

Research and Discussion on the Treatment of Gastric Cancer with Hedyotis Diffusa

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Abstract. Gastric cancer is a type of malignant tumor originated from gastric mucosal epithelial cells, which is associated with *Helicobacter pylori* infection, poor dietary habits, genetics and other factors. Its early symptoms are concealed, and its late prognosis is poor, which provides a great challenge for global public health. *Hedyotis diffusa*, as a traditional Chinese medicine, has the effects of clearing inflammation, strengthening blood circulation, eliminating swelling cysts and regulating internal circulation. Its terpenoids, flavonoids and anthraquinones show significant anti-tumor effects. Combined with the theory of traditional Chinese medicine and modern pharmacological research, this research systematically analyzed the active ingredients, pharmacological effects and clinical application of *Hedyotis diffusa* in the treatment of gastric cancer, and discussed the efficacy of *Hedyotis diffusa* and its compound in the treatment of gastric cancer, building a theoretical basis for the future research. With the development of network pharmacology and multi omics technology, in-depth analysis of the molecular mechanism of *Hedyotis diffusa*, the mechanism of its synergistic anti-tumor network will provide a new sight for new drug discovery.

Keywords: *Hedyotis diffusa*, gastric cancer, antitumor, clinical application

1. Introduction

Cancer, also known as malignant tumor, is caused by malignant proliferation of cells and is invasive and metastatic. The main classification includes cancer, sarcoma and carcinosarcoma [1]. The pathogenesis of cancer is usually concerning the long-term joint action of chemical, physical, viral and other factors, causing a series of abnormal gene changes. In 2022, there were an estimated 20million new cases of cancer worldwide, with a standardized incidence of 196.9/100000; The number of cancer deaths was about 9.7 million, and the standardized mortality rate was 91.7/100000. Compared with the standardized incidence rate (201.0/100000) in 2020, the standardized mortality rate (186.0/100000) decreased significantly, with gastric cancer accounting for 6.8% of the total cancer deaths [2]. Gastric cancer is a common malignant tumor of the digestive system. The main symptoms include long-term dyspepsia, dull pain in the upper abdomen, and decreased appetite. It is initially formed from the protective layer cells in the inner wall of the stomach, and the most common type is called adenocarcinoma.

Hedyotis diffusa (*Scleromitron diffusum*), also known as "*Hedyotis diffusa*" and "bamboo leaf grass" in ancient Chinese medicine, is a plant of *Hedyotis* genus in Rubiaceae. The herb of *Hedyotis*

diffusa is slightly bitter, sweet and cold, affecting the stomach, large intestine and small intestine. According to the dictionary of traditional Chinese medicine, its efficacy is "anti-inflammatory, promoting blood circulation and detumescence, and regulating the internal circulation of the human body". It is commonly used for lung heat, asthma, sore throat, intestinal carbuncle, cancer, etc [3]. Modern pharmacological studies have confirmed that its terpenoids, flavonoids, anthraquinones and polysaccharides have anti-tumor effects of inhibiting tumor cell proliferation, invasion and metastasis, inducing apoptosis and regulating the inflammatory microenvironment [4]. In this paper, combined with the theory of traditional Chinese medicine and modern research, the mechanism and clinical application of *Hedyotis diffusa* in the treatment of gastric cancer were systematically discussed, providing reference for its research and new drug development.

2. Pathogenesis of gastric cancer

From the perspective of Western medicine, Lauren's classification divides gastric cancer into intestinal type, diffuse type and mixed type. It is generally believed that diffuse gastric cancer is significantly associated with genetic predisposition factors, while intestinal gastric cancer is closely related to *Helicobacter pylori* (HP) infection and people's lifestyle [5]. HP infection drives the Correa cascade by inducing chronic inflammation, atrophic gastritis, intestinal metaplasia, and dysplasia, ultimately leading to carcinogenesis [5]. According to research, heavy drinking will lead to an increase in the probability of gastric cancer, while ethanol and its metabolite acetaldehyde can promote the development of gastric cancer through DNA damage, point mutation and inhibition of DNA repair. At the same time, the deficiency or gene mutation of enzymes involved in ethanol metabolism, especially ADH and ALDH, further increases the toxic effect of acetaldehyde and increases the risk of cancer [3]. According to the research, there is a close association between DMBT1 and gastric cancer. The expression of DMBT1 is upregulated, which is a specific marker of intestinal metaplasia and is involved in the progression of precancerous lesions [6]. TsRNA such as tRF-3017A are up-regulated in gastric cancer tissues and cells. They form RNA induced silencing complex by binding ago protein, bind and silence the tumor suppressor gene neuroepidermal like growth factor 2 in a sequence dependent manner, also promote the migration and invasion of cancer cells [7].

