Progress in the Study of the Effects and Mechanisms of Medicinal and Food Herbs and Their Active Ingredients on Colorectal Cancer

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Abstract: Colorectal cancer (CRC) is the fourth deadliest cancer in the world, with nearly 900,000 deaths annually. Although environmental and genetic factors as well as population aging are key in the pathogenesis of colorectal cancer, numerous studies have shown that dietary habits and nutrition may play both causal and protective roles in the development of colorectal cancer. "With the in-depth development and research of traditional Chinese medicine (TCM), the anticolorectal cancer effects of "medicinal food and herbs" have been gradually explored, and have received widespread attention due to their safe and significant therapeutic and healthcare effects. This paper summarizes and discusses the effects and mechanisms of "medicinal food" herbs and their active ingredients in colorectal cancer. This review is intended to serve as a reference for future research on anticolorectal cancer ingredients from "medicinal and food" herbal sources as drugs or food supplements.

Keywords: "medicinal food" herbs, Colorectal cancer, Diet, Mechanism of action.

1. Introduction

Colorectal cancer (CRC) accounts for approximately 10% of all cancer deaths [1]. With the aging of the population and changes in dietary habits, the incidence of colorectal cancer is expected to increase to 2.5 million new cases worldwide by 2035 [2]. Currently, colorectal cancer is often treated with surgery, radiotherapy, chemotherapy, immunotherapy and targeted therapy, but in many cases this does not result in complete tumor control. Epidemiologic studies have shown that more than half of the risk of colon cancer can be prevented by modifiable risk factors, including diet [3][4].

Chinese medicine has a certain understanding of colorectal cancer since a long time ago, and there are records of colorectal cancer in the "Neijing" as well as in ancient Chinese medical books of different generations, such as "blood in the bowel from dirty toxins", "intestinal mushrooms", "obstruction in the abdomen ", "lock-anal hemorrhoids", "blood in stool", "dysentery", "intestinal fetish", etc. These ancient Chinese medical texts have recorded colorectal cancer such as etc. These ancient texts provide valuable clinical experience for the treatment of colorectal cancer. As a kind of safe and non-toxic food and medicinal material, "medicinal food and medicinal material" has been used for thousands of years, from which we have a unique advantage to screen and develop medicines that can effectively prevent and treat CRC and have low toxicity and side-effects when taken for a long period of time. At present, a variety of "food and medicine" herbs and active ingredients have been found to be effective in preventing and treating colorectal cancer in various ways, as well as improving the toxic side effects of radiotherapy and immunotherapy. Therefore, this paper provides a scientific basis for the further development of functional foods for the prevention and treatment of CRC by describing the anti-CRC mechanism of "medicinal food" herbs and active ingredients.

2. Anti-colorectal Cancer Herbs from the Same Source as Food and Medicine

In the 2021 edition of the Chinese Pharmacopoeia, there are 110 kinds of herbs with the same origin as food and medicine. Through summarizing the literature on "medicines and foods with the same source" against colorectal cancer in recent years, it is found that most of the "medicines and foods with the same source" against colorectal cancer are tonic medicines. The "External Testimonies of Medicine" said, "If the positive qi is weak, then it will become rock." When the human body's positive qi is insufficient, cancerous toxins are easy to invade, and cancerous tumors will occur [5]. In his research, Professor Yu Rencun put forward a viewpoint called "internal deficiency doctrine", which believes that the key to tumor formation is due to insufficient function of internal organs and lack of positive qi [6]. One of the important principles of Chinese medicine in the treatment of colorectal cancer is to support positive energy and detoxification, and to support positive energy as the first priority, including tonifying qi and yang, nourishing yin and blood, and tonifying spleen and kidney. The drugs that can replenish the deficiency of qi, blood, yin and yang of the organism are called tonic drugs, which are also known as deficiency replenishing drugs [7]. They include licorice, eucommia, astragalus, ginseng, ganoderma lucidum and so on. The anticolorectal cancer effects of tonic drugs are summarized as follows, respectively.

