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RESEARCH ARTICLE

DIETARY DETERMINANTS IN THE INITIATION AND PROGRESSION OF CANCER

Venkata Vijaya lakshmi[1], Antonydas[2], B Devasena [3] , Senthilkumar G P[4]* and B Nazreen [5]
[1]PERI Institute of Technology, Chennai - 48
[2]PERI College of Arts and Science, Chennai -48
[3]PERI College of Physiotherapy, Chennai -48
[4]PERI College of Pharmacy, Chennai -48
[5] PERI College of Nursing, Chennai -48

*Corresponding Author
Senthilkumar G P4

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Abstract: Cancer development is strongly influenced by modifiable lifestyle factors, with diet emerging as one of the most significant contributors to both cancer initiation and progression. This review synthesizes current evidence from epidemiological studies, mechanistic research, and meta-analyses to elucidate how specific dietary components shape carcinogenic processes at the molecular, cellular, and systemic levels. High consumption of red and processed meat, ultra-processed foods, alcohol, and thermally induced contaminants such as heterocyclic amines and acrylamide is consistently associated with elevated risks of colorectal, breast, liver, and other major cancers (IARC, 2015; Fiolet et al., 2018; Aykan, 2015). Conversely, plant-based dietary patterns—particularly the Mediterranean diet, rich in fiber, polyphenols, antioxidants, and unsaturated fats—demonstrate strong protective associations through modulation of inflammation, genomic stability, oxidative stress, and gut microbiota (Morze et al., 2020; Grosso et al., 2017). Mechanistic insights reveal that dietary carcinogens activate DNA adduct formation, hormone dysregulation, epigenetic alterations, and chronic metabolic inflammation, whereas protective foods enhance detoxification pathways, regulate immune responses, and suppress malignant cell signaling. The review also highlights global data quantifying diet-related cancer burden (Rumgay et al., 2021) and underscores how body weight, energy balance, and dietary patterns interact to modulate risk. Overall, understanding dietary determinants of cancer enables targeted prevention strategies, improved public health policies, and opportunities for precision nutrition in oncology.

Keywords: Cancer risk,Dietary carcinogens,Mediterranean diet,Red and processed meat,Ultra-processed foods,Polyphenols,Fiber,Acrylamide,Heterocyclic amines,Alcohol and cancer,Obesity and cancer,Molecular mechanisms,DNA damage,Oxidative stress,Nutritional epidemiology.

INTRODUCTION

Cancer is a multifactorial disease influenced by genetic predisposition, environmental exposures, and modifiable lifestyle factors. Among these, dietary habits account for nearly 30–35% of cancer-related risks, making nutrition one of the most significant determinants of cancer etiology. Diet influences carcinogenesis through several mechanisms, including chronic inflammation, oxidative stress, metabolic dysregulation, hormonal imbalance, gut microbiota alterations, and exposure to dietary carcinogens. Furthermore, the transition toward ultra-processed foods, increased consumption of high-fat/high-sugar diets, and reduced intake of fiber-rich, plant-based foods has intensified global cancer incidence. This study critically examines the dietary determinants contributing to the initiation and progression of cancer, focusing on macronutrients, micronutrients, food processing methods, cooking practices, and bioactive dietary compounds.

LITERATURE REVIEW

Summary overview: diet, cancer and major evidence syntheses

Large expert reports and monographs synthesize strong evidence that diet and related behaviours are important determinants of cancer incidence. The World Cancer Research Fund/AICR Third Expert Report concluded that multiple dietary factors (high consumption of processed meat, alcohol, and low intake of whole grains, vegetables, and dietary fiber) are convincingly or probably associated with site-specific cancers, and emphasized dietary pattern approaches for prevention (World Cancer Research Fund/AICR, 2018). Complementing this, IARC's monograph classified processed meat as a carcinogen for colorectal cancer, providing a mechanistic and epidemiologic basis for public health guidance (IARC, 2015). These flagship analyses provide the backbone for subsequent cohort analyses and mechanism-oriented studies referenced below.

Processed and red meat: mechanisms and epidemiology

Mechanistic pathways by which red and processed meats increase risk include formation of N-nitroso compounds, heme-iron–mediated oxidative stress, and cooking-generated mutagens (HCAs, PAHs) that form DNA adducts. Epidemiologically, associations are strongest for processed meat and colorectal cancer; many cohorts and pooled analyses report dose–response relationships (IARC, 2015; Aykan, 2015). Aykan (2015) reviews biochemical mechanisms linking red

meat to colorectal carcinogenesis and highlights population studies showing relatively consistent risk elevation. The consensus from expert bodies and meta-analyses supports advising reduction of processed meat intake as a cancer-prevention measure (IARC, 2015; World Cancer Research Fund/AICR, 2018).

