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Progress in the study of the active ingredients and pharmacological effects of Duyiwei

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Abstract: *Lamiophlomis rotata (Benth.) Kudo is a plant of the family Labiatae and genus Striga. The active ingredients of Duyiwei are complex and have a variety of pharmacological effects. In this article, we refer to the recent literature and related studies to elaborate the active ingredients and pharmacological effects of Duyiwei, with a view to providing a theoretical basis for the clinical application of Duyiwei. Although some results have been achieved in the study of the pharmacological effects of Duyiwei, the study of its chemical composition and pharmacological mechanism is still not complete, and in-depth research can be carried out from cellular, tissue, molecular biology, metabolism and other multidisciplinary aspects, with a view to providing theoretical basis for the clarification of Duyiwei's active ingredients and the development of the mechanism of Duyiwei's active ingredients and its clinical applications.*

Keywords: *Duyiwei; Chemical composition; Active ingredient; Pharmacological study; Review*

1. Introduction

Duyiwei is a plant of the family Labiatae, genus Striga, and is mostly used for its roots and rhizomes. The plant is widespread in Tibet, but only sporadically scattered in Qinghai, Gansu, Sichuan and Yunnan, growing in rocky meadows, riparian zones or strongly weathered gravel beaches at an altitude of 3900 to 5100 metres. Duyiwei was first published in the 'Sichuan Journal of Traditional Chinese Medicine', 'bitter taste, slightly cold nature, a small poison. Into the liver meridian', "blood circulation and stasis, pain relief, qi and swelling, renewal of the tendons and bones", "where there is no stasis and pregnant women should not be served" and so on. It mainly contains cyclic enol ether terpene glycosides, phenylethanol glycosides, flavonoids, volatile oils and other chemical components, with analgesic, haemostatic, antibacterial, anti-inflammatory, immunomodulatory, anti-tumor and other pharmacological effects. In this paper, we systematically collated the research reports on Duyiwei at home and abroad in recent years, and summarised them from the aspect of modern pharmacological effects, in order to provide more ideas and thoughts for more scientific research workers, and also to provide references for the in-depth development and rational application of Duyiwei, which are summarised and reviewed as follows:

2. Anti-inflammatory effect

Studies have shown that Duyiwei has good anti-inflammatory effects, and the pharmacological substance basis involves cycloenol ether terpenoids, flavonoids, and phenylethanol compounds [1-2]. In a study of postoperative subcutaneous effusion in patients with craniocerebral injury, Fu Zengbin concluded that the clinical therapeutic effects, serum TNF-α, IL-8, PCT levels, quality of life, and complication responses were much better than those of the conventional treatment group when the traditional Chinese medicine (Duyiwei) was administered orally or nasally in addition to conventional treatment. And the postoperative flap effusion appeared to a certain extent due to its inflammatory reaction or allergic reaction, which further confirmed the pharmacological effect of Duyiwei can inhibit inflammatory reaction by down-regulating serum TNF-α, IL-8 and PCT levels [3]. Based on network pharmacology and the theory of component structure, Kang dot explored the anti-inflammatory effect of Duyiwei, and the three components of Duyiwei can play synergistic effect, and the ratio structure of the components has a greater impact on the efficacy of the drug. When the ratio of cyclic enol ether terpene

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glycosides (gardenia gardenia glycoside methyl ester: 8-O-acetyl gardenia gardenia glycoside methyl ester) is 1.21:1, and the ratio of 3 kinds of components (cyclic enol ether terpene glycosides: phenylethanol glycosides: flavonoid glycosides) is 4.8:1.6:1, it can exert the optimal effect of anti-inflammation. This study may provide a new experimental basis for the intrinsic quality control of Duyiwei [4]. Wang Lijuan et al.[5] used aqueous and ethanol extracts of Duyiwei to treat acute inflammation of the foot in rats by gavage, and the results showed that the aqueous and ethanol extracts were able to reduce the swelling of the foot on the inflamed side and the contralateral side of the foot in rats. The novel preparation of Duyiwei, Babu paste, and its active ingredients showed excellent effects in anti-inflammatory experiments. Experimental data from Zheng Yannan and Wang Xi et al [6-7] showed that the paste had significant anti-inflammatory ability, with cycloenol ether terpene glycosides effectively reducing swelling, while phenylethanol glycosides and flavonoids had relatively weak anti-inflammatory effects.

