

# Research Progress of Buyang Yiwei Decoction in Regulating Intestinal Flora for Gastric Cancer

Yu Li<sup>1</sup>, Manya Wang<sup>2</sup>, Huixie Zhao<sup>3</sup>

<sup>1</sup>Oncology Department, The First Affiliated Hospital of Heilongjiang University of Traditional Chinese Medicine, Harbin, People's Republic of China;

<sup>2</sup>Department of Traditional Chinese Medicine, Shanghai Pudong New Area Nanhui Xincheng Community Health Service Center, Pudong New Area, Shanghai, People's Republic of China; <sup>3</sup>Department of Traditional Chinese Medicine, Shijiazhuang TCM Hospital, Shijiazhuang, People's Republic of China

Correspondence: Manya Wang, Email wangmanya@126.com

**Abstract:** Intestinal flora is a complex micro-ecosystem in human body, which is called the second genome of human body. Intestinal flora imbalance plays an important role in the occurrence and development of gastric cancer through circulation, metabolism and immunity. Gastric cancer is associated with dysbacteriosis. Traditional Chinese medicine (TCM) compounds in Buyang Yiwei Decoction can reduce the clinical signs and symptoms of gastric cancer by regulating intestinal microbiota, alleviate the adverse reactions of gastric cancer after radiotherapy and chemotherapy, and improve the quality of life of patients. This article reviews whether Buyang Yiwei Decoction can reduce the risk of gastric cancer or play a therapeutic role in gastric cancer by improving the intestinal microbiota.

**Keywords:** traditional Chinese medicine, gastric cancer, intestinal microbiota, treatment

## Introduction

Gastric cancer is one of the most common digestive tract malignant tumors, and its incidence and mortality are at the forefront worldwide. According to the World Health Organization's Global Cancer Statistics Database in 2020, the incidence of gastric cancer ranks fifth and the mortality rate ranks fourth in the world. However, there are 19.29 million newly diagnosed and registered cancer patients in the world, of which about 23.7% occur in China. Gastric cancer ranks fourth in the incidence of cancer in China, and its mortality rate ranks third.<sup>1,2</sup> At the same time, reducing the incidence and mortality of gastric cancer in China is a major public health problem that needs to be solved urgently. The morbidity of gastric cancer is related to many factors, and the clinical signs and symptoms of patients in the early stage are not obvious, so about 80% of patients with gastric cancer have progressed to the middle and late stages, so the 5-year survival rate of gastric cancer is less than 50%.<sup>3</sup>

Gastric cancer is one of the malignant tumors with high morbidity and mortality. The current survey found that the incidence of gastric cancer in the world is on the rise.<sup>1</sup> The prognosis of gastric cancer is good in the early stage, but the clinical diagnosis rate is low. Most patients with gastric cancer are in the middle and late stages when they are diagnosed, and the 5-year survival rate of advanced gastric cancer is low. At present, the first-line treatment recommended by clinical guidelines is surgery, and different surgical treatment methods are adopted according to different conditions; with the development of medicine, immunotherapy has become one of the treatment methods for advanced gastric cancer; with the development of precision medicine, targeted therapy has also become a good choice for the treatment of advanced gastric cancer. At the same time, for patients receiving radiotherapy, chemotherapy, targeted therapy, or patients with toxic side effects after the above treatment, who cannot tolerate the treatment, can be given TCM syndrome differentiation, and then take Chinese medicine treatment, so as to alleviate the pain of patients brought by cancer to a certain extent, and alleviate the clinical signs and symptoms of gastric cancer. The combination of traditional Chinese medicine therapy and modern therapy can improve the therapeutic effect to a certain extent and reduce the adverse reactions caused by modern medical technology.<sup>4</sup> The overall prognosis of patients with advanced gastric cancer is poor, and the main treatment is still systematic treatment. However, traditional chemotherapy drugs have entered the bottleneck period, the choice of targeted drugs is limited, and immunotherapy has some limitations, such as the poor effect of single

drug. Therefore, new treatment strategies are urgently needed to further prolong the survival time and improve the quality of life of patients with gastric cancer.

