REVIEW ARTICLE

Drink your prevention: beverages with cancer preventive phytochemicals

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KEY WORDS

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ABSTRACT

Specific alimentary habits, including a high consumption of vegetables, fruits, cereals, and olive oil, characteristic of the Mediterranean diet, are associated with a reduction of risk of cardiovascular pathologies, type 2 diabetes, neurodegenerative diseases, and some cancers. Numerous beverages contain diverse natural compounds, termed phytochemicals, that have been reported to exert antitumor, antiangiogenic, and antioxidant properties. Here we review the chemopreventive and angiopreventive properties of selected phytochemicals found in common beverages: epigallocatechin (green tea), triterpenoids (citrus juices), resveratrol (red wine), xanthohumol (beer), procyanidin (chocolate), and caffeine (coffee), focusing on their molecular mechanisms, providing "ready to drink" prevention approaches.

Introduction Changes in the world food economy are reflected in shifting dietary patterns, for example, increased consumption of energy-dense diets rich in fat, mainly saturated fat, and low in unrefined carbohydrates and vitamins. These alimentary patterns are often associated with reduced energy consumption and a sedentary lifestyle.[1-4] Given the changes occurring in diet and lifestyle habits, chronic noncommunicable diseases are becoming increasingly significant causes of disability and premature death in both developed and newly developing countries. It is known that specific alimentary habits, including the Mediterranean diet characterized by a high consumption of vegetables, fruits, cereal, spices, and olive oil, are associated with a reduction of risk of cardiovascular diseases, type 2 diabetes, neurodegenerative diseases, and some cancers. Prevention still remains the principal approach to manage such diseases.

Dietary factors, found in solid foods and beverages, could contribute to the prevention of approximately 30% of cancers in industrialized countries, making diet the second preventive approach in cancer. Fruit and vegetable consumption, both as solids and liquids, provides different nutrients and a range of bioactive compounds including vitamins (vitamin C, folate, and provitamin A), minerals (potassium, calcium, and magnesium), phytochemicals (flavonoids, phenolic acids, alkaloids, and carotenoids), and fibers that have been associated with reduced cancer risk. However, translation into the clinic of nutraceuticals as drugs has been a major hurdle. Several studies have demonstrated that diet, along with early screening, represents a crucial point in cancer management, suggesting that prevention starts from what we eat and what we drink. Chemoprevention is defined as the use of natural, synthetic (laboratory-made), or biologic (living source) agents able to delay, reverse, or inhibit tumor progression, in order to decrease the risk of developing invasive or clinically significant disease.[5,6] Michael Sporn coined this term in 1979 while testing the effect of vitamin A and retinoid-supplemented diets on animal models of epithelial cancer.[7] When referred to cancer, a potential chemopreventive agent should be a well-tolerated compound with no toxicity or side effects yet administered for an extended period of time to healthy subjects.

Several common beverages are rich in phytocompounds that have been shown to have antiproliferative, proapoptotic, antioxidant, and anti-inflammatory activities, and many of those have been extensively investigated for their potential in cancer therapy and prevention. Thus, beverages can be considered as a prevention tool, easily administered and "ready to drink".

In the present paper, we aimed to discuss the potential use of diet derivatives, focusing on

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TABLE Biological activity associated with flavonoids contained in green tea, fruit juice, beer, chocolate, coffee, and red wine

Beverage	Molecules	Biological effects	References
green tea	epigallocatechin-3-gallate	anti-inflammatory	8,15
		cardioprotection	8
		antiproliferative/proapoptotic	11,12,13
		antiangiogenic	14
fruit juice	triterpenoids	anti-inflammatory/antioxidant	21, 22, 26
		antiangiogenic	19, 20
		antiproliferative/proapoptotic	23, 24, 25
red wine	resveratrol	cardioprotection	57
		anti-inflammatory/antioxidant	49, 50
		antiproliferative/proapoptotic	41, 42, 44, 45
		antiangiogenic	51, 52
beer	xanthohumol	anti-inflammatory/antioxidant	64, 74
		antiangiogenic	73
		antiproliferative/proapoptotic	68, 69, 71
		antiestrogenic	65, 66, 67
chocolate	procyanidins	anti-inflammatory/antioxidant	81, 83
		antiangiogenic	87
		antiproliferative/proapoptotic	84, 85, 86
coffee	caffeine	antiproliferative/proapoptotic	90, 91, 92

beverages as an approach to prevent or interfere with cancer development, summarizing the key features of some common diet-derived natural compounds with chemopreventive properties. We will discuss a few of these compounds, emphasizing how the efficacy of the "natural molecules" or their derivatives are associated with safety for healthy subjects (in a prevention approach) or as an integration to therapy for cancer patients (in an intervention approach).

