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RESEARCH ARTICLE

THE INFLUENCE OF FUNCTIONAL FOODS IN THE TREATMENT OF GASTROINTESTINAL CÂNCER

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ABSTRACT

The efficacy of functional foods in stages of gastrointestinal cancer is evidenced by compounds such as prebiotics, probiotics, antioxidants, phenolic compounds, and dietary fibers. Objective: To evaluate the influence of functional foods on the treatment of gastrointestinal cancer. Methodology: This was a bibliographic study of an exploratory-descriptive type with a qualitative approach. The data collection began with a bibliographic survey conducted through research of scientific productions on the proposed theme, covering the period from 2014 to 2024. The literature search was carried out in the following databases: Latin American and Caribbean Health Sciences Literature (LILACS) and PubMed. It is noteworthy that the LILACS and BDENF databases were consulted through the Virtual Health Library (VHL). The searches were conducted using the Descriptors: Intestinal Neoplasms, Functional Foods, and Gastrointestinal Cancer, in Portuguese and English, with the aid of the Boolean operator "AND". Results and Discussion: Functional foods have chemopreventive properties, inhibiting the proliferation of cancer cells and promoting apoptosis. They are most effective in the early stages of the disease and may include probiotics and prebiotics to maintain intestinal health and reduce the adverse effects of chemotherapy. They also modulate the microbiome, improving the efficacy of treatments and aiding in the recovery of microbial diversity during oncological treatment. Conclusion: Dietary strategies that include prebiotics, probiotics, polyphenols, and fibers can optimize therapeutic outcomes and improve the quality of life of patients with gastrointestinal cancer.

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INTRODUCTION

Functional foods have gained prominence as allies in combating chronic diseases, including gastrointestinal cancer. These foods, rich in bioactive compounds such as fibers, polyphenols, and short-chain fatty acids (SCFAs), possess properties that go beyond basic nutrition, playing a crucial role in modulating gut health and the immune system. Recent studies indicate that a diet rich in functional foods can aid in the prevention and treatment of neoplasms by improving gut microbiota, reducing inflammation, and promoting tumor cell apoptosis (MOLDANDO, 2017; FIBERS, 2023). Specifically, in the case of gastrointestinal cancer, the interaction between gut microbiota and functional foods proves critical. The fermentation of dietary fibers by gut bacteria generates SCFAs, such as butyrate, which not only strengthens the intestinal barrier but also regulates the immune system and inhibits tumor cell growth. Additionally, prebiotics and probiotics have been shown to restore microbial balance, increasing diversity and reducing cancer-associated gut dysbiosis (PROBIOTICS, 2015; REALIZATION, 2021).

Epidemiological data show that Western diets high in fats and low in fiber are associated with an increased risk of colorectal cancer, while populations with dietary habits rich in vegetables and whole grains exhibit lower rates of neoplasia. On the other hand, conventional treatments may impact gut microbiota, exacerbating adverse effects and reducing therapeutic efficacy. In this context, strategies that include functional foods emerge as a promising approach to mitigate these impacts and enhance treatments (DYSBIOSIS, 2018; RELATION, 2020). Clinical studies suggest that the use of probiotics can not only alleviate gastrointestinal symptoms associated with oncological treatments but also improve immune responses. For instance, certain strains of *Lactobacillus* and *Bifidobacterium* have been associated with modulating inflammatory responses and enhancing tolerance to chemotherapy. These findings underscore the importance of a personalized diet that considers individual microbial composition to optimize therapeutic outcomes (PREBIOTICS, 2014; CURCUMIN, 2019). The objective of this study is to analyze the influence of functional foods on the treatment of gastrointestinal cancer, focusing on efficacy in different disease stages and the role of gut

microbiota. The relevance of this investigation lies in the growing need for integrative approaches that complement effective treatments, improving patients' quality of life and enhancing therapeutic effects. The justification is grounded in extensive scientific evidence supporting the benefits of functional foods in cancer prevention and control, highlighting the importance of dietary strategies as an integral part of modern oncology (PROBIOTICS, 2015; FIBERS, 2023).

