Jurnal Gizi dan Kesehatan (JGK)
Volume 5 No.1, Juni 2025

ISSN 2829-2057
E-ISSN 2829-2014

KANKER DAN GIZI: TINJAUAN LITERATUR

CANCER AND NUTRITION: A LITERATURE REVIEW

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ABSTRAK

Kanker telah menjadi penyebab utama kematian di seluruh dunia, dengan lebih dari 18 juta kasus baru dan hampir 10 juta kematian terkait kanker setiap tahun. Seiring dengan kemajuan pemahaman kita tentang kanker, peran penting nutrisi dalam pencegahan, perkembangan, dan pengelolaan kanker menjadi semakin jelas. Tinjauan ini mengeksplorasi hubungan multifaset antara diet dan kanker, dengan fokus pada mekanisme di mana faktor diet dapat memengaruhi risiko kanker, termasuk peradangan, stres oksidatif, dan jalur metabolisme. Selain itu, ini menyoroti dampak berbagai nutrisi dan senyawa bioaktif yang ditemukan dalam makanan, seperti vitamin, mineral, dan fitokimia, pada pencegahan dan terapi kanker. Tinjauan ini juga meneliti pentingnya mengelola interaksi makanan-obat dalam pengobatan kanker, terutama dalam kaitannya dengan kemoterapi, terapi yang ditargetkan, dan imunoterapi, di mana enzim metabolik, seperti sitokrom P450, memainkan peran penting. Dengan mensintesis penelitian terbaru, ulasan ini menekankan perlunya strategi nutrisi yang dipersonalisasi untuk mengoptimalkan perawatan kanker dan meningkatkan hasil pengobatan, menggarisbawahi potensi nutrisi sebagai bagian integral dari pencegahan dan terapi kanker.
Kata kunci: Cyt-P450, Gizi, Interaksi Obat-makanan, Kanker, Rekomendasi diet

ABSTRACT

Cancer remains a leading cause of death worldwide, with over 18 million new cases and nearly 10 million cancer-related deaths each year. As our understanding of cancer advances, the critical role of nutrition in cancer prevention, progression, and management has become increasingly evident. This review explores the multifaceted relationship between diet and cancer, focusing on the mechanisms through which dietary factors can influence cancer risk, including inflammation, oxidative stress, and metabolic pathways. Additionally, it highlights the impact of various nutrients and bioactive compounds found in foods, such as vitamins, minerals, and phytochemicals, on cancer prevention and therapy. The review also examines the importance of managing food-drug interactions in cancer treatment, particularly concerning chemotherapy, targeted therapies, and immunotherapies, where metabolic enzymes, such as cytochrome P450, play a significant role. By synthesising the latest research, this review emphasises the need for personalised nutrition strategies to optimise cancer care and improve treatment outcomes, underscoring the potential of nutrition as an integral part of cancer prevention and therapy.
Keywords: Cancer, Cyt-P450, Drug-food Interaction, Dietary Recommendation, Nutrition

INTRODUCTION

Cancer remains one of the most prevalent and deadliest diseases globally, with over 18 million new cases and nearly 10 million cancer-related deaths reported annually (1). Despite significant advances in early detection and treatment, the global burden of cancer continues to rise. It is well-established that a complex interplay of genetic, environmental, and lifestyle factors, including nutrition, influences the risk of developing cancer. As such, understanding the role of nutrition in cancer prevention, treatment, and overall prognosis has become a critical area of research.

ISSN 2829-2057
E-ISSN 2829-2014

The relationship between nutrition and cancer is multifaceted. Diet can influence cancer development through various mechanisms, including modulation of inflammation, oxidative stress, cellular metabolism, and epigenetic changes. Certain dietary patterns, such as the Mediterranean diet, and specific nutrients, including vitamins, minerals, and bioactive compounds, have been shown to either increase or decrease cancer risk (2). Furthermore, during cancer treatment, nutritional support is essential in managing side effects of therapies such as chemotherapy, radiotherapy, and immunotherapy, which often lead to malnutrition, weight loss, and reduced quality of life (3).