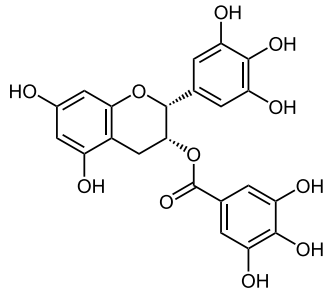
Green tea and epigallocatechin Green tea is obtained from the evergreen plant *Camellia Sinensis* leaves, and it can be considered as the most ancient beverage apart from water. Drinking green tea for disease prevention is a traditional Chinese recommendation. Considering its high content of flavonoids, green tea possesses antiproliferative, antimutagenic, antioxidant, antibacterial, antiviral, and chemopreventive activities.[8] Catechins (epicatechin, epigallocaetchin, epicatechin-3-gallate, and epigallocatechin-3-gallate [EGCG]) are the major classes of flavonoids contained in green tea,[9] and EGCG is the most abundant one, representing from 50% to 75% of the total amount of catechins.

The effects of EGCG have been extensively investigated. EGCG has been found to be endowed with anti-inflammatory, antioxidative, anti-infective, and neuroprotective properties.[10] Furthermore, it shows a chemosensitizing effect on a wide range of malignancies by inhibiting tumor cell growth, invasion, angiogenesis, and the promotion of metastasis.[11] The antineoplastic properties of EGCG have been tested in vitro and in vivo, and, more recently, in clinical trials.[12]

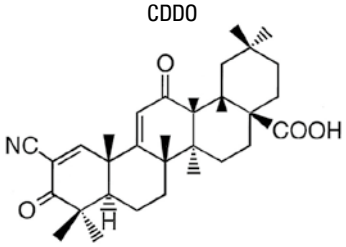
Epidemiological studies conducted on the Japanese population reported the preventive activities of EGCG in breast cancer. These effects are supported by numerous in-vitro and in-vivo studies. Numerous molecular mechanisms have been associated with the anticancer activities of EGCG, including impairement of tumor growth by inhibiting the activation of HIF-1α and NK-κB, and repression of vascularization.[13] Other studies have shown the ability of green tea polyphenols to inhibit angiogenesis in breast cancer by downregulating vascular endothelial growth factor (VEGF) and matrix metallopeptidase 9 (MMP-9) expression through signal transducers and activators of transcription (STAT) 3.[14] EGCG also reduces tumor volume in mouse models of breast cancer.[15] The biological activities of EGCG on breast cancer are related to its ability to modulate estrogen target gene expression such as trefoil factor 1 and progesterone receptor. EGCG also decreases P-glycoprotein and breast cancer resistance protein (ABCG2) expression in drug-resistant cancer cells of many types of tumors.

Several studies have shown the ability of EGCG to inhibit tyrosine kinase receptors and their downstream effectors such as pAKT and pERK.[16,17] The laminin receptor has been identified as a potential EGCG receptor that modulates