2.1 Licorice

Glycyrrhiza glabra belongs to the family of legumes, is sweet and flat in nature, and is known as "the oldest of the nation", with the efficacy of harmonizing all medicines [8]. Traditionally, licorice has been used as a sweetener and flavoring agent for food. The treatment of colorectal cancer has been challenged by the development of drug resistance. It was found that licorice chalcone H inhibited the growth of oxaliplatin-resistant colorectal cancer cells [9]. Also, Kwak Ahwon et al. found that licorice chalcone B could induce ROS-dependent apoptosis in oxaliplatin-resistant colorectal cancer cells via p38/JNK MAPK signaling [10]. In addition, several studies have shown that active compounds such as photoglycyrrhizidine [11], dihydroflavonoids from licorice [12], glycyrrhizic acid [13], and isoglycyrrhizin [14] can inhibit the proliferation, invasion, and migration of colorectal cancer cells and induce apoptosis. These findings suggest that the important role of licorice in anticolorectal cancer, especially licorice can reverse the resistance to chemotherapeutic drugs, is less in clinical studies and insufficiently articulated with basic research, which deserves our attention.

2.2 Eucommia Ulmoides

Eucommia ulmoides, a plant of the genus Eucommia in the family of Eucommiaceae, has been used in China for more than two thousand years. The Divine Husbandman's Classic of the Materia Medica (神农本草经云) "Duzhong flavor Xinping, the main lumbar and spinal pain, tonic, beneficial to the essence of the gas, firm sinews, strong will, in addition to the yin under the itchy wet, urinary residual leaching. Taken for a long time to lighten the body and resistance to old age, a Si Xian, born in the valley". So far, the effective active compounds isolated from Cortex Eucommiae mainly include lignans, flavonoids, terpenoids, polysaccharides, etc., according to the structure, and these active compounds have a wide range of pharmacological activities [15]. In the current reports on Cortex Eucommiae, the anticolorectal cancer effects of Cortex Eucommiae are mainly related to the promotion of tumor cell apoptosis. As early as 2016, Luan Fangfei et al. intervened human colorectal cancer cells HCT116 with eucommia leaf extract and found that eucommia leaf extract could promote apoptosis as well as inhibit the anti-angiogenic activity of human colorectal cancer cells at high concentrations [16]. In addition, Eucommia gum latex extract also prevented DMH-induced early colorectal carcinogenesis in rats by modulating xenobiotic metabolism, inflammatory response, cell proliferation and apoptosis [17].

2.3 Astragalus Membranaceus

Astragalus is a plant of Leguminosae family and Astragalus genus, with sweet taste and slightly warm nature, belonging to lung and spleen meridians, it has the function of tonifying gi and consolidating the surface, diuretic and toxin-supporting, draining pus, astringing sores and generating muscles, and is one of the most important tonic medicines. The main active ingredients of Astragalus are polysaccharides, flavonoids, and saponins. In recent years, Astragalus has been actively studied for its potential use in the treatment of inflammation and gastrointestinal tumors. Astragalus extracts have been shown to inhibit the growth of several colon cancer cells in vitro [18]. Tin et al. in 2007 found that total Astragalus saponins promoted apoptosis in HT-29 human colon adenocarcinoma cells and inhibited cell proliferation by blocking the cell cycle in the S-phase and G2 / M-phase, as well as inhibiting p21 expression and cell cycle protein-dependent kinase activity [19]. The prickly aristolochicin is Astragalus isoflavone (Astragalus isoflavone), the first astragalus isoflavone to be explored. Astragalus isoflavone was also found to promote apoptosis and inhibit the growth of human colon cancer cells, and it was demonstrated in nude mice transplantation tumors that Astragalus isoflavone could also inhibit angiogenesis and colorectal cancer cell invasion through the down-regulation of pro-angiogenic factors, such as VEGF and MMPs [20]. In summary, most of the anticolorectal cancer effects of astragalus are related to the promotion of apoptosis as well as the inhibition of angiogenesis in colorectal cancer cells.