Prevention and treatment of gastric cancer with traditional Chinese medicine is the characteristic and advantage of treatment of gastric cancer in China. In recent years, traditional Chinese medicine has achieved good results in the treatment of gastric cancer, showing a good prospect, and its multi-mechanism and multi-level therapeutic effect has also been widely concerned and valued. At present, more than 70% of cancer patients in China have been treated with traditional Chinese medicine. The data show that traditional Chinese medicine can significantly enhance the sensitivity to chemotherapy drugs, enhance the anti-cancer effect, and significantly improve the adverse reactions such as cancer-related fatigue and bone marrow suppression. Studies have shown that the functional mechanism of traditional Chinese medicine in the treatment of tumors is related to the positive regulation of cytotoxic T cells, natural killer cells, dendritic cells and interleukin-12.<sup>5</sup> A large number of clinical studies have shown that traditional Chinese medicine plays an active role in the prevention and treatment of gastric cancer, especially in improving clinical signs and symptoms, preventing the further development of precancerous lesions, preventing recurrence and metastasis after operation, and enhancing the efficacy and attenuation of chemotherapy.<sup>6</sup> Chinese medicine has been widely used in the treatment of precancerous lesions of gastric cancer, Chinese medicine can significantly improve the patient's clinical signs and symptoms and gastroscopic pathology, and prevent the further development of the tumor.<sup>7</sup>

## Relationship Between Intestinal Microbiota and Gastric Cancer

Intestinal flora remains stable under the joint action of the external environment and the body, which is of great significance to the body's absorption and digestion, nutritional metabolism, inflammatory response and immune regulation. In recent years, with the rapid development of the second and third generation sequencing technology and biochip technology, the role of human intestinal flora in health and disease has been further discovered.<sup>8</sup> *Helicobacter pylori*, one of the intestinal flora, is the strongest risk factor for the occurrence and development of gastric cancer. Cytotoxin-associated protein and vacuolating toxin released after *Helicobacter pylori* infection are the key toxic factors leading to gastric cancer.<sup>9</sup> At the same time, *Helicobacter pylori* can stimulate immune response and inflammation, induce atrophy of gastric mucosal epithelium, destruction of gastric oxyntic glands and dysplasia. The development of most gastric cancer is from normal gastric mucosa to non-atrophic gastritis to chronic atrophic gastritis to intestinal metaplasia of gastric mucosa to dysplasia of gastric mucosa to gastric cancer, and *Helicobacter pylori* is the initiator of this process.<sup>10</sup>

Relevant studies have shown that cytotoxin-associated proteins can promote the occurrence and development of gastric cancer by regulating multiple pathways in the body. The most common pathways include extracellular regulated protein kinase/mitogen-activated protein kinase (ERK/MAPK), phosphatidylinositol 3-kinase/protein kinase B (PI3K/Akt), nuclear factor- $\kappa$ B (NF- $\kappa$ B), Ras, tyrosine protein kinase/signal transducer and activator of transcription inhibitor (JAK/STAT3), Wnt/-catenin, etc., and simultaneously induce the mutation of the classic tumor suppressor gene p53, which significantly increases the risk of gastric cancer.<sup>11</sup> *Helicobacter pylori* infection of gastric epithelial cells is related to MAPK signaling pathway, which can cause the production, increase, apoptosis, proliferation, differentiation and other changes of inflammatory cytokines, and ultimately lead to the transformation of epithelial cells into mesenchymal cells.<sup>12</sup> Among them, vacuolating cytotoxin can promote the expression of vascular endothelial growth factor in gastric cancer by up-regulating Wnt/-catenin signaling pathway, and also inhibit GSK3-induced autophagy and promote the occurrence of inflammatory response through PI3K/Akt signaling pathway.<sup>13,14</sup> NF- $\kappa$ B has been found to be an important regulatory factor, which is highly involved in the control of cell differentiation, proliferation, survival, invasion and angiogenesis during tumorigenesis and progression. Aberrant and sustained activation of NF- $\kappa$ B signaling contributes to the malignant transition from inflammation to cancer. Thus, the association between pathogens and NF- $\kappa$ B through blockade of the NF- $\kappa$ B signaling pathway shows therapeutic potential and benefits for cancer therapy.<sup>15</sup> There is sufficient evidence that NF- $\kappa$ B signaling pathway plays a driving role in the occurrence and progression of gastric cancer. NF- $\kappa$ B signaling pathway plays a crucial role in the immunity of gastric cancer and is currently considered as a potential therapeutic target for gastric cancer patients.<sup>16</sup>