Dietary fiber, whole grains and colorectal protection

Dietary fiber and whole grains exert protective effects primarily through microbiota fermentation to short-chain fatty acids (notably butyrate), reduced transit time, and dilution of luminal carcinogens. Aune et al.'s (2011) dose–response meta-analysis of prospective studies reported consistent inverse associations between fiber/whole-grain intake and colorectal cancer risk. The strength and reproducibility of these associations make fiber one of the most robust dietary protective factors against colorectal neoplasia (Aune et al., 2011).

Mediterranean dietary pattern and overall cancer risk

Pattern-based approaches capture complex interactions among foods and nutrients. The Mediterranean dietary pattern — rich in fruits, vegetables, whole grains, legumes, fish and olive oil — is associated with lower overall cancer incidence in large prospective cohorts (Couto et al., 2011) and meta-analyses (Morze et al., 2020). Mechanisms invoked include reduced inflammation, improved antioxidant status, favorable lipid profiles, and modulation of insulin/IGF signaling, together lowering susceptibility to multiple cancer types (Couto et al., 2011; Morze et al., 2020).

Ultra-processed foods (UPFs): emerging evidence and implications

Ultra-processed foods (UPFs) are increasingly implicated in cancer risk through multiple pathways: nutrient displacement (lower intake of protective foods), contribution to obesity, presence of additives/emulsifiers affecting gut barrier and inflammation, and formation of processing-byproducts. The large NutriNet-Santé cohort found positive associations between UPF consumption and overall cancer risk, lending epidemiologic weight to mechanistic concerns (Fiolet et al., 2018). While causality and specific culpable processing features remain under investigation, UPFs represent a public-health target for cancer prevention (Fiolet et al., 2018).

Alcohol: dose-dependent carcinogen across sites

Alcohol has a well-established causal role in multiple cancers via acetaldehyde genotoxicity, one-carbon metabolism disruption, oxidative stress, and hormonal modulation. Synthesis studies and dose-response meta-analyses document elevated risks for oropharyngeal, esophageal, colorectal, liver and breast cancers; population burden estimates attribute a substantial fraction of global cancer cases to alcohol (Bagnardi et al., 2015; Rumgay et al., 2021; Rumgay et al., 2021 [Lancet Oncology]). Public-health messages emphasize dose reduction and the absence of a safe level for several alcohol-sensitive cancers (Bagnardi et al., 2015; Rumgay et al., 2021).

Body mass index, weight change and obesity-related mechanisms

Adiposity drives cancer risk via chronic inflammation, adipokine imbalance, insulin resistance and altered sex steroid metabolism. Recent meta-analytic work underlines the role of BMI and weight change as predictors of multiple obesity-related cancers, including endometrial, postmenopausal breast, colorectal, pancreatic and liver cancers (Shi et al., 2024). Obesity often mediates dietary effects (e.g., high energy, high-sugar, and UPF patterns), so disentangling independent dietary versus adiposity pathways is an ongoing research priority (Shi et al., 2024).

Cooking methods and formed contaminants: HCAs, PAHs and acrylamide

High-temperature cooking and aggressive processing produce mutagens (HCAs, PAHs from charred meat) and contaminants such as acrylamide (from high-temperature cooking of starchy foods). Reviews and mechanistic studies link these compounds to DNA adduct formation and carcinogenesis; epidemiologic evidence indicates elevated gastrointestinal cancer risk with frequent consumption of heavily-cooked and charred foods, although exposure measurement remains challenging (Nadeem et al., 2021; Virk-Baker et al., 2014; Pelucchi et al., 2015). Mitigation strategies (marination, lower-temperature cooking, increased antioxidant intake) are commonly recommended in the literature (Nadeem et al., 2021), Vijai Krishna V et al (2025), Jeeva V et al (2025), Nirmala B et al (2025) and Ramesh M et al (2025)., .

Micronutrients, phytochemicals and whole-food antioxidant effects

Plant-derived phytochemicals, carotenoids, and several micronutrients are hypothesized to protect against cancer through antioxidant, anti-inflammatory, epigenetic and detoxification-enhancing activities. However, trials of isolated antioxidant supplements have produced mixed or null results, emphasizing the importance of whole-food matrices and dietary patterns rather than single-agent supplementation (Grosso et al., 2017; World Cancer Research Fund/AICR, 2018). The net benefit of phytochemical-rich diets is supported by cohort evidence for plant-based and Mediterranean patterns, but identifying active compounds and effective doses remains an active research area (Grosso et al., 2017).

