects were measured by enzyme-linked immunosorbent assay, and the improvement of gastrointestinal function and symptoms and signs was significantly better than that in the group treated with Western medicine alone. The pro-inflammatory factor HMGB1 can bind to the RAGE receptor, thereby activating tumor necrosis factor- α , adhesion factors, interleukins, etc., leading to systemic inflammatory response syndrome (SIRS) and causing secondary damage to pancreatic tissue. The liver is one of the organs most susceptible to damage in AP. Various factors such as endotoxemia and microcirculation disorders caused by AP can cause liver damage. Therefore, controlling acute liver injury caused by AP is one of the effective methods

to prevent the development of multiple organ dysfunction syndrome in the body. Liver damage will also prolong the course of AP in reverse, and its incidence rate is positively correlated with the severity of pancreatitis [33]. Scholars found through animal experiments that Yinchenghao Tang can reduce the levels of serum alanine aminotransferase (ALT), serum amylase (AMY), aspartate aminotransferase (GOT), and inflammatory markers (TNF- α , IL- β), and inhibit the expression of autophagy adapter protein (p62), keap1, and nuclear factor E2-related factor 2 (Nrf2) in liver tissue, thereby inhibiting the p62-keap1-Nrf2 signaling pathway and alleviating the inflammatory response and liver damage caused by SAP[34].

4. Summary and Outlook

In summary, traditional Chinese medicine (TCM) formulations have demonstrated significant therapeutic effects in the treatment of severe acute pancreatitis (SAP). The main mechanisms of action include: (1) reducing pro-inflammatory factors and increasing anti-inflammatory factors to control the inflammatory response of SAP, thus alleviating damage to the pancreas and other organs; (2) inhibiting the release of pancreatic enzymes to slow down the process of self-digestion of the pancreas; (3) treating intestinal functional disorders and complications by regulating intestinal neurotransmitters and reducing endotoxin levels in the intestine; (4) slowing down SAP lung injury by inhibiting the expression of JNK-related signaling pathways; (5) accelerating apoptosis of pancreatic acinar cells to prevent excessive autophagy of cells; and (6) regulating the binding of relevant proteins to their corresponding receptors to prevent progression to the systemic inflammatory response syndrome (SIRS) stage and subsequent liver damage.

A large amount of clinical data indicates that TCM has significant advantages in the combined clinical treatment of SAP with various methods. However, it is still necessary to note that the mechanism of TCM in treating SAP has not been fully revealed, the exact pharmacological components of single TCM formulations are not fully understood, and there is still a lack of large-sample, high-quality clinical studies. This article aims to review the efficacy of TCM formulations in treating SAP. Despite the lack of clinical research on TCM syndrome differentiation and treatment, future research should focus on reviewing the progress of TCM clinical syndrome differentiation and treatment of SAP, in order to better utilize the characteristics of integrated Chinese and Western medicine in the treatment of SAP.

References

- [1] Tian Jiyun; Chen Yafeng; Feng Dianxu. Progress in the Treatment of Severe Acute Pancreatitis with Integrated Traditional Chinese and Western Medicine [J]. Journal of Traditional Chinese Medicine, 2010, 21(07): 1755-1757.
- [2] Cao Feng, Li Fei, Zhao Yupei. Interpretation of "Guidelines for the Diagnosis and Treatment of Acute Pancreatitis in China (2021)" [J]. Chinese Journal of Practical Surgery, 2021, 41(07): 758-761.

