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Exploration on the Mechanism of Wound Healing Effect of the Pair of Muscle-building Jade Red Paste based on the Theory of "Simmering Pus and Long Meat"

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Abstract: ***A wound refers to the damage and rupture of the human skin and mucosal surface caused by external forces such as collision, cutting, tearing, and burns. Wound healing refers to a series of pathological and physiological processes in which local tissue is repaired through regeneration, repair, and remodeling after tissue loss caused by external forces. Currently, wound healing faces problems such as prolonged healing cycles, unbearable pain, and the possibility of scar tissue affecting aesthetics after healing, which seriously affects the quality of life of patients. Shengji Yuhong Gao, as a good medicine for treating chronic wounds, can effectively regulate the levels of growth factors, improve wound microcirculation, and enhance the body's immunity. "Boiling pus and growing flesh" is a traditional Chinese medicine external treatment method that promotes wound healing. Therefore, using the "simmering pus and growing flesh" method to guide the use of Shengji Yuhong Gao has a significant healing effect on wounds.***

Keywords: Stewed pus and long meat, Sheng Ji Yu Hong Gao, Chronic wounds, Mechanism of action**.**

1. Introduction

A wound [1] is a damage to normal skin or tissue in the human body caused by external factors (such as surgery, heat, external forces, electricity, chemicals, low temperatures, etc.) or internal factors (such as tissue hypoxia, local blood circulation disorders, etc.). Wound healing [2] refers to the process of recovering the damaged tissue to its original structure and function through a series of complex biological processes after the body has suffered various wounds or injuries. However, due to various reasons (such as infection, ischemia, diabetes, etc.), the healing process may be blocked, leading to the formation of chronic wounds or scars. Due to the lengthy and complex process of wound healing, often accompanied by high economic costs, promoting wound healing and reducing scar formation have become an important area of medical research. According to statistics [3], the chronic wound incidence rate in Wales was 6% in 2012-2013, equivalent to 5.5% of national healthcare expenditure. In 2012, the cost related to wound management in the UK was approximately £ 4.5-51 billion. This indicates that patients with chronic wounds have poor health-related quality of life and high medical expenses, which bring huge costs to the healthcare system and society. In recent years, due to the unique advantages of high safety, few side effects, precise efficacy, and long-term use of traditional Chinese medicine in promoting wound healing, more wound patients tend to choose traditional Chinese medicine for treatment. As a classic formula commonly used in traditional Chinese medicine surgery to treat chronic wounds, Shengji Yuhong Gao has received more attention and application. There is research confirming [4] that Shengji Yuhong ointment can reduce thrombus formation in wound capillaries, improve blood circulation in patients, increase or decrease tissue oxygen supply, thereby promoting wound healing and repair.

2. Theoretical Basis of Traditional Chinese Medicine Surgery for Wound Healing

Chronic wounds in traditional Chinese medicine belong to the categories of "ulcers," "ulcers," "ulcers," and "carbuncles. The four members of the Jin and Yuan dynasties conducted a systematic analysis of the etiology and pathogenesis of chronic wounds, which essentially boils down to organ deficiency and invasion of pathogenic toxins. The "Essential Methods of Surgery" [7] states that "carbuncle is originally caused by fire and toxin, and blockages in meridians and collaterals lead to the coagulation of qi and blood. That is to say, when the meridians are blocked, the circulation of qi and blood is not smooth, which can easily lead to stagnation of qi and blood. And this kind of obstruction may be caused by external invasion, emotional disorders, or improper diet, which hinders the circulation of qi and blood, leads to insufficient local nutrition supply, and metabolic waste cannot be eliminated in a timely manner. Evil toxins accumulate inside, causing local tissues to rot, and deficiency, stasis, evil, and decay combine, resulting in further deficiency of qi and blood, which cannot nourish the wound. The wound is difficult to heal, and ultimately may lead to the formation of abscess. According to the three stages of initial wound formation, pus formation, and collapse, internal treatment methods can adopt three methods: detoxification and swelling reduction, pus penetration and decay removal, and muscle growth and closure. Based on this, the treatment of wounds with traditional Chinese medicine can be divided into three mechanisms: detoxification and swelling reduction, blood circulation and stasis removal, and pus lifting and decay removal. The sentence is:. This is not in line with the role played by the method of simmering pus to grow flesh at different stages of wound healing. During the inflammatory phase, it promotes the shedding of pus and carrion by "penetrating pus and removing decay", and during the repair

phase, it promotes the growth of new flesh through "simmering pus to grow flesh". And this method also follows the growth law of traditional Chinese medicine, which is "removing rotten meat and developing new muscles".