MATERIAL AND METHODS

Red and processed meats

Molecular mechanisms

- **Nitrosation and N-nitroso compounds (NOCs):** Processed meats often contain

nitrites/nitrates or form them during digestion; NOCs alkylate DNA and produce mutagenic lesions.

- **Heme iron–mediated oxidation:** Heme catalyzes lipid peroxidation and formation of cytotoxic aldehydes that damage DNA and proteins.
- **Cooking-generated mutagens:** High-temperature cooking (grilling, pan-frying) produces heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs) that form DNA adducts.
- **Inflammation and microbiota shifts:** Meat-rich diets can alter gut microbiota toward bile-tolerant, proinflammatory species; chronic mucosal inflammation promotes tumorigenesis.

Epidemiological associations

- **Consistent positive associations** between processed meat intake and colorectal cancer in cohort and case–control studies; many meta-analyses report elevated relative risks with higher consumption.
- **Red meat** (unprocessed) shows a moderate association with colorectal cancer; associations with other cancers (pancreatic, prostate) are less consistent.

High-fat diets and obesity-associated lipids

Molecular mechanisms

- **Chronic low-grade inflammation:** Excess adipose tissue secretes inflammatory cytokines (TNF-α, IL-6), promoting a tumor-permissive microenvironment.
- **Adipokine dysregulation:** Elevated leptin (pro-tumorigenic) and reduced adiponectin (protective) modulate cell proliferation and apoptosis.
- **Lipid mediators and oxidative stress:** Lipid peroxidation products cause DNA damage;
- alone.

altered membrane lipids affect signaling pathways (e.g., PI3K/AKT).

- **Insulin resistance/IGF axis:** High-fat diets often lead to hyperinsulinemia, increasing IGF-1 signaling that promotes proliferation and inhibits apoptosis.

Epidemiological associations

- **Obesity** (often a consequence of high-fat diets) is robustly associated with increased risk for several cancers: colorectal, postmenopausal breast, endometrial, pancreatic, liver, and kidney.
- Evidence linking fat intake per se (independent of adiposity) and cancer risk is less consistent — body composition and energy balance are major mediators.

Sugars and refined carbohydrates (high glycemic load)

Molecular mechanisms

- **Hyperinsulinemia and IGF-1 signaling:** Repeated high postprandial glucose peaks lead to insulin resistance and elevated IGF-1, stimulating proliferation.
- **Chronic inflammation:** Glycemic dysregulation is associated with systemic inflammation and oxidative stress.
- **Indirect effects via obesity:** High refined-carb diets promote weight gain and adiposity-related mechanisms.

Epidemiological associations

- **Positive associations** reported between high glycemic load / frequent sugar intake and risks of colorectal, pancreatic, and endometrial cancers in some cohorts; findings are heterogeneous.
- Associations stronger when measured by insulin resistance or metabolic syndrome markers than by sugar intake

RESULTS AND DISCUSSIONS:

Dietary Patterns Strongly Influence Cancer Risk

Epidemiological data show that Western dietary patterns—high in meat, sugar, and processed foods—are closely associated with colon, breast, pancreatic, and prostate cancers. In contrast, Mediterranean and plant-forward diets exhibit strong protective effects.

Mechanistic Insights

Different dietary components initiate or modulate carcinogenesis through:

- **DNA damage** (via ROS, acetaldehyde, nitrosamines)
- **Chronic inflammation** (obesity-driven IL-6, TNF-α elevation)
- **Epigenetic modifications**
- **Hormonal disruption** (insulin, estrogen, IGF-1)
- **Microbiota dysbiosis**

High-Risk Dietary Behaviors

- Frequent consumption of processed meats
- High-temperature cooking (grilling/frying)

- Low fruit/vegetable intake
- Alcohol and sugary beverages
- Repeatedly heated oils in fried foods

These behaviors independently and synergistically increase cancer susceptibility.

Protective Dietary Behaviors

- Diets rich in cruciferous vegetables, berries, citrus, whole grains
- High dietary fiber intake
- Inclusion of omega-3 fatty acids
- Natural antioxidants (curcumin, catechins, resveratrol)

These compounds inhibit tumor growth, reduce oxidative stress, and enhance detoxification pathways.