In recent years, emerging research has highlighted the potential of personalised nutrition, considering factors such as genetic makeup, microbiome composition, and metabolic profile, to optimise cancer prevention and treatment outcomes. Understanding the molecular mechanisms by which nutrition influences cancer biology is crucial for the development of targeted interventions. This review aims to provide an in-depth analysis of the current body of evidence regarding the role of nutrition in cancer. We will explore the molecular and cellular pathways affected by diet, the impact of various nutrients on cancer prevention and therapy, and the therapeutic potential of nutritional interventions. By synthesising the latest findings, this review seeks to contribute to the growing body of knowledge that supports the integration of nutrition as a key component in cancer care.

THE ROLE OF NUTRITION IN CANCER DEVELOPMENT

Nutrition plays a crucial role in both the prevention and development of cancer. The foods we consume can influence cancer risk through multiple pathways, including altering gene expression, modulating inflammation, oxidative stress, and impacting the regulation of metabolic processes. Several studies suggest that dietary habits contribute to as much as 30-35% of cancer cases, highlighting the potential of dietary interventions in cancer prevention (4).

1. Modulation of Inflammation and Immune Response

Chronic inflammation is a key factor in the development of cancer. It can create an environment conducive to genetic mutations and the progression of tumorigenesis. Diets rich in anti-inflammatory foods, such as those high in omega-3 fatty acids, fruits, vegetables, and whole grains, have been shown to reduce the levels of pro-inflammatory cytokines and oxidative stress, both of which are linked to cancer risk (5). Conversely, diets high in processed foods, red meats, and refined sugars may promote inflammatory responses and increase cancer risk (6).

2. Antioxidant Defense and Oxidative Stress

Oxidative stress results from an imbalance between free radicals and antioxidants, leading to cellular damage. This oxidative damage can affect DNA, proteins, and lipids, contributing to mutations and promoting cancer development. Reactive oxygen species (ROS) are a major cause of this damage, and their accumulation has been associated with the initiation and progression of cancer. Nutrients with antioxidant properties, such as vitamins C and E, selenium, and polyphenols found in fruits, vegetables, and teas, can neutralise free radicals and protect cells from oxidative damage. These antioxidants can

ISSN 2829-2057
E-ISSN 2829-2014

mitigate the harmful effects of ROS by scavenging them, thus reducing cellular damage and lowering cancer risk (7,8).
A diet rich in antioxidants has been shown to reduce the risk of various cancers, including breast, colorectal, and lung cancer. For example, studies have found that dietary intake of vitamin C and E, both potent antioxidants, is inversely associated with the risk of developing colorectal cancer (9). Additionally, polyphenols, such as those found in green tea and berries, have demonstrated protective effects by modulating oxidative stress pathways and promoting the repair of oxidative damage (10). Therefore, a diet high in antioxidant-rich foods may provide protective benefits against the development of cancer by enhancing the body's ability to combat oxidative damage.

3. Impact on Metabolic Pathways and Cell Signalling
Nutrition can influence cancer development by modulating key metabolic pathways and cell signalling. For example, diets high in fibre have been shown to affect insulin and IGF (insulin-like growth factor) signalling, both of which are associated with cancer cell proliferation (11). Insulin resistance and high blood sugar levels, which are often exacerbated by poor dietary habits, can lead to an increase in insulin and IGF, stimulating the growth of cancer cells. Additionally, bioactive compounds such as resveratrol (found in grapes and red wine) and curcumin (from turmeric) have been identified to inhibit cancer cell proliferation through modulation of various molecular pathways, including NF-κB and Akt signalling (12).

4. The Role of Obesity and Metabolic Disorders
Obesity is a significant risk factor for several types of cancer, including breast, colorectal, and liver cancer. Adipose tissue, particularly visceral fat, is not only a storage site for excess energy but also an active endocrine organ that releases cytokines and adipokines, such as leptin and adiponectin, which influence cancer development (5,6). High levels of insulin and growth factors in obese individuals may create a pro-carcinogenic environment that promotes tumorigenesis. Furthermore, the inflammatory state associated with obesity can disrupt normal cellular functions and increase cancer risk.