2.4 Angelica Sinensis

Angelica is the umbelliferae angelica herb, "Compendium of Materia Medica" cloud: "the ancients married wife, for the continuation. Angelica regulates blood, for women to medicine, there is the intention of thinking of husband, so there is the name of angelica." Angelica sinensis is warm in nature, sweet and pungent in flavor, and belongs to the liver, heart, and spleen meridians, and is a large bulk of Gansu Taoist medicinal herbs [21]. Zhu Lijuan et al. found that the volatile oil of Angelica sinensis may inhibit the proliferation and migration of human colorectal cancer cells HCT-116 and induce apoptosis through the Wnt/\beta-catenin signaling pathway [22]. In addition, FENG et al. found that Angelica sinensis blood tonic soup could significantly reduce the volume of colon tumors, as well as reduce the nucleoplasmic ratio, and induce apoptosis of colon cancer cells by up-regulating the expression of Bax and Caspase-3, and regulating the expression of Bcl-2 to achieve anti-tumor effects [23]. In the clinical study, it was found that when Angelica sinensis blood replenishing sugar was given for 7d after colon cancer surgery, IgG, IgM, IgA and CD4+/CD8+ increased in the Angelica sinensis blood replenishing soup group compared with the conventional treatment, so it was shown that the Angelica sinensis blood replenishing soup could improve the immunity of patients with colorectal cancer [24]. Regardless of Angelica sinensis or Angelica sinensis complex, it can achieve the effect of treating colorectal cancer by inhibiting apoptosis as well as improving the immune function of the body. From the perspective of traditional medicine, colorectal cancer is mostly related to deficiency and stagnation, and both Angelica sinensis and Angelica sinensis blood tonic soup can replenish qi and generate blood, exerting their antitumor advantages.

2.5 Ginseng

Ginseng is a plant of the family Wujiaceae, which is sweet, complementary and slightly warm, with the effects of tonifying vital energy, restoring pulse and fixing detachment, tonifying the spleen, benefiting the lungs, and generating fluids and tranquilizing the mind, and is an important medicine for tonifying vital energy and strengthening the body [25]. Cheng et al. intervened in HT-29 human colorectal cancer cells with ginseng pectin and found that the HT-29 cells were blocked in the G2/M phase of division so as to achieve the antiproliferative effect, and after further research, it was found that the structure of ginseng polysaccharides can be altered by high temperature to produce some modified polysaccharides that promote apoptosis [26]. Similarly, Wang Chongzhi et al. found that two ginseng polysaccharides, GBPP and GBPE, could inhibit the proliferation of HT-29 and HCT-116 cells by blocking at G2/M division [27]. In addition, the combination of ginsenoside CK with antitumor drugs can increase the sensitivity of antitumor drugs [28]. The above

studies suggest that ginseng exerts its therapeutic effects through multiple mechanisms of action, including inducing tumor cell cycle blockade as well as assisting antitumor drugs to increase their efficacy and reduce their toxicity.

2.6 Ganoderma Lucidum

Ganoderma lucidum is the dried substrate of Ganoderma lucidum or Ganoderma lucidum of the family of Polyporaceae, which is a valuable medicinal material for supporting and strengthening the body, nourishing and strengthening the body, as pointed out in Shennong Ben Cao Jing: "Ganoderma lucidum is sweet and warm in taste, and it is the master of deafness, good for the joints, preserving the spirit and benefiting the spirit, firming up the tendons and bones and good for the color, and it is a long time serving to lighten up and not aging and prolonging the years [29]." In clinical practice, Ganoderma lucidum can be used in conjunction with a variety of traditional Chinese medicines for combating tumors and adjuvant chemotherapy. Extracts of Ganoderma lucidum paired with camphor and deer antler have inhibitory effects on proliferation and metastasis of colon cancer cells by regulating cell cycle control proteins, promoting apoptosis, and decreasing the level of p53 protein [30]. Li et al. demonstrated that Ganoderma lucidum triterpenes can induce human colorectal cancer by inducing the release of c-Myc, which leads to the up-regulation of Caspase-3 and Caspase-9 expression, and induce SW620 cell apoptosis [31].

