Emergence of nutrigenomics and dietary components as a complementary therapy in cancer prevention

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Received: 23 April 2022 / Accepted: 2 November 2022 / Published online: 11 November 2022
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Abstract
Cancer is an illness characterized by abnormal cell development and the capability to infiltrate or spread to rest of the body. A tumor is the term for this abnormal growth that develops in solid tissues like an organ, muscle, or bone and can spread to other parts of the body through the blood and lymphatic systems. Nutrition is a critical and immortal environmental component in the development of all living organisms encoding the relationship between a person’s nutrition and their genes. Nutrients have the ability to modify gene expression and persuade alterations in DNA and protein molecules which is researched scientifically in nutrigenomics. These interactions have a significant impact on the pharmacokinetic properties of bioactive dietary components as well as their site of action/molecular targets. Nutrigenomics encompasses nutrigenetics, epigenetics, and transcriptomics as well as other “omic” disciplines like proteomics and metabolomics to explain the vast disparities in cancer risk among people with roughly similar life style. Clinical trials and researches have evidenced that alternation of dietary habits is potentially one of the key approaches for reducing cancer risk in an individual. In this article, we will target how nutrigenomics and functional food work as preventive therapy in reducing the risk of cancer.

Keywords Cancer · Dietary components · Nutrigenomics · Nutrigenetics · Polyphenols

Introduction
Everyone responds differently to the treatment whether it involves a diet, a lifestyle change, or a medication. Disparities in the likelihood of getting diseases like cancer may be due to genetic differences. SNPs (single-nucleotide polymorphisms) account for over 90% of all human genetic diversity; people contain between 5 and 8 million SNPs (Nicastro et al. 2012). The risk of acquiring a disease like cancer is increased by genetic differences or mutations that are brought on by changes in the DNA of an individual living cell. This alternation in DNA is triggered by numerous aspects like environmental, improper nutrition uptake, and chemical uptake. Next comes the second stage known as carcinogenesis in which the genetically altered cells get initiated and get affected by carcinogens. These initial cells are further transformed into malignant cells that are specified via up-regulation or stimulation of various signaling pathways which are included in apoptosis, angiogenesis, proliferations, and invasion. The third and last stage of progression in which uncontrolled proliferation of cells are irreversibly changed and metastasis occurs in which cancerous cells spread out in the whole body (Pitot et al. 1981). The majority of the mortality rate associated with cancer occurs due to metastasis. The mechanism of inhibition or promotion of the nutritional requirements can affect the process of carcinogenesis. A huge percentage of human cancers is pointedly allied with lifestyle and diet according to epidemiological data (Setlow 2001). Numerous studies indicated that the cancer cases and tumor behaviors are influenced by dietary habits as a part of environmental factors (Davis et al. 2004; Milner 2006; Anand et al. 2008b, a; Ross 2010;
Papadimitriou et al. 2021). Nutrition holds relevance in the prevention and management of cancer as it is related to our daily lifestyle, and this is not any new perception. About more than 2000 years ago, Hippocrates said “Let food be the medicine and medicine be the food” (Nasir et al. 2020).

Observational study has shown that adopting a Mediterranean diet is not only linked to a lower risk of overall cancer-related mortality but also reduces chance of specific types of cancer (particularly tumors of the colon and rectum, gastrointestinal tract, breast, abdomen, pancreatic, prostate, liver, and neck and head) (Schwingshackl et al. 2016; Sellami et al. 2020). According to genomic studies, DNA methylation is the most common epigenetic modification that happens post-translationally, and nutrition’s impact on DNA methylation and other epigenetic events is crucial in the fight against cancer. (Feero et al. 2010). Some of the bioactive components which modulate cell signaling, hormonal balance, ontogenesis, cell death, mutagen metabolic rate, and cell cycle regulation are polyphenols; flavonoids; folate; zinc; vitamins D, E, and C; calcium; carotenoids; N-3 fatty acids; and conjugated linoleic acids (Surh 2003; Ramos 2008). By targeting numerous molecular pathways, phytonutrients have been discovered to reduce breast cancer cell proliferation, differentiation, invasion, metastasis, and angiogenesis and induce apoptotic cell death (Bhattacharya et al. 2021).

Two key concepts that emerge here are nutrigenomic and nutrigenetics. Nutrigenetics is the exploration of how a person’s genotype effects their phenotypic response to dietary consumption, whereas nutrigenomics means how the nutrients transform protein expression and genetic material which eventually impact cellular metabolism (Marcum 2020). Therefore, it is a combination of molecular nutrition and genomics. Nutrigenomics target is to examine the effects of diet and nutrition on gene expression, particularly using high-throughput epigenomic (histone methylation), transcriptomic (RNA transcription), proteomic (protein synthesis), and metabolomic (metabolite production) assays (Marcum 2020; Sales et al. 2014). The goal of this review is to explore the impact of dietary food and bioactive compounds in the management of cancer.

### Nutrigenetics

According to reports, genetic variability may change nutritional needs and dietary intake among human sub-populations, opening the possibility of personalizing nutrient intake for the optimal disease prevention based on a person’s genome (Farhud et al. 2010). Therefore, the genetic profile has an impact on the body’s reaction to bioactive food components by altering their absorption, metabolism, and location of action (Farhud et al. 2010). Nutrigenetics look into the effect of genetic variation particularly as a single-nucleotide polymorphism (SNP) on an individual’s reaction to dietary intake particularly in terms of how genetic variation affects metabolic status (Or dovas and Mooser 2004). Some specific genes persuade both food preferences and how much food is to be consumed. For example, the genetic polymorphism in GLUT2 (glucose transporter type 2) is linked to sugar eating habits, implying a glucose-sensing mechanism that controls food intake (Eny et al. 2008). An individual’s sensitivity to caffeine differs due to genetic variation in the CYP1A2 gene. This gene codes for a caffeine demethylating enzyme produced in the liver, and some variants of the gene demethylate caffeine faster than others (Cornelis 2012; Thorn et al. 2012). Another example is polymorphism in the glutathione peroxide gene. Human studies have indicated a link between selenium supplementation and a lower risk of liver, colon, prostate, and lung cancer (Farhud et al. 2010). However, no two people will react in the same way. Glutathione peroxide is an antioxidant enzyme that requires selenium to activate. Human glutathione peroxide polymorphism at codon 198 causes a substitution of proline to leucine amino acid which has been linked to an increased risk of lung cancer. The function of lycopene in reducing prostate cancer risk is another case where preclinical research suggests protection but epidemiologic evidence is contradictory. The XRCC1 (Arg399Gln) polymorphism may affect lycopene responsiveness (Goodman et al. 2006). Enzymatic activity is influenced by genetic variants in catechol-O-methyltransferase, sulfotransferase, and UDP-glucuronosyltransferase. Some food substances are metabolized by these enzymes. Green tea was linked to a decreased risk of breast cancer in women who had the catechol-O-methyltransferase low-activity variant. This enzyme catalyzes the methylation of catechins allowing them to be removed more quickly (Wu et al. 2003; El-Sohemy 2007). Genetic polymorphisms can impact the speed of digestion, absorption, metabolism, and uptake of dietary components, which could explain some of the discrepancies in diet-health outcomes studies.

