

Exploring food and medicine homology: potential implications for cancer treatment innovations

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ABSTRACT

The concept of food and medicine homology (FMH) is deeply embedded in traditional Chinese medicine and carries historical importance. The recent rigorous definition of FMH pertains to substances that exhibit both pharmacological and nutritional functions, and have active ingredients that are fundamentally non-toxic and appropriate for extended consumption. With the progression of modern biotechnology, the application of this concept in treating diseases has markedly expanded, and its intrinsic mechanisms have been examined in detail. The use of FMH substances in cancer therapy, as either a primary treatment or an adjuvant therapy, has paved the way to low-toxicity cancer treatments. This commentary examines the theoretical underpinnings, potential advantages, and practical applications of FMH substances in cancer prevention, treatment, and nutritional support enhancement. Advantages including low toxicity, long-term edibility, minimal adverse effects, and high patient compliance are discussed. Moreover, owing to its multicomponent and multitarget characteristics, FMH may provide novel opportunities for cancer therapy. Given the high lethality of cancer and associated ethical implications, current research should prioritize fundamental studies investigating potential FMH applications in cancer therapy. Concurrently, preliminary preclinical studies would be appropriate to establish a solid foundation for subsequent clinical trials.

Keywords: Food and medicine homology, Cancer, Pharmacological and nutritional functions, Hypotoxic treatment

1. INTRODUCTION

The concept of food and medicine homology (FMH), an extension of traditional Chinese medicine theory, has a rich historical context. With the growing focus on health and natural remedies, FMH research is attracting increasing attention. Recently, Cong has defined FMH as relating to substances with both pharmacological and nutritional characteristics, whose pharmaceutical

components are safe for long-term consumption [1]. Currently, the scope of FMH in the treatment of diseases comprises three main areas: herbal formulas exhibiting FMH properties, single edible herbs or foods, and bioactive compounds extracted from these sources. The integration of traditional medical knowledge with modern scientific techniques in these interdisciplinary studies has promoted the development of novel strategies for innovative disease treatment [2].

Commentary

Cancer remains a leading cause of death worldwide, and its high mortality rates, disease complexity, and treatment challenges place a substantial burden on healthcare systems. In particular, cancer metastasis, recurrence, and drug resistance pose major challenges in the treatment of tumor diseases. Additionally, tumor heterogeneity results in varying drug sensitivity among patients [3]. Currently, the main cancer treatment approaches involve surgery (such as tumor resection, organ transplantation, ablation therapy, cryosurgery, and laser therapy), chemotherapy, and radiation therapy. Although these strategies can yield favorable outcomes, they are also associated with considerable adverse effects and complications. Consequently, extensive research aimed at minimizing damage while increasing treatment effectiveness has focused on discovering novel therapeutic strategies, such as targeted therapy, immunotherapy, cell therapy, hormone therapy, nanotherapy, and stem cell transplantation [4]. The development of drugs with diminished toxicity and adverse effects is critical for improving patient prognosis and overall quality of life.

Growing evidence indicates the enormous potential of FMH substances for the treatment of various diseases; consequently, their anti-inflammatory, antioxidant, antiaging, and antibacterial properties are being actively explored. These substances also show promise in minimizing the low-toxicity adverse effects associated with cancer treatments [5]. These foods or herbs contain a wide array of natural compounds, including polyphenols, flavonoids, coumarins, vitamins, alkaloids, fatty acids, and minerals, each with unique functions. Some compounds exhibit antitumor properties or serve as standalone nutritional supplements [6]. For example, resveratrol and pterostilbene, among other bioactive compounds obtained from edible plants, have been shown to inhibit tumor progression by suppressing tumor cell proliferation, migration, and invasion, as well as inducing apoptosis, without exhibiting any toxicity to the human body. Other substances have shown enhanced effectiveness through mechanisms such as covalent coupling, self-assembly, or synergistic interactions. Polyphenols, monosaccharides, saponins, sterols, and terpenoids can self-assemble into nanoparticles, micelles, vesicles, and hydrogels through mechanisms including electrostatic interactions, hydrophobic interactions, and hydrogen bonding [7]. This self-assembly process significantly increases the efficacy of pharmaceutical drugs. Additionally, certain compounds have protective effects in the human body or mitigate the toxicity of other molecules. For example, several preclinical and clinical studies have shown that curcumin decreases the adverse effects of chemotherapy in patients. In addition, imperatorin enhances the antitumor activity of gemcitabine when used in combination therapy [8]. These results highlight that bioactive compounds from edible plants have excellent potential in tumor therapy and adjuvant tumor therapy (Figure 1).