3. "Anti-colorectal Cancer Active Ingredients

3.1 Flavonoids

Flavonoids are plant secondary metabolites, which are a series of compounds with diverse and complex structures consisting of two benzene rings interconnected by three carbon atoms. Flavonoids are present in almost all higher green plants and have a wide range of biological activities [32]. Flavonoids in the "medicinal food" class of anticolorectal cancer Chinese medicines are mainly found in plants such as licorice, dandelion, hakufu, eucommia, etc. They are quercetin, glycyrrhizin, glycyrrhizin chalcone, lignocerol, hesperidin, eucommia, and rutin, respectively. It has been found that high intake of flavonols (e.g., quercetin) as well as flavonoids (e.g., apigenin (apigenin)) in the daily diet may reduce the risk of colon cancer [33]. Flavonoids utilize their antioxidant activity to prevent intestinal morphophysiological damage induced by the anticolorectal cancer drug fluorouracil [34]. Quercetin is the main representative of the flavonol flavonoid subclass. It is commonly found in fruits and vegetables and is one of the most common dietary flavonols in the diet. Quercetin has been widely reported in the scientific literature as an anticancer agent. So far in ex vivo colorectal cancer model reports, quercetin anticolorectal cancer has been mainly associated with Wnt/β-linker protein, PI3K/AKT, MAPK/Erk, JNK, or p38, p53 and NF-kB signaling pathways [35]. Quercetin can be used as a drug or dietary ingredient to achieve anticancer activity. In addition, Zhang Lei et al. found that quercetin combined with epicatechin may regulate the inflammatory response through the miR-124-3p/IL-6 signaling pathway through a mouse model of colorectal cancer to achieve an anticolorectal cancer effect [36]. Lignan is a common flavonoid widely found in various fruits and

vegetables. It has excellent anti-inflammatory, antioxidant and anticancer properties. Chan Ho Jang et al. found that the combination of lignocaine and oxaliplatin was able to stimulate apoptosis and inhibit proliferation of colorectal cancer cells through an ampk-related mechanism, resulting in inhibition of the growth of HCT-116 xenograft tumors in mice [37]. Therefore, we can conclude that intake of lignan-rich diet helps to improve the efficacy of oxaliplatin when treating colorectal cancer. In addition to this the flavonoid rutin volatile oil inhibits colorectal genesis through apoptosis that can be induced by TRAIL / Apo2L [38]. In recent years, flavonoids have been the focus of much attention, and studies of their oncological effects over the last 10 years have shown that flavonoids can be used as precursor drugs to antitumor drugs.

3.2 Terpenoids

With isoprene as the basic structure, different ways of the first place connected are terpenoids. Currently, terpenoids in "medicinal and food" class of anticolorectal cancer traditional Chinese medicines mainly include ursolic acid, carotenoids, glycyrrhizic acid, porinic acid, ginsenoside, dandelion terpene alcohol, Ganoderma triterpenes, etc., which are found in "medicinal and food" class of traditional Chinese medicines, such as ursine, xiakouqiuqiang, licorice, poria, ginseng, dandelion and Ganoderma lucidum. "class of traditional Chinese medicine. Ursolic acid is a pharmacologically active pentacyclic triterpenoid, which can be extracted from medicinal plants, fruits and vegetables, and the main antitumor component of ume and Xiaku Cao is ursolic acid. Triterpenoids are one of the most critical chemical constituents in the plant kingdom, and about 20,000 different structures have been identified [39]. Abnormal activation of the Wnt/β-catenin signaling pathway is an important factor involved in the pathogenesis of colorectal cancer [40]. In ex vivo experiments, after intervening with ursolic acid in human colorectal adenocarcinoma cells (SW620) and a mouse subcutaneous SW620 graft tumor model, it was found that ursolic acid induced apoptosis and inhibited the proliferation and migration of colorectal cancer cells, and also inhibited the growth of xenografts by decreasing the Wnt/β-catenin signaling cascade response [41]. Dietary carrot and terpenoid carotenoid intake has been found to reduce the risk of colorectal cancer in several clinical studies [42][43][44]. Glycyrrhizic acid can inhibit the proliferation, invasion and migration of colorectal cancer cells and induce apoptosis by regulating SIRT3 [45].