### Nutrigenomics

The multidisciplinary knowledge which deals with the effect of food on genes and the response of an individual towards it is termed as nutrigenomics (Riscuta 2016). The important concepts of the nutrigenomics are that the progression from a healthy phenotype to a chronic illness phenotype arises by alteration in gene expression or via variation in activities of enzymes and proteins that are controlled directly or indirectly via chemicals present in the diet (Kaput and Rodriguez 2004). Nutrigenomics is associated with the effects of diet and nutrition on gene expression particularly using high-throughput epigenomic (histone methylation), transcriptomic (RNA transcription), proteomic (protein
synthesis), and metabolomic (metabolite production) (Mar- cum 2020; Sales et al. 2014) (Fig. 1). This inter-relationship exerts a major impact on the pharmacokinetic parameters of the human body. The extensive variability in cancer prevention and risk is basically due to nutrigenetics and transcriptomics combined with metabolomics and proteomics (Riscuta 2016). According to the nutrigenomics theory, naturally bioactive constituents can affect the human genome either directly or indirectly and hence influence gene and gene product expression. Nutritional elements can influence a variety of biological processes including maturation as well as the development, occurrence, development, and/or severity of a variety of infections, particularly cancers; and the health consequences of a dietary are dependent on an individual’s genetic heritage of illness and health (Riscuta 2016). Thus, it can be stated that bioactive components and nutrient of diet influence the expressions of several genes either through differential regulation of genes or by silencing or activating genes that are not functional at a given moment of development (Ordovas and Corella 2004). Nutrigenomics defines nutrients as dietary signals that are recognized by cellular sensor systems and alter gene and protein expression and hence metabolite synthesis. “Dietary signatures” are patterns of gene expression, protein expression, and metabolite synthesis in response to certain foods or nutritional regimens (Müller et al. 2003). The study of nutritional signatures in individual cells, organs, and species to better understand how diet impacts homeostasis is known as nutrigenomics. Furthermore, nutrigenomics seeks to identify and comprehend the genes that impact the risk of diet-related illnesses on a genome-wide scale as well as the processes that allow these genetic predispositions to exist (Müller et al. 2003). In molecular nutrition research, genomic technologies can be employed in two different but complimentary approaches (Fig. 2) (Müller et al. 2003). The following nutrigenomics research goals can be identified using these two main approaches (Fig. 3).

Epigenetics

In 1942 Conrad H. Waddington designated the word “epigenetics” to characterize irreversible hereditary gene expression patterns that occur without changing nucleotide sequence yet are powerful enough just to modify transcriptomic patterns. DNA methylation, histone modification, and gene silencing via microRNA are all epigenetic mechanisms (Link et al. 2010). Epigenetics is a very promising and appealing path from a clinical point of view. This is due to the fact that unlike genetic changes (mutations, gene deletions), epigenetic alterations can be reversed. Nutrients are significant because they may impact epigenetic alterations such as DNA methylation and histone modifications, altering the transcriptional activation genes linked to various metabolic and clinical mechanisms such as cancer and aging (Link et al. 2010; Choi and Friso 2010).

DNA methylation which alters a cytosine base at the CpG dinucleotide residues with methyl groups is catalyzed by DNA methyltransferase and controls gene expression patterns by varying chromatin structures (Choi and Friso 2010). Folate, vitamin B-12, methionine, choline, and betaine may influence DNA methylation and histone methylation through changing 1-carbon metabolism. Two 1-carbon metabolites that can affect DNA and histone methylation are S-adenosylmethionine, a methyl donor for methylation processes, and S-adenosylhomocysteine, a product inhibitor of methyltransferases (Choi and Friso 2010). Green tea high in epigallocatechin-3-gallate inhibits DNA methyltransferase enzymatic activity and reactivates methylation-silenced genes in cancer cells (Fang et al. 2003). Histone modification is another epigenetic process

Fig. 1 Branches of nutrigenomics
that results in gene silencing and unsilencing (Nicastro et al. 2012; Glozak and Seto 2007; Myzak and Dashwood 2006). Besides from direct epigenetic changes, different histone modifications frequently alter chromatin structure, which seem to be equally important in gene regulation and cancer (Ellis et al. 2009). Histones can be methylated, acetylated, phosphorylated, biotinylated, ubiquitinated, sumoylated, and ADP-ribosylated (Choi and Friso 2010). Because of their propensity to trigger cell cycle progression and death by boosting the expression of particular apoptosis, inducing or cell cycle-mediating genes, HDAC (histone deacetylase) inhibitors have been discovered as potential cancer therapeutic medicines (Johnstone 2002). HDAC is inhibited by resveratrol, butyrate, sulforaphane,
and diallyl sulphide, whereas histone acetyltransferases are inhibited by curcumin.

**Transcriptomics**

Functional genomics techniques are ways for investigating an organism’s genetic code, which is the total amount of RNA transcripts (including mRNA, rRNA, tRNA, and other noncoding RNA). The information content of an organism is stored in its genome’s DNA and expressed through transcription. Non-protein-coding RNAs have additional functions, whereas mRNA functions as a brief intermediate molecule in the information network (Lowe et al. 2017). mRNA transcripts are regularly validated as a good biomarker for disease danger identification (Nicastro et al. 2012). Microarrays, which assess a set of preset sequences, and RNA sequencing, which employs high-throughput sequencing to capture all sequences, are amongst the most significant modern techniques in the domain (Lowe et al. 2017). For definite food components, transcriptomics studies present evidence regarding molecular targets. For example, 9000 genes were used to resolve the transformation in colonocytes gene expression in carcinogen injected rat’s DNA microarrays. The diets for animals varied only in fat type: n-6 polyunsaturated fatty acids (PUFAs), n-3 PUFAs for fish oil, and n-9 monounsaturated fatty acids for olive oil. The transformation has been shown in the colonic epithelium’s molecular portrait of gene expression, at the initiation of malignancy (DNA adduct configuration) and promotional (Aberrant Crypt Foci) stage (Davidson et al. 2014).

**Proteomics**

Proteomics is the comprehensive examination of peptide development and differentiation in distinguishing development of the disease via protein pathways that connect the extracellular microenvironment to transcriptional activation (Petricoin and Liotta 2003). Proteomics is an essential element of nutrigenomics since it describes how our genome reacts to dietary changes (Kussmann and Affolter 2009). Proteomics may be utilized in nutrition to discover and quantify bioactive proteins and peptides, as well as to answer questions concerning nutritional bio efficacy (Kussmann and Affolter 2006). Proteomics is being used by the nutritional science community to identify biomarkers of fitness, illness, treatment, and prediction (Xiao et al. 2009). The flavonoid quercetin alters a variety of proteins. A proteomic investigation of quercetin-treated human colon cancer cells found changes in the levels of a number of proteins involved in colon cancer cell proliferation, differentiation, and apoptosis. Their discovery as quercetin’s molecular targets could explain the flavonoid’s anticancer properties (Wenzel et al. 2004). Breikers et al. investigated the influence of increasing vegetable intake on expression levels in the intestinal epithelium of healthy mice, finding 30 proteins that were expressed differentially in the intestinal mucosa of healthy mice with enhanced vegetable consumption (Breikers et al. 2006). Six proteins revealed to have varied degrees of activity might help prevent colorectal cancer. As a result, the observed alterations in protein content support the prevention of colorectal cancer by vegetables (Breikers et al. 2006). Stierum et al. used DNA microarrays, subtractive hybridization, and proteomics to explore the impacts of multifunctional dietary constituents with anti-colorectal cancer benefits that have been advocated and to create colon-epithelial cell line–based screening methods for such nutrients. (Stierum et al. 2001).