Moreover, different researchers found that the intestinal flora of gastric cancer patients had changed significantly compared with normal patients in 16s sequencing of biopsy tissues of gastric cancer patients, in which the number of

*Lactobacillus*, *Klebsiella pneumoniae* and *Nitrospirillum* increased, while the number of *Porphyromonas* and *Neisseria* decreased, and these bacteria had specific functions to promote the occurrence of gastric cancer.<sup>17</sup> It has been found that lactic acid produced by lactobacilli can promote the development of tumors by activating hypoxia-inducible factor 1 (HIF-1) pathway in tumor cells, and lactic acid can be used as an energy source for tumor growth and angiogenesis.<sup>18</sup> *Nitrospirillum* was found to be present in all patients with gastric cancer, while it was completely absent in patients with chronic gastritis. Several members of the *Nitrospirillum* phylum are known to play a role in the metabolism of nitrate and nitrite, and nitrate consumption is an important risk factor for the development of gastric cancer.<sup>19</sup> At the same time, the pathogenic factors secreted by these flora, such as outer membrane protein, phospholipase, BAK protein and nickel binding protein, can help them colonize the gastric mucosa, promote the progress of chronic gastritis and increase the risk of gastric cancer.<sup>20</sup>

## Regulatory Effect of Buyang Yiwei Decoction on Intestinal Flora in Patients with Gastric Cancer

In ancient books of traditional Chinese medicine, there is no disease named after “gastric cancer”, but according to its clinical signs, gastric cancer is classified into “epigastric pain”, “dysphagia”, “nausea”, “upset stomach”, “accumulation”, “consumptive disease” and so on.<sup>21</sup> At the same time, ancient and modern Chinese medicine experts summarized the etiology and pathogenesis of Gastric cancer as insufficient healthy qi, uncontrolled diet, daily bad mood and feeling of external evil, among which insufficient healthy qi is the most important morbidity mechanism, blood stasis, heat toxin, phlegm these pathological products interact with each other, leading to the occurrence and development of the disease. Li Dongyuan mentioned in his Treatise on the Spleen and Stomach: “When the vitality of the spleen and stomach is insufficient, diseases will occur.” Therefore, it is believed that the weakness of the spleen and stomach is the root cause of the disease. At the same time, on the basis of inheriting the clinical experience of ancient physicians, combining with the changes of living conditions and dietary habits of modern people and taking into account the physical condition of gastric cancer patients after surgery, radiotherapy and chemotherapy, modern Chinese medicine scholars continue to innovate and put forward new ideas for the diagnosis and treatment of gastric cancer.

