

## 55 Anticancer Fruits, Vegetables, Beverages, Oils and Spices

Maliheh Najari Beidokhti<sup>1\*</sup>

### \*Corresponding author:

Maliheh Najari Beidokhti

<sup>1</sup> Department of Studies in  
Biotechnology, University of Mysore,  
Manasagangotri, Mysore 570006, India

### Abstract

Cancer is one of the most devastating diseases, and despite good understanding of the molecular basis of the disease and advances in treatment, globally cancer is still a major cause of death. It has been estimated that 30–40 percent of all cancers can be prevented by lifestyle and dietary measures alone and a diet rich in fruits and vegetables is associated with a reduced risk of many common forms of cancer. Several *in vitro* and *in vivo* studies have demonstrated the antitumor properties of various fruit and vegetable extracts and beverages. Epidemiological data suggest that ingestion of bioactive compounds from fruits and vegetables, such as polyphenols and terpenes, may contribute to reduce the incidence of cancer in humans. The mechanisms by which these compounds inhibit tumourgenesis include inhibition of tumour cell mediated protease activity, attenuation of tumour angiogenesis, induction of cell cycle arrest and promotion of apoptosis. In addition, it has been reported that combining natural compounds with chemotherapeutic agents is a promising strategy to enhance the inhibition of tumour survival. Also a wide variety of phenolic substances derived from spice possess potent antimutagenic and anticarcinogenic activities. Such spices have been known to be effective on large intestine, liver, stomach, breast, skin, bladder, and colon cancer. Hence, an attempt has been made to review some fruits, vegetables, beverages, oils and spices used for the prevention and treatment of cancer.

**Keywords:** Cancer; Antioxidant; Apoptosis; Polyphenols; Flavonoids

### Introduction

Cancer is one of the most devastating diseases [1], and despite good understanding of the molecular basis of the disease and advances in treatment, globally cancer is still a major cause of death [2].

According to WHO reports the deaths from cancer worldwide are projected to continue rising, reaching an estimated 13.1 million in 2030. The number of all cancer cases around the world reached 12.7 million in 2008 and is expected to increase to 21 million by 2030. Approximately one in five people before age 75 will suffer from cancer during their lifetime, while one in ten in this age range is predicted to die due to cancer [3].

It has been estimated that 30–40 percent of all cancers can be prevented by lifestyle and dietary measures alone [4]. Natural products are the source of numerous therapeutic agents. Table 1 displays various properties of some known natural products [5]. Recent progress in the discovery of drugs from natural products has resulted in development of compounds for use in cancer treatment [6, 7, 8].

Wide arrays of phenolic substances, particularly flavonoids, those present in dietary and medicinal plants, have been reported to possess substantial anti-carcinogenic and anti-mutagenic effects [9, 10]. These flavonoids are naturally occurring low molecular

weight polyphenolic compounds widely distributed in fruits, vegetables and beverages [9].

Epidemiological data suggest that ingestion of bioactive compounds from fruits and vegetables, such as polyphenols and terpenes, contribute to reduce the incidence of cancer in humans. The mechanisms by which these compounds inhibit tumourgenesis include inhibition of tumour cell mediated protease activity, attenuation of tumour angiogenesis, induction of cell cycle arrest and promotion of apoptosis. In addition, it has been reported that combining natural compounds with chemotherapeutic agents is a promising strategy to enhance the inhibition of tumour survival [11]. Effect of polyphenols on human cancer cell lines, is most often protective and induce a reduction of the number of tumors or of their growth. These effects have been observed at various sites, including mouth, stomach, duodenum, colon, liver, lung, mammary gland or skin [12].

Nowadays, spices are used to develop commercial disease-preventing foods by utilizing physiological activities such as anticancer activity, antibiotic activity and physiological-pharmaceutical activity [13]. A wide variety of phenolic substances derived from spice possess potent antimutagenic and anticarcinogenic activities [14, 15]. Also such spices have been known to be effective on large intestine, liver, stomach, breast, skin, bladder, and colon cancer [13].

Table 1. Properties of known natural products.

Common name	Properties
Beetroot	anti-cancer, anti-viral, anti-inflammatory, antioxidant and detoxifying
Tomato	anti-cancer, anti-viral and antioxidant
Rhubarb	anti-bacterial, anti-cancer, antioxidant and healthy heart
Pumpkin	anti-cancer and antioxidant
Chili pepper	anti-bacterial, anti-viral, antioxidant and antiseptic
Avocado	anti-allergenic, anticancer, anti-inflammatory, antioxidant and healthy heart
Pineapple	anti-cancer, anti-inflammatory, antioxidant and healthy heart
Papaya	anti-cancer, anti-inflammatory, antioxidant and healthy heart
Apricot	anti-cancer, antioxidant and detoxifying
Guava	anti-cancer, anti-viral, antioxidant and detoxifying
Apple	anti-allergenic, anti-inflammatory, detoxifying and healthy heart
Mango	anti-viral, anti-inflammatory, antioxidant, detoxifying and healthy heart
Blueberry	anti-bacterial, anti-cancer, anti-inflammatory, antioxidant and healthy heart
Cherry	anti-cancer, anti-inflammatory, anti-oxidant and detoxifying
Raspberry	ant-bacterial, anti-cancer, antioxidant, detoxifying and healthy heart
Cranberry	antibacterial and antioxidant
Green tea	anti-allergenic, anti-cancer, anti-inflammatory, antioxidant and healthy heart
Ginger	antiseptic and detoxifying
Black cumin	anti-allergenic, anti-bacterial, anti-inflammatory and healthy heart
Turmeric	anti-allergenic, anti-cancer, anti-inflammatory, antioxidant and healthy heart

### Cranberry (*Vaccinium oxycoccos*)

Studies showed that the unique combination of phytochemicals (flavonols, proanthocyanidin oligomers, and triterpenoids) found in cranberry fruit may produce synergistic health benefits [16, 17]. *In vitro* studies show that cranberry reduced tumor cell growth for various types of cancer including, breast, colon, prostate and lung [16, 17, 18]. Proanthocyanidins (PACs) and other cranberry constituents are thought to contribute to the observed anticancer properties. The synergistic effects of the myriad phytonutrients are thought to inhibit oxidative DNA damage that is linked to cancer promotion and inhibit cell proliferation [19, 20]. Cranberries are one of the leading fruit sources of quercetin. It has been reported that Quercetin inhibited the growth of MCF-7 human breast

adenocarcinoma, HT-29 human colon adenocarcinoma, and K562 human chronic myelogenous leukemia cell lines [16].

### Papaya (*Carica papaya*)

Papaya is an example of the rich source of lycopene. Lycopene which is one of the carotenoids is endowed with powerful anticancer properties and now is considered to be potentially for the prevention of cancer and other diseases [21]. Important experiments have shown that *Carica Papaya* has antitumor and free-radical scavenging activities. *C. papaya*, with abundant bioactive phytochemicals, has the potential to be of use in combating cancer [22]. Rahmat *et al.* reported that papaya juice has anticancer property against liver cancer cell line (HepG2) [21].

### Cherry (*Prunus avium*)



Cherries are considered to be a rich source of polyphenols, which are powerful antioxidant compounds reported to have many health promoting activities, including anticancer. Cherry contains perillyl alcohol [23] and this compound was pointed to be one of the major responsible compounds for anticancer properties of cherry extracts [11, 23] as it was detected in the most promising products [23], and can use as anticancer drug by stimulating different types of tumours to apoptosis, inhibiting their proliferation or overcoming their resistance to chemo-/radiotherapy [11]. Lee *et al.* reported that the methanolic extract of cherry blossom has shown inhibition against growth of human colon cancer cell line HT-29 [24].