3. Boil Pus and Grow Meat

Stewing pus and growing flesh is a characteristic therapy in traditional Chinese medicine surgery for treating chronic wounds. "Stewing pus and growing flesh" can also be written as "snuggling pus and growing flesh", where "snuggling" means being close to and adjacent to each other. His argument was first recorded in Shen Douyuan's "Surgical Qixuan: The Theory of Applying Plaster to Ulcers and Ulcers", where he mentioned: "In cases where the ulcer has already subsided, the pus has decreased, the ulceration has settled, or there is little pain or itching, and the muscles have not yet developed, if the ointment is not applied, the red flesh will not be protected and the wind will be difficult to resist. Therefore, applying Taiyi ointment and other ointments will result in the growth of pus and flesh. The method of simmering pus and growing flesh is mainly used in the middle and late stages of wound healing, when there is not enough rotten flesh or new flesh, mainly through the absorption of external drugs on the wound surface. Through a series of effects, it promotes the sufficient and smooth flow of qi and blood in the local wound, increases the leakage of pus, provides a moist environment conducive to wound healing, and increases the amount of pus that can carry pathogens out. The simmering one is warm; the pus one is qi and blood. The "pus" produced by simmering pus and meat is not the "pus" referred to in modern medicine, but the "pus" produced by simmering traditional Chinese medicine. There are significant differences in the formation stage, characteristics, and microscopic differences between it and the "pus" referred to in modern medicine. At present, the method of simmering pus and growing flesh is clinically applicable to chronic wounds such as diabetes feet, burns, perianal diseases, pressure sores, herpes zoster, etc. These diseases have large wounds and are not easy to heal. In Wang Weide's "The Complete Life of Surgery", it is mentioned that "when poison comes, it must come from pus, and when pus comes, it must come from qi and blood". If there is sufficient qi and blood, the pus produced by "simmering" will be yellow, thick, and abundant, and the wound is easy to heal; On the contrary, if the qi and blood are weak, the pus produced by "simmering" will have a light and thin color, a foul odor, a small amount, and the wound will persist and not heal, which can easily lead to chronic wounds [11]. Therefore, traditional Chinese medicine believes that pus is a medium for carrying pathogenic factors out of the body, emphasizing the importance of expelling pus. In the "Xue Ji Medical Case", it is mentioned that "after the rupture of a carbuncle, the stagnant flesh must be removed, which is a way to promote the growth of new flesh." It also emphasizes the importance of pus drainage, believing that in order to heal the wound, the rotten flesh must be completely removed so that new flesh can grow. So, in treating chronic wounds, the focus is on "decay" and the key is to eliminate "pus". In modern clinical practice, the goal of removing necrotic tissue is often achieved through surgical procedures. However, even though the necrotic tissue on the wound has been removed, the possibility of "new decay" still exists. If the wound shows a positive syndrome and heals slowly, new decay will occur due to the residual toxins of dampness and heat. Therefore, simmering pus is a supplement and continuation of lifting pus and removing decay. Combining "simmering pus" and "removing decay" is a refinement and supplement to the "simmering pus and growing flesh" method. Therefore, in the treatment of chronic wounds, ointments or powders containing both "simmering pus" and "removing decay" effects should be used. Shengji Yuhong ointment, as a good medicine for treating chronic wounds, has the ability to remove purulent tissue and promote wound healing. It can effectively prevent the increase of new decay and hinder wound healing, and is now widely used to treat chronic wounds such as perianal diseases after surgery and skin ulcers, This article aims to explore the pharmacological mechanism of Shengji Yuhong ointment in promoting wound healing, which has shown good therapeutic effects in clinical practice, in order to better guide clinical medication.