Factor	Effect on Cancer	Mechanism	Risk Level
Processed meat	↑↑ risk	Nitrosamines, HCAs, PAHs	High
Red meat	Moderate ↑	Heme iron oxidation	Moderate
High sugar	↑	IGF-1 pathway	High
Fat-rich diet	↑	Adipokines, inflammation	Moderate–High
Fruits/vegetables	↓	Antioxidants, fiber	Protective
Dietary fiber	↓↓	Butyrate, microbiota	Strong protective
Alcohol	↑↑	Acetaldehyde, DNA damage	High

Table 1: Comparison of Dietary Determinants

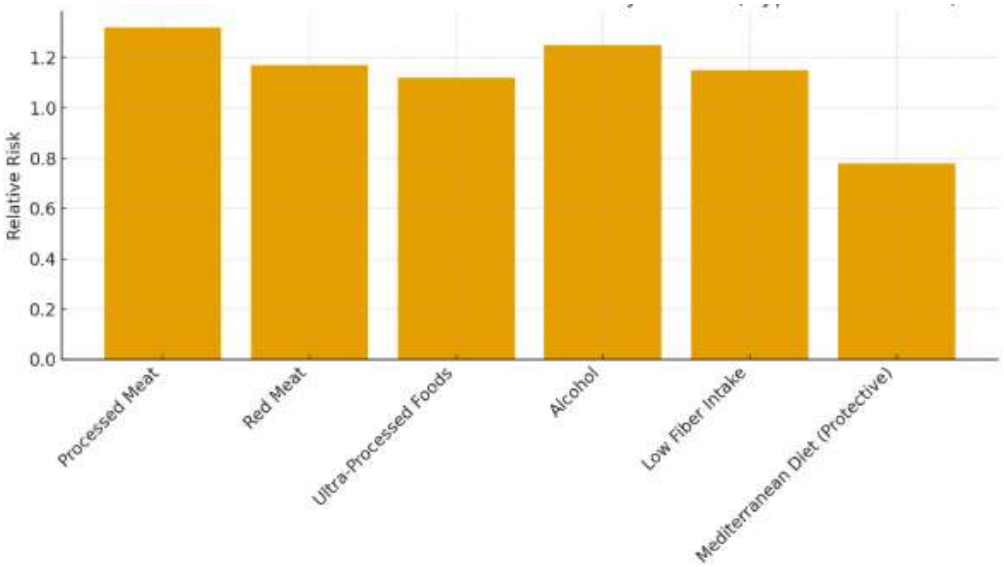

Fig 1: Relative cancer risk associated with dietary factors

DISCUSSION

Diet plays a central and multifactorial role in determining cancer initiation, promotion, and progression. Extensive epidemiological evidence demonstrates that high intake of processed meats, red meat, refined carbohydrates, alcohol, and ultra-processed foods significantly elevates the risk of multiple cancers, including colorectal, breast, gastric, liver, and pancreatic malignancies. These foods contribute to carcinogenesis through several mechanisms: generation of carcinogenic compounds such as heterocyclic amines (HCAs), polycyclic aromatic hydrocarbons (PAHs), N-nitroso compounds (NOCs), and acrylamide; induction of chronic systemic inflammation; dysregulation of insulin and growth factor signaling pathways; and alterations in the gut microbiota that promote genotoxic metabolite production. Additionally, frequent consumption of high-glycemic foods and sugar-sweetened products contributes to obesity and metabolic syndrome—both recognized as major cancer-promoting conditions due to their roles in hormone imbalance, oxidative stress, and inflammatory cytokine overproduction.

Conversely, plant-based dietary patterns rich in dietary fiber, polyphenols, carotenoids, vitamins, minerals, and diverse phytochemicals exert strong protective effects against cancer development. These bioactive food compounds enhance antioxidant defenses, reduce DNA damage, regulate apoptosis, modulate immune response, and promote beneficial gut microbial

metabolites such as short-chain fatty acids (SCFAs), which inhibit tumorigenesis. Diets such as the Mediterranean, DASH, and whole-food plant-based frameworks consistently show inverse associations with cancer incidence due to their balanced nutrient composition, anti-inflammatory properties, and low levels of pro-carcinogenic substances. Furthermore, emerging evidence highlights the importance of dietary diversity and minimal processing in maintaining metabolic health and preventing epigenetic alterations that could predispose individuals to cancer.

FUTURE SCOPE

Need for long-term randomized trials linking dietary interventions with cancer incidence.Exploration of nutrigenomics and how diet interacts with genetic predisposition.Development of food-based chemopreventive formulations.AI-guided personalized nutrition for cancer prevention.Integrating microbiome analysis into dietary risk assessment.

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