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Fruit phytochemicals: Antioxidant activity and health-promoting properties

Emmanuel Kormla Danyo*, **Maria N. Ivantsova**

Ural Federal University named after the first President of Russia B.N. Yeltsin, Yekaterinburg, Russia

* e-mail: e.kdanyo@gmail.com

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Abstract:
Synthesized in plants, polyphenols are powerful antioxidants and protect against stressful conditions. We aimed to identify different kinds of phytochemicals in fruits and provide detailed information on the roles they play in promoting good health in the human body. We also discussed the biological activities of phytochemicals found in several fruits.

Google Scholar and PubMed databases were used to search for relevant information that could assist in answering our research questions. We selected and reviewed both research and review articles related to the purpose of our study.

Fruits contain numerous antioxidants which neutralize the negative impact of free radicals on the body. Free radicals are destructive species that can be produced during normal body metabolism or come from exogenous sources such as smoking or exposure to radiation. Due to their unstable nature, they can cause damage to cellular macromolecules, resulting in the development of degenerative diseases. Phytochemicals are diverse groups of bioactive compounds found in fruits that have potent antioxidant activity and exhibit several health-promoting properties in both *in vivo* and *in vitro* studies. There are two major groups of antioxidants: natural (or dietary) antioxidants and synthetic antioxidants. Natural antioxidants have gained much popularity in recent times because of the safety concerns surrounding the use of synthetic antioxidants.

The consumption of fruits plays a critical role in disease prevention, especially diseases resulting from oxidative damage to cells. The inclusion of fruits in one's daily diet helps improve their overall wellbeing.

Keywords: Fruits, antioxidants, bioavailability, polyphenols, carotenoids, biological activity

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INTRODUCTION

Fruits are important in the human diet because they provide the body with nutrients that promote growth and development, as well as maintain good health. Insufficient intake of fruits is one of the top ten risk factors responsible for death globally. Increasing fruit consumption can save the lives of about 2.7 million people each year [1]. Many individuals recognize the importance of diet in promoting good health and preventing disease. This is driving the search for new diet regimens with a positive impact on human health. Scientists are vigorously screening various food products, such as fruits, for potential disease-preventing properties. Fruits are referred to as "functional foods", and studies have established the need to include them in the human diet [2].

Reactive oxygen species are free radicals involved in oxidation reactions in the body. They are harmful and can cause the breakdown of cell membranes, damage to membrane proteins, and DNA mutations. This can result in aging and many diseases such as arteriosclerosis, cancer, diabetes mellitus, liver injury, inflammation, skin damage, coronary heart disease, or arthritis. Antioxidants can inhibit the oxidation of molecules by breaking the chains of free radical reactions by donating their own electrons to free radicals [3]. Fruits are endowed with many bioactive compounds such as vitamin C, vitamin E, carotenoids, flavonoids, tannins, and other phenolic constituents, which act as potent antioxidants [4].

Although mostly consumed fresh, fruits can be processed into different kinds of food products such as canned foods, juices, pastes, etc. due to their free radical scavenging and health-promoting properties [2]. The consumption of bioactive compounds from fresh fruits or their processed products is linked with the prevention and decreased risk of many degenerative diseases [2]. Fruit-based products such as juices are widely available on the market, and they have been shown to contain a lot of compounds that exhibit antioxidant properties [5, 6]. Studies have found that polyphenols present in grape juice can protect individuals from heart disease, while juice from berries and apples can inhibit hypercholesterolemia [7]. Also, juice obtained from oranges, pineapples, and grapefruits contains good quantities of folic acid derivatives that are involved in the prevention of diseases of the nervous system and malformations such as spina bifida [8].

Studies are demonstrating that plant-based diets containing a lot of fruits and other nutrient-rich plant foods can lower the risk of diseases associated with oxidative stress [9]. Antioxidants from natural sources such as fruits are now gaining much popularity, especially in the food industry, due to their safety, unlike synthetic antioxidants, as well as their preventative and therapeutic effects on the body. Although synthetic antioxidants are used in food production to prevent lipid oxidation, butylated hydroxyanisole and hydroxytoluene are suspected to cause cancer and liver damage in animal studies [10, 11]. Diets containing adequate amounts of plant-based foods are highly important for maintaining good health. Food from plants such as fruits, vegetables, and whole grains contains enough antioxidants and minimizes the occurrence of chronic diseases [12]. Individuals who consume fruits in large quantities have a reduced risk of developing cancer and early death, especially from cancers involving epithelial cells, such as those in the cervix, lungs, stomach, esophagus, pancreas, and colon [12].

This review provides current information on phytochemicals present in fruits and shows them as potent antioxidants that promote good health by preventing diseases such as cancer, diabetes, etc. It also discusses some of the factors that can reduce fruit phytochemical bioavailability and thus decrease their health benefits for the human body.

STUDY OBJECTS AND METHODS

We reviewed relevant scientific literature found in Google Scholar and PubMed. Some of the search terms we used to retrieve articles included the effect of free radicals on the human body; phytochemicals and their fruit sources, biological activity, digestion, and bioavailability; and the importance of antioxidants for human health. The articles were selected based on the purpose of this review and our research questions.