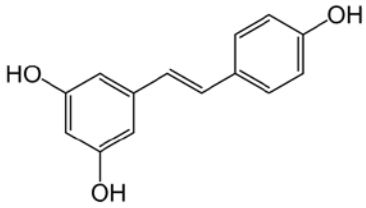
epigallcatechin-3-gallate



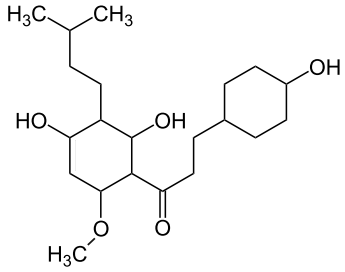
CDDO



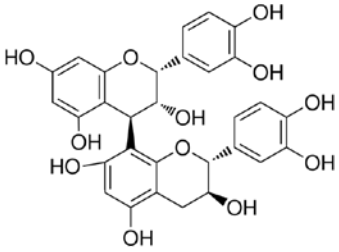
resveratrol



xanthohumol



procyanidin B_2



caffeine

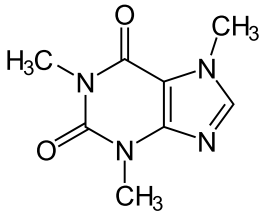


FIGURE 1 Phytochemicals in beverages: green tea (epigallcatechin), fruit juice (triterpenoids), red wine (resveratrol), beer (xanthohumol), hot chocolate (procyanidins), and coffee (caffeine).

several crucial intracellular signaling pathways.[18] In addition, EGCG exerts indirect effects on epidermal growth factor receptors (EGFRs), STATs, and activator protein 1.

In a recent study, EGCG has been used in combination with arctigenin and curcumin on prostate and breast cancer cells, resulting in a strong effect on cell cycle arrest and apoptosis associated with an increase in the ratio of Bax to Bcl-2 proteins, a decrease of NF-κB, PI3K/Akt, and STAT3 pathway activation.

Fruit juice and triterpenoids Fruit consumption is a key feature of the Mediterranean diet as supported by the food pyramid, in consideration of their high content of vitamins, mineral salts, antioxidant, phytochemicals, and water. Fruit juice represents a rapid solution for immediate fruit consumption and is commercially available. Triterpenoids are one of the most representative compounds in the groups of naturally-derived molecules. They can be found in vegetables and fruits such as bearberry, coffee, aniseed, olives, apples, blueberry, asian pear, bell pepper, eggplant, grapefruit, sweet cherry, cranberry, grapes, tomatoes, oranges, and mandarins. Triterpenoids have been studied for their promising activities since 1988 and these include a wide range of biological effects like antiviral, antifungal, anti-inflammatory, and antitumor activity. Among triterpenoids, oleanolic acid represents one of the most promising and widely studied categories, for its antitumor, protective (heart, liver, stomach), and antidiabetic properties. This leads to the production of synthetic analogues of oleanolic acid, where the introduction of chemical modifications significantly increased activity. Some of the most studied triterpenoids are represented by CDDO (2-cyano-3, 12-dioxooleana-1,9(11)-dien-28-oic acid) as well as its C28 methyl ester (CDDO-Me) and C28 imidazole (CDDO-Im) variants.

The antiangiogenic and angiopreventive potential of triterpenoids has been previously studied by our group.[19,20] Two other groups also demonstrated that triterpenoids mediated their proapoptotic and anti-inflammatory effects through NF-κB pathway inhibition.[21,22] Several studies have speculated on the promising use of triterpenoids to inhibit colorectal cancer,[23] prostate cancer,[24] and lung cancer growth.[25] Choi et al.[26] demonstrated that CDDO derivatives exert anti-inflammatory effects in colorectal cancer by downregulating cyclooxygenase 2 and upregulating 15-hydroxyprostaglandin dehydrogenase. Liu et al.[27] demonstrated its anti-inflammatory effects in ischemia-reperfusion injury through the activation of Nfr2 signaling. It has also been reported that CDDO-Me reduced both inflammatory and fibrotic cytokine expression (tumor growth factor β and interleukin [IL] 6) and early upregulation of fibrotic gene expression in the lung (α smooth muscle actin, fibronectin, and collagen type 1).[28] The antitumor efficacy of several

