

The Preventive and Therapeutic Effect of Coptidis Rhizoma on Inflammatory Bowel Diseases and Colorectal Cancer

Peng Hai Yan^{*}, Shen Wei Xing, Cheng Hai Bo

The Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, China

Email address:

260615@njucm.edu.cn (Peng Hai Yan)

^{*}Corresponding author

To cite this article:

Peng Hai Yan, Shen Wei Xing, Cheng Hai Bo. The Preventive and Therapeutic Effect of Coptidis Rhizoma on Inflammatory Bowel Diseases and Colorectal Cancer. *International Journal of Chinese Medicine*. Vol. 5, No. 4, 2021, pp. 53-56. doi: 10.11648/j.ijcm.20210504.11

Received: November 22, 2021; **Accepted:** December 8, 2021; **Published:** December 24, 2021

Abstract: Background: Colorectal cancer has high incidence and mortal rate in China. Chronic inflammatory intestine diseases are ascribed to precancerous lesion of colorectal cancer because of its close relationship with each other. TCM therapy has good effect in the prevention and treatment of inflammatory bowel diseases related colorectal cancer. Objective: To explore the preventive and therapeutic effects of Coptis chinensis and traditional Chinese medicine compound containing Coptis chinensis on inflammatory bowel disease and colorectal cancer. Methods: This paper reviews the sections in classical TCM books and recent report of clinical and experimental research on the formulars composed of Coptidis Rhizoma and the single drug in treating ulcerative colitis, intestinal polyps and colorectal cancer. By analyzing the data reported in the original literature, The mostly applied herbal formulas in the clinic including Gegen Qinlian Decoction, Dark Plum Pill and Banxia Xiexin Decoction were studied in detail. Results: Coptidis Rhizoma has the function of clearing away heat and drying dampness, purging fire and detoxification, benefiting intestine and stopping diarrhea. Several formulas composed of Coptidis Rhizoma are applied to treat inflammatory bowel diseases and colorectal cancer. Conclusion: Coptidis Rhizoma and its composition has the function of inhibiting intestinal inflammation, regulating intestinal flora, protecting intestinal barrier, and etc.

Keywords: Coptidis Rhizoma, Inflammatory Bowel Diseases, Colorectal Cancer, Clinical Study, Experimental Research

1. Introduction

Colorectal cancer (CRC) is the third most common cancer in males and second in females, and the fourth most common cause of cancer death worldwide [1]. Inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, strongly increase a person's risk of developing colorectal cancer [2]. Reverse the process of transformation of inflammation to carcinoma is considered as the effective method to prevent the incidence of CRC [3]. CRC can also begin as a benign adenomatous intestinal polyp, evolving to adenoma with high grade dysplasia, invasive adenocarcinoma and metastatic disease [4].

Traditional Chinese medicine (TCM) has been extensively used as an alternate treatment and prevention for cancers and precancerous lesion [5]. The disease names related to inflammatory bowel disease and colorectal cancer include "intestinal wind", "organ toxin", "Chang Xvn", and etc [6]. There are lots of herbal medicine formulas are applied to

treat chronic intestinal diseases and relieve the clinical symptoms of patients'. Coptidis Rhizoma is one of the most widely used traditional Chinese herbs in China and the medical records in past thousands of years have fully confirmed its therapeutic effect on intestinal diseases [7].

2. Review

2.1. Clinical Application of Coptidis Rhizoma in the Classical Medicinal Formulas

In the classic Chinese medicine books of "Treatise on Febrile Diseases" there are several formulas containing Coptis chinensis Franch such as Gegen qinlian Decoction [8], Dark Plum Pill [9] and Banxia Xiexin Decoction [10] which are commonly used in treating ulcerative colitis (UC), intestinal polyps, colorectal cancer and etc. The following is the summary of the clinical application of the above-mentioned formulas (Table 1).