2. FOOD AND MEDICINE HOMOLGY IN CANCER PREVENTION

The genesis and progression of tumors is a gradual process influenced by various risk factors, including genetic predisposition, lifestyle choices, and dietary habits. The gradual nature of progression highlights the importance of long-term cancer prevention strategies consisting primarily of lifestyle adjustments and regular screening for tumor markers [9]. Although pharmacological interventions have been found to effectively prevent tumor development, this strategy is influenced by factors such as safety, cost-effectiveness, and patient adherence, among other considerations. In contrast, FMH substances offer notable advantages, including high safety, low toxicity, affordability, excellent patient compliance, and suitability for prolonged use (Figure 2).

The American Institute for Cancer Research report "Diet, Nutrition, Physical Activity, and Cancer: A Global Perspective" highlights that proper dietary choices have greater efficacy than dietary supplements in cancer prevention. High-dose supplement trials have not consistently demonstrated the protective effects indicated by observational epidemiological studies, and some trials have even reported unforeseen adverse effects. The Global Diet and Cancer Research Report has identified 26 foods with anticancer properties. Although no single food can fully prevent cancer, a diet rich in vegetables, fruits, whole grains, legumes, and other plant-based foods has been found to significantly decrease cancer risk. This preventive approach aligns with the principle of FMH, emphasizing the role of nutrition in health maintenance and disease prevention.

Numerous fundamental and clinical studies have validated the effectiveness of FMH substances in preventing tumor development through diverse mechanisms. These substances enhance the immune response, thus increasing the body's ability to recognize and eliminate cancer cells. For example, *Astragalus membranaceus* (Fisch.) and *Codonopsis pilosula* (Franch.) have been shown to promote T lymphocyte proliferation and activation while increasing macrophage phagocytic activity. Additionally, through their antioxidant properties, they neutralize free radicals and decrease oxidative damage, thereby decreasing cancer risk. Notable examples include polyphenols from green tea and polysaccharides from *Lycium chinense* Miller. These substances also significantly contribute to tumor prevention by exerting anti-inflammatory effects and inhibiting inflammatory pathways associated with carcinogenesis. For example, berberine, extracted from *Coptis chinensis* Franch., inhibits the release of inflammatory mediators, whereas saponins from *Panax notoginseng* (Burkill) decrease the expression of inflammatory factors. The multitargeted actions of these compounds enable concurrent cancer prevention through various pathways, thereby providing a holistic approach to decreasing