RESULTS AND DISCUSSION

Generation of free radicals in the body and their role in cellular pathology. Free radicals are highly reactive molecules produced from either endogenous metabolic processes or external sources. They consist of reactive oxygen species and reactive nitrogen species. The endogenous sources include peroxisomal metabolism, mitochondrial respiration, phagocyte activity, inmation, arachidonate pathways, ischaemia, exercise, and reactions involving iron and other transition metals. The external sources involve exposure to radiation, ozone, cigarette smoke, air pollutants, and industrial chemicals [13, 14]. Nitric oxide radical ($NO^•$), superoxide anion radical ($O_2^{•-}$), perhydroxyl radical ($HOO^•$), hydrogen peroxide (H_2O_2), hydroxyl radical ($^•OH$), singletoxygen ($^1O_2$), hypochlorous acid (HOCl), peroxynitrite ($ONOO^-$), hypochlorite radical (ClO^-), and lipid peroxides (LOPs) are examples of free radicals capable of causing damage to biomolecules such as DNA, proteins, and lipids [15]. Polyunsaturated fatty acids can undergo peroxidation to produce compounds such as malondialdehyde, isoprostanes, 4-hydroxy-2-nonenal, etc. These compounds are known to cause diabetes, neurodegenerative diseases, and heart disease. Lipoproteins can be destroyed by peroxynitrites, resulting in the lipid peroxidation of cell membranes. The production of free radicals can interfere with protein synthesis and protein functions [15].

Oxidative stress is defined as an imbalance between the production of reactive oxygen species and the body's antioxidant defense system [16]. Excessive production of free radicals may lead to a buildup of oxidative stress in cells and subsequent damage to proteins, DNA, lipids, and carbohydrate molecules. Many human diseases can be caused by oxidative stress, including brain dysfunction, heart disease, inflammatory diseases, diabetes, cardiovascular malfunctions, autoimmune diseases, and aging [2, 17]. Overproduction of reactive oxygen species may lead to overexpression of oncogenes, mutagen formation, and the initiation of atherogenic processes or inflammation. Maintaining redox homeostasis in the body is necessary for good health and disease prevention [11]. Since excessive production of free radicals is harmful, organisms possess natural antioxidant defense enzymes such as glutathione peroxidase, catalase, superoxide dismutase, and glutathione reductase to neutralize the effect of free radicals on the body [13]. However, certain conditions such as stress, illnesses, a high intake of processed foods, and environmental pollution can cause an imbalance in the body's natural antioxidant defense processes [8].

Free radicals become a problem for the body when its antioxidant defense system is inadequate to neutralize or scavenge them [18]. Oxygen plays a crucial role in supporting human metabolic processes. However, in the process of certain metabolic events, oxygen can be transformed into highly reactive species that are destructive to cells in the body. Most of these reactive species are free radicals, possessing unpaired electrons. Since free radicals are unstable, they can either donate or accept electrons from other cellular molecules [14]. Increasing the intake of dietary antioxidants from fruit sources can reduce the stress imposed on the body by reactive oxygen species by protecting biomolecules (proteins, nucleic acids, and lipids) from oxidative damage, suppressing inflammatory responses, and controlling vascular homeostasis [19, 20].

Major phytochemicals in fruits. Fruits are important sources of phytochemicals for human consumption. About 200 000 phytochemicals have been identified, of which 20 000 can be found in vegetables, fruits, and cereals. Phytochemicals are bioactive compounds of plant origin that do not supply the body with energy but possess essential health benefits [21]. They are secondary metabolites present in plants. The main phytochemicals are phenolic compounds, carotenoids, and glucosinolates [12]. These chemicals are produced in plants to protect them from predators or diseases. They are referred to as "non-essential" nutrients because the human body can function without them [22]. Fruits contain different kinds of phytochemicals, such as phenolic acids, carotenoids, and flavonoids. These phytochemicals exert a wide range of biological activities and provide protection against chronic diseases. For instance, they may prevent the proliferation of cancer cells and regulate inflammatory and immune responses [23].

Carotenoids are lipid-soluble compounds synthesized in plants and microorganisms but not in animals. They are found in subcellular organelles such as chloroplasts and chromoplasts. Carotenoids are mainly conjugated with proteins in chloroplasts and serve as an additional pigment for photosynthesis. However, they exist in chromoplasts in crystalline form or as oil droplets. Carotenoids impart yellow, orange, and red colors to different kinds of plants and fruits. They are used in food processing as colorants and food supplements. During photosynthesis, they act as photosensitizers and protect plants from photodamage [12, 24]. Many carotenoids bind to chlorophylls, giving rise to xanthophyll-chlorophyll and carotene-chlorophyll complexes (giving fruits a variety of colors). When fruits mature, their chlorophyll content is reduced, retaining only colored pigments [25]. Fruit color can indicate the type of carotenoids present; for example, yellow-orange fruits are high in β-carotene and α-carotene [26].

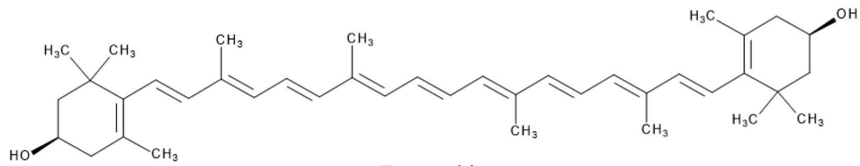
Typically, carotenoids contain the C40 skeleton, also known as tetraterpenoids. Humans can obtain approximately 50 carotenoids through diet. There are two classes of carotenoids, namely carotenes and xanthophylls. Carotenes include α-carotene, β-carotene, β,ψ-carotenes, and lycopene, whereas xanthophylls include β-cryptoxanthin, zeaxanthin, lutein, astaxanthin, fucoxanthin, and peridinin. These carotenoids contain oxygen in the form of hydroxy, aldehyde, carbonyl, carboxylic, furanoxide, and epoxide groups. Chemical structure of major carotenoids in fruits is shown in Fig. 1. There is a growing interest in screening plants and underutilized fruits for carotenoids. This is because fruits are identified as rich sources of carotenoids in the human diet [27–29]. There are a lot of health benefits associated with the intake of foods containing carotenoids. Table 1 shows some major carotenoids, their fruit sources, and their potential biological activities.