Table 1. Clinical application of Coptis Chinese French in the classical formulas.

| number | medicinal formulas | composition | action | reference |
|--------|-------------------------|---|--|-----------------------|
| 1 | Gegen qinlian Decoction | Pueraria Lobata, Scutellaria baicalensis, Coptidis Rhizoma, liquorice | dispersing exopathogens and clearing away internal heat | 8, 11, 12, 13, 14, 15 |
| 2 | Dark plum pill | dark plum, Asarum, dry ginger, cassia twig, aconite, pericarpium zanthoxyli, Coptidis Rhizoma, golden cypress, Ginseng, Angelica sinensis | clearing upper heat and warming lower cold, moderating liver and harmonizing middle-Jiao | 9, 16, 17, 18 |
| 3 | Banxia xiexin decoction | Pinellia ternate, Dried ginger, Scutellaria baicalensis, Coptidis Rhizoma, Ginseng, jujube, liquorice | harmonizing liver and spleen, dissolving lumps and resolving masses | 10, 19, 20, 21 |

2.2. Gegen Qinlian Decoction (GGQL)

Gegen qinlian Decoction are composed of Pueraria Lobata, Scutellaria baicalensis and liquorice besides Coptidis Rhizoma. The action of the formula is dispersing exopathogens and clearing away internal heat. The monarch drug is Pueraria Lobata which is ascribed to the channel of spleen and stomach. Pueraria Lobata can not only expel exopathogens, clear away heat, and ascending clear-Yang to stop diarrhea. Scutellaria baicalensis and Coptidis Rhizoma are both minister drugs. With bitter taste and cold nature, the two minister drugs can clear away heat and dry dampness to stop diarrhea. Liquorice plays as assistant and guide with the function of moderating the property of herbs. Combined with replenishing Qi, strengthening spleen, clearing away heat, or warming Yang respectively, GGQL can treat ulcerative colitis with the function of regulating immunity and relieving inflammation [11]. According to the results of clinical study, modified GGQL is effective in treating damp-heat syndrome of intestinal polyps [12]. Experimental research showed that the actional mechanism of GGQL includes anti-inflammation, anti-virus, inhibiting gastrointestinal motility, improving immunity, and, etc [13]. As to diarrhea of postoperative colorectal cancer because of damp-heat accumulation, GGQL can stop diarrhea by clearing away heat and drying dampness [14]. It is proved to have synergetic effect with Mesalazine [15].

2.3. Dark Plum Pill (DP)

Dark plum pill is composed of warm and cold drugs, tonify drugs and purging drugs. It has the function to clearing upper heat and warming lower cold, moderating liver and harmonizing middle-Jiao. Dark plum is the monarch drug with the function of astringing bowel to stop dysentery. Asarum, dry ginger, cassia twig, aconite and pericarpium zanthoxyli have the function of warming viscera and dispersing cold pathogen. Coptidis Rhizoma and golden cypress have the function of clearing away heat. Ginseng and Angelica sinensis have the function of replenishing Qi and nourishing blood. DP can relieve the symptoms of abdominal pain and diarrhea of patients of ulcerative colitis [16]. Modified DP can prevent the recurrent of intestinal polyp and the incidence of colorectal cancer [17]. Modified DP is also applied to treat late stage of colorectal cancer with metastasis of lungs and brain [18].

2.4. Banxia Xiexin Decoction (BXXX)

Banxia xiexin decoction is a harmonizing prescription. It

has the function of harmonizing liver and spleen, dissolving lumps and resolving masses. The monarch drug is Pinellia ternate which has the function of dissolving lumps and resolving masses, descending adverse reverse and stopping vomit. Dried ginger can warm middle-Jiao, Scutellaria baicalensis and Coptidis Rhizoma can clear away internal heat which are minister drugs. Ginseng and jujube are assistant drug with the function of replenishing qi and strengthening spleen. Liquorice is the guide drug with the function of moderating the property of herbs. BXXX is applied to treat UC with the function of alleviating infiltration of inflammatory cells, inflammation reaction, balancing gut flora, and promoting the repairment of intestinal mucosa [19]. BXXX can prevent the recurrence of intestinal polyp and better the pathological change of atypical hyperplasia of intestinal mucosa [20]. Combined with chemotherapy to treat colorectal cancer, BXXX can not only relieve the patients' adverse reaction of peptic tract, but also relieve the liver injury and decrease of white blood cells [21].

3. Experimental Research of the Herb of Coptidis Rhizoma

Coptis Rhizoma mainly contains isoquinoline alkaloids, lignans, flavonoids, organic acids and other chemical compositions [22-25]. Up to now the results show that the most actively ingredient of Coptis Rhizoma is berberine [26-30] which has the function of anti-inflammation, regulating gut flora, and protecting the intestinal mucosal barrier (Table 2).