Buyang Yiwei Decoction is the empirical prescription of Professor Li Ji of Heilongjiang University of Chinese Medicine. Its research found that Buyang Yiwei Decoction can help patients with advanced gastric cancer recover physically, improve their clinical signs and symptoms, reduce the level of tumor markers, and combine with SOX chemotherapy to enhance efficacy and reduce toxicity, alleviate the damage of chemotherapy. This prescription can improve the quality of life of patients. It is of great significance to delay the progress of the disease.<sup>22</sup> Radix Astragali, Radix Angelicae Sinensis, Rhizoma Chuanxiong, Radix Paeoniae Alba, Herba Salviae Chinensis, Radix Actinidiae Chinensis, Rhizoma Curcumae, Herba Epimedii, and Flos Pruni mume. The compatibility of Radix Astragali and Radix Angelicae Sinensis in Buyang Yiwei Decoction can tonify qi and blood of the body, so the above two medicines can be used to treat the deficiency of healthy qi caused by the late stage of Gastric cancer and treatment; the combination of Radix Angelicae Sinensis, Rhizoma Chuanxiong and Radix Paeoniae has the effects of enriching the blood, promoting blood circulation and removing blood stasis, aiming at the blood stasis in the etiology and pathogenesis of Gastric cancer; At the same time, Rhizoma Curcumae is effective in promoting the circulation of qi and eliminating lumps, while Herba Salviae Chinensis is effective in promoting blood circulation and removing blood stasis and eliminating lumps, and Herba Epimedii is effective in replenishing the body's Yang qi. The combination of the three can support healthy qi and dispel pathogenic qi; Radix Actinidiae Chinensis (Radix Actinidiae Chinensis) is an empirical drug for cancer, and Fructus Mume has the effects of promoting the circulation of qi and promoting the production of body fluid, and can protect the body's body. The formula is based on that theory of qi and blood, treats both qi and blood, tonifies and disperses simultaneously, emphasizes tonifying qi and promoting blood circulation, and has remarkable curative effect on improving the hypercoagulable state of gastric cancer chemotherapy with the syndrome of qi deficiency and blood stasis and improving the quality of life of patients.

Buyang Yiwei Decoction is a commonly used prescription in our department for the treatment of advanced gastric cancer and weakness after radiotherapy and chemotherapy. Astragalus is a plant of Astragalus of Leguminosae, which is recorded in Shen Nong's Herbal Classic. It is a top-grade medicinal material with the functions of promoting qi

circulation, consolidating the exterior, diuresis, detoxification and suppuration. Modern pharmacological studies have found that it mainly contains flavonoids, saponins, polysaccharides and other chemical components, which have many pharmacological effects, such as regulating immunity, anti-tumor, protecting cardiovascular and nervous system, anti-aging and so on.<sup>23</sup> At the same time, clinical trials and animal experiments have also verified that the anti-tumor pharmacological effect of Astragalus.<sup>24</sup> Astragalus polysaccharide can regulate various cancer signaling pathways of Wnt, p53 and NF- $\kappa$ B and interact with specific transcription molecules to play an anti-tumor role. The active components extracted from Astragalus membranaceus can play an anti-tumor role by mediating VEGF/MMP signaling pathway to resist angiogenesis, and can also play an anti-tumor role through PI3K/Akt/mTOR signaling pathway.<sup>25,26</sup> The main chemical components of Angelica sinensis are volatile oil, coumarins, organic acids, flavonoids, polysaccharides, etc. The volatile oil, polysaccharides, organic acids and other components in Angelica sinensis have anti-tumor effects.<sup>27</sup> Modern studies have found the potential benefits of Astragalus and Angelica in cancer and cachexia patients, which can inhibit the growth of tumor cells, the release of inflammatory cytokines, the expression of NF- $\kappa$ B and STAT3, and the activation of primary tumor macrophages and T cells.<sup>28</sup> Angelica sinensis and Astragalus membranaceus reduce immune injury, improve intestinal barrier function, increase species diversity and richness, and regulate intestinal flora imbalance by increasing body weight and thymus index, reducing spleen index and CD4/CD8 ratio of T lymphocyte subsets, and regulating the level of phyla and order of *Bacteroides*.<sup>29</sup> Radix Angelicae Sinensis, Rhizoma Chuanxiong, and Radix Paeoniae Alba are modified from Siwu Decoction, and studies have found that Siwu Decoction can improve the nutritional status and immune function after gastric cancer surgery.<sup>30</sup> At the same time, it was found that Siwu Tang could regulate 10 different bacterial genera, especially it could up-regulate the abundance of three dominant strains norank\_f\_muribaculaceae, Lactobacillus, and prevotella\_9,<sup>31</sup> in which Lactobacillus played a key role in the morbidity and treatment of gastric cancer. This may also be one of the ways to treat gastric cancer with Angelica sinensis, Ligusticum chuanxiong and Paeonia lactiflora.