In animal studies perillyl alcohol has been shown to induce pancreatic, mammary and liver tumours regression and to exhibit possible application as a chemopreventive agent for colon, skin, and lung cancer, as well as a chemotherapeutic agent for neuroblastoma, prostate and colon cancer [23].

### Pineapple (*Ananas comosus*)

Bromelain is an aqueous extract of pineapple that contains a complex mixture of thiol proteases and non-protease components [25]. Bromelain is known for its clinical applications such as modulation of tumor growth and anti-inflammatory properties [26]. Antitumor properties of bromelain have been demonstrated in both, *in vitro* and *in vivo* studies and bromelain may have the potential of being developed into an effective anticancer agent for malignant peritoneal mesothelioma (MPM) [27]. The anti-cancer activity of bromelain [25, 28] is attributed predominantly to its protease components and it has been reported that bromelain was shown to increase expression of p53 as well as another activator of apoptosis, Bax, in mouse skin papillomas [25].

### Guava (*Psidium*)

Guava leaves can interfere with multiple signaling cascades linked with tumorigenesis and provide a source of potential therapeutic compounds for both the prevention and treatment of cancer. Guava leaf hexane fraction (GHF) specifically suppresses AKT/mTOR/S6K kinase signaling and leads to the induction of apoptosis through the down-modulation of proteins that mediate tumor cell survival, proliferation, metastasis, and angiogenesis in human prostate cancer cells [29]. Lupeol, a triterpene, of guava has been reported as an anticancer compound. It has been demonstrated that acetone extracts of guava branch (GBA) had cytotoxic effects on HT-29 cells. GBA may be a potential candidate for a novel therapeutic agent in the field of anticancer drug discovery [30].

### Apple (*Malus domestica*)

Some fruit peels have to combat variety of cancers, including cancer of the liver, colon, breast, and lung. Peels from different varieties of apples (Rome Beauty, Idared, Cortland, and Golden Delicious) are reported to have an antiproliferative effect [1]. It has been indicated that triterpenoids isolated from apple peels have potent antiproliferative activity and may be partially responsible for the anticancer activities of whole apples [31]. Golden delicious apple peels have been reported to inhibit the cell proliferation of HepG2 human liver cancer cells and MCF-7 human breast cancer cells and Caco-2 colon cancer cells [1, 31]. Some of the active principles present in these peels, such as quercetin and quercetin-3-*O*-beta-D-glucopyranoside, have been found to be responsible for the anticancer activity observed [1] (Table 2). Several reports indicate that apples play an important role in the prevention and treatment of prostate cancer [32, 33].

**Table 2. Active principles isolated from apple peel with anticancer and antioxidant Properties.**

Scientific name	Common name	Isolated compound	Biological activity
<i>Pyrus malus</i>	Apple	Flavonoids including quercetin-3- <i>O</i> -beta-D-glucopyranoside, quercetin-3- <i>O</i> -beta-D-galactopyranoside, quercetin, (-)-catechin, (-)-epicatechin, quercetin-3- <i>O</i> -alpha-L-arabinofuranoside, 2 alpha-hydroxyursolic acid	Anticancer
<i>Pyrus malus</i>	Apple	Various triterpenoids including ursolic acid, 3 beta- <i>transp</i> -coumaroyloxy-2 alpha-hydroxyolean-12-en-28-oic acid, (-)-epicatechin, procyanidin B2, chlorogenic acid, and catechins and flavonol glycosides, especially rutin	Antioxidant



### Grape (*Vitis Vinifera*)

Grape antioxidants have drawn an increased attention for their potential anticancer effects. A number of studies suggest that the high consumption of grape components could be associated with the reduced risk of certain cancers such as breast cancer and colon cancer. The anticancer effects of grape antioxidants have been demonstrated in *in vitro* and *in vivo* models [34].

Both grapes and grape-based products are excellent sources of various anticancer agents and their regular consumption should thus be beneficial to the general population. Grape seeds are a potential source of anticancer and cancer chemopreventive phytochemicals, the other parts of the grape such as the skin, the whole grape by itself, grape-derived raisins, and phytochemicals present within the grapes have also demonstrated potential anticancer efficacy in various preclinical and clinical studies [35].

It has been reported that grape seed extract (GSE), a rich source of proanthocyanidins, is against colorectal cancer [36]. Also the effects of oligomeric proanthocyanidins on human colorectal cancer cell line SNU-C4 have been demonstrated [37]. GSE also play an important role in the prevention and treatment of prostate

cancer [32, 38]. Grape seed proanthocyanidins (GSPs) have been shown to induce apoptosis of Non-small-cell lung cancer (NSCLC) cells: A549 and H1299 and GSPs *in vitro* are also effective on oral squamous cell carcinoma [34].

### Mango (*Mangifera indica*)

Lupeol, a triterpene present in mango and other fruits, has shown to possess anticancer properties in *in vivo* and *in vitro* assays. The apoptogenic activity in mouse prostate by lupeol and mango pulp extract has been recorded [39]. Noratto *et al.* compared the anticancer properties of

polyphenolic extracts from several mango varieties (Francis, Kent, Ataulfo, Tommy Atkins and Haden) in cancer lines, including Molt-4 leukemia, A-549 lung, MDA-MB-231 breast, LnCap prostate, and SW-480 colon cancer cells and non-cancer colon cell line CCD-18Co. Overall, polyphenolics from several mango varieties exerted anticancer effects, where compounds from Haden and Ataulfo mango varieties possessed superior chemopreventive activity [40]. Table 3 displays isolated compounds from peel of mango with antioxidant property [1].

**Table 3. Isolated compounds from peel of mango with antioxidant property.**

Scientific name	Common name	Isolated compound	Biological activity
<i>Mangifera indica</i> L.	Mango	Mangiferin, penta- <i>O</i> -galloyl-glucoside, gallic acid, methyl gallate, quercetin <i>O</i> -glycosides, kaempferol <i>O</i> -glycoside, xanthone <i>C</i> -glycosides, mangiferin, isomangiferin, gallotannins	Antioxidant

### Peach (*Prunus persica*)

Commercial varieties of peaches contain a mixture of phenolics that may possess anticancer activity. Peach phenolics may have potential in therapy and chemoprevention of metastatic breast cancer. It has been reported that yellow fleshed peach "Rich Lady" (RL) extracts preferentially inhibited the proliferation of the estrogen-independent MDA-MB-435 breast cancer cells over the estrogen-dependent MCF-7 and the normal MCF-10A breast cells [41].

### Plum (*Prunus*)

Plums can cure cancer such as breast and colon. Plums even in their dried form known as prunes are high in unique phytonutrients or their anti cancer agents called neochlorogenic and chlorogenic acid [42]. *Eugenia jambolana* Lam., commonly known as black plum or 'jamun' is an important medicinal plant in various traditional systems of medicine. It has been reported that whole Jamun extract possess cytotoxic effects on the cultured human cervical

cancer cells, the HeLa (HPV- 18 positive) and SiHa (HPV-16 positive). Preclinical studies have shown it to possess antineoplastic, chemopreventive and radioprotective properties. [2]. Also the fruit pulp extract possesses selective antineoplastic effects against breast cancer. It has been reported that red fleshed plum "Black Splendor" (BS) extracts showed great effects on MDA-MB-435 cells as compared to the other breast cancer or the normal breast cell lines [41].