**Metabolomics**

A metabolome is a collection of metabolites and tiny molecular weight intermediates that changes depending on the physiology or development of a cell, tissue, or organ (Beger et al. 2016). To outline cells at different phases of carcinogenesis, metabolomics techniques are used based on shifts in glucose metabolism and also to know the mechanism of action of bioactive food components (Gatenby and Gillies 2007; Kim and Milner 2010). Metabolomics is a powerful technique for determining how diet affects an individual’s health. Inter-individual variations in metabolizing identical foods in normal and illness states can be identified by detecting food-derived biomarkers. Metabolomics might help with nutrition evaluation in three ways: food intake biomarker identification, diet-related disorders research through cohort studies, and dietary intervention assessment using metabolic patterns (Tebani and Bekri 2019). Solanky et al. evaluated urine metabolites in premenopausal women who received soy in the form of textured vegetable protein containing conjugated isoflavone glycosides or miso containing unconjugated isoflavone. Urinary metabolites from women who ate soy demonstrated significantly greater alteration in metabolites than those who consumed textured vegetable protein, suggesting that the isoflavone’s involvement in detecting any biological effects is substantial (Solanky et al. 2005).

**Dietary supplements in cancer prevention: mechanistic approach**

The American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention have revealed a link between an elevated consumption of red meat/processed meat (bacon, luncheon meats, sausage) and an increase in the rate of cancer and mortality (World Cancer Research Fund 2007; Kushi et al. 2012). Consuming 100 g of red meat or 50 g of processed meat each day raises the risk of colon or rectum cancer by 15–20%. On the other hand, diet...
high in vegetables and fruits, whole grains, fish, or chicken has been related to a decreased risk of several malignancies (Miller et al. 2010).

Nutritional variables inhibit carcinogenesis through the following mechanisms: (a) The induction of phase 2 drug metabolizing enzymes facilitates the detoxification of carcinogenic intermediates, (b) monoxygenases that are reliant on cytochrome P450 are suppressed, (c) cancerous cells are targeted for apoptotic (cell death), (d) alterations in the cell cycle’s progression, and (e) vasculogenesis and metastases targeted for apoptotic (cell death), (d) alterations in the cell cycle’s progression, and (e) vasculogenesis and metastases suppression (Stan et al. 2008; Kelloff 2000; Milner 2004). Cancer begins with exposure to a carcinogen, DNA damage, and oncogene activation (Land et al. 1983). The mutagenic and cancerous effects of carcinogens are regulated via bio-transformation enzymes commonly called xenobiotics or drug-metabolizing enzymes (Phase I and Phase II enzymes) (Davis 2007; Lee and Surh 2005). The superfamily of enzymes activates a wide variety of known carcinogens via phase I metabolism as cytochrome P450 form (CYP450) (Mittal et al. 2015). Several mechanisms such as oxidative stress and antioxidant profile, phase I and phase II enzyme activity have been associated to cancer genesis. Antioxidant phytochemicals can bind to free radicals, altering antioxidant responses, DNA damage/repair, and tumor growth (Chen and Liu 2018). Phytochemicals such as cytochrome P450 and antioxidant enzymes have been found to affect carcinogen bio-activation or detoxification by altering phase I and phase II enzyme activity (Chen and Liu 2018). Flavonoids have been shown to influence the CYP450 system by inducing, activating, and inhibiting certain CYP isozymes in the diet (Moon et al. 2006). Many flavonoids naringenin, tangeritin, and tea flavonoids have been demonstrated to inhibit CYP450 2B, 2E1, and 3A-dependent processes (Obermeier et al. 1995; Fuhr et al. 1993).

The antioxidant response element (AORE), which is found in the promoter region of particular genes, is substantially responsible for the stimulation of phase II enzymes. The transcription factor Nrf2 binds to the AORE region to kick-start gene expression. Glutathione S-transferase, gamma-glutamyl cysteine ligase, and heme-oxygenase-1 are examples of AORE-regulated gene products that mediate detoxification and/or antioxidant properties, thereby protecting cells from carcinogenic and mutagenic degradation (Lee and Surh 2005). The nuclear transcription factor erythroid 2p45 (NF-E2)–related factor 2 (Nrf2), which is sequestered in the cytoplasm by Kelch-like ECH-associated protein 1 (Keap1), regulates the transcription of AORE-driven genes. By activating de novo manufacturing of phase II detoxifying or antioxidant genes via the Nrf2-AORE core signaling pathway, anethole dithiolthiones, sulforaphane, curcumin, caffeic acid phenethyl ester, 4′-bromoflavone, and other compounds protect DNA and other essential cellular components (Lee and Surh 2005). Dietary cocoa protects against colitis-related cancer by activating the Nrf2/Keap1 pathway resulting in increased amounts of enzymatic antioxidants and lower levels of inflammatory promoters (Pandurangan et al. 2015).

To produce biological consequences, activated carcinogens form covalent adducts with individual nucleic acids of DNA or RNA. Reactive oxygen species (ROS) such as superoxide anions, hydrogen peroxide, and hydroxyl radicals have also been found to damage DNA bases and the deoxyribose backbone (Bartsch 1996). There are various DNA repair pathways that prevent damage from persisting and are critical for genomic integrity and cancer prevention (Cooke et al. 2005). A deficiency of folate has been found to affect DNA repair processes (Friso and Choi 2005).

Following signal transduction, cells produce reflecting responses and engage in activities that affect cell fate including cell growth, death, and cell cycle arrest (Chen and Liu 2018). The most common final targets of cell signaling pathways are apoptosis regulators like Bax, Bad, Bcl-2 family proteins, and caspases; cell cycle regulators like myc and Chks (checkpoint kinase); and proliferation regulators like cyclins, CdcS (cell-division cycle proteins), and CDKs (cyclin-dependent kinases) (Chen and Liu 2018). Limiting the course of tumorigenesis by triggering growth arrest using nutritional bioactive compounds as a viable option. The cell cycle is a sequential process that guides dividing human cells through discrete phases (G1, S, G2, and M phases) (Davis 2007). The balance between interactions among cyclins, cyclin-dependent kinases, and CDK inhibitors (CDIns) regulates cell cycle progression. By inhibiting CDK4, CDK2, cyclin D1, and cyclin E and generating CDIns, phenolic compounds such as genistein and epigallocatechin-3-gallate cause cell-cycle arrest (Agarwal 2000).

One of the most effective cancers defenses is apoptosis, often known as programmed cell death as it eliminates potentially dangerous aberrant cells. (Reed 1999). A range of novel approaches are currently being investigated to target individual apoptotic regulators involving regenerative medicine, RNAi techniques, recombination biology, and traditional molecular and computational chemistry (Fischer and Schulze-Osthoff 2005). Nutritional management by bioactive components present in functional meals is a well-known and effective method that is gaining traction (Martin 2006). There is a lot of evidence that dietary bioactive compounds can trigger apoptosis by interacting with a number of molecular targets (Martin 2006). Resveratrol, EGCG, vanilloids (including capsaicin and curcumin), and minerals like selenium have all been shown to induce apoptosis in a variety of cell types, including colon cancer cells, epidermoid cells, glioma cells, leukemia cells, prostate cells, and transformed bronchial epithelial cells (Martin 2006).