3.3 Polysaccharides

Dietary plant polysaccharides are one of the major sources of natural polysaccharides with significant anticancer activity and potential developmental value in food and medicine. Plant polysaccharides fight tumors by enhancing immune regulation, inhibiting tumor cell growth, and preventing tumor cell invasion and metastasis, among other mechanisms [46]. Compounds such as licorice polysaccharide, kombucha polysaccharide, jujube polysaccharide, ginger polysaccharide, lycium polysaccharide, poria polysaccharide, platycodonopsis polysaccharide, galangal polysaccharide, flavonoid polysaccharide, astragalus polysaccharide, etc. are active ingredients in "medicinal food" class of anticolorectal cancer traditional Chinese medicine. Ginger polysaccharide (UGP1) inhibits the growth of human colon cancer by potentially promoting apoptosis of tumor cells and modulating the activity of the immune system [47]. The relationship between the anti-tumor effects of glycyrrhiza polysaccharides and the intestinal microbiota was verified in depletion of intestinal flora and fecal transplantation experiments, and when fecal transplantation experiments were carried out, it was found that transplantation of feces from glycyrrhiza polysaccharides-treated mice to other mice prevented the growth and spread of the tumors to a certain extent [48]. Licorice polysaccharides have also been shown to be immunologically related to colorectal cancer. Ayeka et al. found in their study that licorice polysaccharides inhibited the proliferation of colorectal cancer cells CT26 in a dose-dependent manner while increasing the expression of IL-7, which is known to be an antitumor immunomodulationrelated anticancer gene [49]. Tao et al. found that dendrobium polysaccharides in a study based on a zebrafish xenograft model, Astragalus polysaccharides and mushroom polysaccharides could all inhibit the growth of HT29 cells, and Dendrobium polysaccharides had the most significant effect [50]. Polysaccharides have complex and diverse anti-tumor mechanisms, especially in the regulation of the tumor immune microenvironment, which is getting more and more attention and has a broad application prospect.

4. Anti-colorectal Cancer Mechanism of Action

4.1 Inducing Apoptosis and Autophagy of Tumor Cells

There are many mechanisms of Chinese medicine against colorectal cancer, and inducing apoptosis is one of the important ones. Apoptosis is an orderly and programmed cell death, which is an active death process triggered by specific gene regulation. For cancer cells, if the apoptotic process is interrupted, it means that the cancer will get further development and and spread, the core mechanism of apoptosis is the caspases family, and there are three pathways that can activate the caspases family, the most common pathways are the intrinsic (or mitochondrial) and extrinsic (or death receptor) pathways of apoptosis, and in addition to endoplasmic reticulum pathway [51]. Cellular autophagy is not only an important mechanism to maintain normal cellular life activities, but also a special means for cells to cope with extreme environments, and the process of autophagy is generally divided into four steps, namely initiation, extension, closure and degradation [52]. Several studies have indicated that Platycodonopsis saponin D plays an important role in the induction of apoptosis, including the regulation of Bcl-2 family proteins, mediation of ROS generation, obstruction of the cell cycle, activation of the MAPK-related signaling pathway, inhibition of Akt activity, and inhibition of telomerase activity, among other pathways [53]. Arti Nile et al. demonstrated in an in vitro cellular model that treatment with cinnamon extract rich in cinnamaldehyde inhibited the proliferation and migration ability of colon cancer cell lines Hct-116 and Ht-29 cells and found that the number of cells in the sub-G1 phase was significantly increased, and the G2 phase was blocked; lastly, treatment with cinnamon extract through junction led to the activation of apoptosis-associated proteins calpain I and PARP [54].

4.2 Inhibition of Tumor Growth

The quality of life and prognosis of tumor patients depend most importantly on controlling the spread and growth of tumor cells. Research results point out that certain herbal extracts can exert therapeutic effects, such as inhibiting tumor growth, by adjusting the amount of intestinal flora. Colon cancer cells (CT-26) were used to establish a hormonal mouse model as a research object, and in order to deeply investigate the role of intestinal microorganisms in the anticancer effect of licorice polysaccharides, a fecal transplantation test was designed, in which licorice polysaccharides lost their inhibitory effect on tumor growth when the intestinal microbiota was depleted. By performing fecal transplantation experiments, it was found that transplanting the feces of mice treated with licorice polysaccharides to other mice could slow down the growth and metastasis of tumors to a certain extent, and in summary, licorice polysaccharides can inhibit colorectal cancer growth by regulating the intestinal flora [55]. Immune cells play an extremely important role in inhibiting tumor growth, which can recognize and remove tumor cells in a specific manner without causing harm to normal cells. Administration of dandelion polysaccharide not only significantly increases the activity of NK cells, but also stimulates the proliferation of lymphocytes and increases the proportion of lymphocyte subpopulations. Therefore, dandelion polysaccharide has the effect of protecting and enhancing the function of lymphocytes, alleviating the impact caused by tumors on the function of the immune system, and effectively inhibiting the growth of tumors in vivo [56].

