JOP. J Pancreas (Online) 2007; 8(6):704-714.

REVIEW

Progress in the Study of Therapeutic Effects of Traditional Chinese Medicine and Extracts in Treating Severe Acute Pancreatitis

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SUMMARY

This review summarizes the effects and mechanisms of traditional Chinese medicine and herb extracts in treating severe acute pancreatitis. Substances used in traditional Chinese medicine can inhibit pancreatic enzymes and improve microcirculation as well as immunoregulation by blocking the pathological progress of severe acute pancreatitis. Extracts of Chinese herbs not only act on the pancreas, stomach and intestine, but also have markedly therapeutic effects on other viscera damaged as a result of the systemic inflammatory response to acute pancreatitis. Therefore, the application of extracts of Chinese herbs for treating severe acute pancreatitis has significant clinical value and good prospects.

INTRODUCTION

Severe acute pancreatitis is one of the three main causes of acute abdomen constantly accompanied by multi-system and multi-organ impaired function or failure. Its onset and development is characterized by rapid change, complicated illness and is difficult to treatment. With the continuous development of traditional Chinese medicine in recent years, it has been proven that traditional Chinese medicine and its extracts have remarkable effects in treating severe acute pancreatitis and enjoys unique advantages. Therefore, this article summarizes traditional Chinese medicine, its extracts and the marked therapeutic effects on severe acute pancreatitis documented in recent years, and demonstrates their curative effects and mechanisms.

PROGRESS RESULTING FROM EXPERIMENTAL STUDY

Traditional Chinese Medicine

Gardenia Jasminoides Ellis

The medicinal part of the gardenia is its fruit. Its main active ingredient is geniposide and its degradation product is genipin [1]. Its pharmacological effect includes a choleretic effect, conscious-sedation, improved micro-circulation, antibiosis and anti-inflammation.
Mao, Jia and some other scholars [2, 3, 4], in carrying out a series of empirical studies on the use of extract of *Gardenia jasminoides Ellis* in treating severe acute pancreatitis, found that *Gardenia jasminoides Ellis* remarkably reduced the serum amylase and myeloperoxidase levels of both serum and pancreatic tissue as well as the level of TNF-alpha and IL-6 as well as reducing injury by oxygen-free radicals, NO and endotoxins. The mechanism of the extract of *Gardenia jasminoides Ellis* in treating severe

acute pancreatitis may be that it can lower the activity of lipid perhydride in serum and tissue, protect the antioxidation ability of the organism itself, and lessen injury by oxygen-free radicals and their cascade reaction during the severe acute pancreatitis process. Jia *et al*. [5, 6] found that the extract of *Gardenia jasminoides Ellis* can lower vasopermeability and inflammation, improve pancreatic hemodynamics, protect the function of the cellular membrane and alveolar subcellular organelles, strengthen the defense mechanism and inhibit the release of pancreatic enzymes and biotic active factors.

Acanthopanax

The medicinal part of Acanthopanax is its root and rhizome with flavonoids as the major functional components, exerting its effects in many aspects: dilating blood vessels and reducing blood viscosity to promote blood circulation and increase cardiac and cerebral blood flow, decreasing the heart rate and lowering tissular oxygen consumption and metabolism as well as the effects of anti-fatigue, anti-stress and anti-inflammation, bidirectional regulation on the central nerve system and leukocytes, thus enhancing non-specific resistance of the body [7].
Acanthopanax presents a favorable "adaptogen-like" action, as discovered in modern studies, demonstrating that this material can successfully improve the tissular tolerance of hypobaric hypoxia, augment erythrocyte oxygen saturation, normalize the pathological process, antagonize oxidation, ameliorate microcirculatory function, and alleviate pancreatic pathological changes through reducing oxygen-free radicals production and increasing the NO level [8]. When injected intraperitoneally into severe acute pancreatitis rats in the research of Wang *et al*. [9], acanthopanax led to apparently a higher serum NO level and superoxide dismutase activity in the treated group in relation to the severe acute pancreatitis group, and a notable decline in serum amylase ($P<0.05$ for every indicator) as well as a decreased pathological state of the pancreas at all time points in treated rats.