METHODOLOGY

This study was a bibliographic, exploratory-descriptive investigation with a qualitative approach, using data to develop the scientific article. Data collection was carried out through a bibliographic review of scientific productions on the proposed theme, covering the period from 2010 to 2023. The inclusion criteria for selecting the contents were full-text publications related to the theme, documents, regulations, health entity guidelines on the topic, and articles published in Portuguese, English, and Spanish. Exclusion criteria encompassed articles unrelated to the theme, duplicate materials, incomplete documents, debates, reviews, abstracts, and materials unavailable in full. The literature search was conducted in the following databases: PubMed, Virtual Health Library (VHL), Scientific Electronic Library Online (SciELO), and ScienceDirect. The LILACS and BDENF databases were accessed via the Virtual Health Library (VHL). The searches employed the Health Sciences Descriptors (DeCS), including terms such as Gastrointestinal Cancer, Gut Microbiota, and Functional Foods, in Portuguese and English, with the aid of the Boolean operators “AND” and “OR.”

The methodology adopted for this study began with the careful selection of keywords in the DeCS, followed by searches across various indexed databases. Using both the keywords and their alternative terms, tables were prepared containing all relevant articles related to the searches with the descriptors and alternative terms in each database consulted. Duplicate articles were excluded, and a selection by title relevance was conducted. After this screening, the selected articles underwent abstract readings, and those meeting the relevant inclusion criteria were subjected to exhaustive reading. For a comprehensive analysis of the selected articles, three discussion axes were outlined based on the study's specific objectives:

- The efficacy of functional foods in different stages of gastrointestinal cancer.
- Dietary strategies based on functional foods.
- The relationship between gut microbiota and functional foods.

These questions guided the reading of the selected articles, providing a conceptual framework for the critical and in-depth analysis of the information contained within. The responses obtained for each question from the exhaustive article readings formed the basis for writing the results and conducting the discussion. This structured and meticulous methodology enabled a systematic and well-founded investigation of relevant literature, reinforcing the validity and robustness of the results presented in this scientific study.

RESULTS AND DISCUSSION

Efficacy of Functional Foods in Different Stages of Gastrointestinal Cancer: The consumption of dietary fibers has been widely associated with a reduced risk of colorectal cancer (CRC), as demonstrated by numerous epidemiological studies. This protective relationship can be explained by physiological and metabolic mechanisms, such as fibers' ability to bind to bile acids in the intestine, reducing their reabsorption and preventing the formation of secondary carcinogenic compounds. Moreover, fiber fermentation by gut microbiota produces short-chain fatty acids (SCFAs), such as butyrate, which possess anticancer properties. Butyrate induces apoptosis in tumor cells, regulates gene expression, and attenuates local inflammatory processes. Fibers also modulate gut microbiota, favoring beneficial bacteria such as *Lactobacillus* and *Bifidobacterium*, which help maintain intestinal barrier integrity and microbial balance, reducing the risk of chronic inflammation and cancer (Celiberto F, *et al*., 2023; Otles S, *et al*., 2014).