### Date (*Phoenix dactylifera* L.)

Date fruits possess free radical scavenging, antioxidant, antimutagenic, anti-inflammatory, gastroprotective, hepatoprotective, nephroprotective, anticancer and immunostimulant activities [43, 44]. Glucans isolated from Libyan date (*Phoenix dactylifera* L.) were found to exhibit potent antitumor activity. This activity could be correlated to their (1-3)- $\beta$ -D-glucan linkages. In a preliminary study, water-soluble glucan exhibits potent antitumor activity against implanted sarcoma-180 solid tumor growth in mice [45]. In another study Barzin *et al.* reported



that *Phoenix dactylifera pollen grains* with rat liver extract displayed anticancer activity [46].

### Avocado (*Persea Americana*)

Avocado (*Persea americana*) fruits are consumed as part of the human diet and extracts have shown growth inhibitory effects in various types of human cancer cells. Studies have shown that avocado fruit extracts exhibit antiproliferative effects in human cancer cell lines. Avocado fruit meat only recently has been identified as containing cancer-preventing phytochemicals not found in other fruits and vegetables. The potential anticancer activity of avocado fruits is due to a combination of specific aliphatic acetogenins that target two key components of the EGFR/RAS/RAF/MEK/ERK1/2 cancer pathway [47]. Avocado is one of the richest sources of dietary lutein among commonly eaten fruits and also contains other carotenoids and vitamin E. It has been reported that the acetone extract of avocado inhibited proliferation of the human prostate cancer cell lines. The high lutein content of the avocado and the known antiproliferative and antitumor properties of this carotenoid suggested that lutein might be responsible for this effect [48].

### Chiku (*Manilkara zapota*)

Nitric oxide is a free radical involved in the pathogenesis of cancer by increasing tumour vascularization and metastasis. Studies using nitric oxide inhibitors have shown decrease in tumour growth and a role in cancer therapy. The 13 plants analysed by Jayakumar and Kanthimathi scavenged nitric oxide and inhibited the growth of MCF-7 cell. On the breast cancer cell line (MCF-7), chiku fruit showed high inhibitory activity. Phytochemicals present in fruit scavenge nitric oxide and inhibit MCF-7 cell proliferation. Also Chiku is a rich source of polyphenols and has been shown to display anticancer effects on human colon cancer cells [49].

### Watermelon (*Citrullus vulgaris*)

Watermelon is one of the leading sources of lycopene, second only to the tomato. A number of studies have indicated that a lycopene-rich diet lowers the risk of certain chronic diseases such as cancer and heart diseases [21]. The anticancer activity of lycopene has been demonstrated in both in vitro and in vivo tumor models as well as in humans [50]. Lycopene inhibits the proliferation of human MCF7 mammary cancer cells. Watermelon juice, which contains high lycopene, has anticancer properties against breast cancer cell line (MDA-MB-231). It has been observed that higher the concentration of lycopene, higher the amount of cell death [21].

### Pomegranate (*Punica granatum*)

Treatment and prevention of cancer is the potential therapeutic property of pomegranate [51, 52]. Previous studies have demonstrated the anticarcinogenic activity of pomegranate extracts and genistein in a series of human cancer cells. Both pomegranate

extracts and genistein inhibit the growth of MCF-7 breast cancer cells through induction of apoptosis, with combination treatment being more efficacious than single treatments [53].

*In vitro* assays utilizing three prostate cancer cell lines (DU-145, LNCaP, and PC-3) demonstrated various pomegranate extracts (juice, seed oil, peel) potently inhibit prostate cancer cell invasiveness and proliferation, cause cell cycle disruption, induce apoptosis, and inhibit tumor growth. Research in mice has shown pomegranate fruit extract (PFE) inhibits tumorigenesis in lung cancer and skin cancer models. Also the effect of flavonoid-rich pomegranate juice (PJ) and fermented pomegranate juice (FPJ) and pomegranate pericarp extracts on HL-60 human leukemia cell differentiation and proliferation has been reported [51]. A series of studies indicated the peel extracts of Egyptian pomegranate showed the highest antioxidant activity, as well as, a pronounced anticancer activity against MCF-7 human breast cancer cells and HCT-116 colon cancer cells [54].

### Berry (*Rubus*)

Anthocyanins, a class of flavonoids, are reddish natural pigments extensively distributed in fruits and especially in berries [55]. Berries contain a diverse range of phytochemicals with biological properties such as antioxidant, anticancer, anti-neurodegenerative, and anti-inflammatory activities [56, 57].

Epidemiological studies have positively correlated the consumption of berries with reduced mortality by cardiovascular disease and some types of cancer [55]. Seeram *et al.* evaluated the berry extracts for their ability to inhibit the growth of human oral (KB, CAL-27), breast (MCF-7), colon (HT-29, HCT116), and prostate (LNCaP) tumor cell lines. With increasing concentration of berry extract, increasing inhibition of cell proliferation in all of the cell lines was observed, with different degrees of potency between cell lines. The berry extracts were also evaluated for their ability to stimulate apoptosis of the COX-2 expressing colon cancer cell line, HT-29. Black raspberry and strawberry extracts showed the most significant pro-apoptotic effects against this cell line [56].

### Citrus fruits (*Citrus*)

Numerous therapeutic properties have been attributed to citrus fruits, like anticancer, antiviral, anti-tumor, anti-inflammatory activities. The phytonutrients and vitamins may be responsible for the antioxidant, anticancer and anti-inflammatory properties of the citrus species. Although sweet orange (*Citrus sinensis*) is the major fruit in this group accounting for about 70% of citrus output. The group also encompasses small citrus fruits such as tangerine tree (*Citrus reticulata*), grapefruit tree (*Citrus vitis*), lime tree (*Citrus aurantifolia*) and lemon tree (*Citrus limonum*). There are about 40 limonoids in citrus with limonin and nomilin being the principal ones. These compounds, which occur in high concentration in grapefruit (*C. vitis*) and orange juice (*C. sinensis*) provide the bitter taste in citrus. Limonoids possess the ability to inhibit tumor formation by stimulating the enzyme glutathione S transferase (GST) [58]. The potential of citrus limonoids as anticancer agent in



mice has been reported and it was found that five limonoids aglycones (limonin, nomilin, obacunone, isoobacunoic acid, ichangin) induced significant amounts of GST in the liver and intestinal mucosa [59]. Reduction of skin tumours by limonoids has been also shown by animal studies [60]. In another study Entezari *et al.* reported Antimutagenicity and Anticancer Effects of *Citrus Medica* Fruit Juice [61].

Orange and lemon oil contain substantial amounts of GST that also possesses anti-cancer activity. Flavonoids are another phytochemicals found in citrus fruits [58] and they have strong anti-cancer activity [58, 62] and inhibit all stages carcinogenesis. *In vitro*, flavonoids display anti-proliferative effect on various human neoplastic cell lines as observed in myeloid and lymphoid leukemia cells, gastric cancer cells, ovarian cancer cells prostate cancer cells and squamous cell carcinoma.

Quercetin, myricitin, rutin, tangeritin, naringin and hesperidin are found amongst the common flavonoids in citrus fruits [58]. Furthermore quercetin seems to inhibit angiogenesis [63] and also shows remarkable anti-tumor properties. Tangeritin is a polymethoxylated flavone that is found in tangerine and other citrus peels. Tangeritin shows potential as an anti-cancer agent. It strengthens the cell wall and protects it from invasion. Pink grapefruit have a high content of  $\beta$ -carotene [58]. Pink grapefruit also contains a high level of lycopene, the red pigment that has a significant anti-tumor activity [5, 58].

Different *Citrus* varieties including *C. reticulata*, *C. unshiu*, and *C. natsudaoidai* are known to prevent tumorigenesis. It has been reported that *C. reticulata* peels have displayed potent tumor-suppressing activity in SNU-C4 human colon cancer cells [1]. Health properties of some citrus fruits have been shown in table 4 [5].