Polyphenols are among the most abundant groups of substances present in fruits, with about 8000 phenolic structures identified so far [15, 42]. They are mainly classified into flavonoids, phenolic acids, lignans, and stilbenes. Flavonoids are the most abundant group of phytochemicals [21]. They possess a minimum of one hydroxyl group linked to an aromatic ring. Dietary polyphenols are grouped into flavonoids and nonflavonoids. Flavonoids include flavones (luteolin and apigenin), flavonols (quercetin, kaempferol, and myricetin), flavonones (narigenin), isoflavonoids (daidzein and genistein), anthocyanidins (malvidin and cyanidin), and flavanols (epicatechin, catechin, epigallocatechin, epigallocatechin gallate, epicatechin gallate). Chemical structure of selected polyphenols in fruits is shown in Fig. 2. Nonflavonoids include stilbenes, phenolic acids, tannins, lignans, anthocyanidins, anthraquinones, and coumarins. They are characterized based on their carbon atom arrangements. Most polyphenols derived from plants, such as flavonoids and phenolic acids, are conjugated. They are bound to one or more sugar moieties or residues through their hydroxyl groups [37, 43]. They can also be conjugated to amines, organic acids, lipids, carboxylic acids, and other phenolic compounds [44].

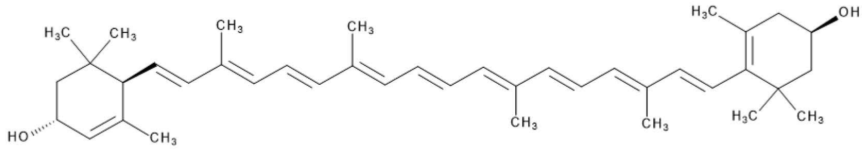
Polyphenols are synthesized in plants as a form of protection against stressful conditions such as exposure to UV, temperature fluctuations, and infection by pathogens [45]. They are powerful antioxidants with metal chelating properties that can reduce lipid peroxidation and trap nitrates to prevent the formation of mutagenic nitroso compounds [13]. Phenolic acids, flavonoids, and tannins constitute the most common polyphenols present in the human diet [46]. The composition of phenolic compounds found in fruits is determined by fruit ripeness, cultivar, physiological conditions, weather, and soil conditions. Postharvest treatments (e.g., processing) and storage can also influence the content of polyphenols in fruits [47]. Higher concentrations of polyphenols can be found in the outer parts of fruits such as apples, watermelons, oranges, etc. The concentration of polyphenols present in some plant food can be as high as 500 mg per 100 g of food [48]. Table 2 lists various polyphenolic compounds and the fruits that contain them

Antioxidant and health-promoting properties of fruit phytochemicals. ***The role of phytochemicals in cancer prevention and management.*** Cancer is a disease characterized by the abnormal growth of cells able to invade and metastasize to other areas of the body. This disease develops due to the changes taking place within the genes that control normal body functions [71]. It is one of the major health problems affecting people globally, both in developed and developing countries. About 18.1 million new cases of cancer were recorded in 2018 worldwide, and this number is expected to increase to about 23.6 million by 2030 [72].

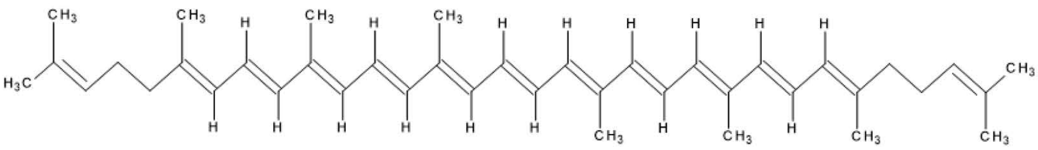
The current remedies for cancer treatment include surgical removal and treatment of cancer cells with radiation accompanied by chemotherapy [73]. Chemoprevention of cancer makes use of natural and/or artificial mediators to interrupt carcinogenesis by inhibiting specific molecular signaling pathways. The chemotherapeutic mediators involved in cancer treatment may be grouped as blocking and suppressing agents [74, 75]. Chemotherapy has certain disadvantages, such as drug resistance, cancer recurrence, and harmful effects on non-targeted tissues. These are some of the challenges arising from the