3. Immunomodulatory effects

Duyiwei has some immunomodulatory effects and can improve immunity. Bai Rong et al[2] demonstrated that Duyiwei Babu Ointment showed a significant effect in reducing the inflammatory response triggered by delayed-type hypersensitivity reaction in mice and enhanced the phagocytosis ability of mouse macrophages, showing its immunomodulatory function. Kang Li et al.[8] also found that the total saponins in Duyiwei had a significant effect on both non-specific and specific immunity. In addition, the saponin and alcohol extracts in Duyiwei were able to increase spleen and thymus weights in hormonal mice[9]. Cang Xiaofeng [10], in a clinical trial exploring the adjuvant treatment of rheumatoid arthritis with Duyiwei capsule combined with Bone Melon Extract Injection, found that patients in the test group were treated with Duyiwei capsule and Bone Melon Extract Injection in combination with the treatment of the control group, and the time of morning stiffness as well as the number of swollen joints, DAS28 as well as VAS scores, and laboratory indexes (levels of rheumatoid factor, CRP, and ESR) of the test group were better than those of the control group, with statistically significant differences (differences were statistically significant). Control group, and the difference was statistically significant ($P < 0.05$). Duyiwei capsule can improve the immune function, eliminate joint swelling, improve microcirculation, and promote the improvement of patients' conditions.

4. Hemostatic and analgesic effects

The haemostatic and analgesic targets of the unique constituents from different entry sites of Duyiwei were screened, and the five core constituents in the molecular docking (glycyrrhetinic acid, ursolic acid, levosigmoidine, α-coumarinone, and donglingchuetin) were well combined with the top 5 DC-ranked targets (TNF, IL6, CASP3, JUN, and PPARG). Levosigmoidine can be used to treat vascular headache and is more effective than phenothiazine [11]. The main components of its efficacy are glycyrrhizic acid and paeoniflorin, in addition to the elevation of platelets after long-term gavage of glycyrrhizic acid in rats [12-13]. In terms of haemostasis, ursolic acid induces differentiated macrophages to become M2-type wound-healing-promoting macrophages, leading to angiogenesis and epithelial cell proliferation, thus achieving haemostasis [14-15]. α-Coumarinone [16] has an analgesic effect, and it is the main active ingredient in antidysmenorrheal drugs. As an important medicinal active ingredient of Cordyceps militaris has anti-inflammatory and analgesic pharmacological effects [17] and is able to reduce the apoptosis of human umbilical vein endothelial cells caused by high glucose and high-fat [18].TNF- is a potential pain mediator in neurovascular inflammatory diseases and promotes the development of inflammatory nociceptive sensitization [19].TNF participates in the mechanisms associated with haemostasis and effectively triggers the pro-coagulant properties of the endothelial cell properties and promotes the state of clots [20]. It has been shown that activation of spinal nuclear transcription factor (NF-κB) leads to a massive release of IL6 in an animal model of bone cancer pain, inducing bone cancer pain [21]. In addition, studies have found an association between IL6 and cerebral haemorrhage, with high expression of IL6 inhibiting the inflammatory response and neuronal injury, reducing necrosis of perihemorrhagic tissues, and facilitating haematoma resorption.CASP3 expression was elevated by assessing the degree of injury to the brain parenchyma following cerebral haemorrhage, and it was pointed out that apoptosis plays a role in neuronal cell injury secondary to cerebral haemorrhage [22].

Several academic researchers have demonstrated this role in various experiments. Liao Yingqiong et al [23] showed that the aqueous extract of Duyiwei increased the amount of fibrinogen contained in rats and inhibited the reduction of prothrombin time in rats. Zhang Quanlong et al [24] showed that topical

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application of total cyclic enol ether ether terpene glycosides of Duyiwei had significant haemostatic effects on severed tails of mice, abdominal aorta and middle ear artery of rabbits, and livers of rats, and that it was superior to that of the aqueous extract. Yang Yang, Wang Lijuan and other researchers [25-26] conducted analgesic experimental studies on the analgesic effect of Duyiwei Babu Paste, aqueous extract, and alcoholic extract using five different methods, respectively, and the results proved that the analgesic effect was obvious. Chen Xiang [27] found that the capsule of Duyiwei significantly shortened the bleeding time and plasma recalcification time in mice, and the analgesic effect was significant. The effect of the aqueous extract of Duyiwei on different pain models in rats, the experiments proved the analgesic and effective inhibition of chronic pain effect, and initially revealed its analgesic mechanism [28]. Bai Rong et al[2] verified the analgesic effect of phenylethanol glycoside extracts from Duyiwei by the classical hot plate method and twisting method.