Probiotics play a crucial role in gut health and disease prevention, including CRC. They can alter gut microbiota composition, strengthen the intestinal barrier, and reduce inflammation—factors linked to carcinogenesis. Probiotics such as *Lactobacillus* and *Bifidobacterium* produce SCFAs that inhibit tumor cell proliferation and promote apoptosis. Additionally, these microorganisms enhance immune responses, creating a less hospitable environment for cancer development. Studies suggest that probiotics can increase the efficacy of conventional therapies, such as immunotherapy and chemotherapy, while reducing side effects like diarrhea and mucositis. Probiotics also reduce inflammatory processes, modulate cytokines, and aid in microbiota recovery after disruptions caused by antibiotics (Nami Y, *et al*., 2023; Gao G, *et al*., 2021; Eslami *et al*., 2019). Beyond probiotics, postbiotics—products derived from microbial fermentation—exhibit immunomodulatory and anti-inflammatory effects that may help prevent gastrointestinal diseases, including cancer. They strengthen the intestinal barrier, reduce chronic inflammation, and restore microbiota balance, critical factors in carcinogenesis. Similarly, bioactive compounds from functional foods, such as phytochemicals, lignans, and polyphenols, play important roles in CRC prevention and treatment. These compounds possess antioxidant and anti-inflammatory properties, help reduce oxidative stress, and modulate cellular pathways associated with tumor progression. For example, pectin induces apoptosis and regulates inflammation in CRC, while compounds like curcumin have demonstrated efficacy across multiple critical molecular pathways in cancer (Jastrząb, *et al*., 2021; Greiner, *et al*., 2014; Yu *et al*., 2019).

Curcumin, found in turmeric, is one of the most studied bioactive compounds in CRC. It regulates tumor progression by inhibiting inflammatory pathways such as NF-κB and COX-2 and activating apoptotic processes. Research also highlights advanced curcumin formulations, such as deuterated curcuminoids, which offer greater bioavailability and potency. Combining curcumin with conventional treatments like chemotherapy has been shown to significantly increase patient survival and reduce adverse effects. Other compounds, such as resveratrol, zingerone, and thymol, have also demonstrated anticancer efficacy by inhibiting cellular signaling pathways and promoting apoptosis. These compounds are emerging as valuable tools for chemoprevention and treatment of gastrointestinal cancer (Ismail *et al*., 2019; Laali *et al*., 2019;

Wu *et al*., 2019). Functional foods, including flaxseed, oat bran, soy, and phenolic-enriched lettuces, exhibit notable anticancer properties. Components in these foods, such as lignans, beta-glucans, and phenolics, modulate gut microbiota, control inflammation, and promote cellular apoptosis. For instance, flaxseed lignans have antioxidant and antiproliferative properties, while beta-glucans act as immunomodulators and antitumor agents. Studies also show that reducing nitrogen availability in plants can increase the concentration of bioactive compounds like phenolics, which inhibit tumor cell proliferation. These findings underscore the importance of functional foods in CRC prevention and management (Mendonça *et al*., 2018; Zhou *et al*., 2019; Parikh *et al*., 2019).

The role of gut microbiota in modulating conventional therapies is also significant. A balanced microbiome can enhance the efficacy of immunotherapies, such as PD-1 blockade, by improving T-cell activation and antitumor responses. Beneficial microorganisms like *Akkermansia muciniphila* have been associated with better therapeutic outcomes. Conversely, the microbiota can impact treatment toxicity, such as in the case of irinotecan, a chemotherapeutic drug whose reactivation by microbiota can cause severe toxic effects. Strategies like the use of probiotics and prebiotics can mitigate these adverse effects and improve therapy effectiveness (Cho; Chinnapen, 2018; Guthrie, *et al*., 2019). Integrating functional foods, probiotics, and nutraceuticals into CRC management offers a promising approach to improving gut health, reducing inflammation, and enhancing the effects of conventional therapies. Beyond their anticancer properties, these components demonstrate additional benefits, such as reducing treatment side effects and improving patients' quality of life. Future studies should focus on optimizing these interventions to expand their clinical application and maximize their therapeutic benefits (Yang, *et al*., 2017; Mendonça *et al*., 2018; Pyo, Yeonhee *et al*., 2024).