When NF-κB is suppressed, cells become more vulnerable to apoptosis (Courtois 2005). NF-κB downregulation
makes cells more susceptible to death, and NF-κB activation encourages cell survival and proliferation. Overexpression of Bcl-xL, IAPs (XIAP and cIAP-2), and the death receptor signaling antagonist switching helps to integrate a variety of survival signaling pathways, including NF-κB (Cummings et al. 2004). In cell lines originating from cancer tissues genistein, indole-3-carbinol, curcumin, EGCG, and apigenin were reported to block NF-κB activation (Martin 2006; Sarkar and Li 2004). Pro-apoptotic (Bcl-2, Bcl-xL) or anti-apoptotic (Bax and Bak) proteins can be influenced by dietary bioactive components allowing cytochrome c to be released from mitochondria (Chen and Kong 2005). Curcumin causes apoptosis in cancer cell lines by down-regulating the apoptosis suppressor proteins Bcl-2 and Bcl-xL (Martin 2006). Beta-carotene reduces the production of apoptotic Bcl-2 in colon cancer cells (Martin 2006). Apoptosis can be induced through the activation of caspases by dietary components. Resveratrol enhances caspase activity (caspases 6, 3, and 9) in a range of cell types including normal and hematopoietic cells (Ferry-Dumazet et al. 2002).

An additional approach by which bioactive constituents can help prevent cancer is by slowing the growth of angiogenesis. The suppression of angiogenesis eventually results in a reduction in tumor size and ultimately limits tumor development (Hofseth and Ying 2006; Rose and Connolly 2000; Cao et al. 2002; Dulak 2005). Angiogenesis is an important stage in tumor development because it provides nutrition and oxygen to malignant cells (Oak et al. 2005). Growth factors such as vascular endothelial growth factor (VEGF) and fibroblast growth factor stir endothelial cells during angiogenesis and get enchanted by the angiogenesis site which also contains inflammatory cytokines and chemo-attractants (Fayette et al. 2005; Presta et al. 2005; Albini et al. 2005).

Mechanisms of action of polyphenols in chemoprevention

Polyphenolic compounds particularly stimulated the interest of investigators over the last couple of years due to their powerful antioxidant properties (Luo et al. 2021). Grapes, various blueberries, pear, apple, and cherry provide around 200–300 mg polyphenols per 100 g fresh weight. A cup of tea, a glass of red wine, or a cup of coffee typically contains about 100 mg polyphenolic compounds (Scalbert et al. 2005). Red wine polyphenols, stilbenes, and flavonoids have been linked to cancer prevention and promote human health with no discernible detrimental consequences (He et al. 2008). Polyphenolic compounds are explicit molecules or very complex chemicals that are derived from phenylalanine or its precursor shikimic acid and are categorized as flavonoids, phenolic acids, stilbenes, and lignans (Dreţcanu et al. 2021). They can inhibit DNA methyltransferases (DNMT), alter histones, and affect the epigenome of cancer cells.
proving that they have a defence mechanism against cancer prevention (Hardy et al. 2011).

Flavonoids

Flavonoids are pigments and phytohormones present in fruits and vegetables that have antiviral, antibacterial, analgesic, anti-inflammatory, anti-proliferative, cytotoxic, estrogenic, anticovulcants, and antiparasitic properties (Busch et al. 2015). Flavones, isoflavones, flavanones, anthocyanidins, and flavanols (catechins and proanthocyanidins) are the subclasses based on chemical structure (Niedzwiecki et al. 2016). Flavonoids are the most frequent polyphenols in foods, and they may be found in small amounts in almost any meal. Quercetin and kaempferol are the most prominent representatives (Manach et al. 2004). Parsley and celery are the best sources of flavones, and citrus fruits contain significant amount of flavanones (Manach et al. 2004). Isoflavones are categorized as phytoestrogens because they have characteristics similar to estrogens and have the capacity to bind to estrogen targets (Manach et al. 2004). Flavanols are categorized into two kinds: catechins (a monomer) and proanthocyanidins (a polymer) (Niedzwiecki et al. 2016). Catechins are an antioxidant that may be found in a wide range of foods. Galloycatechin, epigalloycatechin, and epigallocatechin gallate (EGCG) are found in teas, dicotyledous plants’ seeds, and grapes (Arts et al. 2000).

Natural flavonoids have been shown to suppress the proliferation of numerous kinds of cancer cells via multiple molecular targets and metabolic pathways (Sak 2014). Flavonoids have been shown to readily attach to cell membranes, enter in vitro–grown cells, and control metabolic processes in cells (Sak 2014). Oxidative damage reduction, carcinogen inactivation, proliferation inhibition, differentiation promotion, cell cycle arrest and apoptosis induction, tumor angiogenesis blockage, and metastasis suppression are all anticarcinogenic characteristics of flavonoids (Sak 2014; Kilani-Jaziri et al. 2012; Li et al. 2008). Preclinical research has revealed that flavonoids such as epigallocatechin-3-gallate, quercetin, apigenin, hesperidin, and genistein have anticancer potential by slowing cell cycle and/or activating apoptosis (Aiello et al. 2021). Green tea consumption on a regular basis has been linked to a lower risk of cancer (Ahmed et al. 2004). EGCG has been shown to influence growth factor–mediated pathways, mitogen-activated protein kinase–dependent pathways, and ubiquitin/proteasome degradation pathways (Khan et al. 2006). Quercetin’s cancer-preventive properties include cell cycle arrest, apoptosis, and antioxidant activity (Gibellini et al. 2011). When administered as an intra-tumoral injection, quercetin suppresses tumor development in mammary glands (Devipriya et al. 2016). In a population-based investigation, dietary quercetin was found to reduce the incidence of stomach cancer, colorectal cancer, and lung cancer (Ekström et al. 2011; Theodoratou et al. 2007; Lam et al. 2010). Due to large levels of glucosinolates, which may be hydrolyzed to isothiocyanates by the enzyme myrosinase or intestinal microbiota, increased consumption of Brassica plants such as broccoli and cabbage lowers the risk of cancer in a variety of organs (Navarro et al. 2011). Isothiocyanates, which are found in cruciferous family, prevent cancer cells from forming and developing by inhibiting carcinogen-activating cytochrome P450 monooxygenase, activating carcinogen-detoxifying phase 2 enzymes, inducing apoptosis, and inhibiting the cell cycle (Lu et al. 2006a, b). Although case–control studies have revealed a link between dietary flavonoid intake and particular cancers (upper aerodigestive tract, colorectal, breast, and lung cancers), additional prospective cohorts evaluating dietary polyphenol metabolism are needed to confirm health benefits (Aiello et al. 2021; Knekt et al. 2002; Grosso et al. 2017).