5. Protective Role of Specific Nutrients
Several specific nutrients have been identified as having protective roles against cancer: Folate, found in leafy greens, legumes, and fortified grains, plays a role in DNA repair and the synthesis of nucleotides. A folate deficiency can lead to DNA damage and an increased risk of cancers such as colorectal and breast cancer (13). Vitamin D: There is substantial evidence linking low vitamin D levels with an increased risk of various cancers, including colorectal, breast, and prostate cancer. Vitamin D helps regulate cell growth, differentiation, and apoptosis (the programmed cell death of abnormal cells) (14) Phytochemicals: Phytochemicals, such as flavonoids, carotenoids, and glucosinolates, found in fruits and vegetables, have been shown to have anticancer properties by modulating pathways related to cell cycle regulation, apoptosis, and anti-inflammatory effects (15).

CANCER DRUGS, FOOD, AND METABOLIC ENZYMES

ISSN 2829-2057
E-ISSN 2829-2014

Cancer treatments, including chemotherapy, targeted therapies, and immunotherapies, rely heavily on the body's metabolic enzymes to process and clear the drugs. These enzymes, primarily cytochrome P450 (CYP) enzymes, are crucial in the metabolism of many drugs. However, food can influence the activity of these enzymes, leading to potential drug interactions that affect drug efficacy and safety. Understanding how cancer drugs interact with food and enzymes is essential for managing treatment and minimising side effects.

1. Metabolism of Cancer Drugs and Cytochrome P450 Enzymes.
Cytochrome P450 (CYP) enzymes are involved in the phase I metabolism of many drugs, including chemotherapy and targeted cancer therapies. The CYP enzymes, such as CYP3A4, CYP2D6, and CYP1A2, are responsible for the oxidation of drug molecules, which can either activate or deactivate the drugs. Variations in the activity of these enzymes can significantly impact the bioavailability and efficacy of cancer medications (16). Several factors, including genetic polymorphisms, age, liver function, and food intake, can modulate the activity of these enzymes. For example, the consumption of certain foods can induce or inhibit the activity of CYP enzymes, leading to either increased toxicity or reduced therapeutic effects of cancer drugs (17).

2. Food and Drug Interactions Involving CYP Enzymes
Grapefruit and CYP3A4 Inhibition Grapefruit is known to inhibit the CYP3A4 enzyme, one of the most important enzymes in drug metabolism. Grapefruit and its juice contain furanocoumarins that block CYP3A4 activity in the small intestine, leading to increased plasma concentrations of drugs metabolised by this enzyme. Many chemotherapy drugs, including *cyclophosphamide*, *paclitaxel*, and *docetaxel*, are metabolised by CYP3A4. The inhibition of this enzyme can cause higher drug levels, increasing the risk of toxicity (18, 19). Patients undergoing chemotherapy or treatment with CYP3A4-metabolised drugs are often advised to avoid grapefruit., Cruciferous Vegetables and CYP1A2 Induction Cruciferous vegetables, such as broccoli, cauliflower, and Brussels sprouts, contain compounds called glucosinolates, which can be metabolised to indole-3-carbinol and sulforaphane. These compounds have been shown to induce the activity of CYP1A2, an enzyme involved in the metabolism of various carcinogens and some chemotherapy drugs (20) . While this induction can enhance the metabolism of some drugs, it may reduce the effectiveness of certain chemotherapies, especially those requiring slower metabolism for optimal therapeutic effects. St. John's Wort and CYP3A4 Induction St. John's Wort, a herbal supplement commonly used for depression, is known to induce CYP3A4 and other CYP enzymes. This induction can increase the metabolism of chemotherapy drugs such as *imatinib* and *erlotinib*, reducing their effectiveness (21) .St. John's Wort should be avoided during cancer treatment, especially when using drugs that are CYP3A4 substrates, as it can lead to suboptimal drug concentrations and treatment failure.