- [3] Zhuo Yuzhen; Cui Lihua; Li Caixia; Cui Naiqiang; Zhang Shukun. Research Progress on the Mechanism of Action of Traditional Chinese Medicine Compound in the Treatment of Acute Pancreatitis [J]. *Chinese Journal of Integrative Medicine in Surgery*, 2019, 25(03): 394-398.
- [4] Pancreatic Surgery Group, Surgical Branch of Chinese Medical Association. Guidelines for the Diagnosis and Treatment of Acute Pancreatitis in China (2021) [J]. *Zhejiang Practical Medicine*, 2021, 26(06): 511-519+535.
- [5] Zhuo Yuzhen, Cui Lihua, Li Caixia, et al. Research Progress on the Mechanism of Action of Traditional Chinese Medicine Compound in the Treatment of Acute Pancreatitis [J]. *Chinese Journal of Integrative Medicine in Surgery*, 2019, 25(03): 394-398.
- [6] Shen Weixing. Discussion on the Positioning and Treatment of Acute Pancreatitis in Traditional Chinese Medicine [J]. *Zhejiang Journal of Traditional Chinese Medicine*, 2007, 42(3): 136-137.
- [7] Zhang Shengsheng; Li Huizhen. Expert Consensus on Traditional Chinese Medicine Diagnosis and Treatment of Acute Pancreatitis (2017) [J]. *Chinese Journal of Traditional Chinese Medicine*, 2017, 32(09): 4085-4088.
- [8] Zhang Zhe, Zhao Jingjie, Wang Yongzhi, Li Li. Research Progress on Pharmacological Effects and Mechanisms of Chaihu Shugan Powder [J]. *Chinese Journal of Traditional Chinese Medicine Information*, 2017, 24(09): 128-131.
- [9] Ni Xinqiang, Cao Meiqun, Wu Zhengzhi, et al. Research Progress on Chemical Composition and Pharmacological Effects of Chaihu Shugan San [J]. *Shanghai Journal of Traditional Chinese Medicine*, 2017, 51(09): 109-113.
- [10] Lu Weiwei, Qian Xiaoqiang, Yang Min, et al. Effect of Chaihu Shugan San Combined with Zusanli Acupuncture on Serum Inflammatory and Immune Indexes in Patients with Acute Pancreatitis [J]. *Shanghai Journal of Traditional Chinese Medicine*, 2023, 57(06): 80-83.
- [11] Shi Xianli, Zeng Huilin. Clinical Study on Chaihu Shugan San Enema in the Treatment of Acute Pancreatitis [J]. *Journal of North Sichuan Medical College*, 2019, 34(05): 619-621.
- [12] Sun Wenjie, Chen Yafeng, Li Hongchang, et al. Clinical Research Progress of Da Chengqi Tang in the Treatment of Acute Pancreatitis [J]. *Chinese Journal of Experimental Formulae*, 2019, 25(12): 221-226.
- [13] Gao Xiang, Liu Meimei, Yao Qiqi, et al. Clinical Study of Da Chengqi Tang Combined with Octreotide in the Treatment of Acute Severe Pancreatitis [J]. *Journal of Chinese Medicine*, 2023, 41(02): 238-242.
- [14] Li Jie, Chen Yafeng, Feng Dianxu. Effect of Da Chengqi Tang on Expression of Pancreatic Interleukin 18 [J]. *Journal of Traditional Chinese Medicine*, 2020, 31(11): 2681-2684.
- [15] Wang Xiaoyan, Li Chunyu, Zhang Yanan, et al. Effect of Electroacupuncture at Different Acupoints on Expression of 5-HT7 Receptor in Gastric Antrum and Colon Tissues of Rats with Functional Diarrhea [J]. *Acupuncture Research*, 2021, 46(07): 549-554.
- [16] Shen Yanping, Tang Xiaoyue, Jiang Shengyang, Wang Wenyuan, Wu Yanmin, Xia Beilei. Mechanism Study of Da Chengqi Tang in Treating Intestinal Dysfunction in Severe Acute Pancreatitis [J]. *Journal of Chinese Medicine*, 2017, 35(05): 1138-1141+1347-1348.
- [17] Gershon MD. Nerves, reflexes, and the enteric nervous system pathogenesis of the irritable bowel syndrome [J]. *J Clin Gastroenterol*, 2005, 39(5 Suppl 3): S184-193.
- [18] Xiang Hong, Wang Zhizhou, Shang Dong. Effect and Molecular Pharmacological Mechanism of Qingyitang in the Treatment of Acute Pancreatitis [J]. *Journal of Traditional Chinese Medicine*, 2018, 29(02): 408-411.
- [19] Wu Zhishui, Long Zhengmin. Clinical Efficacy of Qingyitang in Patients with Severe Acute Pancreatitis [J]. *Shenzhen Journal of Integrative Chinese and Western Medicine*, 2023, 33(11): 32-34.
- [20] Shi Yujie, Liu Jingya, Sun Guangyuan. Effect of Qingyitang Combined with External Chinese Medicine on Gastrointestinal and Pancreatic Function Indexes in Patients with Severe Acute Pancreatitis [J]. *Chinese Emergency Medicine*, 2021, 30(08): 1450-1453.
- [21] Chen Guanghua, Wang Tao, Shu Bo. Mechanism of Qingyitang Mediated JNK Signaling Pathway in Regulating Immune System Response and Anti-inflammatory Response to Systemic Inflammation in Acute Pancreatitis Mice [J]. *Journal of Chinese Medicine*, 2023, 41(08): 249-253.
- [22] Li Chuan, Fang Changtai. Relationship between TREM-1, PCT, sICAM-1 Expression Levels and Severity of Acute Pancreatitis [J]. *Sichuan Medicine*, 2019, 40(07): 714-717.
- [23] Luan Xiaofeng, Wang Lei, Gai Xuefeng. Effect of Qingyitang Plus and Minus on Severe Pancreatitis and Its Influence on Amylase, Tumor Necrosis Factor- α , Interleukin-6 Levels [J]. *Journal of Chinese Medicine*, 2020, 38(03): 50-53.
- [24] Hu Wei, Liu Hongbin, Wang Manxue, et al. Mechanism of Qiyi Decoction and Curcumin Adjusting Intestinal Microecology for the Treatment of Severe Acute Pancreatitis. *Tianjin Medicine*, 2018, 46(11): 1155-1160.
- [25] Zhu Ranpei, Sang Tianqing, Xie Hui, et al. Research Progress of Da Chaihu Tang in Digestive System Tumors. *Chinese Journal of Experimental Traditional Medical Formulae*: 1-11 [2023-12-02].
- [26] Zhou Jing, Lu Xianyan. Clinical Efficacy Analysis of Modified Da Chaihu Tang in the Treatment of Acute Pancreatitis. *Modern Medicine and Health Research Electronic Journal*, 2023, 7(12): 95-97.
- [27] Feng Wentao, Yang Zhonghai, Zhang Dapeng, et al. Effect of Modified Da Chaihu Tang Combined with Shengjiang San on the Efficacy of Acute Hyperlipidemic Pancreatitis and Its Influence on Blood Lipid Levels, Inflammatory Factors, and AMS. *Journal of Modern Integrated Traditional Chinese and Western Medicine*, 2022, 31(12): 1658-1661.
- [28] Lin Yaoyao, Lin Xianping, Mai Ye, et al. Effect of Modified Da Chaihu Tang on Serum TNF- α , SOD, LPS, Gas, and Intestinal Flora Levels in Patients with Acute Pancreatitis of Fushi Heat Syndrome. *Shandong Journal of Traditional Chinese Medicine*, 2022, 41(01): 50-55+77.
- [29] Gao Hua, Nie Jinshan. Efficacy Study of Modified Da Chaihu Tang Combined with Conventional Treatment on Intra-abdominal Hypertension in Moderate Severe

