Analysis of pharmacological action and clinical application of DaXueTeng based on its anti-inflammatory action

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Highlights

DaXueTeng (Caulis Sargentodoxae) belongs to Angiospermae, Dicotyledons, Lardizabalaceae, Sargentodoxa, deciduous woody liana. Caulis Sargentodoxae was first recorded in the “BenCaoTuJing”, saying that it can attack blood and cure blood clots. This dissertation first overview relevant literatures of DaXueTeng recent years. We review the anti-inflammatory effects and clinical application of the current active components of DaXueTeng, which provides a good application prospect in clinic.

Abstract
As one of the representative drugs for clearing heat-toxicity, Chinese medicine DaXueTeng (Caulis Sargentodoxae) contains various chemical substances such as tannins, glycosides, cyclic polyphenols, triterpenoids, lignins, flavonoids, terpenoids and organic acids. It has a wide range of pharmacological effects. Meanwhile, it is valued by the doctor. Modern research suggests that DaXueTeng has antibacterial, antiviral, anti-inflammatory, anti-tumor, and immunosuppressive effects. It has been experimentally and clinically proven that the active constituents of DaXueTeng have a good therapeutic effect on inflammatory diseases. It is widely used in the treatment of pelvic inflammatory disease, annexitis, prostatitis, appendicitis, periappendiceal abscess, inflammatory intestinal obstruction, UC, endometriosis, inflammatory secondary infertility, gouty arthritis, pharyngitis, and stomatitis. Here we review the anti-inflammatory pharmacological effects and clinical applications of Caulis Sargentodoxae.

Keywords: DaXueTeng, Anti-inflammatory effect, review
Background

DaXueTeng (Caulis Sargentodoxae) is the stem of Sartopodoxa cuneata (Oliv.) Rehd. et Wils. The plant is endemic to China and is a relict plant of the Tertiary ancient tropical flora. It is mainly produced in the central and eastern parts of China, the provinces of Jiangxi, Hubei, Henan and Jiangsu in the northern part of the Indo-China Peninsula [1]. DaXueTeng is bitter and calm, belonging to stomach meridian and large intestinal meridian. It has the functions of promoting blood circulation, eliminating toxic phlegm, relieving pain, clearing the pain, and strengthening the bones and stagnation. It is used to treat pelvic inflammatory disease, acute appendicitis, chronic appendicitis, menstrual disorders, prostatitis, rheumatoid arthritis and other diseases. All have good results [2]. Previous phytochemical studies of DaXueTeng have described several components from the acetocetate portion, including anthraquinones, triterpenoids, lignans, flavonoids and organic acids, as well as phenolic glycosides and lignans from the n-BuOH and water-soluble fractions. DaXueTeng has played a major role in anti-inflammatory, anti-bacterial, anti-viral, etc [3-5]. Four phenolic glycosides, cuneatasides A-D [6-8], and one ionone glycoside cuneataside E [9], together with seven known phenolic Compounds were isolated from the water-soluble constituents of the stem of Sargentodoxa cuneata [10-14]. The active ingredient of DaXueTeng can effectively inhibit two Gram-positive bacteria, Staphylococcus aureus and Micrococcus epidermidis [15]. The inhibitory effect of tannin on Staphylococcus aureus is especially obvious [16]. Rutin and salidroside have been proved to be effective in inhibiting the development of inflammation in aqueous extract of DaXueTeng. The anti-inflammatory effects of these chemical constituents of DaXueTeng have attracted wide attention of scholars at home and abroad, and have been widely used in clinical practice. In this paper, the anti-inflammatory effects and clinical applications of the active components of DaXueTeng are reviewed.

Pharmacodynamic effects on different inflammation

Treatment of gynecological inflammation

Treatment of pelvic inflammatory disease Pelvic inflammatory disease is a common clinical gynecological disease, including inflammation of the ovaries, fallopian tubes, uterus and surrounding connective tissue, as well as the peritoneum and pelvis. Pelvic inflammation is a common gynecological disease of ovary, fallopian tube, uterus and its surrounding connective tissue, peritoneum and pelvic inflammation. Chinese medicine classifies pelvic inflammatory disease as abdominal mass, mass in abdomen, menstrual disorders, and leukorrheal diseases. Traditional Chinese medicine DaXueTeng and compound DaXueTeng have treated this disease and achieved remarkable results. Chinese medicine with single DaXueTeng and compound DaXueTeng is effective in treating this disease. Modern pharmacological experiments have also fully proved that DaXueTeng which can clear away heat and promote blood circulation, detoxify and dredge collaterals, has remarkable curative effect on pelvic inflammation. In pharmacological experiments, Huang Shufeng et al. found that DaXueTeng can reduce the ratio TXA2 / PGI2 ratio and TXA2 content in serum of model rats, alleviate endometrial swelling and improve the degree of endometrial lesion [17]. It showed that DaXueTeng could improve the edema and inflammatory state of uterine tissue in model rats.