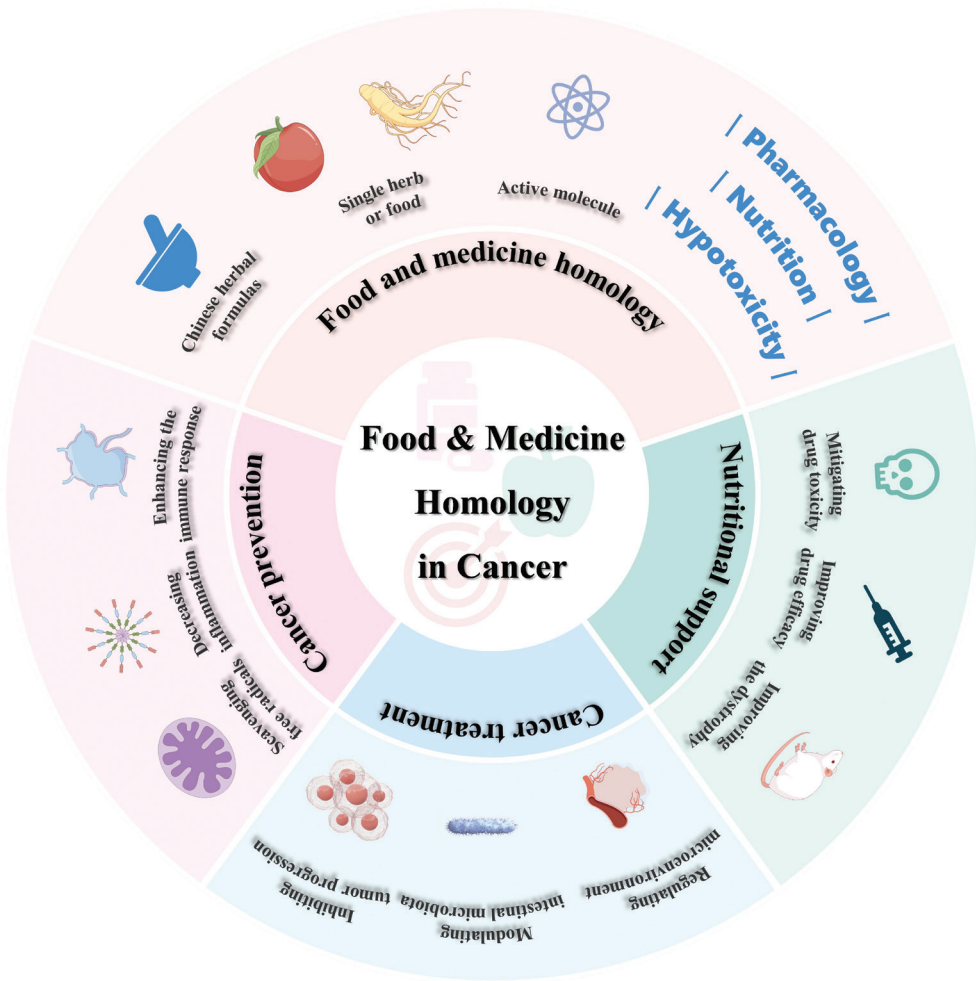


Figure 1 | Food and medicine homology in cancer.



Figure 2 | Advantages of food and medicine homology substances.

cancer risk and enhancing overall health. In addition, FMH substances have been found to prevent tumor development via the antimicrobiota pathway. Beyond several oncomicrobes that have been definitively identified from current epidemiological and experimental evidence, numerous microbial species have been found

to directly induce cancer [10]. Furthermore, a category of “complicit” microorganisms continually produce carcinogenic metabolites, thereby escalating tumorigenesis risk [11]. Certain FMH herbs that exhibit antimicrobiota functions have been found to effectively mitigate cancer risk through this mechanism. For example,

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glycyrrhizic acid and isoliquiritigenin from *Glycyrrhiza uralensis* Fisch. have shown significant efficacy in alleviating symptoms associated with *Helicobacter pylori*-associated gastritis, thus potentially decreasing gastric cancer risk [12, 13]. Additionally, curcumin and gingerol, active compounds in *Zingiber officinale* Roscoe, have been shown to eradicate *Helicobacter pylori* in murine models [14] (Figure 3).