**Table 4. Health properties of some citrus fruits.**

Common name	Properties
Lemon	anti-cancer, antioxidant and antiseptic
Orange	anti-bacterial, anti-cancer, anti-viral, antioxidant, detoxifying and healthy heart
Grapefruit	anti-cancer, anti-viral, anti-inflammatory, antioxidant, detoxifying and healthy heart
Lime	anti-allergenic, anti-cancer, anti-viral, antioxidant and detoxifying

### Apricot (*Prunus armeniaca*)

Recently, several investigators have reported that apricot inhibits the growth of various cancer cells including gastric, breast, hepatocellular, colon and pancreatic cancer cells. It has been reported that Japanese apricot extract (MK615) dramatically suppressed cutaneous in-transit metastases in a patient with

advanced malignant melanoma [10]. These results suggest that MK615 is useful for treating human malignant tumors. The growth of all of the cancer cells tested was inhibited by MK615 in a concentration-dependent manner. Among the cell lines, pancreatic cancer MIA PaCa-2 cells were highly sensitive to MK615. Since MK615 contains several triterpenoids that exhibit antitumor activities [64]. It has been reported by Goma that the extracts of sweet apricot and bitter almond kernels could inhibit the growth of human breast (MCF-7), colon (HCT-116), and hepatocellular (Hep-G2) carcinoma cell lines [65].

### Musk-melon (*Cucumis melo*)

Musk melon (*cucumis melo*) possesses useful medicinal property such as anti-inflammatory, antioxidant, free radical scavenging and anticancer. Cucurbitacin B is a natural anti cancer agent isolated from the stem of *cucumis melo*. The anti cancer activity of Cucurbitacin B in human leukemia cells has been reported. Cucurbitacin B inhibits STAT3 activation and the Raf/MEK/ERK pathway in leukemia cell line K562. Cucurbitacin A and E also possess significant antitumor activity [66].

### Litchi (*Litchi chinensis*)

Litchi fruit pericarp (LFP) contains significant amounts of polyphenolic compounds, including condensed tannins (polymeric proanthocyanidins), epicatechin, procyanidin A2, and flavonoids which would be useful for anticancer drug discovery [67, 68]. The litchi fruit pericarp extract and its constituents have been reported to possess anti-cancer activity against human breast cancer [68, 69, 70, 71] and hepatocellular carcinoma *in vitro* and *in vivo* [67, 69] through proliferating inhibition and apoptosis induction of cancer cells [67].

### Blackberry (*Rubus fruticosus*)

Blackberries are an excellent source of natural antioxidants. Based on the high antioxidant potential of the fruits, as indicated by the lipid peroxidation inhibitory activity of their extracts, their incorporation in the diet is highly recommended. It has been reported that the hexane extracts of the Jamaican *Rubus* spp. demonstrated moderate COX inhibitory activity and exhibited the greatest potential to inhibit cancer cell growth, inhibiting colon, breast, lung, and gastric human tumor cells [72].

### Blueberry (*Vaccinium*)

Yi *et al.* evaluated the bioactivities of phenolic compounds in rabbiteye blueberries and assessed their potential antiproliferation and apoptosis induction effects using two colon cancer cell lines, HT-29 and Caco-2 and they suggested that blueberry intake may reduce colon cancer risk [73].

Faria *et al.* reported that blueberry anthocyanins and the respective anthocyanin-pyruvic acid adduct demonstrated anticancer properties by inhibiting cancer cell proliferation and by acting as



cell antiinvasive factors and chemoinhibitors. Also the anthocyanin-pyruvic acid adduct extract showed a more pronounced effect in MDA-MB-231 [55]. Wedge et al. reported the ethanol extracts of blueberry strongly inhibited CaSki and SiHa cervical cancer cell lines and MCF-7 and T47-D breast cancer cell lines [74].

### Raspberry (*Rubus idaeus*)

Raspberries are high in phenolic phytochemicals, particularly flavonoids such as anthocyanin pigments, which give raspberries their deep red color. Raspberries have significant antioxidant and anticancer activity. Darker raspberries show greater antioxidant activity than lighter ones but not significantly greater anticancer activity. It is assumed that phytochemicals other than anthocyanins in the raspberries were responsible for the inhibition of tumor cells to inhibit liver cancer cell growth [75]. The biological activity of black raspberry against esophageal, colon, [72, 76] and oral cancers has been demonstrated. It has been indicated that *Rubus* berries exhibited the greatest potential to inhibit cancer cell growth, inhibiting colon, breast, lung, and gastric human tumor cells [72]. Ellagic acid and a whole range of flavonoids, carotenoids and terpenoids present in *Rubus idaeus* (raspberries) have been reported to be responsible for antioxidant activity. These chemicals block various hormone actions and metabolic pathways that are associated with the development of cancer [77].

### Olive (*Olea europaea*)

The anticancer properties of olives have been highlighted in two research papers. First, a study from Spain has shown that the major complex phenols in extra-virgin olive oil suppress overexpression of the HER2 cancer gene in human breast cancer cells [78]. In another study, also from Spain, researchers found that maslinic acid, found in the skin, leaves and wax of olives, inhibited the growth of HT29 colon cancer cells [79].

### Persimmon (*Diospyros virginiana*)

Methanolic extract of persimmon calyx (PCE) contains bioactive materials and it is highly cytotoxic against human cancer cells and induces cell death through apoptosis. Therefore, PCE may have potential for development as a novel cancer chemotherapeutic agent originating from a natural product [6]. In another study fractionated extracts of persimmon (*Diospyros kaki*) peels were studied for cytotoxic activity and multidrug resistance (MDR). The results indicated the therapeutic value of persimmon peel extracts as potential antitumor and MDR-reversing agents [80].

### Pumpkin (*Cucurbita maxima*)

The plant *Cucurbita maxima* Duchesne (commonly known as pumpkin) is used in most countries as anti-diabetic, antitumor, antihypertensive, anti-inflammatory, immunomodulatory and antibacterial agents. Several *in vitro* and *in vivo* studies with crude pumpkin fruit extract as well as various purified fractions, including

proteins and poly-sacharides, have shown anticancer activity against melanoma, Ehrlich ascites carcinoma and leukaemia which may be due to its cytotoxicity and antioxidant properties [81, 82].

### Barberry (*Berberis*)

Barberries have long been used as herbal remedy for the treatment of a variety of complaints [83]. Barberry contains a wealth of anticancer, antitumor, antioxidant and mutation preventing compounds as well as cancer preventing properties. The *Berberis vulgaris* extract play a prominent role in promoting apoptosis upon the treatment and suppression of the liver cancer diseases [84]. Among several alkaloids of *Berberis* species, berberine is considered to be responsible for most of the biological activity [85]. Berberine shows inhibitory effects on the proliferation and reproduction of certain tumorigenic microorganisms and viruses, such as *Helicobacter pylori* and hepatitis B virus. It has been reported that berberine shows proapoptotic effects in many cancer cell lines and nontumor cells, including HL-60 cells, Balb/c 3T3 cells, HeLa and L1210 cells, SNU-5 cells, U937 cells, B16 cells, Ehrlich ascites carcinoma (EAC) cells, WEHI-3 cells, A431 cells, prostate cancer cells, human oral epithelioid carcinoma cell lines (KB), SW620 cells, and SMMC-7721 cells [86]. Berberine inhibits proliferation and induces apoptosis in primary effusion lymphoma cells [87]. It has been reported that berberine suppresses the androgen receptor (AR) signaling and berberine or its derivatives, presents a promising agent for the prevention and/or treatment of prostate cancer [88]. Studies have shown that berberine can induce both autophagy and apoptosis in hepatocellular carcinoma cells HepG2 and MHCC97-L [89].