Stilbenes

Because of the antioxidant, cell death activation, and anti-inflammatory properties stilbenes, another family of polyphenols have a lot of potential for disease prevention and therapy including cancer (Sirerol et al. 2016). Stilbenes have been discovered to suppress cancer by interfering with molecular processes across all stages of carcinogenesis, including initiation, progression, and promotion (Sirerol et al. 2016). Resveratrol which is abundant in red wine, mulberries, peanuts, and grapes is one of the most significant stilbenes (Jang et al. 1997). Resveratrol has been shown to have cytotoxic effects in vitro against myeloid and lymphoid cancer cells, as well as breast, skin, cervix, ovary, stomach, prostate, colon, liver, pancreatic, and thyroid cancer cells (Kundu and Surh 2008; Aggarwal et al. 2004; Ko et al. 2017). Resveratrol has also been demonstrated to make tumor cells more susceptible to chemotherapy treatments effectively reversing drug resistance (Ko et al. 2017; Mondal and Bennett 2016). Resveratrol’s anticancer action is caused by non-coding RNAs epigenetic control of cell homeostasis (especially protein synthesis, autophagy, and organelle turnover), cell metabolism (e.g., glucose absorption and the Warburg effect), cell proliferation, cell death,
and cell motility (Vallino et al. 2020). Future research could look into molecules that are structurally similar to resveratrol. Pterostilbene is a natural analogue of resveratrol with better bioavailability and considerable antioxidant activity in vitro as compared to resveratrol (Kapetanovic et al. 2011; Rimando et al. 2002). Based on its antineoplastic activities in various malignancies, pterostilbene demonstrates the hallmark qualities of an effective anticancer drug (Obrador et al. 2021).

**Phenolic acids**

Phenolic acids are classified into two types: hydroxybenzoic acids and hydroxycinnamic acids. Gallic acid represents hydroxybenzoic acids, ellagic acid represents hydroxycinnamic acids, and p-coumaric, caffeic, ferulic, and sinapic acids constitute hydroxycinnamic acids (Manach et al. 2004). Both hydroxy and carboxy groups are present in these compounds. Proteins like phenylalanine and tyrosine provide a steady source of phenolics in the diet. 4-Hydroxybenzoic acid inhibited the histone deacetylase enzyme causing the acetylation process to be altered and eventually kill the cancer cells (Seidel et al. 2014). Phenolic acids are an ester of caffeic and quinic acids found in yerba mate, coffee, Hawthorn, artichoke, blackberry, nettles, and raw potatoes. Chlorogenic acid was found to be mostly cytotoxic to malignant cells (MCF-7 cell line) in vitro causing cell death while having no impact on normal human lymphocytes even at low doses (El-Nabi et al. 2018). Caffeic acid activated the Nrf2/Keap1 pathway and had direct antioxidant action in ovarian cancer cell lines resulting in anticancer effects (Sirota et al. 2015). By triggering ROS-dependent apoptosis, gallic acid inhibited the growth of colon cancer cells and prostate cancer cells (Subramanian et al. 2016; Russell et al. 2012).

**Lignans**

Lignans can be found in flax seeds, legumes, cereals, grains, fruits, algae, and a variety of plants (Niedzwiecki et al. 2016). Arctigenin, a natural lignan compound derived from *Arctium lappa* seeds has been found to cause apoptosis in breast cancer cells by activating the ROS/p38 MAPK pathway and altering Bcl-2 epigenetic regulation (Hsieh et al. 2014). Arctigenin therapy suppresses ovarian cancer cell growth and promotes caspase-3-dependent apoptosis (Huang et al. 2014). Arctigenin reduced cell cycle arrest from G(1) to S phase in the human gastric cancer cell lines SNU-1 and AGS via altering the expression of cell cycle regulatory proteins (Jeong et al. 2011). Arctigenin inhibits cell development in glioma cells and may cause apoptosis and cell cycle arrest during the G0/G1 phase (Maimaitili et al. 2017). Flaxseed is employed as both a chemopreventive and a cancer therapy (De Silva and Alcorn 2019). Flaxseed lignans have the ability to target numerous complex interdependent mechanisms associated with tumor development and sustainability at the very same time, implying that lignans might be employed in a broad-spectrum combination chemotherapeutic strategy (De Silva and Alcorn 2019). The flax seed lignans include secoisolariciresinol diglucoside, pinoresinol, lariciresinol, and matairesinol (Kezimana et al. 2018). Because of its powerful anti-proliferative, antioxidant, antiestrogenic, and/or anti-angiogenic properties, secoisolariciresinol diglucoside has been reported to prevent various cancers including breast, lung, and colon cancers (Kezimana et al. 2018). Secoisolariciresinol diglucoside’s anticancer activity has been attributed to the inhibition of carcinogenesis-related enzymes (Imran et al. 2015). Secoisolariciresinol diglucoside also reduces local inflammation, NF-κB signaling, and mammary tumor formation (Bowers et al. 2019).

**Curcumin**

The principal active component of turmeric (*Curcuma longa* L.) has been studied as an antioxidant, anticancer, and anti-inflammatory agent (Tomeh et al. 2019). Curcumin’s anticancer action has been demonstrated in a number of studies on breast cancer, ovarian cancer, lung cancer, gastric cancer, head and neck squamous cell carcinoma, prostate cancer, and brain tumors revealing its ability to target a wide range of cancer cell lines (Anand et al. 2008b, a). Curcumin’s anticancer effectiveness is principally achieved by inducing apoptosis and reducing tumor growth and invasion by suppressing a variety of cellular signaling pathways (Kunnunakkara et al. 2017). Curcumin’s safety and effectiveness in patients with cancer have been demonstrated in many clinical investigations involving human participants either alone or in conjunction with several other chemotherapeutic medicines. Curcumin works as an anticancer agent by interfering with several cellular pathways and inhibiting/inducing the production of many cytokines, enzymes, or growth factors such as COX-2, EGF, MAPK, PKD1, NF-κB, TNF-α, STAT3, and others (Kabir et al. 2021).

**Role of PUFAs (polyunsaturated fatty acids) in chemoprevention**

There are two main types of PUFAs: n-6 and n-3. Both n-6 and n-3 polyunsaturated fatty acids are beneficial to human health and therefore must be consumed as part of a well-balanced diet since they cannot be produced by the body (Liu and Ma 2014). The n-3 PUFAs are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), whereas the n-6 PUFAs include linolenic acid (LA) and arachidonic acid (Azrad et al. 2013). In vitro
and in vivo experimentation studies show that n-6 PUFAs induce carcinogenesis, but n-3 PUFAs may be cytotoxic (Liu and Ma 2014; Bagga et al. 2002; Chajès et al. 2012). n-3 PUFAs are important for cell signaling, cell structure, and membrane fluidity. They help to resolve inflammation and have anti-inflammatory properties (Vega et al. 2021). It has been hypothesized that n-3 PUFAs and associated intermediates have an impact on critical pathways driving lung cancer development and outcomes (Vega et al. 2021).