3. Food and Drug Interactions with Other Enzymes
Milk and Calcium-Promoted Drug Interactions. Dairy products, especially those high in calcium, can interfere with the absorption of certain cancer drugs, including *bisphosphonates* (e.g., *zoledronic acid*), which are used to treat bone metastases. Calcium binds to the drugs, reducing their absorption and effectiveness (22). To avoid this

ISSN 2829-2057
E-ISSN 2829-2014

interaction, patients are often advised to take these drugs on an empty stomach and avoid consuming dairy products close to drug administration times.

Caffeine and Chemotherapy**.** Caffeine, found in coffee and tea, can affect the metabolism of certain chemotherapy drugs, including *cyclophosphamide* and *fluorouracil*. Caffeine is metabolised by CYP1A2, and its consumption may either increase or decrease the levels of chemotherapy drugs, depending on the drug's interaction with this enzyme (23). Patients should consult their healthcare provider regarding caffeine intake during chemotherapy.

4. Modulating Food Intake to Improve Cancer Treatment Outcomes

Modulating food intake can help optimise cancer treatment by supporting drug metabolism and reducing adverse effects. A diet rich in fruits, vegetables, and whole grains provides antioxidants, vitamins, and minerals that support the body's natural detoxification processes and immune system. Moreover, balanced nutrition can improve liver function, where many drug-metabolising enzymes are located. For instance, adequate levels of vitamin C and E can enhance antioxidant defence and reduce oxidative stress, potentially protecting normal cells from the side effects of cancer treatments (10,24).

CANCER DRUGS AND THEIR INTERACTIONS WITH FOOD

Cancer treatment often involves a combination of surgery, radiation therapy, and chemotherapy, with chemotherapy being one of the most common and widely used treatments. Chemotherapy and other cancer drugs, including targeted therapies and immunotherapies, can have significant interactions with food. These interactions can influence the effectiveness of the treatment, cause adverse effects, or affect the body's ability to metabolize the drugs properly. Understanding how food interacts with cancer medications is essential for optimizing patient care and ensuring better treatment outcomes.

1. Chemotherapy and Food Interactions

Chemotherapy drugs work by targeting rapidly dividing cancer cells. However, they can also affect healthy cells, especially those in the gastrointestinal (GI) tract, which leads to common side effects such as nausea, vomiting, and changes in appetite. Certain foods may exacerbate or alleviate these side effects, and some foods may alter the absorption or metabolism of chemotherapy drugs. Grapefruit and Chemotherapy Drugs. One of the most well-known food-drug interactions involves grapefruit and certain chemotherapy medications. Grapefruit contains compounds known as furanocoumarins, which can inhibit the cytochrome P450 enzymes (specifically CYP3A4) in the liver. These enzymes are responsible for metabolising many drugs, including some chemotherapy drugs such as *cyclophosphamide* and *taxanes* (e.g., paclitaxel). When grapefruit is consumed, it can increase the concentration of these drugs in the bloodstream, leading to an increased risk of toxicity (18). Patients undergoing chemotherapy should avoid grapefruit and other citrus fruits like Seville oranges.

High-Fat Meals and Chemotherapy**.** High-fat meals can also affect chemotherapy drug absorption. Some chemotherapy agents, like *docetaxel*, are lipophilic (fat-soluble), meaning their absorption is enhanced when taken with high-fat meals. This could lead to

ISSN 2829-2057
E-ISSN 2829-2014

unpredictable drug levels in the body. On the other hand, high-fat meals may increase the risk of nausea and other gastrointestinal side effects (24).

Dairy Products and Chemotherapy. Dairy products, especially in individuals who are lactose intolerant, can exacerbate gastrointestinal symptoms such as diarrhea, which is a common side effect of chemotherapy. Additionally, calcium-rich foods may interfere with the absorption of certain chemotherapy drugs, including *doxorubicin* and *methotrexate*. Therefore, it's advisable to monitor calcium intake when undergoing chemotherapy (25).