4. Shengji Yuhong Cream

4.1 Drug Components and Their Medicinal Mechanisms

Shengji Yuhong Gao was first recorded in the famous Ming Dynasty physician Chen Shigong's "Surgical Authenticity" [12]. Its main ingredients include light powder, purple grass, angelica, blood dried root, white atractylodes, licorice, and insect white wax. The production method [13] is to first soak the four medicinal herbs of Angelica sinensis, Angelica dahurica, purple grass, and licorice in sesame oil for three days, then slowly simmer to remove the residue. After the herbs are slightly withered, remove them and let the sesame oil cool (below 40 ℃). Add white wax, light powder, and blood and stir continuously until completely dissolved, and cool until the paste is formed. The formula uses light powder as the main medicine, which was first recorded in the Tang Dynasty's Chen Zangqi's "Bencao Shiyi". Light powder has a pungent, cold, and toxic taste, and its main functions are to attack toxins, kill insects, and promote the growth of granulation tissue. In modern pharmacology, light powder has antibacterial, anti-inflammatory, and granulation tissue growth effects, which can inhibit skin fungi, reduce inflammatory reactions, and accelerate wound healing. However, relevant studies have shown that light powder belongs to mercury containing preparations, also known as silver powder. Long term external use of light powder can cause systemic toxic reactions, the most significant of which are liver, kidney, and neurotoxicity. The official medicines include purple grass, angelica, blood dried and white atractylodes. The main compatibility of purple grass in Shengji Yuhong ointment is to clear heat, detoxify, cool blood, and promote blood circulation. This effect comes from the chemical components in purple grass, such as shikonin, which has detoxifying and anti-inflammatory effects [16]. It can effectively reduce the inflammatory response during wound healing and shorten the wound healing time. Danggui has the effects of promoting blood circulation, removing blood stasis, and relieving pain. In Shengji Yuhong Gao, Danggui has the effect of promoting blood circulation, which is attributed to the ferulic acid in Danggui's organic acids. Ferulic acid can inhibit platelet aggregation, help remove blood stasis and promote wound healing. Blood stasis has the effects of promoting blood circulation, relieving pain, and stopping bleeding. Through its ability to promote blood circulation and

remove blood stasis, blood stasis can eliminate local blood stasis and promote blood circulation. At the same time, the hemostatic effect of blood exhaustion helps to control bleeding from wounds, while its myogenic effect contributes to the repair of wound surfaces and the growth of new flesh. The role of Bai Zhi in Shengji Yuhong Gao is mainly to promote wound healing, reduce inflammation and pain through its effects of promoting muscle regeneration, expelling pus, promoting blood circulation, and relieving pain. The role of licorice in Shengji Yuhong ointment is multifaceted, not only helping to reduce inflammatory reactions and promote wound healing, but also harmonizing medicinal properties, enhancing immunity, and achieving analgesic and anti-inflammatory effects. These ingredients work together and have the effects of promoting blood circulation, removing blood stasis, detoxifying, and generating muscle.

4.2 Mechanism of Action

4.2.1 Regulating Growth Factor Levels

At present, it is known that Shengji Yuhong Gao can promote fibroblast growth and collagen differentiation, improve microcirculation, and accelerate wound healing by regulating various growth factors in the body. For example, fibroblast growth factor (bFGF), heme oxygenase-1 (HO-1), transforming growth factor beta 1 (TGF-β 1), hypoxia inducible factor-1 alpha (HIF-1 alpha), vascular endothelial growth factor (VEGF), and prostaglandin E2 (PGE2).

According to modern pharmacological research, basic fibroblast growth factor (bFGF) plays a crucial role in the process of wound healing. BFGF is widely present in cells and collagen fibers, which can promote the migration, proliferation, differentiation and maturation of epidermal cells and fibroblasts, attract collagen to focus and generate collagen fibers, promote wound healing, and also have the effect of generating blood vessels, which can promote wound healing [18]. Shengji Yuhong Gao can increase the secretion of bFGF, promote the growth of fibroblasts and collagen synthesis during the inflammatory and proliferative phases of wounds. However, during the remodeling phase of wounds, Shengji Yuhong Gao can inhibit the secretion of bFGF, thereby inhibiting collagen synthesis and providing a material basis for collagen fiber synthesis. This indicates that Shengji Yuhong Gao has different regulatory effects on bFGF at different stages, which is helpful for wound remodeling and repair [19].

Blood red oxygenase is an endogenous immune regulatory, cell protective, and anti-inflammatory system, and this protective function is mainly attributed to heme oxygenase-1 (HO-1) [20]. HO-1 is commonly regarded as an anti-inflammatory and immunosuppressive enzyme, and relevant experimental studies have shown that this stress response enzyme can alleviate inflammation and regulate immune responses both in vivo and in vitro [21], thereby effectively promoting wound healing. During the process of wound healing, transforming growth factor beta 1 (TGF-β 1) also plays a crucial role. Yan Tingting et al. [22] performed skin lesion wounds on 24 New Zealand white rabbits and divided them into three groups. Different drugs were given to each group for wound repair. The research results showed that the traditional Chinese medicine group covered with Shengmu Yuhong collagen sponge had the shortest wound healing time, and the time of TGF-β 1 expression and peak expression in the traditional Chinese medicine group was significantly advanced. This indicates that Shengmu Yuhong collagen sponge can effectively increase the secretion of TGF-β 1 and HO-1, stimulate the proliferation of fibroblasts, and promote wound healing.