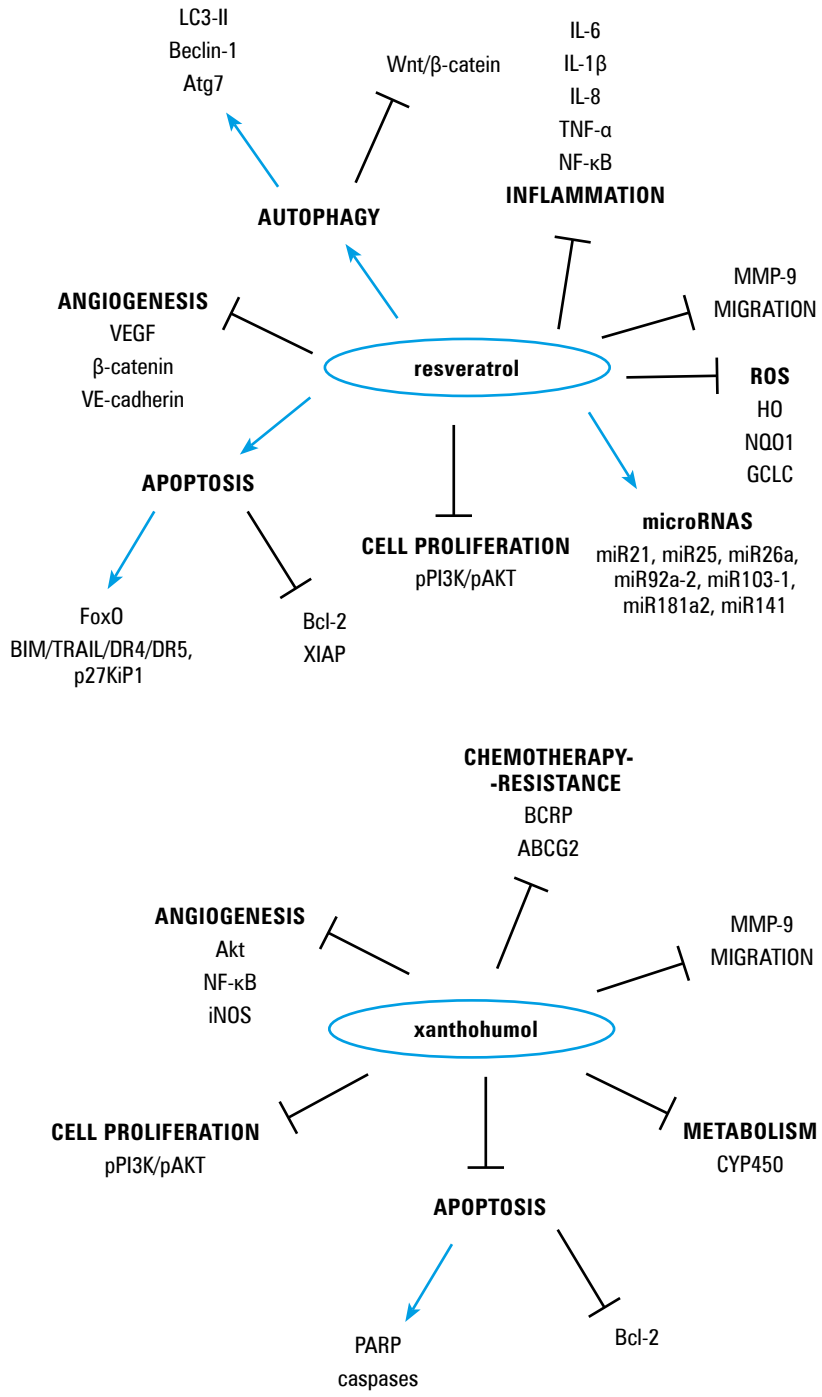


FIGURE 2 Cellular and molecular mechanisms involved in flavonoid-associated (resveratrol and xanthohumol), chemopreventive and angiopreventive activities

Abbreviations: ABCG2 – ATP-binding cassette sub-family G member 2, Atg7 – autophagy-related protein 7, Bcl-2 – B-cell lymphoma 2, BCRP – breast cancer resistance protein, Bim – bcl-2-like protein, CYP450 – cytochrome P450, GCLC – glutamate-cysteine ligase, HO – heme oxygenase, IL – interleukin, LC3-II – LC3-phosphatidylethanolamine conjugate, MMP-9 – matrix metallopeptidase 9, iNOS – induced nitric oxide synthase, NQO1 – NAD(P)H:quinone acceptor oxidoreductase 1, NF-κB – nuclear factor κB, PARP – poly(ADP-ribose) polymerase, PI3K – phosphatidylinositol-3-kinases, ROS – reactive oxygen species, TNF-α – tumor necrosis factor α, TRAIL – TNF-related apoptosis-inducing ligand, VE – vascular endothelial, VEGF – vascular endothelial growth factor, XIAP – X-linked inhibitor of apoptosis protein

triterpenoids is currently being evaluated in phase I/II clinical trials.