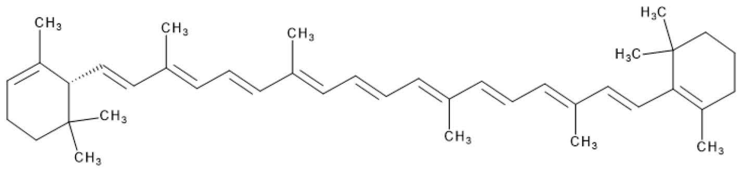
Zeaxanthin



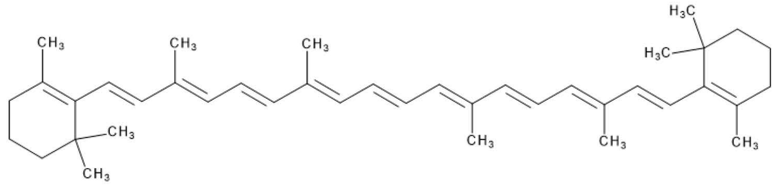
Lutein



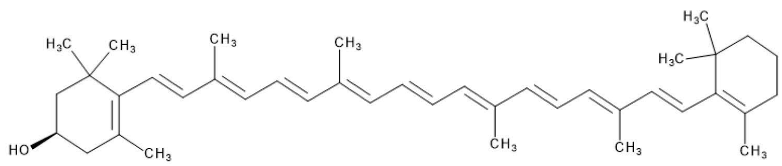
Lycopene



α-carotene



β-carotene



β-cryptoxanthin

Figure 1 Chemical structure of major carotenoids in fruits

Table 1 Carotenoids and their fruit sources

Phytochemical	Fruit sources	Biological activity	References
Lutein	Avocado, melon, rosehips, black chokeberries, sea buckthorn, kiwi, and black currants	Treatment of osteoarthritis and optic nerve injury; antioxidant, anti-inflammatory, neuroprotection, and cardio-protection activities	[30–32]
Zeaxanthin	Avocado, melon, goji berries, Chinese wolfberry, orange, peaches, and mandarins	Prevention of acute and chronic coronary syndromes and age-related macular degeneration; maintenance of normal visual function and anticataract action	[30, 31, 33, 34]
β-cryptoxanthin	Peaches, tangerines, oranges, papaya, grape, mango, and watermelon	Provitamin A and antioxidant activities; promotes bone formation and inhibits bone resorption	[30, 35, 36]
Lycopene	Watermelon, pink grapefruit, red grapefruit, papaya, pink guava, and apricot.	Neuroprotective, antioxidant, cardiovascular, anti-hypertensive, and anti-platelet effects.	[37, 34, 38, 39]
β-carotene	Mango, papaya, banana, grape, melon, orange, watermelon, pear, rosehips, black chokeberries, sea buckthorn, and black currants	Provitamin A, antioxidant, and anticancer activities; prevention of scleroderma and treatment of erythropoietic protoporphyria	[37, 36, 40, 41]
α-carotene	Pineapple, banana, grape, mango, melon, orange, and pear	Provitamin A activity	[36]

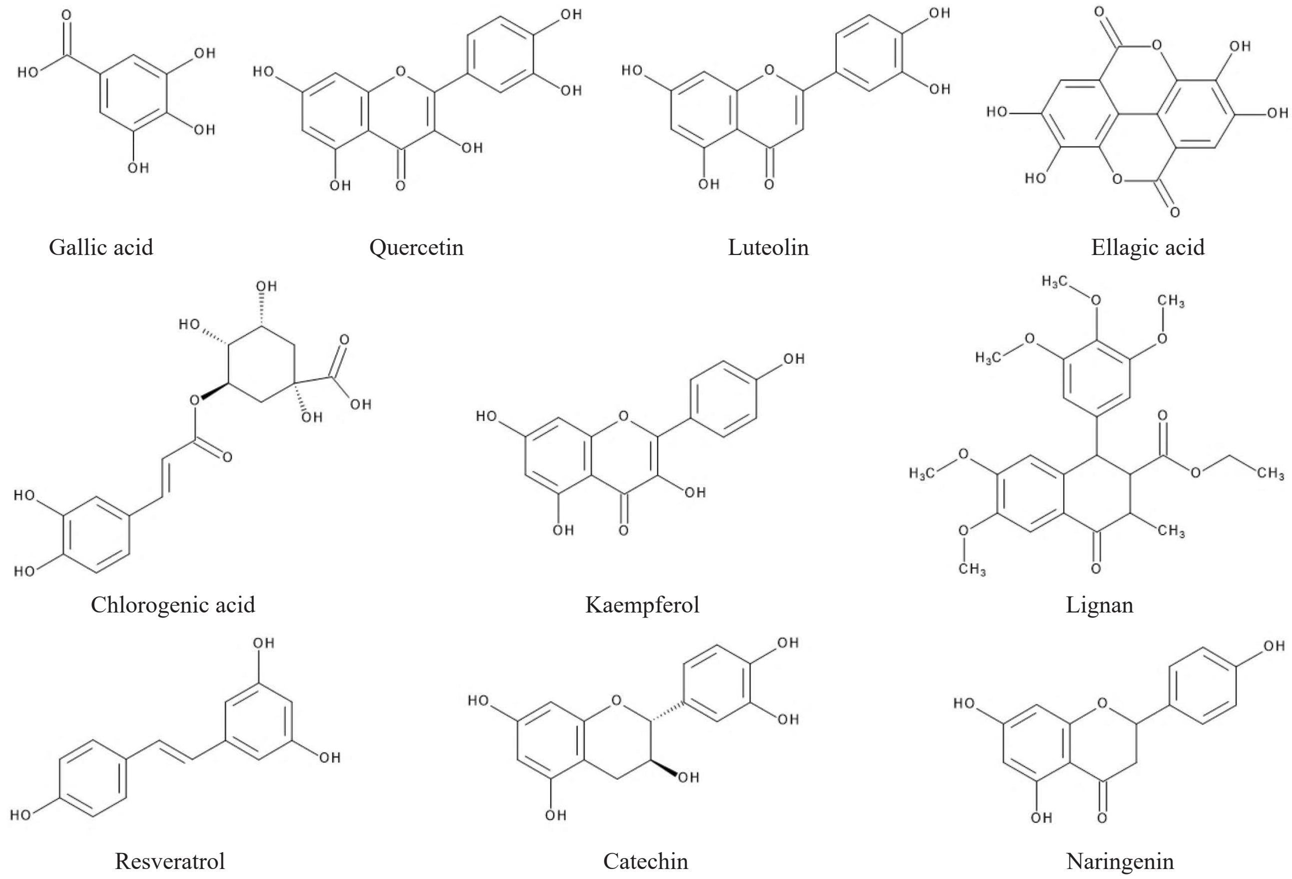


Figure 2 Chemical structure of selected polyphenols in fruits

use of anticancer drugs for cancer treatment. To avoid the side effects emerging from the use of chemotherapeutic agents, scientists are investigating new anticancer agents with better effectiveness and fewer or no side effects [76]. Several epidemiological studies have found that eating fruits on a regular basis can significantly reduce the risk of developing cancer. Polyphenols offer protection to healthy body cells, as well as kill, or are toxic to, premalignant and malignant cells [74].