Wound healing is a dynamic process, and epithelialization, angiogenesis, granulation tissue formation, and wound contraction are all regulated by hypoxia inducible factor-1 alpha (HIF-1 alpha) [23]. And vascular endothelial growth factor (VEGF) can induce cascade components of wound healing, such as angiogenesis, collagen deposition, and epithelialization. Relevant studies have shown that treating fibroblasts overexpressing VEGF can significantly accelerate angiogenesis, enhance connective tissue, and promote wound healing [24]. Ye Lin et al. [25] selected 96 patients with chronic difficult to heal skin ulcers and randomly divided them into two groups. Both groups received basic treatment combined with different drug treatments. The results showed that the content of HIF-1 α and VEGF in wound secretions increased in the Shengji Yuhong ointment group after treatment. Compared with other drug groups, the Shengji Yuhong ointment group could effectively reduce patient pain, promote wound healing, and shorten healing time.

Prostaglandin E2 (PGE2) has significant therapeutic effects in promoting wound healing. It not only has anti-inflammatory properties and promotes angiogenesis, but also has great therapeutic effects in pain relief and scar formation prevention [26]. Dong Xiaopeng et al. [27] conducted experiments on mice using hot plate method to induce pain, acetic acid induced twisting reaction, and ear swelling. The results showed that Shengji Yuhong ointment had inhibitory effects on early wound exudation and edema, as well as anti-inflammatory and analgesic effects. This anti-inflammatory and analgesic effect is related to the purple grass, Angelica sinensis, and inhibition of PGE synthesis contained in Shengji Yuhong ointment.

4.2.2 Regulating Related Signal Pathways

Shengji Yuhong Gao can exert its anti-inflammatory and wound healing therapeutic effects by acting on multiple signaling pathways and targets. In recent years, AGEs RAGE/NF-κ B signaling pathway has been more and more widely used in diabetes refractory wounds. Zhang Jianping et al. [28] randomly divided 60 SD rats into four groups, and conducted diabetes and skin wound modeling. Different drugs were used to intervene. The results showed that the contents of TNF-α, IL-6, CRP, AGEs and the expression level of NF-κ B p65 protein in the wound skin tissue of the Tianshengjiyuhong ointment group 3, 7, and 15 days after the injury were significantly reduced, and the wound healing rate was increased, indicating that Shengjiyuhong ointment could inhibit the activation of AGEs RAGE/NF-κ B signaling pathway. It can reduce the expression of AGEs and RAGE, inhibit the activation of NF-κ B, thereby reducing the release of inflammatory factors, promoting angiogenesis of refractory wounds, and shortening the wound healing time. Some studies

have also shown that [29], the active ingredients in Shengjiyuhong ointment may play a role in promoting the healing of diabetes ulcer wounds by acting on multiple targets such as IL-6, AKF-1, and regulating the activities of AGE-RAGE signaling pathway, IL-17 signaling pathway, IL-1 β/IL-23-IL-17A signaling pathway, TNF signaling pathway, and T-cell receptor signaling pathway.

4.2.3 Improving microcirculation around wounds

Shengji Yuhong ointment can promote angiogenesis, improve microcirculation around wounds, and thus promote tissue repair. Yao Chang et al. [30] divided 60 wound modeling rats into four groups and treated them with Vaseline gauze, Shengji Yuhong ointment dressing, gelatin sponge, and Shengji Yuhong gelatin sponge, respectively. The results showed that the Shengji Yuhong gelatin sponge group had significantly higher values than the other three groups in terms of wound healing rate, hydroxyproline content, hemoglobin content, and microvascular count. Relevant experimental studies have shown [31] that the modified gelatin can cause physiological binding between the heparin inside and the angiogenic growth factors in the granulation tissue of the wound during degradation, which is beneficial for angiogenesis and tissue repair. On the third day after modeling, the granulation tissue around the Shengji Yuhong gelatin sponge showed that.. The number of VEGF positive cells was significantly higher than the other three groups, leading to an increase in microvascular neovascularization, This indicates that Shengji Yuhong ointment and gelatin sponge have a synergistic effect, complementing each other and having good therapeutic effects in promoting wound healing.