Olive oil as beverage supplement Recent epidemiological studies have demonstrated that the Mediterranean diet correlates with a lower incidence of cancer and cardiovascular disease, suggesting that the health-conferring benefits are due mainly to a high consumption of fiber, fish, fruits, and vegetables; furthermore, more recent research has focused on olives and extra virgin olive oil. The potential role of polyphenols present in these foods is extremely important. It has been determined that olives contain up to 16 g/kg of phenols typified by acteosides, hydroxytyrosol, tyrosol, and phenyl propionic acids. Extra

virgin olive oil contains smaller amounts of hydroxytyrosol and tyrosol, but also contains large amounts of secoiridoids and lignans. Both foods contain substantial amounts of other compounds deemed to be anticancer agents, such as squalene and terpenoids.

Because of the high importance of these molecules as chemopreventive agents, several studies have focused on the anticancer and health-benefit effects of olive and its derivatives. The liquid effluent of the olive oil process, referred to as olive mill wastewater (OMWW), is a byproduct of extra virgin olive oil production that comes from the vegetation water and the soft tissues of the olive fruits in addition to the water used in oil production. This product contains high amounts of polyphenols, even greater than the olive and oil (up to 24 g/l).

The presence of these important molecules led several laboratories to focus studies on the use of OMWW as a dietary supplement or functional ingredient in food product formulations. Indeed, phenolic-rich extracts of OMWW present hypocholesterolemic and hypoglycemic effects.[29-31] OMWW has antioxidant and anti-inflammatory potential,[32, 33] in addition to chemopreventive and cell-protective effects.[34,35] Several studies have focused on the safety of the high concentrations of polyphenols and established that these molecules do not exert toxic[36] or genotoxic[37] effects in vitro or in animal models.

Servili et al.[38] functionalized milk beverage with phenol extract from OMWW, like 3,4-DHPEA, 3,4-DHPEA-EDA and verbascoside. A number of studies tried to implement fruit juice with derivatives of OMWW, but many other studies are necessary to evaluate the real potential of these functionalized juices. Furthermore, several studies are necessary to find out the way to stabilize the molecules in these foods.

Red wine and resveratrol The healthful and nutritional properties of wine have been historically recognized for thousands of years and the evidence concerning beneficial effects of polyphenols in red wine has been first reported in 1410 AD. Moreover, in 1819, the physician Samuel Black observed that the French population shows a relatively low incidence of coronary heart disease, despite a relatively high dietary intake of saturated fatty acids (French paradox).[39]

Resveratrol (3,5,4'-trihydroxystilbene), a phytoalexin produced in the skin and seeds of several plants, including grapes, berries, grains, tea, and peanuts, is one of the major components in wine.[40] Its concentration depends on the grape cultivar and geographic condition and is estimated between 0.2 to 5.8 mg/l in red wine and approximately 0.68 mg/l in white wine. Resveratrol has been reported to exert diverse health benefits throughout several biological mechanisms associated with chemopreventive properties that include antioxidant, anti-inflammatory, cardio-protective, and antitumor activity.

The anticancer properties of resveratrol were first reported in 1997, demonstrating its inhibitory effects on tumor initiation, promotion, and progression. Moreover, several studies have investigated the potential cancer chemopreventive properties of resveratrol as well as its therapeutic effects in combination with traditional cancer chemotherapy.[41] Resveratrol has been shown to inhibit the phosphorylation of PI3K/AKT, resulting in a decrease of cell proliferation.[42] Moreover, resveratrol is able to increase the nuclear translocation and DNA binding affinity of FoxO transcription factor[43] to activate Bim/TRAIL/DR4/DR5/p27KIP1 and modulate RAS/MAPK, p21, and Notch-2 pathways, enhancing cell apoptosis and inhibiting migration.[44,45] Furthermore, resveratrol has been shown to induce extrinsic and intrinsic apoptosis pathways and to suppress survival mediators (Bcl-2, XIAP, and survivin).[46,47] Several studies have also demonstrated the role of resveratrol in adhesion molecule downregulation and cell cycle protein modulation, resulting in cycle arrest.[48]