From the perspective of traditional Chinese medicine, the occurrence of gastric cancer is attributed to the imbalance of internal and external circulation. The invasion of external viruses into the human body and the failure of the immune system in the body. "Su Wen Bi Lun" wrote: "if you eat too much, your intestines and stomach will be hurt", which pointed out that if a person eat too much when the climate is too cold or too hot, the spleen and stomach will be damaged, resulting in damp heat accumulation and Qi stagnation. Ye Tianshi, a Qing Dynasty man, pointed out that "when he was just sick, the Qi in his body was blocked in the meridians, and if he felt sick for a long time, the lesion would go deep into the vein", emphasizing that if he was sick for a long time, he would be weak, and if he was sick for a long time, there would be congestion in his body. In the later stage of the disease, tumors appear in the liver, reducing the ability to expel toxic substances from the body, resulting in difficulties in the operation of the spleen and stomach, and the inability of substances to circulate. At the same time, it is accompanied by poor blood circulation, clogging in blood vessels, gastrointestinal dyspepsia, and congestion, which lead to blocked fluid circulation. It is precisely for these reasons that the disease is caused [8]. At the same time, the sludge produced in the body is also a key pathological product. "Danxi mental method" said: "the silt block formed by silt can travel all over the human body with the circulation of the human body", "But those with lumps in the human body are mostly silt". Traditional Chinese medicine has been saying that "most of the causes of

illness are due to the existence of silt" and "rare diseases are mostly due to the formation of silt". Chunjie Li and others proved from the perspective of animal experiments that the traditional Chinese medicine that eliminates the silt and promotes circulation has a good anti-tumor effect on orthotopic transplanted tumor of human gastric cancer MKN-45 cells in nude mice, indicating that the blockage of human internal circulation by silt is one of the important factors in the occurrence of gastric cancer [9]. Professor Pinkang Wei concluded through more than 40 years of clinical practice that the silt blocks the human circulation throughout the whole process of gastric cancer occurrence and metastasis [10]. These theories provide a theoretical basis for the therapeutic effects of *Hedyotis diffusa* on clearing heat, detoxifying, dissipating phlegm and dispersing nodules.

3. Mechanism of *Hedyotis diffusa* on gastric cancer

Hedyotis diffusa contains flavonoids, anthraquinones, sterols, alkanes, terpenes, polysaccharides and other major components, and its effective components have anti-tumor effect [11]. Terpenoids, flavonoids, anthraquinones and polysaccharides significantly inhibit the proliferation, invasion and metastasis of tumor cells, promote the apoptosis of tumor cells, and have obvious anti-tumor effect, especially for digestive system tumors [12].

The total flavonoids of *Hedyotis diffusa* reduced the inflammatory microenvironment and serum tumor markers by down regulating the expression of TLR4, MyD88 and NF - κ B; At the same time, by inhibiting the expression of CLIC4 protein in gastric cancer BGC-823 cells, it can reduce the formation of malignant tumor stroma and prevent tumor invasion and metastasis [13]. In addition, the ethyl acetate extract of *Hedyotis diffusa* has strong anti-5-lox activity, with an inhibition rate of 66.98%, reducing the production of cysteinyl leukotrienes (CysLTs), reducing inflammatory response and vascular permeability, and inhibiting leukocyte chemotaxis and endothelial cell damage [13]. In clinical practice, *Hedyotis diffusa* and *Scutellaria barbata* are often used as drug pairs for synergistic treatment of gastric cancer. The drug can increase the proliferation inhibition rate of gastric cancer SGC-7901 cells, increase the proportion of G0/G1 phase cells, reduce the colony formation rate and the proportion of G2/M phase cells, and significantly reduce the expression levels of Cyclin D1 and c-Myc protein, thereby inhibiting the proliferation of gastric cancer cells. These mechanisms suggest that *Hedyotis diffusa* exerts comprehensive antitumor effects by regulating cell cycle, inhibiting inflammatory signaling pathways and tumor microenvironment.