4.3 Blocking the Proliferation Cycle of Tumor Cells

Cells produce new cells under certain conditions to replace dead senescent cells, which is cell proliferation. Blocking the proliferation cycle of tumor cells in patients is also stopping tumor growth to a certain extent. Natural lignans isolated from Honeysuckle are considered as potential inhibitors of Wnt/ β -catenin signaling and the antiproliferative activity of this natural compound was also found to be associated with the inhibition of the Wnt/ β -catenin-mediated signaling pathway in human colon cancer cells [57]. In a human colorectal adenocarcinoma cell (SW620) model, ursolic acid was found to block the cell cycle of SW620 cells in the G0/G1 phase to achieve an anticolorectal cancer effect [41].

4.4 Improvement of Side Effects Caused by Chemotherapy in Colorectal Cancer

Chemotherapy is widely used in the treatment of colorectal cancer patients, and it plays an important role in improving the prognosis of patients, but it also has side effects such as nausea, vomiting, diarrhea, oral mucositis, and neurotoxicity, which reduces the quality of life of patients. "Medicinal drugs have shown unique clinical efficacy in ameliorating these side effects, and therefore they are used as adjuvants to ameliorate colorectal cancer side effects.

Oxaliplatin is often used to treat locally advanced and metastatic colon or rectal cancer. However, one of the side effects of oxaliplatin, neuropathy, seriously affects the quality of life of patients. The most common symptoms of neuropathy are sensory abnormalities, sensory disturbances, pain and sensory loss. Different astragalus extracts have been shown to improve oxaliplatin-induced neuropathy without affecting the anticancer effects of chemotherapy [58]. Curcumin (curcumin) is the main phenolic compound of turmeric. Curcumin was found to attenuate oxaliplatin-induced neurotoxicity by reducing high plasma neurohypocretin in rats [59].

Fluorouracil and irinotecan are among the most commonly used drugs in patients with advanced colorectal cancer, and intestinal mucositis is one of its common side effects [60]. Tonify Zhong Yi Qi Tang (补中益气汤) with Astragalus as the monarch is a representative formula for tonifying qi and promoting yang. Gou et al. found that Tonify Zhong Yi Qi ameliorate fluorouracil-induced intestinal Tang mav mucositis by inhibiting the up-regulation of inflammatory factors and blocking apoptosis of intestinal mucosal epithelial cells [61]. Nausea and vomiting is one of the common side effects in patients receiving chemotherapy. Ginger is the most widely used supplement to prevent or ameliorate this side effect. Ginger has been used in the treatment of malignant and excessive flatulence after chemotherapy as early as 2007 [62]. Over the years, researchers have been working on chemotherapy-induced side effects, and there is a great potential for research on the toxicity-reducing and potentiating effects of "medicinal food-like" Chinese medicines on chemotherapeutic drugs.

5. Conclusion

In conclusion, Chinese medicines from the same source of food and medicine have great potential in the fight against colorectal cancer. They can interfere with carcinogenesis and regulate the tumor immune microenvironment, as well as reduce the proliferation, migration and invasion of colorectal cancer cells, and most importantly, they can be used as adjuvants to ameliorate the side effects caused by antitumor drugs and to increase their sensitivity. In addition, terpenoids, flavonoids, polysaccharides and other compounds in the "medicinal food" class of anticolorectal cancer traditional Chinese medicines induce apoptosis and autophagy by regulating various signaling pathways, such as MAPK, PI3K/Akt/mTOR, miR-3283p/STAT3, etc., which can block the proliferation cycle of tumor cells, inhibit the growth of tumors and regulate the immune microenvironment of tumors. regulate tumor immune microenvironment.

TCM dietary therapy against colorectal cancer has great potential both in basic experiments and clinical trials, and has many significant advantages over Western medicine in preventing and assisting in the treatment of colorectal cancer, such as fewer toxic side effects and the ability to be taken for a long period of time. Under the theoretical guidance of traditional medicine, improving immunity and nutritional status of colorectal cancer patients through reasonable diet, improving patients' quality of life, and preventing colorectal cancer from its origin is the fundamental way to fight against colorectal cancer. As low-toxicity natural botanicals, "medicinal food" type of colorectal cancer Chinese medicines have broad research prospects in developing new types of colorectal cancer drugs and medicinal dietary formulas, and further studies are needed to find out whether the effect of anticolorectal cancer can be achieved by increasing the daily intake of colorectal cancer patients.

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