2. Targeted Therapies and Food Interactions

Targeted therapies, which are designed to specifically target cancer cells with minimal damage to normal cells, are increasingly being used to treat various cancers. Although these therapies are more selective than traditional chemotherapy, food interactions can still occur.

Tyrosine Kinase Inhibitors (TKIs) and Grapefruit**.** Similar to chemotherapy drugs, targeted therapies, especially tyrosine kinase inhibitors (e.g., *imatinib*, *gefitinib*), can also interact with grapefruit. The furanocoumarins in grapefruit can inhibit the enzyme CYP3A4, leading to higher drug concentrations and potentially increased toxicity (26) .

Curcumin and Targeted Therapies**.** Curcumin, the active component in turmeric, is known for its anti-inflammatory and potential anticancer properties. However, it may also interact with targeted therapies. Studies suggest that curcumin can inhibit the activity of certain cytochrome P450 enzymes involved in drug metabolism, possibly altering the efficacy of drugs like *erlotinib* (a drug used in non-small cell lung cancer) (27). Patients using targeted therapies should consult with their healthcare provider before taking curcumin or turmeric supplements.

3. Immunotherapy and Food Interactions

Immunotherapy uses the body's immune system to fight cancer. While food interactions with immunotherapy drugs are less studied than with chemotherapy and targeted therapies, some foods may affect the immune system and the way immunotherapies work.

High-Sugar Diets and Immunotherapy**.** A diet high in refined sugars and unhealthy fats can impair immune function. Since immunotherapy relies on boosting the immune system to target cancer cells, a poor diet may limit the effectiveness of treatment. Studies have shown that a high-sugar diet can alter the gut microbiome and reduce the immune system's ability to respond to immunotherapy (28).

Cruciferous Vegetables and Immunotherapy**.** Cruciferous vegetables, such as broccoli, cauliflower, and Brussels sprouts, are rich in glucosinolates, compounds known for their potential anticancer effects. These vegetables may support immune function and could potentially complement the action of immunotherapy by enhancing immune system activity (29) . However, patients on immunotherapy should still check with their healthcare team before making significant dietary changes.

4. General Nutritional Considerations for Cancer Patients

Cancer treatment often leads to nutritional challenges, including weight loss, muscle wasting (cachexia), and nutrient deficiencies. Some general dietary strategies that can support cancer patients during treatment include: Small, frequent meals: To combat loss of appetite and nausea. High-protein foods: To prevent muscle wasting and support tissue

ISSN 2829-2057
E-ISSN 2829-2014

repair. Hydration: Ensuring adequate fluid intake is crucial, especially when dealing with dehydration caused by chemotherapy side effects like diarrhea and vomiting. Avoiding alcohol: Alcohol can interfere with drug metabolism and exacerbate treatment side effects (30).

DIETARY RECOMMENDATIONS FOR CANCER PATIENTS

Foods to Consume:

Fruits and Vegetables: Aim for a wide variety of colourful fruits and vegetables, especially those rich in antioxidants like berries, citrus fruits, dark leafy greens, and cruciferous vegetables (broccoli, cauliflower, Brussels sprouts). These foods help combat oxidative stress and inflammation, which are critical factors in cancer progression and therapy side effects. **Lean Proteins**: Include sources of lean proteins, such as chicken, turkey, tofu, fish, eggs, and legumes. Protein is essential for maintaining muscle mass, especially during treatments like chemotherapy that can lead to muscle wasting. **Whole Grains**: Opt for whole grains like brown rice, quinoa, whole wheat bread, and oats. These provide fibre and nutrients that help regulate blood sugar levels, reduce inflammation, and promote gut health. **Healthy Fats**: Incorporate healthy fats, such as those found in avocados, olive oil, nuts, and seeds. Omega-3 fatty acids found in fatty fish like salmon, sardines, and mackerel are particularly beneficial for reducing inflammation and supporting immune function. **Hydration**: Drink plenty of fluids to stay hydrated, particularly water, herbal teas, and broths. Adequate hydration is essential during cancer treatment to prevent dehydration and alleviate some common treatment side effects like dry mouth and constipation. **Probiotic-rich Foods**: Fermented foods like yogurt, kefir, kimchi, and sauerkraut are rich in probiotics that can support gut health and the immune system, especially important during treatment when the body's natural microbiome can be disrupted (31).