Likewise, resveratrol displayed anti-inflammatory properties inhibiting the expression of IL-6, IL-1β, IL-8, and tumor necrosis factor α (TNF-α) cytokines and proinflammatory molecules such as NF-κB, both decreasing IKBβ phosphorylation and activating SIRT1.[49] Several studies have also suggested that resveratrol exerts antioxidant activity through the indirect activation of the Nrf2 pathway, leading to the transcription of several antioxidant defense enzymes (HO-1, NQO1, and GCLC).[50] In multiple myeloma cells, resveratrol is able to inhibit angiogenesis (downregulation of VEGF, β-catenin, and vascular endothelial cadherin), invasion, and metastasis (downregulation of MMP-9).[51,52] Moreover, Fu et al.[53] demonstrated that resveratrol inhibited breast cancer stem-like cells in vitro and in vivo, in addition to inducing the upregulation of LC3-II, Beclin1, and Atg7, key mediators of autophagic process via suppressing Wnt/β-catenin pathway.[53]

Recently, since miRNAs have been recognized as crucial regulators in diverse biological processes, several studies have attempted to elucidate whether resveratrol and other natural compounds are able to modulate miRNAs associated with carcinogenesis and tumor progression. In this context, resveratrol has been shown to induce the upregulation of miR-663, miR-622, and miR-774, which inhibit cell proliferation, and to stimulate the downregulation of miR-21, miR-25, miR-26a, miR-92a-2, miR-103-1 and 2, miR-181a2, and miR-141, which are involved in the regulation of cell apoptosis, survival, and invasion.[54-56]

Since preclinical studies highlighted numerous benefits exerted by resveratrol, several phase I/II clinical trials have been developed in the last decade. In this context, resveratrol has been shown to offer cardioprotective benefits through the improvement of inflammatory markers, atherogenic profile, glucose metabolism, and endothelial function.[57] Although these are promising results,

there are many challenges to overcome in developing resveratrol as an effective therapeutic compound. The major issue concerning resveratrol administration is related to its bioavailability at tolerable doses: resveratrol is a lipophilic agent that is rapidly absorbed and metabolized on oral administration, resulting in a short half-life. Several strategies have been developed to increase resveratrol bioavailability, including synergetic/additive interactions, combining resveratrol administration with other molecules that are potentially able to enhance its effects, and developing resveratrol prodrugs and precursors or nanotechnological approaches (resveratrol nanoformulation) encapsulating resveratrol into liposomes or lipid-core nanocapsules.[58]

Beer and xanthohumol Beer is a common alcoholic beverage in many cultures. It is rich in nutrient as well as nonnutrient components, including carbohydrates, amino acids, minerals, vitamins, and phenolic compounds. Xanthohumol (XN), the most abundant flavonoid in the hop plant (*Humulus lupulus L.*), has been found at a concentration of up to 0.96 mg/l in beer, and it is used as a preservative and to add bitterness and flavor to the drink.[59] XN is a prenylated chalcone (3'-[3,3-dimethyl allyl]-2',4',4-trihydroxy-6'-methoxychalcone) with several biological properties, including anti-human immunodeficiency virus,[60] antiobesity, and anti-infective[61] activities. Moreover, XN shows a potential role in the prevention of bone-destructive diseases.[62] In addition, XN activates the farnesoid X receptor[63] and impairs glucose and lipid metabolism. The anti-inflammatory and antioxidant properties of XN have been extensively documented.[64] Although hop derivatives have been reported to possess affinity to human estrogen receptors in vitro, XN does not show an intrinsic estrogenic potential[65] and reduces estrogen production through inhibition of aromatase activity[66]; the XN antiestrogenic effect was also confirmed in vivo.[67]

Over the last 15 years, increasing evidence has emerged concerning the properties of XN as a chemo- and angiopreventive compound. XN has been described as a good candidate for chemo- and angiopreventive approaches due to its ability to modulate tumor metabolism exerting both cytotoxic and static effects. XN antiproliferative activity is exerted by the induction of poly(ADP-ribose) polymerase-mediated apoptosis in ovarian and prostate cancer as well as glioblastoma cells.[68] In colon cancer cells, XN significantly induces apoptosis by downregulating Bcl-2 and activating the caspase cascade.[69] XN also inhibits cytochrome P-450 CyP enzymes which activate carcinogenesis.[70] XN has also been shown to be an effective antileukemia compound.[71,72]