Screening plants for potent phytochemicals is a better alternative for improving cancer treatment due to their lower side effects. Phytochemicals are biologically active compounds that possess potent anti-tumor properties [76]. They participate in slowing or preventing carcinogenesis by mobbing free radicals, suppressing the survival and spreading of malignant cells, and reducing the invasiveness and angiogenesis of tumors [77–79]. Phytochemicals prevent cancer progression by acting on several molecular targets and signal transduction pathways, such as membrane receptors, downstream tumor-activator or suppressor proteins, kinases, transcription factors, caspases, microRNAs, and cyclins [76].

Apigenin, a flavonoid found in fruits, possesses potent anticancer properties [80]. According to the research, apigenin in the amount of 5 mg/kg suppresses tumor growth while also reducing Ki67 expression and stimulating apoptosis in an athymic nude mouse xenograft with human chondrosarcoma Sw1353 cells. Apigenin can stimulate the expression of Bcl-2 family proteins and activate the caspase cascade to induce G2/M phase arrest and apoptosis [79]. The proliferation of tumor cells such as those in the lung, breast, colon, prostate, and liver can be suppressed by resveratrol (found in fruits such as grapes and berries) [81]. It has been shown to suppress the growth and metastasis of tumors in the lungs of mice with metastatic Lewis lung carcinoma tumors [82]. The antimetastatic and antitumor properties of resveratrol could be due to its ability to inhibit DNA synthesis, angiogenesis, and neovascularization [81]. Several signaling pathways can be altered by resveratrol to reduce the growth and proliferation of cancer cells, initiate programmed cell death, reduce inflammation and angiogenesis, as well as prevent tumor metastases [76]. Diets rich in lycopene content (e.g., fruits) are also shown to reduce the risk of prostate cancer diagnosis in men [83]. Polyphenolic compounds play a crucial role in cancer treatment and prevention by interrupting the initiation, promotion, and progression of cancer cells via the modification of several signal transduction pathways [84]. The role of phytochemicals in cancer prevention at various stages is demonstrated in Fig. 3 [74].

The role of phytochemicals in diabetes management. Diabetes mellitus is one of the main causes of death worldwide, with a prevalence of 8.8% in adults aged 20–79 years [52]. It is generally classified into three major groups, namely type 1 diabetes, type 2 diabetes,

Table 2 Polyphenols and their fruit sources

Phytochemical	Fruit sources	Biological activity	References
Gallotannins	Mangoes and pomegranate	Anti-allergic, anti-hyperglycemic, lipid-lowering, antioxidant, anti-inflammatory, and anticancer properties	[49, 50]
Ellagitannins	Strawberries, raspberries, blackberries, cloudberries, pomegranate, and grapes.	Anti-angiogenic, anti-atherogenic, antithrombotic, anti-inflammatory, antioxidant, and antimicrobial properties.	[49, 51]
Hydroxycinnamic acids	Apple, pear, plums, cherries, peaches, berries, and grapes.	Neuroprotective, antioxidant, hepato-protective, antimicrobial, anti-hypertensive, anticancer, and cardioprotective properties	[40, 41]
Ellagic acids	Blackberry, raspberries, strawberries, mango, and pomegranate	Anti-atherogenic, anti-inflammatory, anti-ulcerative, antidepressant, antidiabetic, antioxidant, and antitumor activities	[40, 52, 53]
Gallic acids	Blackberry, grapes, banana, blueberry, cantaloup, guava, mango, persimmon, and pomegranate	Anti-inflammatory, anti-tumor, anti-obesity, anti-myocardial ischemia, and antioxidant properties	[40, 54, 55]
Anthocyanins	Grapes, blackberries, raspberries, blueberries, Malay apple, red currants, elderberry, and pomegranate	Anti-hypertensive, anti-diabetic, and anti-obesity effects; prevention of stroke, hypercholesterolemia, and hyperuricemia	[30, 40, 56, 57]
Quercetin	Apple, Indian gooseberry, bilberry, cranberries, blackcurrants, raspberry, strawberry, grapes, cherries, passion fruit, and pomegranate	Anti-ulcer, anti-allergic, and antioxidant activities; prevention of osteoporosis and degenerative diseases	[37, 40, 54, 56, 58]
Catechins	Apple, grapes, pear, persimmon, and pomegranate	Antioxidant, anti-allergenic, ant-inflammatory, and antimicrobial activities; protection of skin from UV radiation	[37, 40, 54, 59]
Chlorogenic acids	Cantaloup, apple, carambola, cherries, passion fruit, peach, and pineapple	Anti-obesity, antidiabetic, anti-hypertensive, antimicrobial, and antioxidant effects	[54, 60]
Hesperetin	Citrus fruits (orange, tangerine, lemon, and lime)	Induces apoptosis and cell cycle arrest; anti-angiogenesis, anti-metastases, antioxidant, and anti-inflammatory properties	[37, 40]
Naringenin	Citrus fruits	Anti-inflammatory, antioxidant, anti-atherogenic, anti-convulsant, antibacterial, and immunomodulatory activities	[37, 61]
Naringin	Banana and citrus fruits	Stimulates bone regeneration and repair; anti-inflammatory, anti-cancer, and antioxidant properties; ameliorates mitochondrial dysfunction	[40, 62, 63]
Resveratrol	Red grape, cranberry, blueberry, and plums	Induces apoptosis; cardioprotective, anti-tumor, and antioxidant effects; modulation of estrogen receptor activity	[64]
Lignans	Strawberry, cranberry, blackberry, cloudberry, red and green grapes, grapefruit, orange, tangerine, apricot, melon, kiwi, pineapple, and pear	Antitumor, anti-hypertensive, platelet-activating factor antagonistic, sedative, anti-estrogenic, and antioxidant activities	[64–66]
Kaempferol	Indian gooseberry, blackcurrants, raspberry, strawberry, grapes, banana, apple, guava, and lemon	Induces cell cycle arrest and apoptosis; anti-ulcerogenic, anti-inflammatory, anti-depressive, anticancer, and antioxidant effects; improves wound healing and reduced lung damage	[40, 54 56, 67–69]
Luteolin	Banana, apple, guava, and lemon	Antioxidant, anti-inflammatory, antimicrobial, and anticancer activities	[54, 70]