Dietary Strategies in the Management and Prevention of Colorectal Cancer: The Role of Fiber, Probiotics, and Bioactive Compounds: A diet rich in fiber plays a central role in the prevention and treatment of colorectal cancer (CRC), contributing to gut microbiota regulation and the production of short-chain fatty acids (SCFAs), such as butyrate. This compound has antiproliferative properties, regulating the expression of genes associated with cell survival and promoting apoptosis in cancer cells. Additionally, butyrate strengthens the intestinal barrier, reducing the translocation of toxins and inflammatory substances, factors that increase cancer risk. Fiber also acts as a prebiotic, fostering beneficial microbiota and preventing dysbiosis—a microbial imbalance linked to various diseases, including CRC. Another crucial contribution of fiber is regulating intestinal transit, which reduces the colon cells' exposure time to carcinogenic agents (Celiberto F, *et al*., 2023). Probiotics, alongside fiber, represent another promising nutritional strategy. Microorganisms such as *Lactobacillus* and *Bifidobacterium* modulate gut microbiota, promoting SCFA production and inhibiting enzymes that activate carcinogenic compounds. They strengthen the intestinal barrier, reduce inflammation, and improve immune responses, creating an environment less conducive to cancer development. Studies indicate that probiotics can alleviate side effects of oncological treatments, such as chemotherapy, by reducing toxicity and complications like diarrhea and mucositis. Furthermore, probiotics enhance the effectiveness of immunotherapy by modulating the immune system, particularly in patients undergoing PD-1 blockade treatments (Nami Y, *et al*., 2023; Varsha KK, *et al*., 2021; Gao G, *et al*., 2021). Supplementation with bioactive compounds, such as curcumin, polyphenols, and omega-3 fatty acids, has also proven effective in CRC management. Curcumin, for example, targets multiple molecular pathways, inhibiting inflammation and promoting tumor cell apoptosis. Studies have shown that combining curcumin with chemotherapeutics enhances treatment efficacy and reduces side effects. Polyphenols, found in fruits, vegetables, and teas, modulate cancer-related cellular signaling pathways and exhibit antioxidant and anti-inflammatory effects. Omega-3 fatty acids, such as EPA, can inhibit the growth of cancer stem cells, making them valuable as preventive agents and complementary components in oncological therapies (Yang, *et al*., 2017; Mbese, Zintle *et al*., 2019; Vasudevan *et al*., 2014).

Functional foods, including flaxseed, soy, olive oil, and fermented soy milk, also play a significant role in CRC prevention. Flaxseed, rich in lignans and omega-3 fatty acids, regulates inflammation, promotes cellular apoptosis, and strengthens gut microbiota. Olive oil, a component of the Mediterranean diet, is a source of polyphenols and monounsaturated fatty acids that modulate inflammation and exhibit antioxidant properties. Fermented soy milk, enriched with prebiotics and probiotics, promotes bioactive compound production, regulates microbiota, and reduces inflammation, offering both preventive and therapeutic benefits (Parikh *et al*., 2019; Borzì *et al*., 2018; Le, B *et al*., 2020). Gut microbiota modulation through fecal transplants and personalized dietary interventions has emerged as a therapeutic strategy in CRC management. Diets rich in fiber, probiotics, and bioactive compounds not only improve gut health but also enhance conventional treatments such as chemotherapy and immunotherapy by reducing inflammation and strengthening immune responses. These integrative approaches highlight the importance of diet as an adjunctive tool in controlling colorectal cancer and improving the quality of life for oncology patients (Cho; Chinnapen, 2018; Eslami *et al*., 2019).

The Interaction Between Functional Foods, Gut Microbiota, and Systemic Health: An Approach to Colorectal Cancer Prevention and Management: The interaction between gut microbiota and functional foods results in the generation of bioactive metabolites that play fundamental roles in gut and systemic health. Compounds such as fiber, polyphenols, and lignans are metabolized by gut bacteria, producing short-chain fatty acids (SCFAs) like butyrate, propionate, and acetate. Butyrate, in particular, is essential for maintaining intestinal barrier integrity, strengthening cellular connections, and reducing intestinal permeability. This metabolite possesses anti-inflammatory and anticancer properties, regulating the immune system, promoting tumor cell apoptosis, and inhibiting tumor proliferation. Furthermore, butyrate plays a role in the gut-brain axis, influencing mental health, reducing systemic inflammation, and contributing to neurotransmitter production (Celiberto F, *et al*., 2023; Maiuolo *et al*., 2024). Regular consumption of fiber- and polyphenol-rich foods, such as whole grains, fruits, vegetables, legumes, and seeds, promotes a diverse and balanced microbiota, enhancing SCFA production. Prebiotics and probiotics amplify these benefits by