Liu Qing et al. in exploring the effect of DaXueTeng on serum IL-6, TNF-α and uterine histopathology in rats with chronic pelvic inflammatory disease, it was proved that DaXueTeng could inhibit the expression of inflammatory mediators and inflammatory factors, and regulate the immunity of the body by lowering the levels of serum IL-6 and TNF-α [18]. Xu Hao et al. explored the effect of Hongteng Decoction on integrin αvβ3 expression in endometrium of rats with pelvic inflammation, which proved that Hongteng Decoction enema group was significantly different from gentamicin group and Kangfu Xiaoyan suppository group [19]. Hongteng decoction can increase the expression of integrin αvβ3 protein in endometrium of pelvic inflammatory disease rats, thereby improving endometrial receptivity and increasing pregnancy rate. Xu Xiaoqing used Jiajian Hongteng Decoction in the treatment of 30 cases of chronic pelvic inflammatory disease [20]. There are 30 cases in the control group. The results showed that the total effective rate of the observation group was 93.33 %. It is higher than the control group. The observation group’s results of the clinical symptom scores and B-ultrasound were also better than the control group. The adverse reactions in the observation group accounted for 6.67 %, and the control group accounted for 16.67 %; the recurrence rate of the observation group accounted for 3.33 %, and the control group accounted for 26.67 %. In addition, the quality of life follow-up results showed that the observation group was superior to the control group (P < 0.05). The method of adding and subtracting DaXueTeng retention enema is a kind of treatment for chronic pelvic inflammatory disease with simple operation. It is suitable for promotion in primary medical units, and strong practicality and operability.

Inflammatory secondary infertility

Inflammatory secondary infertility is caused by chronic pelvic inflammatory disease. It belongs to the category of “abdominal mass” of Traditional Chinese Medicine (TCM) syndrome. Liu Daqing et al. made Daxuetong Patrinia Paste enema liquid, using enema retention method to treat inflammatory secondary infertility [21]. The sausage liquid of Patrinia scabra is composed of DaXueTeng, BaiJiangcao (Patrinia scabra), DangGui (Angelica sinensis), ZiHuaDiDing (Herba Violae), SanLeng (Rhizoma Sparganii Stoloniferi), Ezhu (Zedoary rhizome), YanHuSuo (fried Corydalis yanhusuo), JinYinHua (Lonicera japonica), etc. The total number of treatments...
was 100 cases, the total effective rate was 96%, the total pregnancy rate was 90%, and all of them were conceived within one year.

**Endometriosis** TCM holds that congestion and internal obstruction are the main pathogenesis of endometriosis, which belongs to the category of "abdominal mass" and "dysmenorrhea". Promoting blood circulation to remove blood stasis to treat this disease as consensus among physicians.

Dai Deying et al. composed Chinese medicine such as DaXueTeng, TaoRen (Semen Persicae), MuDanPi (Cortex Moutan Radicis), PuHuang (Pollen Typhae) and MuLi (Concha Ostreae) to form Hongteng decoction, which is used for the treatment of endometriosis [22]. The total effective rate can reach 91%. It played a good preventive role, and the total effective rate was 93%. It can also reduce ovarian cysts and improve symptoms of dysmenorrhea and chronic pelvic pain in patients with recurrent endometriosis after operation. The different types of syndromes were treated by the addition and subtraction of the decoction of "red vine". It has achieved good results.

**Annexitis** Annexitis is caused by the dampness of the poisonous phlegm in the hypogastrium. DaXueTeng are scattered and detoxification. It is a good medicine for treating gynecological inflammation. Ma Bangytreated adnexal inflammatory masses with Hongteng Heavy Agent and Guizhi Fuling Pills [23]. Two cases were reported. The inflammatory masses were all dissipated, and the cure rate was 100%.