3. FOOD AND MEDICINE HOMOLOGY IN CANCER TREATMENT

The use of FMH species in cancer treatment has gained widespread recognition, and patient acceptance of herbal and dietary interventions is increasing. Specific food components and traditional Chinese medicines exhibit notable anticancer properties that effectively

inhibit tumor progression through various mechanisms. Currently, 106 traditional Chinese medicines are classified as medicinal or edible substances, nearly 80 of which have been demonstrated to have direct anticancer effects. These foods or herbs, when incorporated into cancer treatment plans, improve therapeutic outcomes and minimize toxicity, thus serving as a valuable complement to conventional cancer therapies. Although FMH bioactive compounds may exhibit lower antitumor effectiveness than traditional chemotherapeutic agents, their minimal adverse reactions have led to satisfactory results after dose escalation or extended treatment [15].

Beyond their direct antitumor effects and provision of essential nutrients, these species support the balance of the intestinal microbiota and positively influence intestinal health. These aspects contribute to the effectiveness of the treatment and nutritional

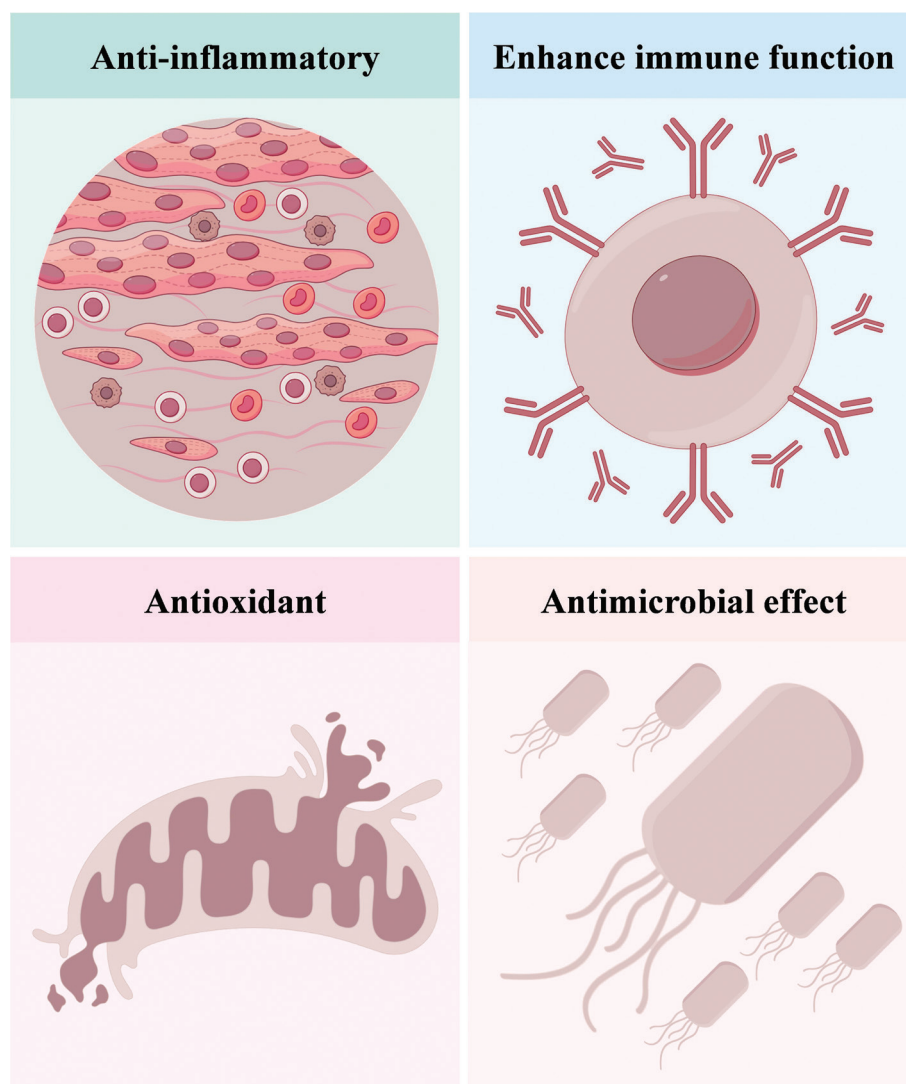


Figure 3 | Food and medicine homology substances for the prevention of cancer.