4.2.4 Improving the body's immune function

The components of Angelica sinensis in Shengji Yuhong ointment have a promoting effect on the immune function of the body, which can activate lymphocytes to produce antibodies, promote the production of lysozyme, and alleviate infections [32]. Zhao Chunlin et al. [33] prepared a mouse model of deep second degree burns and administered different drug interventions, including immune organ index measurement, serum hemolysin antibody level measurement, DNCB induced delayed type hypersensitivity reaction in mice, and mononuclear macrophage phagocytic function measurement. The research results showed that Shengji Yuhong Gao had no effect on the spleen index of burn mice, but could improve the thymus index of burn mice. The research results also showed that Shengji Yuhong Gao could increase the serum hemolysin antibody level, delayed type hypersensitivity reaction degree, and mononuclear macrophage phagocytic function of burn mice, indicating that Shengji Yuhong Gao can improve the specific immune function of burn mice, including humoral immunity, cellular immunity, and non-specific immune function. The, This further demonstrates that Shengji Yuhong Gao can enhance the phagocytic function of the mouse reticuloendothelial system, activate lymphocytes to produce antibodies and lysozyme, and improve the immune function of mice.

4.3 Formulation Innovation

The traditional dosage forms of Shengji Yuhong Gao mainly include ointment, ointment, and powder. However, due to the fact that the paste is carried on gauze, there are still some drawbacks during use [31], such as skin allergies such as redness, papules, blisters, and even ulceration; The barrier effect of gauze is small, and bacteria are easy to invade; The granulation tissue of the wound is prone to grow into the mesh of the gauze, which may damage the newly formed granulation tissue during dressing changes and cause secondary trauma; The moisture absorption of gauze is poor, which can affect the moist environment of the wound and be detrimental to wound healing. In order to overcome these shortcomings, clinical workers and researchers have improved the dosage form of Shengji Yuhong ointment in modern medical practice, such as Shengji Yuhong gelatin sponge and Shengji Yuhong gel. Shengji Yuhong gelatin sponge [34] is a medical material that promotes wound healing. It combines the characteristics of traditional Chinese medicine Shengji Yuhong ointment and gelatin sponge, and has shown better efficacy and mechanism in promoting wound healing, reducing scar formation, and improving wound microcirculation. Collagen [35] plays a crucial role in the process of wound repair, as it promotes tissue healing, can be degraded in vivo, and the degraded fragments have tissue compatibility. The modified collagen can be used as a carrier for the Shengji Yuhong ointment dressing, effectively leveraging the advantages of both in promoting wound healing. Gao Peng [36] used collagen in pig skin and carbomer as collagen materials, determined the value of phenyl isothiocyanate method in the preparation of Shengji Yuhong gel through experimental research, and optimized the process of Shengji Yuhong gel. However, at present, there are few basic research and clinical research data on Shengji Yuhong gel, and its efficacy still needs to be further confirmed.

5. Summary and Prospect

With the rapid aging of China's population, the cost of nursing chronic wounds in China's health care system is increasing, which is a huge challenge to the national economy [37]. Therefore, shortening the healing time of chronic wounds and hospital stay has become an important problem to be solved. As a classic ointment for treating chronic wounds in traditional Chinese medicine and surgery, Shengji Yuhong ointment has been used to this day. Moreover, as an effective medication for the treatment principle of "simmering pus and growing flesh", Shengji Yuhong Gao promotes wound healing through its effects of promoting blood circulation, removing decay, detoxifying, and generating muscle, reflecting the idea that the external treatment principles of traditional Chinese medicine surgery change with the syndrome in different stages of chronic wound development. However, the current application of Shengji Yuhong ointment is limited to the repair of chronic wounds, and its application in plastic surgery is less involved [31]. With the advancement of modernization, people's demand for beauty is increasing day by day, and Shengji Yuhong ointment has the functions of promoting angiogenesis, shortening wound healing time, and scar repair. This has positive significance for plastic surgery, especially for surgeries involving skin incisions. Therefore, if the application of Shengji Yuhong ointment in plastic surgery is promoted, it can provide a more solid scientific foundation

and market support. Moreover, in the future development and application, Shengji Yuhong Gao still faces some challenges [38], such as unclear mechanism of action, quantitative standards for prescription and drug, and unclear toxicity efficacy relationship, which require further research and verification.

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