- Acute Pancreatitis. *Navy Medical Journal*, 2021, 42(06): 736-739.
- [30] Li Gaohui, Lv Wenliang. Brief Introduction to the Clinical Research of Yinchensini Decoction in Ancient and Modern Times. *Journal of Liaoning University of Traditional Chinese Medicine*, 2020, 22(07): 90-95.
- [31] Xiang Hong, Hu Fenglin, Tao Xufeng, et al. Protective Effect of Yinchensini Decoction on Severe Acute Pancreatitis Rat Model by Regulating the lncRNA PVT1/miRNA-30a-5p Signaling Pathway. *Journal of Clinical Hepatology*, 2021, 37(01): 147-152.
- [32] Ma Hui, Li Zheng, Zhang Yingwen, et al. Observation on the Efficacy of Yinchensini Decoction Combined with Longdan Xiegan Decoction in the Treatment of Acute Pancreatitis (Hepatobiliary Damp-Heat Syndrome). *Chinese Journal of Emergency Traditional Chinese Medicine*, 2021, 30(06): 1037-1039.
- [33] Wei Ronghuang, Liang Yalin, Meng Huaying, et al. Application of Fecal Purge Method in Acute Pancreatitis Based on the Theory of Intestine-Liver Axis. *Chinese Journal of Traditional Chinese Medicine Information*, 2023, 30(01): 11-15.
- [34] Zhu Tianhong, Chen Benqi, Zhao Wei, et al. Effect of Yinchensini Decoction on Acute Liver Injury in Rats with Severe Acute Pancreatitis and Its Influence on the p62-keap1-Nrf2 Signaling Pathway. *Chinese Journal of Emergency Traditional Chinese Medicine*, 2019, 28(07): 1167-1170.