3.1. Anti-inflammation

Berberine is the main effective component of Coptidis Rhizoma which has the function of anti-inflammation through inhibiting the activity of neutrophil phospholipase, the chemotaxis of neutrophil cells, the release of oxygen radical, and decreasing the content of PGE2 [31].

3.2. Gut Flora Regulation

The abstract of Coptidis Rhizoma can promote the production of probiotics such as lactobacillus and Bifidobacterium [32].

3.3. Mucosal Barrier Protection

Berberine can protect mechanical barrier of intestinal mucosa through inhibiting the destruction of intestinal stem

cells and tight junction proteins [33]. Berberine can protect intestinal chemical barrier through elevating the expression of

mucoprotein, and increasing the quantity of goblet cells so as to thickening the mucous layer [34, 35].

Table 2. Pharmacological research on the herb of *Coptidis Rhizoma*.

| number | pharmacological action | mechanism | reference |
|--------|----------------------------|---|-----------|
| 1 | Anti-inflammation | inhibiting the activity of neutrophil phospholipase, the chemotaxis of neutrophil cells, the release of oxygen radical, and decreasing the content of PGE2. | 31 |
| 2 | Gut flora Regulation | promote the production of probiotics such as lactobacillus and Bifidobacterium. | 32 |
| | | inhibiting the destruction of intestinal stem cells and tight junction proteins | 33 |
| 3 | Mucosal barrier protection | elevating the expression of mucoprotein, and increasing the quantity of goblet cells so as to thickening the mucous layer | 34, 35 |

4. Conclusions and Perspectives

Coptidis Rhizoma has the function of clearing away heat and drying dampness. According to the records of classical TCM books it is effective in treating diarrhea, dysentery and hematochezia. There are plenty of clinical study on some famous herbal medicine formulas containing *Coptis chinensis* Franch such as GGQL, DP and BXXX in treating ulcerative colitis, intestinal polyp and colorectal cancer. The results showed that those formula composed of *Coptidis Rhizoma* had good therapeutic effect. In GGQL, *Coptidis Rhizoma* combined with *Scutellaria baicalensis* to clear away heat, at the same time take *Pueraria Lobata* as the monarch drug to expel exopathogens and ascending clear-Yang, so the whole formula performs the function of dispersing exopathogens and clearing away internal heat. GGQL is good at treating inflammatory bowel diseases due to dysfunction of separating the clear and excreting the turbid. DP is a complex formula with the function of clearing upper heat and warming lower cold, moderating liver and harmonizing middle-Jiao and is good at treating protracted cases of concurrent coldness and hotness, deficiency and excess. BXXX also contains cold nature drugs and warm nature drugs. good at harmonizing liver and spleen so can be applied to treat inflammatory bowel diseases due to discordance of liver and spleen. The monarch drug is *Pinellia ternate* which is good at drying dampness and resolving phlegm to relieve the distension in the upper abdomen and stomach. According to TCM theory, spleen governs the whole digestive tract including stomach, small intestine and large intestine. Relatively, BXXX is good at relieve the symptoms of abdominal distension and vomit of patients of chronic intestinal diseases.

Lots of experimental research revolved around berberine which is the main component of *Coptidis Rhizoma*. The results showed that *Coptidis Rhizoma* could relieve the inflammatory change of intestine so that inhibit the further transformation from inflammation to carcinoma. *Coptidis Rhizoma* could regulate gut flora so as to promote the generation of beneficial bacteria and kill or inhibit the pathogenic bacteria. Berberine could protect intestinal mucosal barrier so as to cure or relieve the ulcer in the intestine and the surrounding tissue edema.

In conclusion, the further research can focus on either the effective components of *Coptidis Rhizoma* as a single herb for

seeking for drug development, or the clinical application laws of *Coptidis Rhizoma* in different prescriptions to better the therapeutic effect in treating inflammatory bowel diseases and colorectal cancer. It is also hopeful to find out the best scheme and most effective chemicals to prevent the colorectal transformation from inflammation to carcinoma.

Funding

Supported by General Projects of Jiangsu Natural Science Foundation, NO: BK20201400.