Breast cancer can be minimized by fish consumption or consuming long-chain n-3 PUFAs like EPA and DHA (Liu and Ma 2014). DHA has been shown to promote a range of cellular responses that restrict cancer cell survival in vitro and in vivo, as well as to induce apoptosis/reduction of proliferation (Newell et al. 2017). A high-ALA diet reduces cyclooxygenase-2 expression and induces hepatoma cell death (Vecchini et al. 2004). Anorexia-cachexia syndrome, a multifactorial disease characterized by muscle atrophy, fat loss, and progressive loss of function (Freitas and Campos 2019; Argilès et al. 2018), is one of the most prevalent cancer-related consequences, affecting up to 85% of cancer patients. In cancer patients, n-3PUFA supplementation is commonly used to treat anorexia-cachexia syndrome. The efficacy of these drugs in addressing this condition, however, is still up for debate (Laviv et al. 2018). The European Society for Clinical Nutrition and Metabolism (ESPEN) generated cancer patient guidelines in 2017 that only address the use of n-3 PUFAs for cancer cachexia therapy, leaving out other cancer-related disorders that might benefit from n-3 PUFAs (Vega et al. 2021). Cancer patients commonly experience pain, sadness, and paraneoplastic diseases (tumor-induced production of hormones or peptides) (Freitas and Campos 2019). n-3PUFAs are pharmacotnutrients that act as receptor agonists, changing molecular pathways, decreasing inflammatory responses, increasing chemotherapy effectiveness, and extending cancer patients lives (Freitas and Campos 2019; Paixão et al. 2017).

Role of prebiotics, probiotics, and dietary fibers in chemoprevention

Lederberg and McCray developed the phrase “microbiota” to emphasize the importance of bacteria present in the human body in both health and sickness, and the term “microbiome” refers to microorganisms, their genomes, and the surrounding environment (Marchesi and Ravel 2015). Bacteria and their metabolites can interfere with a number of signaling pathways, induce DNA double-strand breaks, promote apoptosis, alter cell development, cause inflammation, and help maintain body homeostasis (Guz et al. 2021). Short-chain fatty acids (SCFAs), choline metabolites, and lipids, among other microbial bioactive substances, play a crucial role in activating host epigenome not just in the gut, but also in the hepatic, cardiac, and central nervous system (Qin and Wade 2018). An altered gut microbiota is associated to the generation of carcinogenic or genotoxic compounds, which is one of the primary microbiome-induced mechanisms implicated in colorectal cancer development (Appunni et al. 2021). The gut microbiota is one of the most affected “organs” by food consumption, and it has emerged as a crucial effector in the diet-cancer association (Song et al. 2015). As a result, dietary patterns appear to have the capacity to directly or indirectly promote or prevent cancer by altering gut bacteria composition and metabolism (Guz et al. 2021). According to ISAPP (International Scientific Association for Probiotics and Prebiotics), probiotics are live bacteria that, when consumed in adequate amounts and provides health advantages to the host body (Gibson et al. 2017). The main metabolites produced by gut microbial fermentation of insoluble dietary fiber, SCFAs (butyrate, acetate, propionate, and valerate) directly stimulates G-protein-coupled receptors, suppress histone deacetylases, and act as energy substrates to link dietary patterns and gut microbiota thereby promoting gut health (Hou et al. 2022). SCFAs suppress cancer cell growth and cause apoptosis and G2-M arrest, resulting in cell death (Matthews et al. 2012). SCFAs (particularly butyrate) block HDAC activity, which increases histone acetylation, which influences gene regulation of cell proliferation, differentiation, and inflammatory response, contributing to intestinal homeostasis and cancer prevention (Parada et al. 2019). The most generally recognized foods having probiotic qualities are fermented dairy products such as kefir, yoghurt (which includes Lactic bacteria, i.e., bifidobacterium), and cheese. Prebiotics, like probiotics, have a big influence on the gut flora. According to the ISAPP (Gibson et al. 2017), prebiotics are substrates that are “selectively utilized by host microorganisms, conferring a health advantage.” According to observational and preclinical research, dietary fiber consumption may lower the incidence of ovarian cancer, breast cancer, stomach cancer, and prostate cancer (Dong et al. 2011; Bravi et al. 2009; Pelucchi et al. 2001, 2004).

Role of vitamins in chemoprevention

Vitamins like the other bioactive metabolites are not produced in the body; therefore, they must be consumed in the form of external supplements. Vitamins A, C, and E are antioxidant vitamins that have protective qualities. Regular antioxidant consumption can also help to avoid cardiovascular and neurological degenerative illnesses as well as cancer. Antioxidant nutrients including vitamin A, vitamin E, beta-carotene, and vitamin C are important in the detoxification of reactive oxygen species (Nepomuceno 2011). Apoptotic and anti-angiogenic activities as well as inhibitory effects...
on cancer cell metastasis have been observed in antioxidants adjuvant vitamins (Jain et al. 2017). Vitamins C, D, and E have been related to a decrease in the side effects of chemotherapy and radiation therapy for colon, gastric, head, and neck, lungs, stomach, and prostate cancers (Jain et al. 2017).

Folate is a water-soluble B vitamin that can be found in a variety of foods such as dark-green green vegetables and beans. Folic acid is a synthetic version that can be found in food supplements such as grains and cereals (Pieroth et al. 2018). Several studies have found a link between folate intake and a decrease in one of the perceived risks associated with various types of cancers like breast cancer, colorectal cancer, prostate cancer, and lung cancer (Kennedy et al. 2011; Figueiredo et al. 2009; Chen et al. 2014). Low folate levels have been associated to carcinogenesis due to uracil incorporation in the DNA helix and the resulting double-stranded breaks which can lead to cancer-causing mutations (Petrone et al. 2021). DNA methylation is an epigenetic change that is necessary for optimal genome regulation and development. Folate is an important source of the one carbon group required to methylate DNA (Irimie et al. 2019). In the methionine route, folate in the form of 5-methyltetrahydrofolate (5-MTHF) is required for homocysteine to methionine conversion, and 5-adenosylmethionine (SAM) is generated from methionine (Pieroth et al. 2018). In crucial processes including DNA and RNA methylation, SAM is a key methyl donor. Inadequate SAM synthesis can result in less methylation of CpG islands in DNA, which can impact transcriptional activity and alter the expression of tumor suppressor genes and proto-oncogenes (Pieroth et al. 2018). A deficiency of folate can also impact the transformation of deoxy uridine monophosphate to deoxythymidine monophosphate, a nucleic acid necessary for DNA synthesis and repair. When uracil is mistaking for thymidine, unstable DNA, DNA strand breakage, and faulty DNA repair can occur (Pieroth et al. 2018). Among the most important genes involved in folic acid conversion is methylene tetrahydrofolate reductase (MTHFR), which catalyzes the production of 5-methyl tetrahydrofolate. C677T is a significant MTHFR gene variation that causes high levels of homocysteine and DNA hypomethylation. MTHFR genetic variants have been linked to an increased risk of malignancies such as breast cancer, glioblastoma, and hepatocellular carcinoma (Petrone et al. 2021).