EXTRACTS OF TRADITIONAL CHINESE MEDICINE

Monomers

Emodin

Emodin, an anthraquinone derivative extracted from the rhizome of *Rheum palmatum L*, is an orange needle crystal whose molecular formula is $C_{15}H_{10}O_5$ and whose relative molecular weight is 270.23 u. The pharmacological effects of emodin are extensive, including inhibiting pancreatic secretion, anti-inflammation, bacteriostasis, immunological regulation, protection of the liver and kidney and antioxidation, thus improving microcirculation, spasmolysis and antitumoral activity, etc. [10].
As a common medicine for treating severe acute pancreatitis, emodin can inhibit anaerobic infection, lead purgation, relieve sphincter of Oddi spasm, protect the intestinal mucosal barrier so as to prevent translocation of intestinal bacteria, eliminate oxygen-free radicals, lower the endotoxin level of plasma and effectively inhibit the abnormal metabolism of vasoactive substances, such as gadoleic acid, and improve microcirculation [11]. It can also promote secretion of pancreatic fluid, interfere with apoptotic genes, induce acinar cell apoptosis of the pancreas, avoid or reduce the release of pancreatic enzymes and inflammatory mediators to block the pathogenic process. By enhancing gene expression by inducing cell factors, emodin can regulate cell proliferation and differentiation, stimulate the synthesis of manifold extracellular matrix, increase DNA synthesis and the protein content of pancreatic tissue, thereby accelerating regenesis and the repair of pancreatic tissue. On the other hand, emodin can markedly lower the serum content of TNF-alpha and IL-6 [12], causing a decrease in serum amylase levels by inhibiting the activity of the pancreatic enzymes and reducing pancreatic necrosis as well as reducing the ascites of severe acute pancreatitis and relieving the pathological changes of pancreatic tissue. Some authors [13, 14] have found that the serum amylase level of severe acute pancreatitis rats dropped

markedly after being treated with emodin; the mRNA expression of EGF increased markedly as compared to the non-treatment group. The total protein and DNA synthesis increased notably; the apoptosis index of pancreatic cells was markedly higher than that of the non-treated group. The Bak mRNA expression, apoptotic gene, was not markedly different from that of the non-treated group, but the Bak mRNA expression was markedly higher than that of the control group. Pancreatic microcirculation dysfunction plays an extremely important role in the pathogenesis of severe acute pancreatitis. While emodin is clearly able to improve the microcirculation and, as a result, inhibit the pathological progress of severe acute pancreatitis, it has been found by Yuan *et al*. [15] that emodin can markedly improve the ischemic state of pancreatic tissue through the normalization of the abnormal metabolism of eicosenoic acid and, consequently, moderate cell necrosis and other pathological damages in the pancreas.

Resveratrol

Resveratrol, an hydroxyl diphenyl-ethylene compound extracted from the root of giant knotweed rhizome, is a colorless needle crystal whose molecular formula is $C_{14}H_{12}O_3$ and whose relative molecular weight is 228.25 u. The pharmacological effect of resveratrol includes antitumoral activity, antioxidation, anti-inflammation, antibiosis, thus inducing apoptosis, protecting the liver and counteracting cardiovascular disease [16]. The mechanism of resveratrol in treating severe acute pancreatitis is the inhibition of the generation, activation and release of inflammatory mediators; it can reduce the generation of NO, IL-1, IL-6, TNF-alpha [17], etc. during the inflammatory process by inhibiting the NF-kappa B activation of macrophages, lymphocytes, etc., and it can block NF-kappa B activation induced by TNF, and inhibit protein kinase activation induced by mitogens. There is evidence that resveratrol can maintain the intestinal mucosa barrier intact, therefore inhibiting bacteria and toxic immigration during severe acute pancreatitis by restraining apoptosis of the intestinal mucosal epithelial cells. Sha *et al*. [18] injected resveratrol (5 mg/mL, 10 mg/kg i.v.) into severe acute pancreatitis rats and found that resveratrol can lead to an apparently lower level of the apoptosis index in intestinal mucosal cells and the positive incidence of the expression of apoptosis regulatory gene bax protein in the treated groups as compared to the control group at the time points of 3, 6 and 12 h ($P<0.01$ for each one).