References

- [1] Chen W, Zheng R, Baade P D, et al. Cancer statistics in China, 2015 [J]. *CA Cancer J Clin*. 2016, 66 (2): 115-132.
- [2] Nitin Singh, Deepak Baby, Jagadish Prasad Rajguru et al. Inflammation and Cancer. *Ann Afr Med*, Jul-Sep 2019; 18 (3): 121-126.
- [3] Connie I Diakos, Kellie A Charles, Donald C McMillan, et al. Cancer-related inflammation and treatment effectiveness. *Lancet Oncol*, 2014 Oct; 15 (11): e493-503.
- [4] Jennifer J Liang, Ian Bissett, Matthew Kalady, et al. Importance of serrated polyps in colorectal carcinogenesis. *ANZ J Surg*, 2013 May; 83 (5): 325-30.
- [5] XU Chao, ZHOU Qing. Discussion on the focus of Traditional Chinese Medicine Intervention based on the Transformation of Early Intestinal Inflammation into Cancer. *World Chinese Medicine*, 2020, Sept; 15 (18): 2819-2822.
- [6] WANG Junyi, CHENG Haibo, ZHOU Zhongying. Discussion on Colorectal Precancerous Lesions Based on the Traditional Chinese Medicine Theory. *Journal of Traditional Chinese Medicine*, 2018, Dec; 59 (21): 1819-1823.
- [7] GUO Renqing. National TCM Master ZHOU Zhongying's Prescriptive Principle on Colorectal Cancer: Data Mining Approach. *Journal of Liao Ning University of TCM*, 2019, Apr; 21 (04): 142-145.
- [8] CHEN Lihong, TANG Yiping, WANG Qiang. Advances in studies on Gegen Qinlian Decoction. *CHINESE TRADITIONAL AND HERBAL DRUGS*. 2010, June; 41 (4): Att. 10-12.
- [9] XIN Fubing. 47 patients of UC treated by Dark Plum Pill. *MODERN TRADITIONAL CHINESE MEDICINE*. 2011, June; 31 (02): 20-21.