A complex of fat-soluble pro-hormones and their metabolites make up the vitamin D system. Photocatalytically generated vitamin D2 (ergocalciferol) in plants and photochemically manufactured vitamin D3 (cholecalciferol) in animal and human skin in response to sunshine (Vuolo et al. 2012). Vitamin D is metabolized to 25-hydroxyvitamin D (calcifediol) in the liver and subsequently to 1,25-dihydroxyvitamin D (calcitriol) in the kidney (Holick 2006). In contrast to its conventional involvement in calcium-phosphorus balance and bone metabolism, vitamin D has been demonstrated to have “non-calcemic” effects in host defense, inflammatory, immunology, and malignancy mechanisms (Vuolo et al. 2012, Holick 2008). High dosages of vitamin D compounds have been demonstrated to inhibit tumor cell proliferation and promote differentiation in a number of in vitro studies. Numerous epidemiologic studies have discovered a link between factors that are thought to lower vitamin D levels (such as geography and latitude, history of sun exposure, and lifestyle) and higher cancer rates, emphasizing the protective effects of sunlight and high vitamin D levels on various types of tumors (Ishihara et al. 2008; Mizoue et al. 2008; Zhang et al. 2020a, b; Pérez-López 2008; Abbas et al. 2007). Vitamin D acts as a transcription factor, impacting tumor development, cell differentiation, and apoptosis essential processes. Higher vitamin D levels are considered to protect against a range of cancers, likely through genomic and non-genomic effects mediated by the vitamin D receptor (vdr) and autocrine/paracrine metabolism of the vdr’s ligands (Vuolo et al. 2012). The (vdr) transcription factor is a ligand-inducible transcription factor that targets genes involved in metabolic, inflammatory, cell growth, and differentiation processes (Ramagopalan et al. 2010). Genetic variations in the (vdr) genes and the vitamin D metabolism pathway initiators, CYP27B1 and CYP24B1, have been associated to an increased risk of oral squamous cell carcinoma and patient morbidity (Zeljic et al. 2012). Vitamin D may be able to overcome apoptosis resistance in oral squamous cell carcinoma by modifying VDR expression in precancerous lesions (Grimm et al. 2015). By up-regulating p27 and p21, the cyclin-dependent kinase inhibitors implicated in G1 arrest, 1,25-dihydroxyvitamin D, and its analogues produce G0/G1 arrest and an inhibitory influence on the G1/S checkpoint of the cell cycle (Wang et al. 1996).

Vitamin C commonly known as ascorbic acid is another key water-soluble antioxidant that is not generated by humans and must be received through supplementation. Vitamin C may be found in citrus fruits such as oranges, strawberries, grapes, and lemons, as well as cruciferous vegetables and dark leafy greens. Vitamin C has antioxidant, pro-oxidant, and gene expression regulator properties that are connected to cancer (Villagran et al. 2021). Several studies have indicated that ascorbate either alone or in combination with chemotherapeutics has a cytotoxic impact on tumor cells in vitro (Reddy et al. 2001; Woźniak and Anuszewska 2002; Cieslak et al. 2015; Xia et al. 2017). Ascorbic acid acts as an antioxidant by producing modest amounts of hydrogen peroxide. Because cancer cells have limited enzymatic and non-enzymatic hydrogen peroxide-processing mechanisms, excessive quantities of hydrogen peroxide produced by high dosages of vitamin C can be lethal (Chen et al. 2015). Numerous studies show increased growth arrest, p53 up-regulation, declined ATP
production, interrupted cellular metabolism, suppression of antioxidant genomic expression NrF-2, and/or cell lysis by apoptotic cell death as a consequence of oxidative damage induced by hydrogen peroxide produced in cell culture medium when ascorbate concentrations of 1 mM or higher are present (Frömberg et al. 2011; Vissers and Das 2018). Both the sodium-dependent vitamin C transporter (SVCT) and the glucose transporter (GLUT) are transporter proteins that carry vitamin C across cell membranes while also controlling oxidative stress. Dehydroascorbate has a structure similar to glucose and may be absorbed into cells via the GLUT, contributing to the intracellular pool in red blood cells, neutrophils at infection sites, and other regions of the body (Vissers and Das 2018). Once within the cell, GSH, NADH, and NADPH-dependent enzymes break down DHA, possibly depriving the cell of these vital nutrients. KRAS and BRAF mutations are common in colorectal cancer, and they are associated with GLUT overexpression and a glycolytic phenotype (Vissers and Das 2018). The anti-tumor activity of ascorbate in colorectal cancer may be explained by a relationship between these events and GLUT overexpression in KRAS and BRAF mutant cells. DHA was taken up by GLUT in cultured cancer cells with mutations in KRAS and BRAF when they were fed with mM levels of ascorbate, and this was connected to a loss of cell survival (Vissers and Das 2018). In a growing tumor, rapid cell proliferation and inadequate blood vessel development result in localized oxygen and nutrition deprivation, which activates the hypoxia-inducible factor-1 (HIF1) (Semenza 2010). HIF1 is linked to proliferative, metastatic, and treatment-resistant tumor phenotypes and regulates cellular adaptation to the hypoxic microenvironment. As a result, HIF1s are now considered a key target for cancer treatment. Proline and asparagine hydroxylases, both of which require ascorbate as a cofactor, control HIF1 levels and transcriptional activity (Campbell et al. 2015).

Vitamin E is a lipid-soluble vitamin that exists in eight natural variants: α, β, γ, and δ isomers of tocopherol and α, β, γ, δ isomers of tocotrienol. Nuts and edible vegetable oils are excellent sources of vitamin E (Ungurianu et al. 2021). Various empirical studies have been conducted to investigate the relationship between vitamin E and cancer risk (Abraham et al. 2019). Anticancer benefits of vitamin E have been linked to antioxidant, anti-inflammatory, anti-proliferative, anti-angiogenic, and immunological modulatory pathways as well as regulation of the HMG CoA reductase enzyme (Abraham et al. 2019; Miyazawa et al. 2009). Vitamin E isomers, particularly γ- and δ-tocopherol and to a lesser extent α-tocopherol, obstruct E2-induced cell proliferation and upregulate PPARγ and NrF2 expression in mammary carcinoma which subsequently reduces inflammation and oxidative stress (Smolarek and Suh 2011; Smolarek et al. 2013). Tocotrienols cause apoptosis by a variety of methods, including death receptor activation, raising the Bax/Bcl-2 ratio and activating p53 signaling (Agarwal et al. 2004). When malignant human liver cells were cultured with γ-tocotrienols, increased caspase 8 and caspase 9 expressions occur resulting into cell death (Sakai et al. 2006). In ovarian cancer cell lines, δ-tocotrienol cause cell cycle arrest in the G1 phase along with mitochondrial apoptosis (Fontana et al. 2021). α-Tocopherol inhibits esophageal squamous cell carcinoma by regulating the PPAR-Akt signaling pathway early in the carcinogenesis process (Xu et al. 2017).