Herba Salviae Chinensis is rich in polysaccharides, triterpenoids, sterols, polyphenols, etc., has a good anti-cancer effect, and has a good therapeutic effect on a variety of malignant tumors. After acting on human gastric cancer cells SGC-7901, Herba Salviae Chinensis polysaccharide has a significant inhibitory effect on cell proliferation.<sup>32</sup> Radix Actinidiae Chinensis is a specific anti-tumor Chinese herbal medicine. Modern pharmacological studies have found that its components include triterpenoids, phenylpropanoids, flavonoids, steroids, anthraquinones, alkaloids, etc., among which triterpenoids are its main chemical components. Radix Actinidiae Chinensis is a promising anti-tumor drug for the treatment of gastric cancer by regulating apoptosis, iron death and mesenchymal phenotype.<sup>33</sup> Curcumin, volatile oil and phenolic acids are the active components in the rhizome of *Curcuma zedoaria*, which can affect and regulate multiple signaling pathways, such as anti-inflammatory, inhibiting cell proliferation, regulating immunity and promoting apoptosis.<sup>34</sup> Zhou Guixiang et al<sup>35</sup> found that curcumol could significantly inhibit the phosphorylation level of PI3K/Akt/mTOR signaling protein in gastric cancer AGS cells, up-regulate the expression of apoptotic proteins Caspase-3 and Bax, and down-regulate the expression of anti-apoptotic protein Bcl-2, thereby inhibiting the growth of gastric cancer AGS cells and inducing cell apoptosis. At the same time, *Actinidia chinensis* and *Curcuma zedoaria* are often used in combination, which is widely used in gastric cancer and its precancerous lesions.

Icariin, a flavonoid, is one of the most important chemical constituents of Epimedium. Modern pharmacological studies have shown that icariin inhibits the proliferation of tumor cells, induces the differentiation and apoptosis of tumor cells, reduces the ability of metastasis and invasion of tumor cells, enhances the activity of anti-cancer cells, and inhibits the activity of telomerase.<sup>36</sup> Previous studies have shown that icariin can inhibit the proliferation and promote the apoptosis of gallbladder cancer cells, and this anti-cancer activity is related to the down-regulation of the expression of apoptosis-related molecules by NF- $\kappa$ B pathway.<sup>37</sup> Oral administration of icariin I improved the microbial community structure, significantly restored the Lactobacillus and Bifidobacterium colonies, and improved the levels of microbiota-derived metabolites, such as short-chain fatty acids and indole derivatives, thereby promoting intestinal barrier repair and reducing systemic inflammation. Icariin I showed strong immune antitumor activity, which was directly reflected by the upregulation of multiple lymphocyte subsets in the peripheral blood of model mice, including CD4 and CD8 T cells or NK and NKT cells.<sup>38</sup> Pharmacological studies on green calyx plum have shown that the extract of green calyx plum has antidepressant, antioxidant, bacteriostatic, anti-platelet aggregation and



other effects and is mainly used to treat depression, gastropathy, globus hystericus, scrofula and other symptoms in clinic. Its main active ingredients are phenylpropanoids and flavonoids (isorhamnetin, quercetin, kaempferol, etc.).<sup>39</sup>

The main active ingredients in Buyang Yiwei Decoction are flavonoids, and the main chemical components are quercetin, kaempferol and Stigmasterol. Among them, quercetin belongs to the flavonol flavonoid subclass compounds. The anticancer effect of quercetin depends on its ability to reduce proliferation, induce apoptosis, cause cell cycle arrest, and inhibit the mitotic process by regulating cyclin, pro-apoptotic, PI3K/Akt, and MAPK molecular pathways.<sup>40</sup> Quercetin was found to play an anti-gastric cancer role by regulating Akt-mTOR/HIF-1 $\alpha$  signaling to activate autophagy and induce apoptosis.<sup>41</sup> Quercetin can significantly enhance the antioxidant system by regulating the Nrf2/HO-1 signaling pathway and effectively reduce the inflammatory response (COX-2 and iNOS) by regulating the NF- $\kappa$ B, AMPK and TLR signaling pathways, thereby reducing the onset of various gastrointestinal cancers, especially colorectal cancer and gastric cancer; Rats dosed with quercetin showed improved gut flora, which in turn suppressed gut inflammation and slowed or inactivated immune cells (Th/T17 cells), thereby reducing complications associated with gut dysbiosis and thereby maintaining gut health.<sup>42</sup>