- [10] LI Kai. The Clinical and Basic Research of Pungent Dispersion Bitter Purgation Method and Banxia Xiexin Decoction on the Treatment of Colon Cancer. China Academy of Chinese Medical Science. 2015.
- [11] YV Tao. The Experience of Treating Ulcerative Colitis with GGQL. MODERN JOURNAL OF INTEGRATED TRADITIONAL CHINESE AND WESTERN MEDICINE. 2008, May; 17 (5): 763.
- [12] CHEN Na, CHEN Dong, ZHANG Lei. Treating Colonic Polyp with TCM. Hebei Journal of Traditional Chinese Medicine. 2014, 36 (06): 837-838.
- [13] WANG Buijiang, LIO Yvan. The Effect of GGQL on the pathological injury, inflammatory reaction and Intestinal Microecology of colonic cancer mice. Modern Practical Medicine. 2020, Dec; 32 (10): 1185-1188.
- [14] LI Yi, GUO Lihua. LI Siwen treat diarrhea of postoperative colorectal cancer patients with GGQL. CHINESE JOURNAL OF INFORMATION ON TRADITIONAL CHINESE MEDICINE. 2010, Aug; 17 (6): 85-86.
- [15] GAO Dong, SHAO Xi-feng. Efficacy of Puerariae and Scutellariae and Coptidis Decoction in Treatment of Patients with Ulcerative Colitis and Its Effects on Inflammatory Reaction and Immune Function. Medical & Pharmaceutical Journal of Chinese People's Liberation Army. 2018, Nov; 30 (10): 89-92.
- [16] ZHENG Caihua, CHANG Yvjan, ZHANG Na, et al. Professor GUO Guangye's Experience in Treatment of Patients with Ulcerative Colitis with modified Dark Plum Pill. Journal of Hebei Traditional Chinese Medicine and Pharmacology. 2018, Sep; 33 (4): 58-61.
- [17] Zhang Lingyun. Observation of The Clinical Therapeutic Effect on Preventing Colonic Adenoma Postoperative patients' Recurrence and Canceration Applying Modified "WuMeiWan". Nanjing University of Chinese Medicine. 2017.
- [18] WANG Sai, XU Xin, ZHANG Mengzhe, et al. Professor JIANG Shiqing's Experience of treating colorectal cancer on the base of syndrome differentiation of JVE YIN Channel. ACTA CHINESE MEDICINE. 2016, April; 31 (4): 467-469.
- [19] HU Chuanwen, JIANG Hongjuan, ZHENG Xiaochun, et al. Effect of Banxia Xiexin Tang Combined with Retention Enema on Ulcerative Colitis at Remission Stage and on Levels of Intestinal Bacteria. JOURNAL OF NEW CHINESE MEDICINE. 2020, Feb; 52 (03): 10-12.
- [20] LI Jicong. The Experience of Treating Discomfort of Patients of Polyp of Peptic Tract after operation with BXXX. Yiyao Qianyan. 2018, Sep; 8 (22): 326-327.
- [21] WANG Xiaoyan. Professor Baojin Hua's Experience in Treatment Colon Carcinoma with Banxia Xiexin Decoction. China Journal of Chinese Medicine. 2019, July; 34 (06): 1201-1204.
- [22] Kamath S, Skeels M, Pai A. Significant differences in alkaloid content of *Coptis chinensis* (Huanglian), from its related American species. Chin Med, 2009, Aug; 4 (1): 17-20.
- [23] Thao Quyen Cao, Quynh-Mai Thi Ngo, Su Hui Seong. Cholinesterase inhibitory alkaloids from the rhizomes of *Coptis chinensis*. Bioorg Chem, 2018 Apr; 77: 625-632.
- [24] Hui Teng, Yong Hee Cho. Optimization of ultrasonic-assisted extraction of bioactive alkaloid compounds from rhizoma *coptidis* (*Coptis chinensis* Franch.) using response surface methodology. Food Chem, 2014 Jan 1; 142: 299-305.
- [25] Fan G, Tao L H, Yue Q H, et al. Metabolic discrimination of *Rhizoma Coptidis* from different species using ¹H NMR spectroscopy and principal component analysis [J]. Planta Med, 2012, April; 78 (6): 641-648.
- [26] Ning Li, Lili Gu, Linlin Qu. Berberine attenuates pro-inflammatory cytokine-induced tight junction disruption in an in vitro model of intestinal epithelial cells. Eur J Pharm Sci, 2010 Apr 16; 40 (1): 1-8.
- [27] Shao-Jung Wu, Trong-Ming Don, Cheng-Wei Lin. Delivery of berberine using chitosan/fucoidan-taurine conjugate nanoparticles for treatment of defective intestinal epithelial tight junction barrier. Mar Drugs, 2014 Nov 24; 12 (11): 5677-97.
- [28] Rodrigo Alzamora, Fiona O'Mahony, Wing-Hung Ko. Berberine Reduces cAMP-Induced Chloride Secretion in T84 Human Colonic Carcinoma Cells through Inhibition of Basolateral KCNQ1 Channels. Front Physiol, 2011 Jun 30; 2: 33.
- [29] Jiang G, Li L, Wu X, et al. cisplatin antineoplastic effect Influence of berberine on in A549 cells. Chin J Lung Cancer, 2015, Aug; 18 (8): 481-486.
- [30] Park S H, Sung J H, Kim E J, et al. Berberine induces apoptosis via ROS generation in PANC-1 and MIA-PaCa₂ pancreatic cell lines. Brazilian J Med Biol Res, 2015, Feb; 48 (2): 111-119.
- [31] GENG Dong-Sheng. Effects of Berberine on Anti-inflammation and Immune Regulation. PHARMACEUTICAL JOURNAL OF CHINESE PEOPLE'S LIBERATION ARMY. 2000, Jan; (06): 317-320.
- [32] CUI Xiang, TAO Jin-hua, JIANG Shu, et al. Research on interaction between *Coptidis Rhizoma* extracts and intestinal bacteria. Chinese Traditional and Herbal Drugs. 2018, Aug; 49 (09): 2103-2107.
- [33] SHEN Yan, WANG Zhangliu, ZHENG Huajun, et al. Protective Effects of Berberine Hydrochloride on the Intestinal Mucosal Mechanical Barrier in Mice with Ulcerative Colitis. Chin J Mod Appl Pharm, 2018 December, 35 (12): 1765-1770.
- [34] Yu X T, Xu Y F, Huang Y F, et al. Berberine attenuates mucosal lesions and inflammation in dextran sodium sulfate-induced colitis in mice [J]. PLoS One. 2018, Mar; 13 (3): e194069.
- [35] Zhu L, Zhang D, Zhu H, et al. Berberine treatment increases Akkermansia in the gut and improves high-fat diet-induced atherosclerosis in Apoe (-/-) mice [J]. Atherosclerosis. 2018, Jan; 268: 117-126.