4. Clinical effects of *Hedyotis diffusa* on gastric cancer

Clinical studies have shown that *Hedyotis diffusa* and its compound have significant curative effect in the treatment of gastric cancer. Qishen Yiwei Decoction contains 10g of *Hedyotis diffusa* and 10g of *Scutellaria barbata*. Weina Shi et al. Gave Qishen Yiwei Decoction to treat chronic atrophic gastritis with precancerous lesions of gastric cancer, and found that the TCM syndrome score of Qishen Yiwei Decoction group (epigastric pain, fullness and stupidity) and pathological score (inflammation, atrophy, intestinal metaplasia, dysplasia) were lower than those in the control Weifuchun group [12]. A randomized controlled trial (RCT) observed the clinical effect of *Hedyotis diffusa* and *Scutellaria barbata* combined with conventional chemotherapy in the maintenance treatment of malignant tumors. The results showed that the progression free survival (PFS) of the combined treatment group was prolonged, the overall improvement rate of quality of life was higher than that of the control group, and the incidence of chemotherapy-related adverse reactions (such as nausea, vomiting, bone marrow suppression) was significantly reduced [14]. These clinical

evidences show that Hedyotis diffusa has significant advantages in prolonging survival, improving symptoms and reducing chemotherapy toxicity.

5. Discussion

Hedyotis diffusa exerts a comprehensive anti-tumor effect against the pathological links such as inflammation, proliferation, invasion and metastasis of gastric cancer through a multi-component, multi-target mechanism. Its traditional efficacy of clearing heat, detoxifying, eliminating phlegm and dispersing nodules is highly consistent with the modern pharmacological mechanism. However, the current study still has limitations. Firstly, clinical trials are mostly small samples or single center studies, lacking large-scale, long-term follow-up randomized controlled trials, and evidence-based medical evidence of efficacy is insufficient. Secondly, the active ingredients of Hedyotis diffusa are complex, and the analysis of the pharmacodynamic material basis and action targets still need to be in-depth, which limits its standardized application. In addition, the bioavailability of traditional drug delivery methods (such as Decoction) is low, which affects the efficacy. Future research should focus on developing new drug delivery systems (such as nanoformulations and sustained-release capsules) to improve drug absorption and targeting. At the same time, multi center, high-quality clinical trials were carried out to determine the optimal dose, course of treatment and combination treatment plan. In addition, combining network pharmacology and multi omics technology, in-depth analysis of the molecular mechanism of Hedyotis diffusa will help reveal its synergistic anti-tumor network and provide a basis for new drug research and development.

6. Conclusion

Hedyotis diffusa shows significant potential in the treatment of gastric cancer by inhibiting tumor cell proliferation, invasion and metastasis, inducing apoptosis and regulating the inflammatory microenvironment. Its traditional Chinese medicine efficacy and modern pharmacological mechanism complement each other, providing a unique perspective for the treatment of integrated traditional Chinese and Western medicine. Existing studies have confirmed that it are able to prolong the progression free survival, improve the quality of life and reduce the side effects of chemotherapy, with good safety and application prospects. In the future, it is necessary to promote its research and application through the following ways. First, analyze its active ingredients and action targets by using multi omics technology, and clarify the molecular mechanism. Second, develop new formulations, such as nanocarriers and mucosal targeting systems, to improve bioavailability. The third is to carry out multicenter, large sample randomized controlled trials to optimize the dose and combination treatment plan; Fourth, strengthen international cooperation and promote the standardization and internationalization of Hedyotis diffusa preparations. These efforts will provide safer and effective treatment options for patients with gastric cancer, and help the development of anti-tumor field of integrated traditional Chinese and western medicine.