**Treatment of male inflammation**

**Chronic prostatitis** Chronic prostatitis belongs to the syndrome of deficiency and excess, kidney deficiency is the basis, blood stasis, heat and dampness-heat is the superficial, should be treated by Tonifying the kidney and promoting urination, removing blood stasis and dredging collaterals. Studies have shown that traditional Chinese medicine regulates immunity and inhibits inflammation, so as to treat chronic abacterial prostatitis CNP. Wang Kelei et al. used SD male rats injected the Xiaohzhiling to replicate chronic nonbacterial prostatitis (CNP) animal model [24]. The SD male rats were treated with compound DaXueTeng. They measured tumor necrosis TNF-A and IL-8 in rat prostate tissue. The results showed that Compound DaXueTeng could improve the histopathological structure of prostate in CNP model rats, alleviate inflammation and decrease the levels of TNF-A and IL-8. Lu Taikun treated chronic prostatitis with Hongteng Patrinia Decoction, 300 cases in the treatment group were treated with Hongteng Patrinia Decoction, 150 cases in the control group were treated with Qianliekang [25]. The results showed that the total effective rate of the treatment group was 90.7%, while that of the control group was 80.7%. It is concluded that Hongteng Patrinia Decoction can promote the absorption of inflammatory lesions, improve hemorhoeology, promote blood circulation, and has a very good effect in the treatment of chronic prostatitis.

**Treatment of digestive tract inflammation**

**Periappendiceal abscess** Periappendiceal abscess occurs after acute appendicitis. Chinese medicine uses clearing heat-toxicity, promoting blood circulation and removing blood stasis, removing toxicity for detumescence. Lou Yi studied that the active ingredients of antibacterial and anti-inflammatory in DaXueTeng are emodin and sitosterol [26]. Tamnin is the main chemical component of DaXueTeng, and has obvious inhibitory effect on many kinds of bacteria and yeasts. Wang Xuejun et al. in the treatment of 102 cases of periappendiceal abscess in Hongteng decoction, it is believed that DaXueTeng contains a large number of flavonoids and has obvious antimicrobial effect [27]. Oral Hongteng Decoction and combined use of antibiotics can accelerate the absorption of severe periappendiceal edema, promote the repair of normal tissues and accelerate the rehabilitation of diseases. Shen Fangmin et al. studied the clinical efficacy of Hongteng Decoction in the treatment of periappendiceal abscess and its effect on prognosis in 70 cases [28]. The results showed that compared with the control group, compound Hongteng decoction had stronger antimicrobial and anti-inflammatory effects, and its total clinical effective rate and prognosis were better than those of the control group.

**Appendicitis** Appendicitis is mostly due to stagnation of intestinal Qi and blood and accumulated dampness-toxicity, and it is a form of traditional Chinese medicine intestinal abscess. Chinese medicine uses promoting blood circulation and removing blood stasis, removing toxicity for detumescence for treatment. DaXueTeng has the effects of promoting blood circulation and removing blood stasis, clearing heat and dredging collateral. Mou Ergu used DaXueTeng and BaiJiangCao (Herba Patriniae) to treat 46 cases of chronic appendicitis and the cure rate was 100% [29]. There were no toxic side effects, and the curative effect was remarkable.

**Acute appendicitis** Acute appendicitis is developing rapidly, and its pain is acute. Traditional Chinese medicine is an important method for non-surgical treatment of acute appendicitis. Yang Hongwu used Hongteng Decoction to treat acute appendicitis [30]. The treatment group consisted of 485 cases, with a total effective rate of 93.40%. In the control group, there are 343 cases with a total effective rate of 71.43%. Xie Shaochu used Hongteng Decoction combined with antibiotics to treat acute appendicitis [31]. It was significantly better than using antibiotics alone. The total effective rate was 90.0% in the treatment group and 67.5% in the control group. And the adverse reactions in the treatment group were significantly less than the control group.

**Inflammatory intestinal obstruction** Xiao Ping applied DaxueTeng Soup oral treatment for postoperative
inflammatory intestinal obstruction [32]. There are 20 cases in the treatment group and the control group. The results showed that the treatment group significantly shortened the time of anal ventilation recovery, alleviated abdominal distention and abdominal pain, promoted the recovery of intestinal function, was conducive to wound healing, and avoided expensive operation costs.

**Chronic atrophic gastritis** Chronic atrophic gastritis is a common disease of digestive system. Promoting blood circulation benefiting qi and clearing heat-toxicity are the therapeutic methods of traditional Chinese medicine. Ma Weiming et al. treated 30 patients with chronic atrophic gastritis with Daxueteng Yuwei Yangwei Decoction, and 30 patients in the control group [33]. The results showed that the clinical efficacy of Daxueteng Yuwei Yangwei Decoction was significantly better than that of the control group. It could eliminate Helicobacter pylori, reduce the expression of Ki-67, Bax and Fax genes, eliminate inflammatory factors to a certain extent, reduce the rate of gene replication loss, and improve the state of gastric mucosa. It also regulates gastrointestinal motility and enhances immune function.