### Tomato (*Solanum lycopersicum*)

Intake of tomatoes and tomato-based products and plasma levels of lycopene, a carotenoid found predominantly in tomatoes, have been relatively consistently associated with a lower risk of a variety of cancers. Evidence is strongest for cancers of the lung, stomach, prostate gland [4, 90] and is suggestive for cancers of the cervix, breast, oral cavity, pancreas, colorectum, and esophagus. The benefits of tomatoes and tomato products are often attributed to the carotenoid lycopene. Numerous other potentially beneficial compounds are present in tomatoes, and, conceivably, complex interactions among multiple components may contribute to the anticancer properties of tomatoes [90].

### Eggplant (*Solanum melongena*)

Eggplant contains Solasodine glycosides that are now used for the treatment of skin cancers.

Eggplant produces glycoalkaloids which are extracted and purified then incorporated into the cream, Curaderm BEC5, which is applied to a skin cancer resulting in the complete removal of all cancer cells without affecting normal cells and healing of the treated lesion with exceptional cosmetic results [91].



### Spinach (*Spinacia oleracea*)

The studies showed that the glycolipids fraction from spinach could help to prevent cancer disease, and become a functional food with anti-cancer activity [92, 93]. Rai *et al.* reported a significant relationship between spinach consumption and the risk of gallbladder cancer [94]. Nyska *et al.* reported that a natural antioxidant in spinach leaves slow prostate cancer in both animal and human prostate cancer cells [95]. Sani *et al.* reported that red spinach (*Amaranthus gangeticus*) showed anticancer potential in *in vitro* and *in vivo* studies. *A. gangeticus* inhibited the proliferation of liver cancer cell line (HepG2) and breast cancer cell line (MCF-7) and it showed that it possess hepatoprotective properties against chemical carcinogenesis [96].

### Mushroom (*Agaricus bisporus*)

Various important pharmaceutical products with proven medicinal applications have been derived from mushrooms for the prevention and treatment of cancer and other chronic diseases [97]. The studies indicated that polysaccharides from mushrooms do not attack cancer cells directly, but produce their antitumor effects by activating different immune responses in the host. The beneficial results of mushroom poly-saccharides are: (a) prevention of oncogenesis by oral consumption of mushrooms or their preparations; (b) direct antitumor activity against various allogeneic and syngeneic tumors; (c) immunopotential activity against tumors in conjunction with chemotherapy; (d) preventive effects on tumor metastasis [98].

*Sparassis crispa*, also known as cauliflower mushroom, is an edible mushroom with medicinal properties. Dietary treatment with *S. crispa* may prove to be a safe therapy for cancer and other chronic diseases [97]. It contains a remarkably high content of 6-branched 1, 3-beta-D-glucan showing anti-tumor activity [99].

### Cabbage (*Brassica oleracea*)

Glucosinolates found in *Brassica* vegetables and their hydrolysis products like Indole and Isothiocyanates derivatives are considered to be cancer chemo-preventive agents, which act at several stages of carcinogenesis. They are known to inhibit the growth of cancer cells to induce apoptosis [100] and they have detrimental activity against various types of cancer such as breast, lung and colon [101]. Sulforaphane (SFN) an isothiocyanate formed by hydrolysis of glucosinolates found in *Brassica oleraceae* is reported to possess anticancer and antioxidant activities. It has been reported that sulforaphane isolated from red cabbage could contribute to the antiproliferative activity and apoptosis in human larynx cancer epithelial cell line and found to have significant anticancer activity [100]. Sulforaphane can decrease the risk of developing different cancers such as breast cancer, gastric cancer and skin cancer. Studies have shown that cabbage demonstrated a pronounced anticancer effect against A-549 lung cancer cells [102].

### Beetroot (*Beta vulgaris* L.)

Currently, there is considerable interest in the anticancer effects of red beetroot (*Beta vulgaris* L.) pigment extract, which is used worldwide as red food color E162 and as a natural colorant in cosmetics and drugs. Of particular significance is its broad spectrum of multi-organ antitumor activity demonstrable in laboratory animal models. Betanin, the betacyanin constituent primarily responsible for red beet color, is an antioxidant with an exceptionally high free radical-scavenging activity and is a modulator of oxidative stress [103]. It has been reported that beetroot (*Beta vulgaris* rubra, BVR) contains secondary metabolites, called betalains and show anticancer activity [104].

### Shallot (*Allium hirtifolium*)

Persian shallot (*Allium hirtifolium*), called as "Mooseer" in Iran belongs to Alliaceae family and is one of the important edible alliums in Iran [105] which has anticarcinogenic [105, 106], hypoglycemic, hypolipidemic, antioxidant, antibiotic properties, kidney and liver protective effects (Fig. 1). The ability of Persian shallot to preferentially suppress the growth of neoplastic over non neoplastic cells provides interesting possibilities for the development of new anticancer strategies in humans. Allyl sulfides, found in processed *Alliaceae* family, possess anticancer properties as shown by their ability to suppress tumor proliferation *in vitro*. Many organosulfur compounds, the major active principles in alliums, inhibit the proliferation of cancer cells, and some of them cause apoptosis in tumor cells of different tissue origin. Effects of chloroformic extract of Persian shallot and its allicin on the proliferation of HeLa (cervical cancer), MCF7 (human, caucasian, breast, adenocarcinoma) have been reported [105].

### Scallion (*Allium fistulosum* L.)

*Allium fistulosum* L., commonly known as scallion, is popularly used as a spice or vegetable worldwide. It has been reported that scallion extracts suppressed the expression of various cellular markers known to be involved in tumor apoptosis, proliferation, angiogenesis and tumor invasion when compared with vehicle control-treated mice. The use of common scallion as a chemopreventive dietary agent to lower the risk of colon cancer has been suggested [107].

### Broccoli (*Brassica oleracea*)

Broccoli is excellent source of phytochemicals [108] which are powerfully anti cancerous [5] and including glucosinolates and their byproducts, phenolics and antioxidant vitamins as well as dietary minerals. Broccoli consumption mediates a variety of functions including providing antioxidants, regulating enzymes and controlling apoptosis and cell cycle [108]. Various epidemiologic





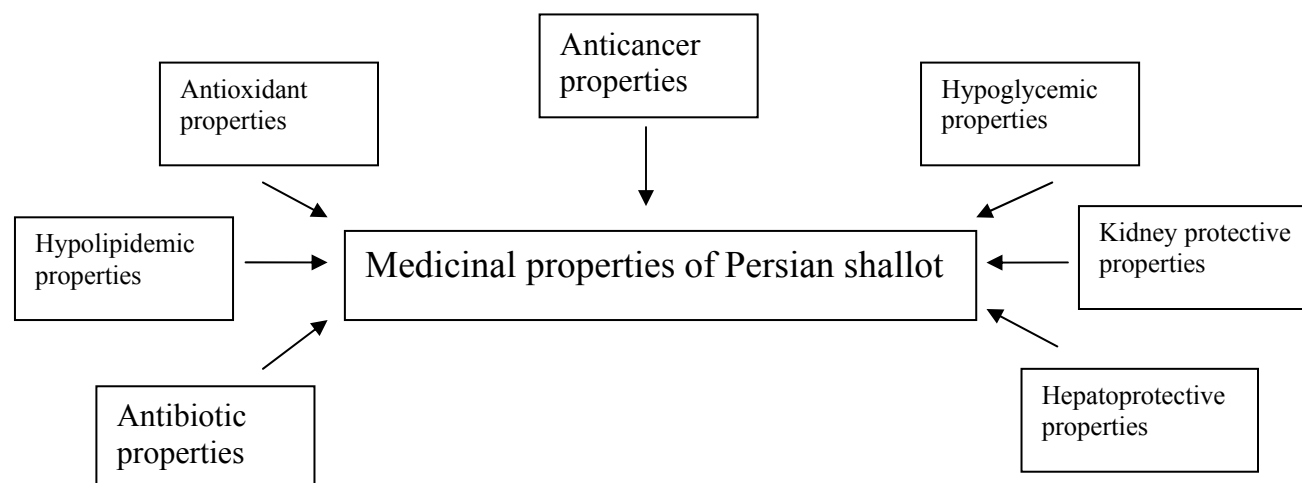


Figure 1. Medicinal properties of Persian shallot.