Baicalin

Baicalin refers to the flavonoids extracted from the root of skullcap, presenting pallide-flavens and thin raphides with a molecular formula of $C_{21}H_{18}O_{11}$ and a molecular weight of 446.35 u. Being the effective antibacterial component of skullcap, baicalin functions with anti-inflammation, antibiosis, antivirus and decreases the inflammatory reaction as well as demonstrating diuresis, cholagogue, antihypertension, sedation, fever reduction, anticancer effects, etc. [19].
It has been proven that baicalin can eliminate oxygen-free radicals, antagonize cellular oxidation in organs, abate tissular ischemia-reperfusion injury, promote cellar apoptosis, resist infection and modulate immunity, etc.. As shown in the latest research, baicalin is capable of avoiding a waterfall-like cascade reaction of inflammatory mediators, lessening tissue damage and inflammatory reaction by its inhibition of NF-kappa B activation and subsequent prevention of gene transcription of pro-inflammatory molecules [20]. Zhang *et al*. [21] injected severe acute pancreatitis rats with a 5% baicalin injection at a dose of 10 mg/100 g using an external jugular-vein passage followed by continuous intravenous administration (10 mg/h/100 g) by microinfusion pump, observed at 3, 6 and 12 h, respectively after surgery. Compared with the control group, in the baicalin treatment group, 12 h survival was higher, the pathological changes were milder at all time points, the plasma amylase level was lower at

3 h, the serum contents of NO and malondialdehyde were lower at all time points, the serum TNF-alpha content was less at 6 h. Zhang *et al*. concluded that baicalin has a protective effect on multiple organs of a severe acute pancreatitis rat model similar to that of octreotide [21].

Compounds

Tripterygium Glycosides

Tripterygium glycosides, a glycoside preparation extracted from the root of *Tripterygium wilfordii*, is a non-steroidal immunosuppressor. Its physiological activity is coordinated with its main components: diterpene lactone, triterpene and alkaloid. The main pharmacological effects are anti-inflammatory and immunosuppressive action [22].

Tripterygium glycosides have an obvious inhibiting effect on T-cell proliferation induced by ConA, can intensively inhibit IL-2 and IL-2 activity induced by T-cells, inhibit IL-1, IL-6, IL-8 and TNF generation induced by monocytes, and it can also inhibit phagocyte generation and block the "waterfall" cascade effect of inflammatory mediators. Tripterygium glycosides have a bi-directional regulating effect on the immunological course which depends on the dose while a therapeutic dose can enhance the cytotoxic activity of the natural killer cell, correct the confusion of the T-cell subgroup distribution and modulate the immune response [23]. Tripterygium glycosides can also directly fight against inflammation itself and markedly inhibit the increase of vasopermeability in inflammation, chemotaxis of the inflammatory cells, the generation and release of prostaglandin E2 (PGE2) and other inflammatory mediators, platelet aggregation and fiber hyperplasia in the late stages of inflammation, etc.. It can be used to inhibit the release of cytokines at multiple levels and block inflammatory reactions for treating severe acute pancreatitis. Jin *et al*. [24] injected a suspension of tripterygium glycoside powder into severe acute pancreatitis rats intraperitoneally for 3 days or less if death occurred earlier. After treatment, amylase, endotoxin, TNF-alpha and IL-1 dropped markedly, and the pancreas pathological grading dropped notably. No marked prolongation of survival or decline of mortality was observed, but long-term survival appeared in the treatment group.

Extract from Ginkgo biloba

The extract from Ginkgo biloba is extracted from the leaf of Ginkgo Biloba; its main active ingredient is ginkgolides (6%) and flavonoid glycosides (24%) and its main pharmacological effects include resisting platelet activating factor (PAF) and antioxidation [25].

Recent studies have proven the important role of PAF in the pathogenesis of severe acute pancreatitis [26]. Since ginkgolides, especially ginkgolide B, are a natural PAF antagonist with strong activity [27], they can improve blood rheology, lower blood viscidity, modulate neurotransmitter release, increase oxygen and glucose supply to ischemic tissues, etc. [28], thus improving the microcirculation of the pancreas and intestines and lowering the endotoxin level. Flavonoid glycosides can eliminate excessive oxygen-free radicals, inhibit the lipid peroxidation of cell membranes, enhance superoxide dismutase activity of red cells, thus protecting the cell membrane and preventing serious body injuries from free radicals. In a study by Xu *et al*. which used intraperitoneal injection of the extract from Ginkgo biloba in severe acute pancreatitis rats [29], pathological damage occurs in the pancreas to an obviously lesser degree in the treated group as compared to the control group. It has an upregulated bcl-2 expression at 3 h after treatment ($P<0.05$), providing an explanation for the repressive effect of the extract from Ginkgo biloba on cellar apoptosis.