supplementation. For example, administration of the dietary fiber *Ganoderma lucidum* polysaccharides significantly decrease the incidence of cancer induced by azoxymethane/dextran sulfate sodium through increasing the abundance of Firmicutes and decreasing the abundance of Bacteroidetes. Additionally, certain natural products derived from food have been found to modulate cytokine secretion and surface marker expression in $\gamma\delta$ T cells, thereby increasing tumor cell recognition ability and cytotoxic ability. A growing body of evidence suggests that various dietary therapies might have antitumor benefits [16]. A phase I clinical trial has revealed that a serine/glycine-free diet enhances antitumor immunity via inhibition of tumor metabolism and modulation of the immune microenvironment. Furthermore, the immune escape mechanism facilitated by PD-L1 expression suggests that combining a serine/glycine-free diet with immune checkpoint inhibitor treatment may increase therapeutic efficacy [17]. These studies underscore the potential roles of FMH substances in enhancing immunotherapy effects.

FMH substances have notable potential in cancer treatment, and their multitarget, multicomponent, and multipathway capabilities facilitate systemic therapeutic effects. Comprehensive research on the bioactivity and mechanisms of these natural compounds might promote the development of new strategies and methods for cancer therapy (Figure 4).

4. FOOD AND MEDICINE HOMOLOGY IN ENHANCING NUTRITIONAL SUPPORT

Nutrition plays a crucial role in human health and is particularly important for patients with cancer, who often experience decreased intake and absorption of essential nutrients [18]. Moreover, the metabolic demands of tumor growth necessitate greater energy and nutrient availability than required by normal tissues. This imbalance exacerbates energy expenditure and worsens

malnutrition in patients with cancer. Nutritional support has been found to greatly improve treatment outcomes and increase survival rates in patients with cancer [19].

Schipper has emphasized that successful cancer treatment is not based solely on complete tumor regression. The main factor in effective oncological therapy is the body's response, thus emphasizing the importance of the active role of the immune system in fighting cancer [20]. Therefore, enhancing overall immune function in patients is essential. Nutritional supplementation during cancer treatment should be aimed at activating the body's innate anticancer mechanisms and increasing therapeutic effectiveness. The use of FMH substances as nutritional supplements can improve patients' nutritional status, thereby strengthening their immune function and anticancer ability. Moreover, these substances can increase patients' tolerance to treatment and mitigate associated toxic effects. Ideally, the medicinal components of FMH substances effectively inhibit tumor progression while bioactive molecules with nutritional functions enhance overall human nutrition (Figure 5).

5. CONCLUSION AND PERSPECTIVE

Overall, FMH herbs can play major roles in tumor prevention and treatment, by enhancing patient immunity and providing nutritional support. Given their low toxicity, these substances can be consumed over extended periods and elicit minimal adverse effects. Moreover, their multicomponent and multitarget nature may enable novel opportunities for tumor therapy. Given the high mortality associated with tumor diseases, conducting clinical research on the therapeutic effects of FMH substances is highly challenging. Although several clinical studies have examined the antitumor efficacy of traditional Chinese medicines, research on FMH substances remains exceptionally scarce. To date, only a limited number of clinical trials have examined the antitumor effects of active compounds derived from FMH herbs. Therefore, further basic research in this area should be



Figure 4 | Food and medicine homology substances for the treatment of cancer.