studies have indicated that consumption of broccoli is associated with a lower risk of cancer, including, prostate, stomach [109], breast, lung, colon [109, 110], ovarian and bladder cancers [110]. The anticancer effect of broccoli has been attributed to sulforaphane (SFN) [4, 102, 109], an isothiocyanate formed by hydrolysis of a precursor glucosinolate called "glucoraphanin". Anticancer effects of SFN have been demonstrated in several malignancies including human colon, bladder, prostate, ovarian, lymphoblastoid, pancreatic, cervical cancer, and lung cancers [109]. This isothiocyanate can decrease the risk of developing different cancers such as breast cancer, gastric cancer and skin cancer [102].

### Garlic (*Allium sativum*)

Garlic (*Allium sativum*) contains plentiful of chemical compounds that are helpful in prevention and treatment of different types of cancer [111, 112]. It has multiple beneficial effects, such as antithrombotic, hypolipidemic, antiarthritic, hypoglycemic, antioxidant [111, 113] and anticancer activity [32, 111, 113, 114], which appear to be due to allicin [111]. Several lines of epidemiological study indicate that the risk of a certain cancer can be prevented by consumption of garlic [115]. Recently, several individual compounds have been isolated from garlic and two major groups of compounds that show active anticancer effects have been identified. One group is the lipid-soluble allyl sulfur compounds such as diallyl disulfide (DADS) and diallyl trisulfide (DATS), and the other one is the water-soluble compounds  $\gamma$ -glutamyl S-allylcysteine group such as S-allylcysteine (SAC) and S-allylmercaptocysteine (SAMC) [116]. Diallyl trisulfide, bound to specific cysteine residues in  $\beta$ -tubulin to form S-allylmercaptocystein and this could be the sole cause of cell cycle arrest and successive apoptosis with activation of caspase-3 [115]. These individual compounds are not only able to suppress the skin, esophageal, stomach, colon, liver, lung and breast cancer growth

in animal models, but also directly inhibit proliferation of a variety of cancer cell lines derived from colon, lung, leukemia, skin, breast, endometrial and prostate cancer cells in vitro [116].

### Sweet potato (*Ipomoea batatas*)

Sweet potato protein (SPP) exerts significant antiproliferative and antimetastatic effects on human colorectal cancer cell lines, both *in vitro* and *in vivo* [117] and the anticancer activity of sweet potato greens extract in prostate cancer have been identified [32]. Previous studies have identified SPP as a type of Kunitz-type trypsin inhibitor (KTI) with potential therapeutic effects in a variety of cancer models. It has been reported that KTI purified from sweet potato inhibited proliferation and induced apoptosis of NB4 promyelocytic leukemia cells. KTIs isolated from other sources, such as human urine and soybeans, have been shown to exert antiproliferative, anti-invasion and antimetastatic activities in a variety of malignant cells, animal models and cancer patients [117]. The constituent polyphenolics of sweet potato greens (SPG) display antimutagenic, antidiabetic, antibacterial, anti-inflammatory, and anticancer activity [32].

### Rhubarb (*Rheum rhabarbarum*)

Several bioactive anthraquinones of rhubarb possess promising anti-cancer properties and could have a broad therapeutic potential. Pharmacological studies have demonstrated that emodin when isolated from rhubarb exhibits anti-cancer effects on several human cancers, including human pancreatic cancer and is capable of inhibiting cellular proliferation, induction of apoptosis, and prevention of metastasis. Aloe-emodin is another major component in rhubarb found to have anti-tumor properties. Its anti-proliferative property has been demonstrated to be through the p53 and its downstream p21 pathway. Rhein is the other major rhubarb anthraquinone, effectively inhibit the uptake of glucose in tumor

cells, caused changes in membrane-associated functions and led to cell death [118].

### Black tea (*Camellia sinensis*)

Tea is a widely consumed beverage and its constituent polyphenols have been associated with potential health benefits. Black tea polyphenols have been demonstrated to suppress proliferation and induce apoptosis in a variety of cancer cell lines by modulating various molecular targets, such as prostate, lung [119] and breast [119, 120]. Various findings suggest that tea and its polyphenolic components possess anticancer effect [121]. Black tea and theaflavins activate an array of apoptogenic signaling events thereby ensuing reduced tumor growth. This beverage not only regress tumor but also protects intrinsic defense machineries

of the host from cancer insult. Black tea even reduces tumor-induced hepatotoxicity and protects against oxidative damage generated by the developing tumor. Therefore, acting in a multi-faceted manner, black tea and theaflavins can successfully bring about regression of the tumor and ensure survival of the host. Fig. 2 illustrates that black tea regresses cancer by directly killing cancer cells and rejuvenating host's suppressed defense machinery [9].

Epidemiological studies suggest a protective effect of tea consumption on some cancer types in human [122]. Black tea has also been shown to inhibit tumorigenesis in animal model systems, including lung, colon, skin [9, 121], fore-stomach, pancreas liver and esophagus of rodents by activating the detoxification systems of the host [9].