The XN antiangiogenic and anti-inflammatory effects are associated with the inhibition of Akt/NF-κB signaling pathway.[73] Further, XN inhibits nitric oxide (NO) production by suppressing inducible NO synthase expression.[74] XN also prevents intravasation and metastasis, suppressing epithelial-to-mesenchymal transition and the expression of cell mobility-associated markers. In-vitro studies have also demonstrated that XN exerts inhibitory effects on migration and invasion in breast cancer, acting on MMP-9 expression.[75]

A recent study has also showed that XN has inhibitory effects on breast cancer resistant protein (BCRP/ABCG2), an efflux transporter crucial for multidrug resistance.[76] In-vivo studies confirmed that XN shows preventive activities on preneoplastic lesion development in mouse mammary gland organ culture and interferes with carcinogenesis in the H4IIE rat hepatoma cell line.[67] Moreover, a toxicity study showed that mice receiving an XN-supplemented diet showed no signs of toxicity on a histopathological examination and biochemical serum analysis as compared with mice on a standard diet.[77] Taken together, XN may be considered as a promising phytochemical in the field of chemoprevention.

Chocolate The origin of chocolate dates back more than 3000 years ago, when it was first discovered in the cocoa bean in the Amazon. Cocoa, the dried and fermented seeds, derives from *Theobroma cacao*. Traditionally, chocolate has been considered an unhealthy food due to its carbohydrate and fat content. However, recent reports have suggested that chocolate consumption is associated with several health benefits ranging from diabetic control and cardioprotection to anticancer effects. These protective properties derive from cocoa bean polyphenol compounds.[78]

Cocoa powder is an abundant source of fiber (26%–40%), proteins (15%–20%), carbohydrates (about 15%), and lipids (10%–24%), and contains minerals and vitamins.[79] In addition, cocoa is rich in flavonoids, including epicatechin, and their dimers (procyanidins B_2 and B_1), have been found to be abundantly represented. Flavonoid content in cocoa products depends on the crop variety, post-harvest handling practices, and manufacturer processing techniques.[80] Fresh and fermented cocoa beans contain 10% of flavonols prior to processing, while the cocoa powder, about 3.6%. Furthermore, cocoa-rich dark chocolate contains more flavones compared with milk and white chocolate. Given the abundance of these flavonoids, cocoa shows potent antioxidant and chemopreventive properties. Several data support cocoa anti-inflammatory and antiapoptotic effects and scavenger activity against oxygen radicals. The scavenger activity is exerted by inhibiting glutathione consumption, reactive oxygen species generation, and increasing γ-glutamylcysteinesynthase and glutathione-S-transferase levels.[81] Polyphenolic cocoa extracts increase CYP1A1 mRNA expression, protein levels, and enzymatic activity.[82]

Cocoa also possesses anti-inflammatory properties, and polyphenolic extracts have been reported to limit the secretion of monocyte chemoattractant protein 1, inhibit the inflammatory mediator prostaglandin E2,[83] TNF-α, and the

associated pathways. Cocoa antiproliferative effects on different cancer cell types are associated with a G1/S and G2/M cell cycle arrest. A cocoa-derived pentameric procyanidin inhibits proliferation in human breast cancer cells through site-specific dephosphorylation or the downregulation of several cell cycle regulatory proteins, finally resulting in the G0/G1 cell cycle arrest phase. Similar antiproliferative mechanisms have been described in human colon cancer cell[84] and in Kras-activated pancreatic ductal adenocarcinoma.[85] Cocoa procyanidin induces mitochondria-dependent apoptosis and decreases the expression of NF-κB-regulated antiapoptotic proteins such as Bcl-x L, Bcl-2.[86] Cocoa polyphenols may also influence endothelial cell growth, thus affecting angiogenesis in vitro.[87] Finally, a recent in-vivo study has revealed cocoa polyphenol properties in chemoprevention of carcinogenesis with a significant reduction in the risk of cancer development.