Panax Notoginoside

Panax notoginoside, extracted from the root of *Panax notoginseng (Burk.) F. H. Chen*, is a dammarane-type triterpene saponin and includes 20 kinds of monomers, among which the main ingredients are panoxadiol saponin

Rb1 and panoxatriol saponin Rg1. Panax notoginoside can dilate blood vessels, improve microcirculation and antioxidation, reduce the Ca^{2+} inflow and anti-inflammation and relieve pain [30].

Antioxidation by panax notoginoside produces a marked effect by improving the activity of superoxide dismutase so as to reduce the generation of free radicals, thus inhibiting lipid peroxidation. In a study of Xiong *et al*. [31], panax notoginoside has been found to downgrade the serum amylase level in severe acute pancreatitis rats at 12 and 24 h after surgery and the positive incidence of germiculture for the pancreas, liver, spleen, lung and mesenteric lymphnodes; it protects the intestinal mucosal barrier, inhibits enteric bacterial translocation and lessens pathological injury, resulting in an elevated survival rate. Ge *et al*. [32] treated severe acute pancreatitis rats with panax notoginoside. They were euthanized after 2 and 4 h, respectively and the pathological injury of pancreatic tissue was markedly improved; serum amylase, thromboxane B_2 and TNF-alpha level were reduced markedly especially during early stage. They found that panax notoginoside could block pathological progress to some extent.

Extract from Caulis Piper Wallichii

The extract of the stem of *Caulis piperis Wallichii* contains alkaloid and flavonoid glycosides, its pharmacological effects include anti-inflammation, the relief of pain and an anti-platelet aggregation effect [33].

It has been proven that the extract of *Caulis piper Wallichii* contains kadsurenone and wallichinine D (V, VI, VIII, IX), which are antagonistic substances to PAF. Xu *et al*. [34] gave extract of *Caulis piper Wallichii* to severe acute pancreatitis rats by intraperitoneal injection, and they found that the levels of serum amylase, PAF and endotoxins in the blood all decreased markedly, pathological lesions of pancreatic tissue were decreased, mean survival time was prolonged and the survival rate increased (all $P<0.05$). It has been suggested that by inhibiting PAF in the blood, the extract of *Caulis piper Wallichii* can promote microcirculation of the intestinal mucosa so as to lower its permeability, relieve translocation of the endotoxins, therefore lowering the level of the endotoxins in the blood which is very important in relieving the pathological process of severe acute pancreatitis.

CLINICAL TREATMENT PROGRESS

Traditional Chinese Medicine

Rhubarb

The medicinal part of rhubarb is its root and rhizome, and anthraquinones and tannin are its main functional components, with extensive pharmacological actions such as purging, the protection of the liver, antibiosis, the elimination of inflammation, immune regulation, anti-tumoral activity, anti-hyper-lipidemia, a decrease in blood pressure, a cardiotonic effect and the increase of gastric activity [35].

The mechanisms of rhubarb in treating severe acute pancreatitis are the following: 1) it facilitates colonic peristalses and evacuation to relieve the symptoms of abdominal pain and distention; 2) it blocks the thrombophilia and improves microcirculation, it can notably decrease the plasmatic levels of TNF-alpha, IL-6 and endotoxin [36], and as a result, remedy the disordered proportion of thromboxane B_2/6-keto-PGF_1alpha attributed to a depressed level of thromboxane B_2 and elevated prostaglandin E_2 in plasma; 3) it reduces the leakage of vessels due to elevated plasma osmotic pressure, lowered hematological hyperviscosity and capillary permeability; 4) it prevents intestinal bacterial translocation by enhancing the intestinal mucosal barrier in order to control autogenous infection and also inhibits endotoxins; 5) it promotes gallstone elimination and controls infection of the biliary tract by greatly relaxing the sphincter, contributing to the smooth flow of bile and pancreatic fluid as well as controlling biliary inflammation; 6) it inhibits the activity of the pancreatic enzymes [37], suppressing the secretion of parenzyme, pancreatic lipase and others, inhibiting the