nourishing beneficial bacteria and introducing new microorganisms to the gut. Probiotics like *Lactobacillus* and *Bifidobacterium* help modulate microbiota, promoting the production of bioactive compounds that prevent chronic inflammation and strengthen the intestinal barrier. Supplementation with probiotics, such as *Lactobacillus rhamnosus* Probio-M9, has been shown to increase microbial diversity, regulate intestinal metabolism, and improve the effectiveness of immunotherapies by boosting immunity and reducing inflammation (Nami Y, *et al*., 2023; Gao G, *et al*., 2021).

Dysbiosis, characterized by an imbalance in gut microbiota, is closely linked to colorectal cancer development. It can impair the effectiveness of treatments such as chemotherapy and immunotherapy, reducing the action of drugs like 5-FU. Dietary strategies incorporating prebiotics and probiotics help restore eubiosis by promoting microbial diversity and improving immune response. Probiotics not only reduce inflammation but also enhance the production of mucins that protect the intestinal barrier, minimizing the risk of infections and gastrointestinal complications (Yuan L, *et al*., 2018; Zhao *et al*., 2023). Bioactive compounds from functional foods, such as curcumin, polyphenols, and lignans, also play crucial roles in colorectal cancer prevention and management. Curcumin modulates gut microbiota, reduces chronic inflammation, and improves intestinal barrier integrity, enhancing the effects of conventional treatments like chemotherapy. Polyphenols, found in fruits, vegetables, and teas, are metabolized by microbiota into bioactive forms with antioxidant and anti-inflammatory properties. Lignans, present in flaxseed, are converted into enterolignans, which regulate hormonal and immune processes, contributing to reduced cancer risk and chronic inflammation (Ismail *et al*., 2019; Baldi, *et al*., 2023; Parikh *et al*., 2019).

Fermented foods, such as kefir and fermented soy milk enriched with prebiotics and probiotics, significantly contribute to gut health and cancer prevention. These foods promote the production of bioactive compounds, such as SCFAs, that strengthen the intestinal barrier, reduce inflammation, and modulate immune responses. Studies indicate that these products can inhibit tumor cell growth and improve the effectiveness of treatments for gastrointestinal cancer (Le, B *et al*., 2020; Sharifi *et al*., 2017). The interaction between gut microbiota and functional foods underscores the importance of personalized nutritional strategies for colorectal cancer prevention and management. By understanding the interactions between diet, microbiota, and metabolism, integrative approaches can be developed to optimize gut health, reduce inflammation, and enhance oncological treatments, promoting not only prevention but also improved quality of life for patients (Seidel *et al*., 2017; Yang, *et al*., 2017).

CONCLUSION

Functional foods play a vital role in the prevention and treatment of gastrointestinal cancer by modulating gut microbiota and influencing biological processes associated with the disease. Bioactive compounds such as fiber, polyphenols, and lignans, metabolized by intestinal bacteria, produce short-chain fatty acids (SCFAs) and other metabolites with anti-inflammatory, antioxidant, and anticancer properties. These interactions strengthen the intestinal barrier, reduce chronic inflammation, and enhance immune responses, inhibiting tumor progression. In prevention, functional foods promote a healthy gut environment and mitigate inflammation; in advanced stages, when combined with conventional therapies, they reduce side effects and improve quality of life. Personalized dietary strategies involving fermented foods, probiotics, and prebiotics integrate nutritional and therapeutic benefits. Thus, functional foods reinforce gut health and offer an integrative approach to managing gastrointestinal cancer, combining prevention, disease control, and treatment support. Further research is needed to explore molecular mechanisms and tailor therapeutic strategies for optimal outcomes.

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