**Ulcerative colitis (UC)** Ulcerative colitis is a refractory disease of the digestive tract. This disease was treated by cooling intestine, cooling blood, regulating qi-flowing and activating collaterals in Chinese medicine. Hu Dingzheng randomly divided 98 cases of chronic non-specific ulcerative colitis into treatment group and control group [34]. 50 patients in the treatment group were treated with Chinese medicine enema (DaXueTeng, KuShen (Radix Sophorae Flavescentis), BaiJiangCao, etc.), and the control group was treated with oral sulfasalazine tablets. The total effective rate of the treatment group was 90 %, and the total efficiency of the control group was 70 %. The therapeutic effect of the treatment group was significantly higher than that of the control group. Zhou Yun used Hongteng Anchang Decoction to treat 60 cases of ulcerative colitis, and 60 cases of the control group were treated with mesalazine [35]. The clinical efficacy of the Chinese medicine group was better than that of the western medicine group. The total effective rate of the Chinese medicine group was 86.7 %, and the total effective rate of the western medicine group was 75.0%. The ESR and CRP in the two groups decreased after treatment, and the difference was not statistically significant. It shows that Hongteng Anchang Decoction can relieve the inflammatory reaction and repair the intestinal mucosa effectively.

**UC patients** Dong Sihai et al retained the enema therapy with Hongteng enema Decoction and combined oral medication [36]. In the effects of immune inflammatory response and intestinal flora in patients with UC, it was found that the levels of ESR, CRP, IL-6, TNF-α in the serum of the two groups were lower, and the level of IL-4 was increased, which was further compared with the control group. The levels of ESR, CRP, IL-6 and TNF-α in the serum of the observation group were lower after treatment, and the level of IL-4 was higher. It is confirmed that the red vine enema retention enema combined with oral medication can effectively inhibit the systemic inflammatory response of patients with UC and increase the anti-inflammatory ability of the body. While taking sulfasalazine routinely, the specific mechanism is directly related to the reversal of intestinal flora imbalance. The therapeutic regimen is worthy of clinical application in the future.

**Treatment of arthrosis**

**Gouty arthritis** Gouty arthritis belongs to the category of "obstructed pain" in traditional Chinese medicine. Methods of treating eliminating dampness by cooling, dispersing wind, expectorantapophlegmatic. Ling Jiayan et al. treated 32 cases of acute gouty arthritis with external application of DaXueTeng with Chinese medicine orally, 32 cases in the control group [37]. It was found that the symptoms of patients with acute gouty arthritis could be effectively alleviated and the pain time of patients could be significantly shortened in the treatment group by applying Daxueteng external application in basic treatment and oral Chinese medicine. It shows that DaXueTeng has obvious anti-inflammatory and analgesic effects on patients with gouty arthritis. Some researchers reported that DaXueTeng has both similar and novel targets as Western pharmaceuticals. Especially noteworthy are MMPs and RelA, which are inhibited by phytochemicals in Hong Teng but not NSAIDs. Hong Teng phytochemicals modulate many different nodes in the osteoarthritic pathway, which may ultimately culminate in a synergistic alleviatory effect on the disease [38].

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**Rheumatoid arthritis (RA)** Recent investigations about Sargentodoxa cuneata concerned to immunosuppressive effects of water decoction, which could be the basis of...
anti-inflammatory and curing rheumatic arthritis [39-40]. FuYu et al. treated adjuvant arthritis rats by intragastric administration of DaXueTeng for 28 days [41]. The expression of MMP-2 and MMP-9 in synovial cells of rats was significantly decreased, which indicated that DaXueTeng could alleviate the damage of synovial tissue, inhibit the secretion of MMP-2 and MMP-9 in synovial cells of adjuvant arthritis rats, prevent the occurrence of synovitis, protect articular cartilage and relieve bone damage. At the same time, FuYu et al. treated 10 rats with DaXueTeng showed that the levels of TNF-α and IL-6 in serum of adjuvant arthritis rats were lower than those of model group, indicating that DaXueTeng inhibited the abnormal secretion of TNF-α and IL-6 in adjuvant arthritis rats, thus preventing the development of immune inflammation, indicating that DaXueTeng regulated TNF-α and IL-6 [42]. It may be an effective mechanism for treating rheumatoid arthritis.