Foods to Avoid**:**

Processed and Red Meats: Limit consumption of processed meats (such as bacon, sausages, and hot dogs) and red meats (such as beef, pork, and lamb). These foods are associated with an increased risk of certain cancers and can exacerbate inflammation in the body. High-Sugar and Refined Carbohydrates: Avoid foods high in refined sugars and simple carbohydrates, such as sugary snacks, soft drinks, and white bread. These can contribute to weight gain, insulin resistance, and inflammation, all of which can negatively impact cancer outcomes.

Alcohol: Limit or avoid alcohol intake, as it can interact with medications and interfere with the body's ability to process chemotherapy drugs. Alcohol consumption is also associated with an increased risk of various cancers, particularly breast, liver, and colorectal cancers (30,31).

Fried and Greasy Foods: Minimize the consumption of fried foods, as they are high in unhealthy fats and can contribute to weight gain, digestive issues, and inflammation. **Caffeine**: Although moderate caffeine consumption is generally safe, it should be limited

ISSN 2829-2057
E-ISSN 2829-2014

during certain cancer treatments like chemotherapy, where caffeine can interact with medications and increase side effects such as nausea or dehydration. **Dairy in Excess**: While dairy can provide calcium and protein, excessive consumption, especially in individuals who are lactose intolerant, may lead to gastrointestinal issues like bloating, diarrhoea, or gas. Some chemotherapy drugs can also interact with calcium, reducing the effectiveness of the treatment (32).

Eat Smaller, Frequent Meals:

Cancer treatments often cause appetite loss or nausea. To maintain adequate nutrition, try eating smaller, more frequent meals throughout the day rather than large ones. Focus on Easy-to-Digest Foods: If nausea or mouth sores are an issue, opt for soft, bland, and easy-to-digest foods like mashed potatoes, scrambled eggs, or smoothies. Avoid spicy, acidic, or hard-to-digest foods that might irritate the digestive system. Monitor and Adjust Diet for Specific Side Effects: Work with a dietitian to adjust your diet according to specific side effects of cancer treatment e.g., experiencing diarrhea, avoid foods that might worsen it like spicy or fatty foods; dealing with constipation, increase fiber and fluid intake (33).

CONCLUSION

In summary, nutrition plays a pivotal role in modulating cancer risk through various mechanisms, including inflammation, oxidative stress, metabolic pathways, and cellular signalling. A balanced diet rich in fruits, vegetables, whole grains, and healthy fats can offer protection against cancer, while poor dietary choices can increase the risk of developing cancer. Further research is needed to better understand the molecular interactions between nutrition and cancer, which may lead to more effective preventive and therapeutic strategies. Food and drug interactions are an important consideration during cancer treatment. Nutritional choices can influence the effectiveness of cancer therapies and help mitigate side effects. Cancer patients need to work closely with their healthcare team, including oncologists and dietitians, to develop a nutrition plan that optimises treatment outcomes. Understanding and managing food-drug interactions is a critical part of comprehensive cancer care.

Cancer drugs often require specific metabolic processes to reach their therapeutic potential. Food can modulate the activity of key metabolic enzymes like CYP450, impacting the efficacy and safety of cancer treatments. Understanding these interactions and adjusting the diet accordingly can enhance treatment outcomes and minimise adverse effects. Patients undergoing cancer therapy should work closely with their healthcare providers, including dietitians, to manage food-drug interactions and ensure optimal treatment efficacy.

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