excessive activation of macrophages and neutrophil infiltration in order to reduce the production of inflammatory cytokines; 7) it decreases catabolism to a lower level by inhibiting Na^+-K^+-ATPase and ATP consumption; 8) it withholds the production of oxygen-free radicals and intensively scavenges the superoxide free radical *in corpore*; 9) it protects pancreatic cells based on its healing effect on damaged structures of the cellular tight junction, nucleus, etc. and stabilizes the lysosomal membrane [38]; 10) by means of immunoregulation, it strengthens the immunity of the body by boosting phagocytosis of the neutrophilic granulocytes and the serum level of total complement. In a study of Li, intestinal function recovery was reached 4-8 days earlier than that of the non-treatment group after the administration of the aqueous extract from rhubarb (containing 30 g of raw rhubarb) through an oral or a stomach tube to 6 severe acute pancreatitis patients [39]. in the study of Yang and Lu, receiving rhubarb powder at 200 mg/kg through a stomach tube results in a better recovery rate from enteroplegia and a lower plasmatic endotoxin level as compared to the control group ($P<0.01$ for both) in treated severe acute pancreatitis patients 48 h after hospitalization [40]. Nasal feeding of 200 mL of 7.5% rhubarb powder mixed liquor to 32 cases with severe acute pancreatitis enrolled in a study by Zhang [41] reached a total effective rate as high as 93.8%.

Salvia Miltiorrhiza

The medicinal parts of salvia miltiorrhiza are the root and rhizome, with the fat-soluble diterpenoid tanshinones and water-soluble phenolic acids as its major functional components: its pharmacological actions include anti-infection, immune response regulation, antagonizing platelet aggregation, dilating blood vessels, multiplying the blood flow in the brain and heart, reducing blood viscosity, improving ischemia-reperfusion injuries in the heart, liver and lung, and eliminating oxygen-free radicals [42].
Salvia miltiorrhiza can alleviate pathological changes in the pancreas due to its inhibitory effect on initial neutrophilic granulocyte and endotheliocyte adhesion by decreasing IL-1, IL-6 and TNF-alpha levels in the blood, pancreatic enzyme production and phospholipase A activation [43]. The active principle, alkanoic acid B and its derivates, can dilate blood vessels, antagonize platelet agglutination and repress thromboxane A_2 production, lower blood viscosity, prevent intramicrovascular coagulation and facilitate fibrinolysis and, as a result, notably decrease the blood flow resistance index and ameliorate the bloodstream self-regulatory mechanism in the pancreas and, finally, remedy the local ischemia of the pancreas. Its action of blocking the calcium channel contributes to the evident blockage of intra-cellular calcium overload caused by extracellular Ca^{2+} inflow and milder pancreatic acinus impairment. The water-soluble phenolic acids have the greatest effect on antagonizing lipid peroxidation and eliminating free radicals. Tanshinol and tanshinone target neutrophil granulocytes directly by inhibiting their respiratory bursts and consequently reduce oxygen-free radical production [44]. They have an apparent preventive effect on biomembrane damages resulting from lipid peroxidation due to their suppression of dihydrocoenzyme consumption, preservation of superoxide dismutase activity and reduction of malondialdehyde in pancreatic, hepatic and renal tissue, and effectively deter the reperfusion injury caused by severe acute pancreatitis [45]. In a study by Ruan and Cai, the administration of a salvia miltiorrhiza injection in the treatment group [46] resulted in a fatality rate of 14.1%, and an obviously shorter average time of recovery of electrolytes and amylase and relief of abdominal pain as compared to the control group ($P<0.05$ for each index). A significant difference in the incidence of complications, frequency of surgery and average hospital stay has been reported by Zhang *et al*. [47] between the salvia miltiorrhiza-treated group and the control group (all $P<0.05$).