Treatment of stomatitis
Xiang Hui found that in the treatment of enteritis with DaXueTeng can achieve better curative effect [43]. At the same time, treating stomatitis in clinical by using of DaXueTeng, found that DaXueTeng has a good therapeutic effect on stomatitis. Oral ulcer was cured by adding red vine. It is concluded that in the future, those who encounter glossitis and oral ulcer will be treated with Hongteng 20 – 30 g on the basis of syndrome differentiation, which has the effect of accelerating the healing of glossitis and oral ulcer.

Treatment of acute pharyngitis
Lv Faqiang reported a case of acute pharyngopharyngitis treated with Hongteng in clinic [44]. The symptoms of the patient were obviously relieved and the curative effect was definite.

Analgesic and anti-inflammatory experiment
Li Hua observed the analgesic and anti-inflammatory effects of DaXueTeng on mice model [45]. It was found that DaXueTeng could prolong the pain threshold latency of acetic acid induced pain model mice, reduce the number of writhing, inhibit xylene-induced ear swelling, reduce swelling and swelling rate, inhibit the proliferation of granulation tissue in mice. The above animal experiments showed that DaXueTeng has obvious analgesic and anti-inflammatory effects, and the mechanism may be related to the influence of DaXueTeng on the levels of inflammatory factors in cells or serum. Z. H. Zhou studied the anti-inflammatory, analgesic effects of Dashui Shui extract and its therapeutic effect on mice with pelvic inflammatory disease [46]. In three experiments with different inflammatory model mice, it was found that SC extracts had similar anti-inflammatory and anti-nociceptive activities to indomethacin. ESC significantly decreased the levels of TNF-α and IL-6 of the model rats compared with indomethacin. ESC can be used to treat both acute and chronic inflammation and to relieve the associated pain.

Cheng Xiaoping stimulated human U937 cells with lipopolysaccharide LPS simulated inflammation model, and then intervened with water extract of DaXueTeng [47]. The results showed that the expression of IL-1beta, IL-10 and TNF-alpha increased after LPS stimulation, and the increase of inflammatory cytokines IL-1beta, IL-10 and TNF-α was significantly inhibited after the intervention of water extract from DaXueTeng, indicating that DaXueTeng could inhibit the progress of inflammatory reaction.

Anti-inflammatory immune activity
Inflammatory reaction plays an important role in the pathogenesis, and the immune response is also involved in its pathogenesis. Through the inhibition of red vine on mouse immune function and allogeneic skin graft rejection, Li Li et al. found that DaXueTeng decoction can make the phagocytic index, IgM production, peripheral blood T lymphocyte count and T, B lymphocyte transformation rate in mice decreased [48]. It can inhibit T lymphocyte-mediated cellular immunity and B lymphocyte-mediated humoral immunity in mice. It can antagonize DNCB-induced delayed-type hypersensitivity by inhibiting the transformation of T cells into effector cells and the activity of macrophages, and alleviate the inflammatory response of DNCB-sensitized mice. It inhibits the number of T cells and T cell proliferative response, and can inhibit the rejection of the same gene skin, indicating that it has significant anti-inflammatory effects. In addition, it was reported that phenolic glycosides from DaXueTeng could significantly inhibit the activity of prostaglandin synthase in sheep’s reproductive gland, and also had obvious anti-inflammatory activity [49-50].

Conclusion
DaXueTeng has a variety of pharmacological activities. It has been proved that there are anthraquinones, three triterpenoids, steroids, lignin compounds and many other compounds in DaXueTeng [51]. Flavonoids with the highest compound content in the leaves of DaXueTeng have been shown to be closely related to antibacterial and anti-inflammatory effects. Pharmacological studies have proved that the total saponins and total tannins in DaXueTeng have antibacterial effects. Rosamultin and kajiehigoside Fl are the first two active triterpenoid saponins isolated by Ruecker G et al. Both of them have strong hemolytic and antiviral activities [52]. Guo et al. used MTT colorimetric method to find that DaXueTeng has antiviral activity, which may be related to triterpenoid saponins in DaXueTeng [53]. In addition, there are many documents that prove that DaXueTeng has the effects of anti-hypoxia, anti-allergy, anti-oxidation, anti-tumor, anti-thrombosis, anti-virus, anti-radiation [54-55]. The study on the pharmacological action of DaXueTeng also provides a theoretical basis for its clinical application.
and the in-depth study on these two aspects will lay a theoretical foundation for us to further study the pharmacological active components of DaXueTeng and develop new drugs. However, there are few reports on the products of DaXueTeng this field, and most of them are still in the research stage. It is suggested that the research on the products of Daxuetong in medical application should be strengthened. Secondly, the clinical application of DaXueTeng mainly concentrated in the traditional Chinese medicine compound, so the author thinks that the application of the single medicine of DaXueTeng deserves further study.

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