## Conclusion

Most importantly, gastric cancer is related to the imbalance of intestinal flora in patients. Buyang Yiwei Decoction and other traditional Chinese medicine compounds with the regulation of intestinal flora imbalance can reduce the clinical signs and symptoms related to gastric cancer and alleviate the side effects of gastric cancer after chemotherapy. TCM diagnosis and treatment based on the comprehensive analysis of the disease and the patient's condition can regulate the species and quantity of intestinal microbiota and achieve the balance and diversity of intestinal microbiota. In addition, the role of traditional Chinese medicine in regulating intestinal microbiota will receive more and more attention in clinical practice. At present, the research on anti-tumor effect achieved by regulating intestinal flora through traditional Chinese medicine is not rich, and although many specific mechanisms have been studied, they are still in the initial stage. In the future, we can conduct in-depth research on the molecular mechanism of intestinal flora regulating tumors, provide new ideas and treatment programs for the prevention and treatment of tumors, and apply the products of related research to clinical practice. Enriching the clinical diagnosis and treatment of cancer.

## Data Sharing Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study. The results of this study will be published in a peer-reviewed journal.

## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

Heilongjiang Province Traditional Chinese Medicine scientific research project; (No.: ZHY19-019) and (No.:ZHY2024-308).

## Disclosure

There are no conflicts of interest.

## References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality Worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209–249. doi:10.3322/caac.21660
2. Qiu H, Cao S, Xu R. Cancer incidence, mortality, and burden in China: a time-trend analysis and comparison with the United States and United Kingdom based on the global epidemiological data released in 2020. *Cancer Commun.* 2021;41(10):1037–1048. doi:10.1002/cac2.12197