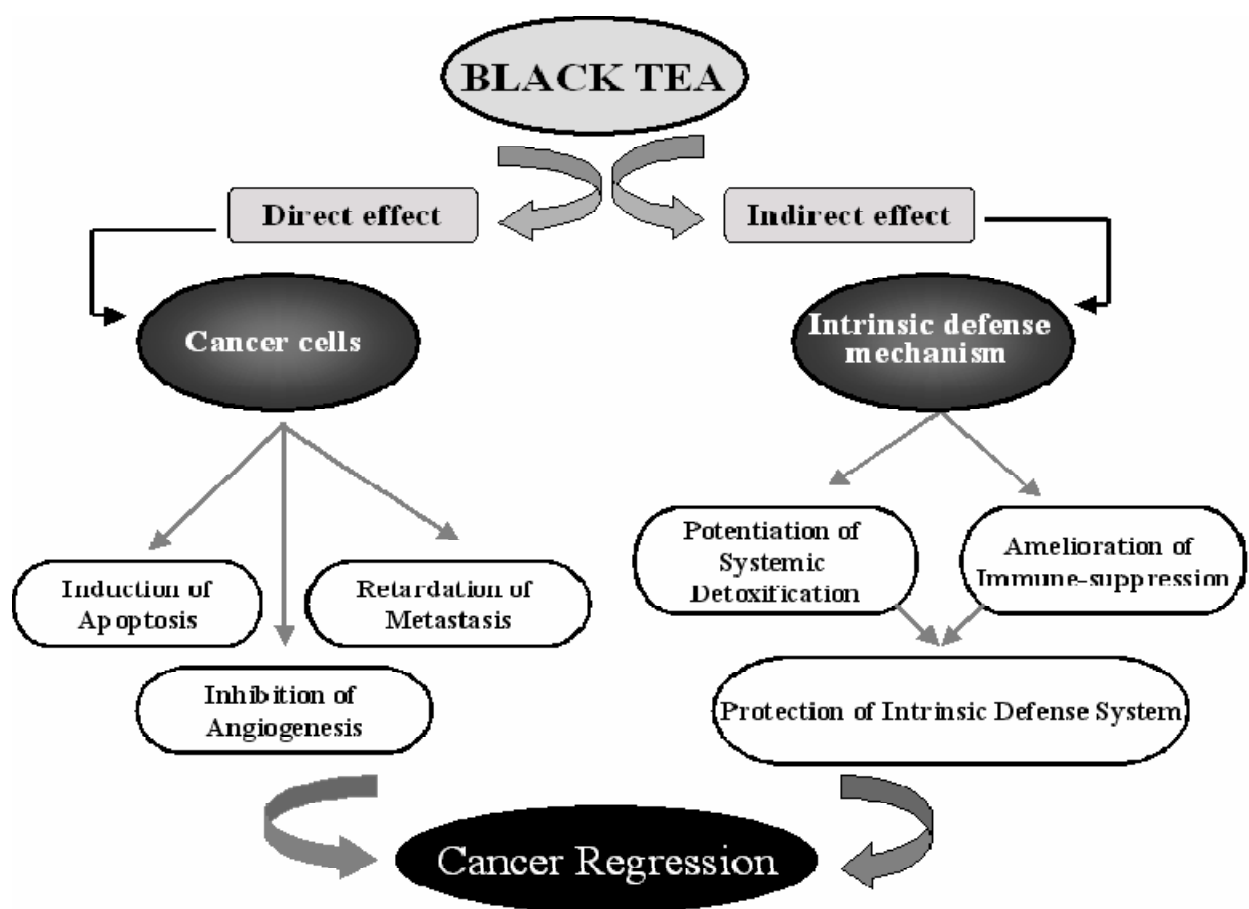


Figure 2. Black tea regresses cancer by directly killing cancer cells and rejuvenating host's suppressed defense machinery.



### Green tea (*Camellia sinensis*)

Green tea is now recognized as the most effective cancer preventive beverage [123]. The consumption of green tea is associated with a lower risk of several types of cancer, including stomach, esophagus, and lung [124]. In some studies, green tea had protective effects on stomach, bladder, skin [125], breast cancer [120, 125]. Green tea has antimutagenic [125, 126] and anticarcinogenic properties [125, 127, 128]. It has been demonstrated that oral administration of tea infusion can inhibit the development of experimental rodent skin tumors, growth of implanted tumor cells and invasion and metastasis of malignant tumors [124]. Green tea extracts contain a unique set of catechins that possess biologic activity in antioxidant, antiangiogenesis, and antiproliferative assays that are potentially relevant to the prevention and treatment of various forms of cancer [128, 129] such as prostate cancer [32].

Cancer patients who consume green tea and take anticancer drugs will have double prevention. Green tea catechins increase the anticancer activity of various anticancer drugs [123]. As for lung cancer, a recent study established that the consumption of green tea was associated with a reduced risk of cancer among non-smoking women [125]. The cancer chemopreventive effect of tea has been attributed to its major phytopolyphenols [124] and tea polyphenols have been shown to inhibit tumorigenesis and tumor progression, at different organ sites, in different animal models for human cancer [130, 131]. Caffeine is another major component of tea responsible for tea's anti-cancer effects. Tea components may also produce anti-cancer effects through mediation of carcinogen metabolizing or detoxification by inhibition of carcinogen-induced mutagenesis, inducing cell cycle arrest and apoptosis or tea components target specific signal transduction pathways leading to AP-1 or NF- $\kappa$ B, which are transcription factors that have been shown to play a key role in carcinogenesis [132].

### Noni fruit juice (*Morinda citrifolia* L.)

*Morinda citrifolia* L. (noni) is one of the most important traditional Polynesian medicinal plants. [44,65] Noni fruit juice made from the fruit of Indian Mulberry has been reported to have a broad range of therapeutic effects; for example, antibacterial, antiviral, antifungal, anticancer, and anti-inflammatory activities including analgesic and immunomodulating effects. For the scientific studies, there are reports that polysaccharide-rich substances in Noni fruit juice have immunomodulating effects and contributed to anticancer activity [133].

An immunomodulatory polysaccharide-rich substance (Noni-ppt) from the fruit juice of *Morinda citrifolia* has been found to possess both prophylactic and therapeutic potentials against the immunomodulator sensitive Sarcoma 180 tumour system.

In advanced cancer patients, there appear to be higher levels of Th2 cytokines and lower levels of Th1 cytokines, thus indicating an

impairment of the cell-mediated immunity. Therefore, it seems that administration of Th1 cytokines and/or Th1 immunostimulators such as Noni-ppt have a great potential for cancer immunotherapy in cancer patients.

In addition to the antitumour potential of Noni-ppt against the syngeneic Lewis lung carcinoma cell line (LLC) tumour that can grow only in the C57BL/6 strain of mice, it has been demonstrated that Noni-ppt also exhibits significant antitumour activity against the allogeneic S180 ascites tumour which can grow in any strain of mice [134].

McClatchey reported that anti-proliferative activity was identified from the water and butanol fractions against a breast carcinoma cell line (MCF-7) and a colon carcinoma line (HCT-116). The active compounds in the water extract appear to affect several genes of the tumor necrosis factor- (TNF) apoptotic pathway and cell cycle, and result in inhibition of cancer cell growth [135].

### Olive oil (*Olea europaea*)

Olive oil when compared to other oils was found that fried olive oil has a protective effect against colon cancer. This agrees with data that unheated olive oil is beneficial in protecting against colon cancer. It has been reported that death rates from prostate cancer was lower in areas with high olive oil consumption, such as Greece and Italy. Also women who intake the olive oil were less likely to be classified into the high mammographic breast density (H-MBD) group [136].

Also the protection of olive oil against breast cancer demonstrated [137, 138] and it may be due to oleic acid components rather than to the acid itself. A study by Menendez of the Northwestern University Feinberg School of Medicine in Chicago revealed that oleic acid blocks the action of HER-2/neu, a cancer-causing oncogene found in about 30% of breast cancer patients [137].

### Palm oil (*Elaeis guineensis*)

Tocotrienols (T3) are vitamin-E constituents that naturally found in palm oil and have been shown to have anticancer effect against a wide range of human cancers. Palm tocotrienols inhibit the growth of skin, stomach, pancreas, liver, lung, colon, prostate, breast and other cancers [136].

### Clove oil (*Syzygium aromaticum*)

Eugenol a natural compound available in various plants extracts including clove is exploited for various medicinal applications [136]. Eugenol is an effective cytotoxic agent for different type of cancer cells and it is endowed with apoptotic inducing capability [139]. It has been reported that the apoptotic effect and anticancer mechanism of eugenol were investigated against colon cancer cells and MTT assay signified the antiproliferative nature of eugenol against the tested colon cancer cells [136]. It has been demonstrated that clove oil and eugenol have significant cytotoxic effect against human fibroblasts and endothelial cells and Hep G2 hepatoma cell lines [139].



### Soybean oil (*Glycine max*)

Soybean contains several components with anticancer activity [106, 136], such as isoflavones, protease inhibitors, phytosterols, saponins, phenolic acids and phytates. Soybean contains three types of isoflavones: aglycone daidzein, genistein and glycitein. Genistein increases concentration of TGF- $\beta$ , which may inhibit the growth of cancer cells has an important role as a potent inhibitor of angiogenesis *in vitro*. Soybean intake may help in preventing the initiation of breast cancer cells. Genistein has been shown to reduce DNA synthesis in human prostate cells *in vitro* and inhibit testosterone effect in prostate cancer development in rats. Prostate cancer is also reported to be associated with increased levels of dihydrotestosterone, and soybean isoflavones are known to inhibit 5-reductase which is involved in the conversion of testosterone to dihydrotestosterone. Isoflavones, the functional components of soybean improves digestive tract function, prevents breast, prostate, and colon cancer. Lectins and peptides act as an anticarcinogenic agent and phytosterols which is another component improves prostate cancer [136].