and gestational diabetes [85]. A lot of factors are responsible for the development of diabetes in individuals, with innate immunity regarded as the main factor in its pathophysiology [86]. Type 1 diabetes is caused by the immune system's inflammatory response to pancreatic islet cells, which causes β-cells to lose function. In type 2 diabetes, low-grade systemic inflammation is a common mediator for the initiation and development of micro- and macro-vascular problems [87]. It is distinguished by insulin resistance and a loss of β-cell function, resulting in an insufficient supply of insulin to meet the body's metabolic needs. People who suffer from type 2 diabetes are unable to control their blood sugar, which results in the excess accumulation of glucose in their blood and urine. Type 2 diabetes is an important public health concern because it accounts for 90% of all diabetes cases worldwide [88].

In recent times, phytochemicals have been under intense consideration for their use as drug candidates to prevent and treat several metabolic disorders such as hyperglycemia and dyslipidemia [52]. Phytochemicals induce important hypoglycemic effects and contribute

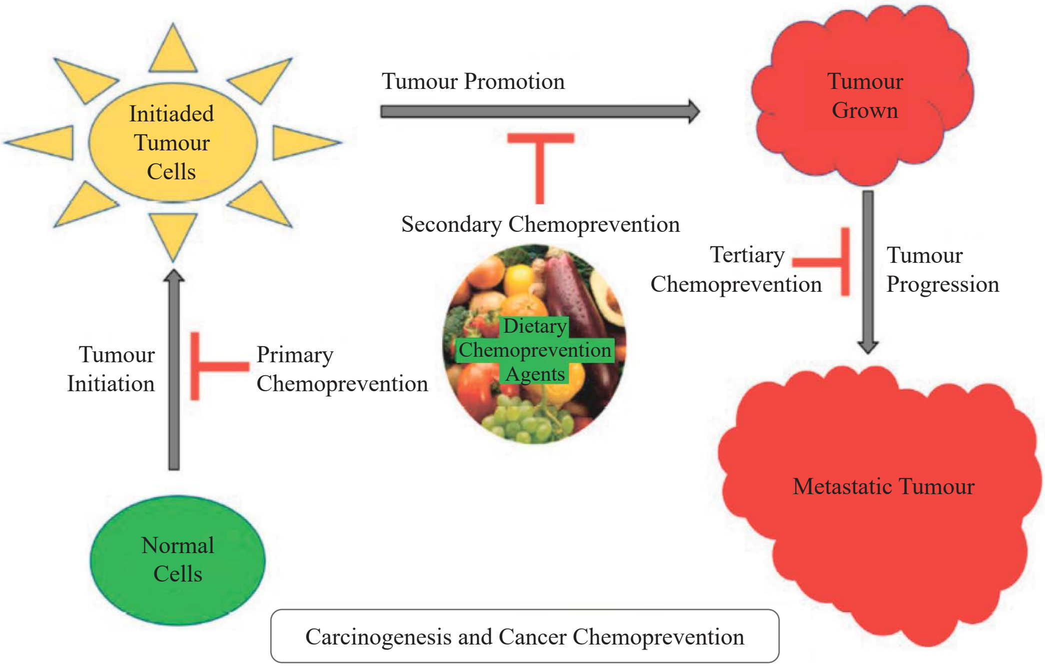


Figure 3 The role of phytochemicals in cancer prevention at various stages of cancer development [74]

to the prevention of diabetes-related vascular complications [89, 90]. Certain groups of flavonoids exhibit potent hypoglycemic properties by enhancing glucose and oxidative metabolism in diabetic conditions. The hypoglycemic property of phytochemicals has been established by studies in human and animal models of type 2 diabetes [91].

According to Keshari *et al.*, flavonoids such as naringenin, apigenin, and quercetin isolated from *Fiscus racemose* stems (these compounds are also present in fruits) demonstrated a hypoglycemic effect by reducing the levels of glucose from 300 to 185 mg/dL after one week of oral administration (100 mg/kg) *in vivo* [92]. Also, the administration of flavonoids to rats improves the glycogen content in the liver when compared with that of untreated diabetic rats. Flavonoids exert their antidiabetic activity by binding to glucose transporter 1 receptors and peroxisome proliferator-activated receptor gamma [92]. This promotes glucose uptake, lipid metabolism, improves insulin activity, and enhanced glucose tolerance in diabetic animals and humans [93]. Flavonoids act through different mechanisms, such as increasing the levels of superoxide dismutase, catalase, and glutathione in the pancreas, normalizing the levels of aspartate transaminase and alanine transaminase in plasma, and enhancing glucose uptake by the cells [94].