Coffee Along with tea, coffee is the most common hot drink in many cultures. Given the widespread consumption of coffee, increasing attention has been given to its possible effects on the development and progression of diverse chronic diseases including cancer. Caffeine (1, 3, 7-trimethylxanthine), a purine alkaloid contained in the seeds of the coffee plant, represents the most abundant component in coffee, and its potential effects on health still represents a controversial issue.

Caffeine has been extensively investigated for its neuroactive properties and for its ability to affect adenosine receptors. In addition, several studies have reported the caffeine effects on cell proliferation and cell cycle progression. Okano et al.[88] demonstrated that caffeine was able to inhibit proliferation in liver cancer cells and to affect MEK/ERK/EGFR signaling pathways. Moreover, high concentrations of caffeine (5–10 mM) alone or in combination with ionizing radiation have been reported to induce apoptosis and p53-independent G1 phase arrest in human A549 lung adenocarcinoma cells through the inhibition of CDK2 activity, the suppression of CDC2 phosphorylation, and interfering with 14-3-3 binding to CDC25C.[89] Furthermore, caffeine increased apoptosis and mitochondrial damage in human leukemia cells and enhanced caspase-8 activity and DNA fragmentation.[90,91]

Lower concentrations (0.25–1 mM) of caffeine have been reported to induce G0/G1 cell cycle arrest without promoting apoptosis. Hashimoto et al.[92] demonstrated that caffeine was able to inhibit the activation of the cyclin D1–CDK4 complex in a dose-dependent manner and to suppress the phosphorylation of Rb protein. In addition, caffeine has been shown to decrease the phosphorylation of AKT and its substrate GSK-3β and to directly inhibit PI3K activity.[92,93] Furthermore, caffeine has been reported to significantly potentiate the effect of chemotherapy with conventional antineoplastic drugs. Among these, caffeine enhanced the cytotoxic activities of ionizing radiation or carboplatin in human leukemic cells, decreasing the levels of an apoptosis inhibitor, glutathione.[94]

Conclusions and future perspectives Taken together, diverse studies suggest that diet significantly contributes to prevention and even intervention approaches in oncology. Daily consumption of phytochemicals from mixed food sources, including beverages, together with balanced diet and physical activity, could provide a "natural" preventive approach to improve individual health status, including potential efficient cancer prevention with minimal toxicity. In this review, we focused our attention on the more common beverages that are rich in phytochemicals. Other vegetable-derived fluids, for example from beets[95-97] and cabbage,[98-100] also appear to possess promising chemopreventive and chemosensitizing properties.

According to this increasing amount of evidence, the public and private sectors should pay more attention to the diet, with educational projects and product attention. Given the fact that the ideal chemopreventive agent does not exist, the consumption of several natural and dietary compounds with chemopreventive molecules could represent a winning strategy for cancer control.

We like the idea that a glass or a cup of a beverage containing healthy phytochemicals could be an easy way to drink our prevention.

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ARTYKUŁ POGLĄDOWY

Łyk prewencji: napoje zawierające przeciwnowotworowe substancje fitochemiczne

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STRESZCZENIE

Pewne nawyki żywieniowe, takie jak duże spożycie warzyw, owoców, produktów zbożowych oraz oliwy z oliwek, charakterystyczne dla diety śródziemnomorskiej, wiążą się ze zmniejszeniem ryzyka chorób sercowo-naczyniowych, cukrzycy typu 2, chorób neurodegeneracyjnych oraz niektórych nowotworów złośliwych. Wiele napojów zawiera różnorodne naturalne składniki, tzw. fitochemiczne, które mają stwierdzone właściwości przeciwnowotworowe, antyangiogenne i antyoksydacyjne. W niniejszym przeglądzie omawiamy właściwości chemioprewencyjne i angioprewencyjne wybranych substancji fitochemicznych obecnych w popularnych napojach: epigallokatechiny (w zielonej herbacie), triterpenoidów (w sokach owoców cytrusowych), resweratrolu (w czerwonym winie), procyjanidyny (w czekoladzie) i kofeiny (w kawie), skupiając się na mechanizmach molekularnych stanowiących „gotowe do spożycia" strategie prewencji.

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