EXTRACTS OF TRADITIONAL CHINESE MEDICINE

Monomers

Anisodamine

Anisodamine also named 654-2, an alkaloid extracted from the root of *Anisodus tonguticus*, is a colorless needle crystal whose molecular formula is $C_{17}H_{23}NO_4$ and whose relative molecular weight is 305.38 u. As one of the anticholine drugs, it can relax the smooth muscle, relieve spasms of the blood vessels (especially the capillaries) [48] and has an analgesic effect together with an inhibiting secretory action of the glandular organ.

The mechanism of anisodamine in treating severe acute pancreatitis is that it can block M and alpha receptors as a blocker of the choline receptor, improve the metabolism of arachidonic acid, relieve vascular smooth muscle spasm, lower vascular resistance, modulate calcium homeostasis, block Ca^{2+} inflow, effectively stop cell calcium overload during ischemia-reperfusion injury, increase energy and oxygen supply to the tissue, protect cells at the cell level, enhance its tolerance to ischemia and hypoxidosis, stabilize the lysosome membrane of the glandular cells, thereby blocking the activation of pancreatic enzymes as well as the occurrence and development of autodigestion in a shorter period, and it can inhibit pancreatic gland secretion allowing the pancreas time to recover [49]. In addition, it can also inhibit the cell factor, oxygen-free radicals and endotoxins at the cell membrane level [50]. One-hundred and twelve severe acute pancreatitis patients were divided randomly into treated and control groups by Zhang and Wang [51] with the former receiving anisodamine through intravenous injection at a flushing dose of 1.5-2.0 mg/kg/day for 5 days leading to an obviously shorter average hospital stay, time of clinical improvement and lower mortality rate in comparison to the control group ($P<0.05$ for each one).

Tetramethylpyrazine

Tetramethylpyrazine, an amide alkaloid extracted from the rhizome of *Ligusticum chuanxiong Hor*., is a colorless needle crystal whose the molecular formula is $C_8H_{12}N_2$ and whose relative molecular weight is 136.20 u. The pharmacological effect of tetramethyl-pyrazine is extensive, including resisting Ca^{2+}, eliminating oxygen-free radicals, improving hemorheology and inhibiting tissue fibrosis, anti-tumoral activity and the effect of diuresis [52].

As a typical calcium channel blocking agent, tetramethylpyrazine can forcefully dilate blood vessels, improve microcirculation, lower blood viscosity, improve blood rheology and increase the volume of blood flow in viscera microcirculation. It can dilate blood vessels indirectly by inhibiting the synthesis of thromboxane A_2 while promoting generation of PGI_2, modulating thromboxane A_2/PGI_2 imbalance, and increasing the stability of the lysosome membrane. Tetramethylpyrazine can increase the surface charge of red cells and platelets, lower platelet aggregation, enhance the transforming capacity of red cells, relieve a high coagulative state, lower blood viscosity thus improving blood rheology, change the condition of the blood flow during blood stagnation, accelerate blood flow, maintain dilation of the blood capillaries, increase total blood flow, prevent thrombogenesis and enhance hemolysis [53]. Li *et al*. [54] randomly divided 61 cases of severe acute pancreatitis patients into two groups; the treatment group was given tetramethyl-pyrazine 120-160 mg together with physiological saline 500 mL, intravenously, once daily and, after 10-14 days of treatment, the targets of blood rheology, hemodiastase and urinary amylase were all significantly better than the control group (all $P<0.05$).

Tetrandrine

Tetrandrine, a bi-benzyl-isoquinoline alkaloid, is extracted from the root of *Stephania tetrandra S. Moore* whose molecular formula

is $C_{38}H_{42}0_6N_2$ and whose relative molecular weight is 622.70 u. Its pharmacological effect is as a calcium antagonist and PAF antagonist [55].

The mechanism of tetrandrine for treating severe acute pancreatitis can perhaps reduce PAF release by inhibiting Ca^{2+} inflow or inner calcium outflow [56], inhibit PLA_2, reduce PAF release and reduce the PLA activation which is induced by PAF [57]. Tetrandrine can reduce peroxidation injury by inhibiting pancreatic enzyme activation, inhibit the calcium overload of pancreatic acinar cells, stop NF-kappa B activation and alleviate the pancreatic inflammatory reaction through its calcium antagonist function. And, in another study, Leng *et al*. [58] divided 26 severe acute pancreatitis patients into treated and control groups; 120-180 mg tetrandrine diluted in 100 mL normal saline was administrated to the treated group twice daily through an intravenous drip lasting 7-14 days, resulting in a better cure rate of 92.3% and a lower incidence and fatality rate from complications such as multiorgan failure and sepsis in the treated group as compared to those in the control group ($P<0.01$ for each index).