Anthocyanins, polyphenols present in fruits such as berries, can prevent type 2 diabetes and obesity. Anthocyanins influence glucose absorption, insulin secretion, level, and action, as well as lipid metabolism in both *in vitro* and *in vivo* studies. Several *in vitro* studies suggested that anthocyanins could decrease glucose absorption from the intestine by delaying the release of glucose during digestion [95]. Some phytochemicals with known anti-diabetic properties include ellagic acid (found in berries, dried fruits, and pomegranate), epigallocatechin gallate (cranberries, strawberries, cherries, pears, kiwi, peaches, black berries, apples, and avocados), naringenin (citrus fruits, cherries, and grapefruit), hesperetin (orange and lemon), chrysin (passion fruit), kaempferol (grapes, raspberry, strawberries, peach, cowberries, and apples), apigenin (grape fruit and orange), quercetin (apples and berries), and resveratrol (grapes) [52].

Anti-inflammatory properties of phytochemicals. Inflammation is a biological response to tissue damage which may be caused by harmful agents produced from biological, physical, or chemical sources. Inflammation can activate several signaling pathways, including phosphatidylinositol-3-kinase (PI3K), Janus-activated kinase (JAK), and mitogen-activated protein kinase (MAPK). Chronic inflammation activates chemokines, cytokines (IL-4, IL-5), inducible nitric oxide synthase (iNOS), signal transducer and activator of transcription 3 (STAT3), and cyclooxygenase enzyme (COX) [96]. Prolonged inflammation interrupts metabolism and induces stress in cells. As a result, it can cause inflammatory diseases such as asthma, autoimmune disorders, allergies, arthritis, and inflammatory bowel disease [96, 97]. Inflammatory diseases can be prevented or suppressed by blocking the pathways that produce inflammatory mediators, particularly proinflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukins (IL-1β, IL-6) [98].

Phytochemicals mediate inflammation through kinases such as mitogen-activated protein kinase and protein kinase C. Phytochemicals inhibit the activity of these enzymes by changing the DNA-binding potential of transcription factors such as nuclear factor kappa-B (NF-kB), one of the main effector molecules that mediates inflammation [99, 100]. Flavonoids such as quercetin inhibit the activity of enzymes such as cyclooxygenase and lipoxygenase in arachidonic acid metabolism to reduce the production of prostaglandins and leukotrienes [101, 102]. Apigenin inhibits the production of prostaglandin E2 (PGE2) and the activity of cyclooxygenase (COX-2), as well as NF-kB-dependent pathways [64]. Hesperidin is another phytochemical that inhibits the synthesis of pro-inflammatory mediators such as arachidonic derivatives, thromboxane A2, and prostaglandins E2 and F2 [103]. Nitric oxide is one of the main mediators of inflammation, and phytochemicals that can prevent its production without damaging endothelial or neuronal nitric oxide synthase (NOS) may be considered potent compounds for treating inflammation [104].

Antioxidant activity of phytochemicals. Antioxidants refer to molecules with the potential to react with free radicals by neutralizing or terminating chain reactions initiated by free radicals to prevent them from destroying other molecules [14]. Antioxidants can protect cells by converting reactive oxygen species to non-radical species, breaking auto-oxidative chain reactions, or reducing the concentration of localized oxygen [105]. Evidence of oxidative stress is implicated in several diseases, such as cancer, cardiovascular, neurological, and pulmonary diseases, rheumatoid arthritis, nephropathy, ocular diseases, and the induction of pre-eclampsia during pregnancy. These conditions develop when free radicals begin to alter cell membranes, proteins, lipoproteins, and DNA; stimulate the overexpression of specific genes; activate various kinases and transcription factors such as AP-1 and NF-kappa B; and contribute to the production of toxic peptides (β-amyloid) [106].

Natural antioxidants are primarily obtained from plants, as well as fruits, in the form of vitamins, carotenoids, flavonoids, tannins, alkaloids, terpenoids, isothiocyanates, lectins, polypeptides, and other phenolic compounds [107–110]. Phenolic compounds exhibit potent antioxidant activity, which is shown through their ability to neutralize the deleterious effects of free radicals and serve as antitumor, cardioprotective, and antimutagenic agents [111]. Studies have shown that the intake of dietary antioxidants, especially from fruits with a high total phenolic content, increases serum antioxidant scavenging capacity and provides a boost for the body's antioxidant defense system [112, 113]. Flavonoids such as quercetin, combined with other bioactive compounds, exhibit strong antioxidant activities and are responsible for the disease-preventing properties of fruits.Quercetin is one of the most potent antioxidant compounds that protects the body against oxidative stress induced by amyloid deposits [64]. Rutin (quercetin 3-O-rhamnoglucoside), which is found in fruits, has a similar level of antioxidant activity. It exertsits antioxidant activity by donating electrons to free radicals to convert them into more stable and less reactive species. Enzymes that are involved in the production of reactive oxygen species can be inhibited by rutin to lower oxidative stress. This can prevent diseases caused by oxidative stress, e.g.,neurodegenerative diseases [64, 114].