3. Gullo I, Grillo F, Mastracci L, et al. Precancerous lesions of the stomach, gastric cancer and hereditary gastric cancer syndromes. *Pathologica*. 2020;112(3):166–185. doi:10.32074/1591-951X-166
4. Ye HN, Liu XY, Qin BL. Research progress of integrated traditional Chinese and Western medicine in the treatment of advanced gastric cancer. *World J Gastrointest Oncol*. 2023;15(1):69–75. doi:10.4251/wjgo.v15.i1.69
5. Zhang Y, Lou Y, Wang J, et al. Research status and molecular mechanism of the traditional Chinese medicine and antitumor therapy combined strategy based on tumor microenvironment. *Front Immunol*. 2021;11:609705. doi:10.3389/fimmu.2020.609705
6. Lu Y, Liu H, Yang K, et al. A comprehensive update: gastrointestinal microflora, gastric cancer and gastric premalignant condition, and intervention by traditional Chinese medicine. *J Zhejiang Univ Sci B*. 2022;23(1):1–18. doi:10.1631/jzus.B2100182
7. Xu W, Li B, Xu M, et al. Traditional Chinese medicine for precancerous lesions of gastric cancer: a review. *Biomed Pharmacother*. 2022;146:112542. doi:10.1016/j.biopha.2021.112542
8. Kuleshov V, Jiang C, Zhou W, Jahanbani F, Batzoglou S, Snyder M. Synthetic long-read sequencing reveals intraspecies diversity in the human microbiome. *Nat Biotechnol*. 2016;34(1):64–69. doi:10.1038/nbt.3416
9. Fengli W, Zhang L. Role of H. pylori infection combined with gastric function testing in the early diagnosis of gastric cancer. *Shenzhen J Integr Tradit Chin West Med*. 2022;32(23):66–68. doi:10.16458/j.cnki.1007-0893.2022.23.021
10. Park YH, Kim N. Review of atrophic gastritis and intestinal metaplasia as a premalignant lesion of gastric cancer. *J Cancer Prev*. 2015;20(1):25–40. doi:10.15430/JCP.2015.20.1.25
11. Yong X, Tang B, Li BS, et al. Helicobacter pylori virulence factor CagA promotes tumorigenesis of gastric cancer via multiple signaling pathways. *Cell Commun Signal*. 2015;13:30. doi:10.1186/s12964-015-0111-0
12. Yousefi B, Mohammadlou M, Abdollahi M, et al. Epigenetic changes in gastric cancer induction by Helicobacter pylori. *J Cell Physiol*. 2019;234(12):21770–21784. doi:10.1002/jcp.28925
13. Liu N, Zhou N, Chai N, et al. Helicobacter pylori promotes angiogenesis depending on Wnt/beta-catenin-mediated vascular endothelial growth factor via the cyclooxygenase-2 pathway in gastric cancer. *BMC Cancer*. 2016;16:321. doi:10.1186/s12885-016-2351-9
14. Li N, Tang B, Jia YP, et al. Helicobacter pylori caga protein negatively regulates autophagy and promotes inflammatory response via c-Met-PI3K/Akt-mTOR signaling pathway. *Front Cell Infect Microbiol*. 2017;7:417. doi:10.3389/fcimb.2017.00417
15. Peng C, Ouyang Y, Lu N, et al. The NF-κB signaling pathway, the microbiota, and gastrointestinal tumorigenesis: recent advances. *Front Immunol*. 2020;11:1387. PMID: 32695120; PMCID: PMC7338561. doi:10.3389/fimmu.2020.01387
16. Chen Q, Du X, Ruan P, et al. Bioinformatics analysis revealing the correlation between NF-κB signaling pathway and immune infiltration in gastric cancer. *Comput Math Methods Med*. 2022;2022:5385456. PMID: 35936362; PMCID: PMC9352505. doi:10.1155/2022/5385456
17. Dias-Jácome E, Libânio D, Borges-Canha M, et al. Gastric microbiota and carcinogenesis: the role of non-Helicobacter pylori bacteria - A systematic review. *Rev Esp Enferm Dig*. 2016;108(9):530–540. doi:10.17235/reed.2016.4261/2016
18. Sonveaux P, Copetti T, De Saedeleer CJ, et al. Targeting the lactate transporter MCT1 in endothelial cells inhibits lactate-induced HIF-1 activation and tumor angiogenesis. *PLoS One*. 2012;7(3):e33418. doi:10.1371/journal.pone.0033418
19. Stewart OA, Wu F, Chen Y. The role of gastric microbiota in gastric cancer. *Gut Microbes*. 2020;11(5):1220–1230. doi:10.1080/19490976.2020.1762520
20. Juozas K, H LG. Other Helicobacters and the gastric microbiome. *Helicobacter*. 2018;23(1):e12521. doi:10.1111/hel.12521
21. Huijun C, Ningsu Z, Xiangrong X. Study on the distribution of primary gastric cancer. *Yunnan J Tradit Chin Med*. 2018;39(09):16–20. doi:10.16254/j.cnki.53-1120/r
22. Li Y, Li J. The decoction was combined with SOX chemotherapy to treat middle and advanced gastric cancer. *Jilin Tradit Chin Med*. 2021;41(02):197–200.
23. Li X, Qu L, Dong Y, et al. A review of recent research progress on the astragalus genus. *Molecules*. 2014;19(11):18850–18880. doi:10.3390/molecules191118850
24. Caixia L, Xiaoye Y, Weihua S, et al. Effect of APS on regulatory T cells in the peripheral blood of elderly patients with advanced gastric cancer. *Practical Geriatrics*. 2021;35(06):564–567.
25. Jiao R, Liu Y, Gao H, et al. The anti-oxidant and antitumor properties of plant polysaccharides. *Am J Chin Med*. 2016;44(3):463–488. doi:10.1142/S0192415X16500269
26. Zhu JJ, An YW, Hu G, et al. Simultaneous determination of multiple sesquiterpenes in curcuma wenyujin herbal medicines and related products with one single reference standard. *Molecules*. 2013;18(2):2110–2121. doi:10.3390/molecules18022110
27. Yan M, Yugui Z, Luping S, et al. Research progress of angelica products and its chemical composition and pharmacological effects. *Chin J Tradit Chin Med*. 2023;48(22):6003–6010.
28. Wu TH, Yeh KY, Wang CH, et al. The combination of astragalus membranaceus and angelica sinensis inhibits lung cancer and cachexia through its immunomodulatory function. *J Oncol*. 2019;2019:9206951. doi:10.1155/2019/9206951
29. Huang H, Xie Y, Li X, et al. Danggui buxue decoction regulates the immune function and intestinal microbiota of cyclophosphamide induced immunosuppressed mice. *Front Pharmacol*. 2024;15:1420411. doi:10.3389/fphar.2024.1420411
30. Shaoyan W. Early weiwei effects of siwei decoction on nutritional status and immune function in early surgery after gastric cancer [J]. *PLA Med J*. 2015;27(06):83–86.
31. Wan D, Liang X, Yang L, et al. Integration of gut microbiota and metabolomics for the hematopoiesis of Siwu paste on anemia rats. *Heliyon*. 2023;9(7):e18024. doi:10.1016/j.heliyon.2023.e18024
32. Yuan L, Rongkang Q, Ronghua Q. Anprograss tumor of anatum and its extracts. *J Modern Integr Tradit Chin West Med*. 2018;27(30):3417–3420.
33. Gao Z, Deng G, Li Y, et al. Actinidia chinensis planch prevents proliferation and migration of gastric cancer associated with apoptosis, ferroptosis activation and mesenchymal phenotype suppression. *Biomed Pharmacother*. 2020;126:110092. doi:10.1016/j.biopha.2020.110092
34. Baoshi L, Ningjun X, Chaolin Z. Impact of zedoary on tumor-related signaling pathways. *J Liaoning Univ Tradit Chin Med*. 2015;17(02):188–191. doi:10.13194/j.issn.1673-842x
35. Guixiang Z, Shuai D, Jiangwen B, et al. Effects and mechanism of zedool on cell proliferation and apoptosis in gastric cancer. *Global Tradit Chin Med*. 2023;16(07):1301–1308.
36. Yuling L, Zhentao M, Wenna L, et al. Progress in the pharmacology of icariin. *Chin J Trad Chin Med*. 2020;38(08):139–142. doi:10.13193/j.issn.1673-7717.2020.08.034