**Vitamin A and carotenoids**

Vitamin A can be obtained from the diet either as preformed vitamin A (mainly as retinyl ester, retinol or retinoic acid) or provitamin A commonly known as carotenoids (Doldo et al. 2015). Retinoids are natural or synthetic derivatives of vitamin A. Retinol is the physiological form of vitamin A, which is metabolized to retinol in target cells and subsequently oxidized to all-trans-retinoic acid and its stereoisomer 9-cis-retinoic acid (Pettersson et al. 2002). After being absorbed by the mucosal cells, provitamin A, i.e., carotenoids, are transformed to retinaldehyde and then to retinol (Doldo et al. 2015). By triggering differentiation and/or growth arrest, the vitamin A metabolite retinoic acid has been found to have chemopreventive and therapeutic effects for malignancies like head and neck, cervical, neuroblastoma, and promyelocytic leukemia (Niles 2004). 9-cis-Retinoic acid induce apoptosis in pancreatic cancer cells via activating RAR- and altering Bcl-2/Bax expression (Pettersson et al. 2002). According to a meta-analysis, a higher dietary consumption of vitamin A may help to prevent the development of ovarian cancer (Wang and He 2020). Plants, fungi, algae, birds, fish flesh, bacteria, microalgae, and yeasts are all sources of carotenoids, which include carotenes, xanthophylls, and apocarotenoids (Koklesova et al. 2020). Despite the fact that certain carotenoids are precursors to vitamin A, many of them are powerful antioxidants and anti-cancer agents (Niranjana et al. 2015). According to epidemiological and experimental studies, carotenoid consumption is inversely associated to cancer prevalence. In colon, liver, breast, prostate, cervix, and leukemia cells, carotenoids such as α-carotene, β-carotene, β-cryptoxanthin, lycopene, lutein, zeaxanthin, violaxanthin, neoxanthin, canthaxanthin, astaxanthin, fucoxanthin, and siphonoxanthin have been demonstrated to have anti-cancer action (Niranjana et al. 2015). Immune modulation, hormone, and growth factor signaling, cell cycle progression, cell differentiation, and apoptosis regulation are the major mechanisms of carotenoids cancer chemoprevention (Niranjana et al. 2015). By interfering with several phases of the cell cycle, β-carotene and lycopene have been shown to decrease tumor cell growth.
| Mineral   | Cancer type                        | Anticancer mechanism                                                                                                                                                                                                                                                                  | References                                                                                     |
|-----------|------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| Selenium  | Prostate, breast, lung, colorectal, ovarian, liver | Reverses the expression of genes linked in carcinogenesis, maintains genomic integrity and slows tumor growth. Activation of tumor suppressor genes, genes involved in phase II detoxifying enzymes, and specific apoptotic genes like caspases. | Tsavachidou et al. 2009; Ferguson et al. 2012; Steinbrenner and Sies 2009; Schrauzer 2009; El-Bayoumy and Sinha 2005; Xiao and Parkin 2006; Björnstedt and Fernandes 2010 |
| Zinc      | Ovarian, prostate, and liver cancer | Protects normal cells from DNA damage, causes apoptosis, and promotes epithelial-mesenchymal transition via an MTF-1-dependent mechanism, all of which help ovarian tumor spread.                                                      | (Singh et al. 2012; Sliwinski et al. 2009; Cheng et al. 2021; Zhang et al. 2020a, b; Costello and Franklin 2014) |
| Vanadium  | Breast, renal, liver, lung and GIT  | Inhibition of cellular tyrosine phosphatases and/or activation of tyrosine phosphorylases protects genomic instability. Both actions activate signal transduction pathways that lead to apoptosis and/or the activation of tumor suppressor genes DNA breakage and fragmentation as well as plasma membrane lipoperoxidation, can cause cell-cycle arrest and/or cytotoxicity. | (Singh et al. 2012; Crans et al. 2018, 2019; Evangelou 2002)                                     |
| Magnesium | Colorectal, liver and esophageal, breast, prostate and ovarian cancer | Mg forms complexes with ATP, ADP and GTP and is required for the action of the glycolysis enzymes glucokinase, phosphofructokinase, and pyruvate kinase, which is known to be the preferred route for neoplastic cells to produce energy. Mg interacts with DNA polymerase, ribonucleases, adenylyl cyclase, phosphodiesterase’s, guanylate-cyclase, ATPases, and GTPases, and is therefore involved in nucleic acid and protein metabolism as well as signal transmission. Mg2+ ions are enzyme cofactors that aid DNA repair pathways in maintaining genomic integrity and fidelity. Any magnesium deficiency might lead these systems to fail causing DNA alterations. | (Leidi et al. 2011; Yang et al. 2000a, 2000b, 2002; Chiu et al. 2004; Blaszczyk and Duda-Chodak 2013) |
| Germanium | Breast, Lung cancer                | Induce interferon, enhance natural killer cell activity, and increase intraperitoneal macrophage action to inhibit tumor and metastases development and change immune system response                                                                                       | (Aso et al. 1985; Kumano et al. 1985; Kuwabara et al. 2002; Kaplan et al. 2004; Jeyaraman and Sellappa 2011; Cho et al. 2020) |
Bioactive dietary components have a substantial influence on genes and nutrition, according to nutrigenomics research. Disease progression may be influenced by both their disease prevention. Nutrigenomics is a crucial science for understanding the gene-nutrient interactions that control illness prevention. Nutritional treatments are fundamental public health strategies because proper nutrition plays a significant role in disease progression. A person’s health and risk of developing diseases like cancer may be influenced by both their genes and nutrition, according to nutrigenomics research. Bioactive dietary components have a substantial influence in cancer prevention and therapy, according to in vitro and in vivo research. According to current research, bioactive dietary components can alter a variety of biological processes connected to carcinogenesis including carcinogen absorption, DNA repair, proliferation and differentiation, necrosis, inflammatory mechanisms, and revascularization. Dietary interventions may lessen toxicity, increase chemotherapy efficacy, and lower the risk of long-term problems in cancer patients, while the evidence is still limited. It is vital to explore the negative effects of dietary supplements as well as the health benefit doses in research studies. Long-term research supporting the use of minerals, vitamins, and antioxidants in cancer patients is currently lacking. Clinicians and researchers must evaluate the dietary demands of individual cancer patients in order to treat cancer and improve life expectancy.

Role of minerals in chemoprevention

Minerals are essential components of micronutrients for humans since they not only aid in the formation of biological structures but also ensure that the body’s fundamental biological processes are operating properly (Prentice and Bates 1994). Some minerals, such as zinc, selenium, magnesium, vanadium, and germanium, are connected to human health and cancer prevention among the multitude of essential and non-essential minerals (Singh et al. 2012). The immune system is the natural mechanism that defends against cancer (Xu et al. 2021), and minerals supplement it. Numerous population studies have discovered that dietary mineral intake may influence the development of some cancers. The Rotterdam Study found a link between dietary zinc and iron intake and a decreased menace of lung cancer (Muka et al. 2017).

As per case–control studies, higher nutritional selenium and zinc consumption may lower the incidence of squamous cell carcinoma and increased calcium, magnesium, and potassium consumption in the diets can help to lower the risk of colon cancer (Lu et al. 2006a, b; Jessri et al. 2011; Meng et al. 2019). Nevertheless, extensive iron consumption may upsurge the risk of colorectal cancer. Nutritional iron may be associated to a higher risk of breast cancer, especially in women who did not receive antioxidants and ingested more lipids during the research (Diallo et al. 2016). Minerals have been linked to oxidative stress, inflammatory response, particular immunity, carcinogenesis, and malignant cell proliferation, among other cancer-related homeostatic systems (Xu et al. 2021). The anticancer mechanism of some minerals is summarized in Table 1.

Conclusion and future perspectives

Nutritional treatments are fundamental public health strategies because proper nutrition plays a significant role in illness prevention. Nutrigenomics is a crucial science for understanding the gene-nutrient interactions that control disease progression. A person’s health and risk of developing diseases like cancer may be influenced by both their genes and nutrition, according to nutrigenomics research. Bioactive dietary components have a substantial influence...
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