Carotenoids such as zeaxanthin, astaxanthin, and lutein are powerful lipid-soluble antioxidants that are involved in mobbing free radicals mainly in lipid-soluble environments. High intakes of carotenoids can prevent lipid oxidation and oxidative stress caused by free radicals [30]. Some carotenoids serve as precursors for vitamin A, while others possess effective antioxidant properties that act to scavenge reactive oxygen species. Carotenoids such as α-carotene, β-carotene, and cryptoxanthin are shown to have provitamin A activity, while lutein and lycopene have strong antioxidant activity [115]. Photo-oxidative damage, which occurs because of UV irradiation of the skin, affects macromolecules such as proteins, lipids, and DNA. This may lead to conditions such as premature skin aging, erythema, photodermatoses, and skin cancer. Intake of carotenoids from diets has been shown to improve skin texture, color, strength, and elasticity. Because of their antioxidant activity, carotenoids offer protection to the skin from the sun and harmful ultraviolet radiation [116]. Several studies have found that diets rich in phytochemicals with high antioxidant activity can help prevent a variety of chronic degenerative diseases caused by oxidative stress. Regular consumption of fruits is important for maintaining good health and disease prevention [117].

Bioavailability of phytochemicals and factors that hinder their bioavailability in the body. ***Digestion and absorption of phytochemicals in fruits.*** The absorption of phytochemicals from the food matrix into the body depends on their solubility, structure, degree of glycosylation or acylation, molecular size, the individual's microbiome, and the presence of complementary compounds [118]. Most of phytochemicals exist as esters, glycosides, or polymers in food, while others covalently bind to cell wall components in food matrices, preventing their release for absorption in the gastrointestinal tract. Apart from isoflavonols, all flavonoids exist in their glycosylated form. However, aglycones and some glucosides, such as resveratrol and quercetin, are easily absorbed from the small intestine [22, 119, 120].

The absorption of phytochemicals from food (e.g., fruits) begins with chewing and digestion in the mouth. Chewing and the action of digestive enzymes, particularly α-amylase, aid in the reduction of food particle size and the release of bioactive compounds (polyphenols or carotenoids) from the food matrix [121]. The digest is delivered to the stomach, where digestive enzymes, an acidic pH, and further mixing disintegrate the food matrix to release more polyphenols or carotenoids. The acidic chyme from the stomach is released into an alkaline environment in the duodenum. Enzymes released by the liver and pancreas and the presence of bile salts at this stage also help release additional bioactive compounds and completely break down the food matrix into simple, absorbable macronutrient units. Polyphenols are then released into the bloodstream and delivered to target tissues. Those phenolic compounds which are not digested are metabolized by the microbiota in the colon to produce metabolites, which are also absorbed into the bloodstream [122]. Carotenoids are lipophilic compounds that are insoluble in aqueous solutions. In the stomach, they are packaged into micelles (which help transport fat-soluble materials) to make them more accessible to the intestinal epithelium for absorption into the bloodstream [34, 36].

Factors that may hinder the bioavailability of phytochemicals in fruits. Bohn defines bioavailability as the amount or concentration of a nutrient or non-nutrient substance absorbed into the human body to stimulate physiological activities or for storage [48]. Bioaccessibility, on the other hand, is defined as the amount of nutrients released from a food matrix during digestion, making the nutrient available or easily accessible for absorption in the gastrointestinal tract [22]. The ability of phytochemicals to exert health-promoting effects on the body depends primarily on their bioaccessibility and bioavailability [123]. Phytochemicals such as polyphenols exist in foods as polymers or in glycosylated form, which may hinder their absorption. To improve the bioavailability of phytochemicals from fruits, they must undergo hydrolysis by colonic microbiota and intestinal enzymes for easy absorption [123, 124]. The involvement of colonic microflora reduces the efficiency of polyphenols absorbed due to the degradation of aglycones to produce several simple aromatic acids during the process [49].

Some phytochemicals, such as tannins, can interact with proteins to form insoluble complexes, and this can limit or prevent their absorption [125, 126]. β-casein can also bind to (+)-catechins and (–)-epicatechin through its proline residues [127]. Phytochemicals can undergo different kinds of changes during gastrointestinal digestion, and those that are able to pass through the intestinal walls can either be metabolized or excreted, which reduces the level (low bioavailability) delivered to target organs or tissues for therapeutic effect [128].

Phytochemicals (such as flavonoids) can bind to components in the digestive system secretions such as saliva, pancreatic, and gastric juices. This may also reduce the amount absorbed into systemic circulation for physiological activities. Research has shown that phenolic compounds have a good affinity for proline-rich proteins and histatins present in human saliva. They either form a covalent or non-covalent bond to increase the size of the phenolic compound to prevent passage through absorptive cells of the small intestine [129]. Enzymes, such as pancreatic α-amylase and trypsin, have been shown to lose activity in the presence of phenolic compounds [130]. In addition, polyphenols can also bind to enterocyte brush border enzymes, and this prevents their release for absorption into the body [129].

CONCLUSION

Fruits are rich sources of phytochemicals which perform several biological activities by acting as potent antioxidant, anticancer, antidiabetic, and anti-inflammatory agents. The modes of action of these bioactive compounds include scavenging free radicals or inhibiting the activity of enzymes and transcription factors that play a critical role in signaling pathways involved in disease initiation and progression. The excess accumulation of free radicals in the body and the inability of the body's antioxidant defenses to effectively destroy free radicals cause oxidative stress and may lead to diseases such as cancer, diabetes, etc. It is therefore imperative that fruits rich in phytochemicals be regularly consumed to reduce an individual's risk of suffering from several chronic disease conditions.

CONTRIBUTION

E.K. Danyo designed the research concept, wrote the original draft, and edited the manuscript. M.N. Ivantsova wrote, reviewed, and edited the manuscript. Both of the authors read and approved the final version of the manuscript.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ORCID IDs
Emmanuel Kormla Danyo https://orcid.org/0000-0003-2183-308X
Maria N. Ivantsova https://orcid.org/0000-0002-2389-0523