Commentary

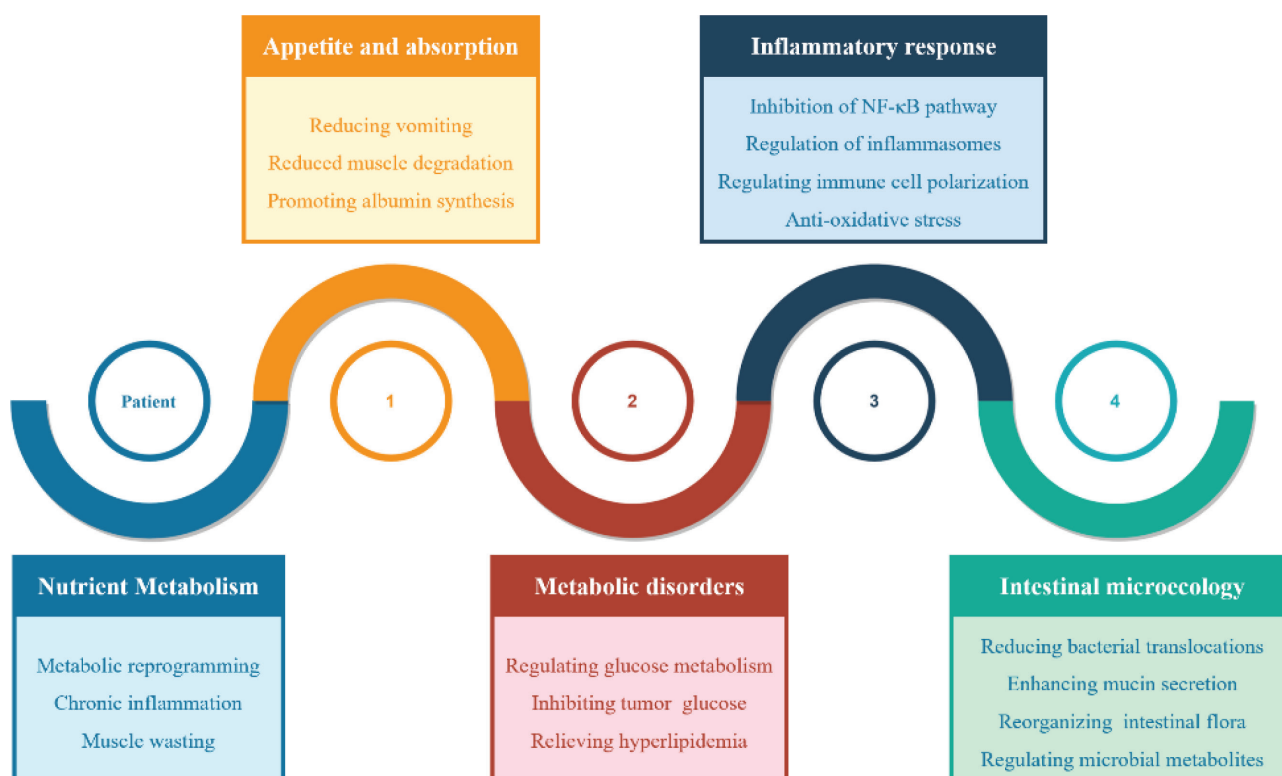


Figure 5 | Food and medicine homology substances for nutritional support.

prioritized. Research should focus on these substances' antitumor effects as well as their nutritional functions, and should clarify the contributions of their nutritional properties to therapeutic outcomes. Concurrently, toxicity findings must be validated through both *in vitro* and *in vivo* experiments. Advanced analytical testing technologies may be used to identify key active ingredients and their respective functions, thus deepening understanding of the chemical reactions, self-assembly processes, or synergistic interactions among functional molecules. The application of machine learning and artificial intelligence will facilitate the exploration of relationships among components, biological targets, and pathways through systems biology and complementary experimental approaches. Because of ethical concerns, conducting clinical trials on FMH substances for tumor treatment is frequently challenging and necessitates use of a substantial number of preclinical models to investigate clinical potential. The use of patient-derived models, such as patient-derived organoids, explants, and xenografts, will increase the clinical relevance of research and provide insights with enhanced applicability to real-world patient scenarios.

DECLARATION OF COMPETING INTERESTS

The authors declare that they have no conflicts of interest.

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