37. Zhang DC, Liu JL, Ding YB, et al. Icaritin potentiates the antitumor activity of gemcitabine in gallbladder cancer by suppressing NF- $\kappa$ B. *Acta Pharmacol Sin*. 2013;34(2):301–308. doi:10.1038/aps.2012.162
38. Chen G, Cao Z, Shi Z, et al. Microbiome analysis combined with targeted metabolomics reveal immunological anti-tumor activity of icaritin in a melanoma mouse model. *Biomed Pharmacother*. 2021;140:111542. doi:10.1016/j.biopha.2021.111542
39. Mengqiu X, Rui W, Xingchen W, et al. Pretive analysis of chemical composition, pharmacological action and quality markers of plum. *Chin J Trad Chin Med*. 2024;42(07):243–250. doi:10.13193/j.issn.1673-7717.2024.07.050
40. Reyes-Farias M, Carrasco-Pozo C. The anti-cancer effect of quercetin: molecular implications in cancer metabolism. *Int J Mol Sci*. 2019;20(13):3177. doi:10.3390/ijms20133177
41. Rong Y, Liu SH, Tang MZ, et al. Quercetin inhibits the proliferative effect of gastric cancer cells by activating the pyroptosis pathway. *Asian J Surg*. 2023;46(11):5286–5288. doi:10.1016/j.asjsur.2023.07.051
42. Chiu HF, Venkatakrishnan K, Golovinskaia O, et al. Gastroprotective effects of polyphenols against various gastro-intestinal disorders: a mini-review with special focus on clinical evidence. *Molecules*. 2021;26(7):2090. doi:10.3390/molecules26072090

## Cancer Management and Research

Dovepress

### Publish your work in this journal

Cancer Management and Research is an international, peer-reviewed open access journal focusing on cancer research and the optimal use of preventative and integrated treatment interventions to achieve improved outcomes, enhanced survival and quality of life for the cancer patient. The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/cancer-management-and-research-journal>