Compounds

Breviscapine

Breviscapine, also named scutellarein, is extracted from *Erigeron breviscapus (Vant.) Hand.-Mazz*. Its main ingredients are total flavonoids and scutellarin. Breviscapine can improve blood circulation, lower vascular resistance, and inhibit intravascular coagulation and platelet aggregation [59].

Breviscapine can improve pancreatic microcirculation, lower blood viscosity, improve the local blood supply to the pancreas, correct ischemia and prevent necrosis. The total flavone can notably improve microcirculation, promote blood flow and eliminate stagnation. It can relax the vascular smooth muscle, dilate the arteriole especially the sphincter muscle of the blood capillaries [60]. Scutellarin can lower hematocrit, inhibit platelet aggregation and raise thromboxane B_2 as well as the thromboxane B_2/6-keto- PGF_1alpha ratio; it can also restore the 6-keto-PGF_1alpha level after ischemia, inhibit intravascular coagulation and promote fibrinolysis so as to lower blood viscosity [61]. Furthermore, breviscapine can enhance the capacity of both the macrophage and the immune systems, eliminate harmful oxygen-free radicals, prevent and treat series of pathological and physiological reactions induced by calcium overload, and prevent neuron injury due to ischemia-reperfusion. There is a significantly lower fatality rate of 8.0% in the treated group as compared to the control group ($P<0.05$), as well as changes of the hematocrit ($P<0.05$) are reported in a study by Huang [62] in which 40 cases of severe acute pancreatitis patients undergoing surgery were randomly divided into two groups: a treated group and a control group with the former receiving an additional intravenous drip of scutellarin.

Conclusions

In this updated article, we extended our previous review [63] reporting that the conservative treatment of severe acute pancreatitis using extracts of Chinese herbs is well-documented. Markedly different from Western medicines such as somatostatin, extracts of Chinese herbs which block the pathological progress of severe acute pancreatitis to some extent not only act on the pancreas, stomach and intestines, but also have markedly therapeutic effects on other viscera due to the systemic inflammatory response complicated by acute pancreatitis. The functions are more extensive than somatostatin and mutually supplementary.

Therefore, the application of extracts of Chinese herbs for treating severe acute pancreatitis has significant clinical value and good prospects. We believe that by further experimental study and clinical application, extracts of Chinese herbs will become a promising formulation for clinically treating severe acute pancreatitis.

Received September 17th, 2006 - Accepted September 6th, 2007

Keywords Drugs, Chinese Herbal; Pancreatitis, Acute Necrotizing; Therapeutics; Extract of Chinese Herbs

Abbreviations PAF: platelet activating factor; PG: prostaglandin

Acknowledgements This review was supported by the technological foundation project of "Traditional Chinese Medicine Science of Zhejiang Province" (No. 2003C130; No. 2004C142), the foundation project for "Medical Science and Technology of Zhejiang Province" (No. 2003B134), the foundation project for "Technological and Development of Hangzhou" (No. 2003123B19), the intensive foundation project for "Technology of Hangzhou" (No. 2004Z006), the foundation project for "Medical Science and Technology of Hangzhou" (No. 2003A004) and the foundation project for "Technology of Hangzhou (No. 2005224)

Conflict of interest The authors affirm that this review is original and they do not have any financial interest in any company, and that all authors meet criteria for authorship

Authors' declaration Some of the contents of this review were previously published in the Journal of Zhejiang University SCIENCE B 2007; 8(2):147-52 [63]. The authors declare that publication in JOP does not violate any existing copyright. The JOP Editors already informed Dr. Wei Yang and Dr. Peter H Byers (Editors-in-Chief) and Helen Zhang (Managing Editor) of the Journal of Zhejiang University SCIENCE B of the publication of the present review.

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Document URL: http://www.joplink.net/prev/200711/09.html

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