References

- [1] Han, X., Zhang, X., Wang, Q., Wang, L., & Yu, S. (2020). Antitumor potential of Hedyotis diffusa Willd: A systematic review of bioactive constituents and underlying molecular mechanisms. *Biomedicine & pharmacotherapy*, *Biomedecine & pharmacotherapie*, 130, 110735.
- [2] Zhang Zheng, Zhang Lifang, liuyanting, Mridul Roy, Lu Ping&Zhang min. (2024). Interpretation of global cancer statistics report 2022 China hospital statistics, 31 (05), 393-400.
- [3] Cheng Xiaolong, Yu Xiao, Wu guobing, Zhang aibin, Liu Min, Hu Zenan&chenzhaofeng. (2022). Research Progress on the relationship between alcohol consumption and gastric cancer *Modern digestion and interventional*

- diagnosis and treatment, 27 (07), 803-807.
- [4] Zhou Xiu&lichangping. (2024). Research progress of *Helicobacter pylori*, deletion gene 1 of malignant brain tumor and the pathogenesis of gastric cancer *Modern clinical medicine*, 50 (06), 471-473+476.
 - [5] Zhou Xin, Ding Jun, Tang Min, chenxufeng, zhangqiaoqiao&Ren Chuanlu. (2025). Dact1 regulates Wnt signaling pathway and inhibits the release of inflammatory cytokines in gastric cancer cells infected with *Helicobacter pylori* *Advances in anatomy*, 1-6.
 - [6] Jiang Jinling, Zhou Chenfei, Wang Chao, zhaoliqin, wujunwei&Zhang Jun. (2023). New progress in gastric cancer research and diagnosis and treatment in 2022 *Chinese Journal of cancer*, 33 (04), 303-314.
 - [7] Liuxinping, zhaojianzhi, Cao Li&chenchangguo. (2024). Research progress of tsrna and its role in the pathogenesis and diagnosis of gastric cancer *Chemistry of life*, 44 (06), 1082-1089.
 - [8] Fengningning&jiangshumin. (2012). On TCM pathogenesis of precancerous lesions of gastric cancer *Journal of Liaoning University of traditional Chinese medicine*, 14 (03), 110-111.
 - [9] Wangchangshong, Lin Kunming, Wu Tongyu, Min Li&Wu Yinpan. (2013). Clinical analysis of TCM pathogenesis of gastric cancer *Journal of Shandong University of traditional Chinese medicine*, 37 (03), 214-215.
 - [10] Xujingyu, Zhang Xuan, peibei, guyufang, liuyongying, Wu Feng.&Wei Pinkang. (2022). Based on NLRP3 inflammasome, this paper discusses the importance of treating precancerous lesions of gastric cancer from the perspective of liver and stomach to block the "inflammation cancer" transformation *Journal of traditional Chinese medicine*, 50 (04), 5-8.
 - [11] Chen, R., He, J., Tong, X., Tang, L., & Liu, M. (2016). The *Hedyotis diffusa* Willd. (Rubiaceae): A Review on Phytochemistry, Pharmacology, Quality Control and Pharmacokinetics. *Molecules* (Basel, Switzerland), 21(6), 710.
 - [12] Zeng Sha, Zhao Hui, Gao Jingshen, Li Ping&Wang Jun. (2025). The latest research progress of anti digestive system tumor active components and its mechanism of action of *Hedyotis diffusa* Willd *Chinese Journal of traditional Chinese medicine*, 1-19.
 - [13] Zhangyufei, liliheng, chenchangjin, Li Yinuo&yuanyoucai. (2025). Research Progress on pharmacological mechanism and pharmacokinetics of *Hedyotis diffusa* Willd *Journal of traditional Chinese medicine*, 53 (01), 111-117.
 - [14] Zhang Yu, Luo Xiaoning&Guo Zheng. (2022). Clinical study of *Hedyotis diffusa* and *Scutellaria barbata* for maintenance treatment of malignant tumor *Journal of Gannan Medical College*, 42 (06), 583-586.