5. Promoting postoperative recovery

Long Liyun [29], in observing 50 patients with incision blepharoplasty, the control group used recombinant human epidermal growth factor gel applied to surgical wounds, and on the basis of recombinant human epidermal growth factor gel applied to surgical wounds, the patients in the observation group began to orally consume sole capsule on the day of the postoperative period, and it was used for 30 consecutive days. The relief of ocular swelling, the degree of swelling of periocular tissues and pain were compared between the two groups of patients. Results The degree of ocular swelling relief, periocular tissue swelling, and pain relief of patients in the observation group was better than that of the control group, and the difference was statistically significant ($P<0.05$). Liu Huanqing in the observation of 97 postoperative limb fracture patients, 49 cases in the observation group took rapid rehabilitation surgical concept (FTS) nursing + Tibetan medicine sole capsule intervention; 48 cases in the control group took conventional nursing. The postoperative rehabilitation indexes, motor function scores, and psychological scores of the observation group were better than those of the control group ($P < 0.05$). The complication rate of the observation group was lower than that of the control group ($P<0.05$). The intervention of FTS nursing + Tibetan medicine sole capsule for Suu limb fracture can promote postoperative rehabilitation, reduce complications, and regulate adverse psychology and restore motor function. Wan Chongxin [30] et al. in collecting 180 patients in vinegar Yanhusuo, Duyiwei granules combined with acupressure to alleviate postoperative pain in anal and intestinal diseases found that in the controlled experiment, the control group did not use any analgesic drugs after surgery, while the western medicine group used oral tramadol hydrochloride tablets for analgesia after surgery, and the acupressure group used vinegar Yanhusuo and Duyiwei granules for acupressure treatment. From the 1st to the 5th postoperative day, the NRS scores of both the western medicine group and the acupressure group were lower than those on the day of surgery and were lower than those of the control group. On postoperative day 5, serum bradykinin and prostaglandin E2 levels decreased in all groups compared with those at 6 hours postoperatively, with the levels in the Western medicine group and the acupressure group lower than those in the control group. The incidence of adverse reactions was only 1.67% in the acupressure group, which was significantly lower than the 11.67% in the western medicine group. Thus, it seems that the analgesic effect of vinegar Yanhusuo granules and Duyiwei granules combined with acupoint compresses is comparable to that of western medicines, but with fewer adverse reactions, which is suitable for promoting its use in clinical practice.

6. Anti-rheumatoid effects

With regard to rheumatoid arthritis (RA), Duyiwei was first mentioned in the Moon King's Pharmacopoeia[31] a Tibetan medical text, and the Jingzhu Materia Medica, which states: 'Duyiwei is able to stabilise the essence, strengthen the sinews and bones, and channel the yellow water within the body.' Both suggest that Duyiwei is commonly used in the treatment of 'yellow water disease'. Both works indicate that Duyiwei has important applications in the treatment of 'yellow water disease'. The literature 'The Four Medical Classics'[32] also mentions that Duyiwei can protect the bone marrow and has a significant therapeutic effect on yellow water disease, which further confirms its potential in the treatment of 'joint-type yellow water disease', also known as rheumatoid arthritis.

Clinical trials have demonstrated that Duyiwei capsule is effective in reducing joint pain and other symptoms caused by rheumatoid arthritis [33]; it has also demonstrated efficacy in the treatment of osteoarthritis of the knee, and no significant side effects have been observed [34]. In addition, it was also found that Duyiwei was able to effectively inhibit the development of initiating lesions and subsequent

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lesions of adjuvant induced arthritis (AIA) in rats, which was particularly prominent in the treatment of subsequent lesions of arthritis [35]. Chen Ruixin [36] et al. established the spectral-effect relationship of total flavonoids of Duyiwei against rheumatoid arthritis, and the results showed that lignoceroside and lignocerotoxin were the key components of total flavonoids of Duyiwei against RA. It can provide some reference for the clinical use of Duyiwei in the treatment of RA.

7. Bacteriostatic effect

The saponins proposed in the extract and infusion of Dioscorea spp. increased the phagocytosis rate of mouse macrophages, the rate of E-wreath formation, and the rate of positive esterase staining after intraperitoneal injection, whereas the leaf saponins of Dioscorea spp. possessed bacteriostatic effects.

8. Anti-tumour activity

Jia Zhengping [37] et al. separated the ethanol extract of Duyiwei, respectively, the total flavonoids, cyclic enol ether ether terpene glycosides, volatile oils, and large polar components of the in vitro antitumour activity of comparative study, preliminary evidence that the volatile oil components of Duyiwei have antitumour activity. Kang Yongjie [38], Yang Yanxia et al [39] also successively found that the petroleum ether extract of Duyiwei and Duiyifenin A (29) derivatives have certain inhibitory effects on different tumour cells.

9. Other pharmacological effects

The aqueous extracts and infusions of Duyiwei have certain hepatoprotective, hepatoprotective, and medullary tonic effects, as well as ameliorating oxidative damage, inflammatory damage, neuralgia, and Parkinson's disease in the brain [40]. In addition, the component of trichoside (71) in Duyiwei has a significant effect on repairing damaged neurons in Alzheimer's disease [41].

10. Conclusion

In recent years, the scientific studies on Duyiwei have been gradually increasing, and Duyiwei was found to contain a variety of chemical components, including but not limited to: cyclic enol ether terpene glycosides, phenylethanol glycosides, flavonoids, volatile oils, amino acids, and so on. In conclusion, it was found that Duyiwei has anti-inflammatory, haemostatic, analgesic, immune-enhancing, and post-operative recovery effects; at present, although the research on the pharmacodynamic substances of Duyiwei has made great progress, the exact mechanism of the pharmacodynamic substances is still unclear, and there exists a reciprocal correspondence between the different pharmacodynamic components, which needs to be further explored for the mechanism of the pharmacodynamic effects and metabolic laws, in order to lay a theoretical foundation for the research and development of this kind of traditional Chinese medicines.

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