### Fennel oil (*Foeniculum Vulgare*)

Fennel seed methanolic extract (FSME) have cytotoxic and antitumor activities. FSME may have remarkable anticancer potential against a breast cancer cell line (MCF7) and liver cancer cell line (HepG-2) [136, 140].

### Black cummin oil (*Nigella sativa*)

*Nigella sativa* seed, its oil and extracts and some of its active principles, particularly thymoquinone and alpha-hederin, possess

remarkable *in vitro* and *in vivo* activities against a large variety of cancers [141, 142] such as liver, lung, pancreas, colon, leukemia, melanoma, prostate, cervix and breast carcinoma [141, 143]. Appropriate modifications in the molecular structure of thymoquinone and alpha-hederin could lead to more effective and safer drugs for the treatment of neoplastic tumors. Moreover, *N. sativa* seed, its oil, thymoquinone, alpha-hederin or their analogs could be used in suitable combinations with already established as chemotherapeutic agents. It has been reported that besides cytotoxic effect of essential oil and ethyl acetate extracts of *N. sativa* against various cancer cell lines, the injection of essential oil into solid tumor in an *in vivo* mouse model (DBA2/P815) significantly reduced the tumor size, inhibited the incidence of liver metastasis and improved the survival chance of the mouse [141].

### Turmeric (*Curcuma longa*)

Curcumin is an orange-yellow component of turmeric (*Curcuma longa*), a spice often found in curry powder. Curcumin is known to have a variety of biologic and pharmacologic activities, including anti-inflammatory, anti-oxidant, and anticarcinogenic potential. Curcumin has anticarcinogenic activity in colon cancer, breast cancer and leukaemia. Curcumin has been reported to cause a marked decrease in cell proliferation and apoptosis in prostate tumours. Curcumin and genistein have been reported as the most potent inhibitors against the growth of human breast tumour cells. It has been reported that the anti-cancer property of curcumin is mediated in part by its anti-angiogenic activity [144].

Curcumin has been shown to have protective and therapeutic effects against cancers of the blood, skin, oral cavity, lung, pancreas, and intestinal tract, and to suppress angiogenesis and metastasis in rodents [145]. Some anticarcinogenic effects of turmeric have been shown in table 5 [13].

Table 5. Anticarcinogenic effects of turmeric.

Common name	Anticancer agent	Functions
Turmeric	Curcumin	<ul style="list-style-type: none"> <li>-Inhibits human colon cancer (HT-29, HCT-15) proliferation</li> <li>-Inhibits mouse skin cancer</li> <li>- Has chemopreventive effect on mice skin, forestomach, colon and oral cancer</li> <li>- Decreases the death rate and hepatocellular carcinoma production in mouse due to the liver cancer induced by diethylnitrosamine</li> <li>- Has cytotoxic activity which repress bladder cancer production</li> </ul>



### Saffron (*Crocus sativus* L.)

Saffron (*Crocus sativus* L.) and their associated carotenoid ingredients are extensively studied for their biomedical properties, especially for their chemopreventive potential against cancer [146]. Saffron and their main constituents possess anticancer and antitumor activities. It has been reported that oral administration of saffron extract inhibited the growth of mouse tumors that were derived from sarcoma-180 (S-180), Ehrlich ascites carcinoma (EAC), Dalton's lymphoma ascites (DLA) and significantly increased the life spans of treated tumor-bearing mice [147].

Crocetin, an important carotenoid constituent of saffron, has shown significant potential as an anti-tumor agent in animal models and cell culture systems. Crocetin affects the growth of cancer cells by inhibiting nucleic acid synthesis, enhancing anti-oxidative system, inducing apoptosis and hindering growth factor signaling pathways [148].

### Red chili pepper (*Capsicum annum*)

Capsaicin, a pungent ingredient of red chili peppers, has been reported to possess antitumor activities. It has been found that treatment of various gliomas with capsaicin significantly upregulated DR5, a death receptor of tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), and downregulated the caspase inhibitor surviving and they also reported that a combined regimen using capsaicin and TRAIL may provide a safe and effective strategy for treating malignant gliomas.

Malignant gliomas are the most common primary brain tumors. They exhibit a relentless malignant progression characterized by widespread invasion throughout the brain, destruction of normal brain tissue, resistance to traditional therapeutic approaches and certain death.

TRAIL, a member of the cytokine superfamily, is a promising candidate for cancer therapy because it induces apoptosis in numerous cancer cell lines but not in normal cells.

Recent studies have shown that capsaicin induces apoptosis in a number of different cancer cells but not in normal cells, indicating that capsaicin may have therapeutic benefits in clinical settings, either as an anticancer agent or as an adjunct to current cancer therapies [149].

### Black pepper (*Piper nigrum*)

Black pepper and cardamom exert immunomodulatory roles and antitumor activities [150] and anticancer activities attributed to capsaicin [151]. Capsaicin may enhance the antitumor effect of BCG in bladder cancer treatment [152] and the potent *in vitro* and *in vivo* antitumor activities of capsaicin suggest that capsaicin might be developed for the treatment of human colon cancer [153].

### Clove (*Syzygium aromaticum*)

Clove (*Syzygium aromaticum*) is one of the most commonly used spices in Indian kitchens. The agent found in the clove extract is capable of killing cancer cells in the human body by proliferation-inhibiting and apoptosis-inducing (causing programmed cell death) effects. It has been shown to be a potent chemopreventive agent. In a research was done by Dwivedi *et al.* water, ethanol and oil extracts were screened for anti proliferative activity against HeLa (cervical cancer), MCF-7 (ER + ve) and MDA-MB-231 (ER – ve) breast cancer, DU-145 prostate cancer and TE-13 esophageal cancer cell lines, along with normal human peripheral blood lymphocytes. Maximum cell death and apoptotic cell demise occurred in TE-13 cells by clove oil whereas DU-145 cells showed minimal cell death [139].

### Cinnamon (*Cinnamomum verum*)

Cinnamon is one of the most widely used herbal medicines with diverse bioactive effects [154]. It has anti-microbial, anti-oxidant, anti-diabetic, anti-inflammatory [155] and anticancer properties [139, 154, 156]. Cinnamon has antiangiogenic protective activities and supports the hypothesis that helps in the prevention of breast cancer [120]. Cinnamon extract has the potential to be an alternative medicine for tumor treatment. Oral administration of cinnamon strongly inhibits not only angiogenesis but also metastasis of tumor tissues [154]. It has been reported that anti-tumor effects of cinnamon extract appear to be mediated by multiple mechanisms. These include inhibition of angiogenesis, potentiating CD8<sup>+</sup> T cell cytotoxicity and apoptosis induction in tumor cells. Anti-tumor effect of cinnamon extracts is directly linked with enhanced pro-apoptotic activity and inhibition of NF $\kappa$ B and AP1 activities and their target genes *in vitro* and *in vivo* mouse melanoma model [155].

### Ginger (*Zingiber officinalis*)

Ginger, the rhizome of *Zingiber officinalis*, one of the most widely used species of the ginger family, is a common condiment for various foods and beverages [157]. Some phenolic substances present in ginger, generally, possess strong anti-inflammatory and anti-oxidative properties and exert substantial anti-carcinogenic, anti-apoptotic and anti-mutagenic activities [15, 157].

Ginger and many of its chemical constituents have been shown, in numerous clinical studies, to be useful in combating postoperative vomiting and vomiting of pregnancy. It may be worthwhile investigating the effect of ginger on vomiting during cancer chemotherapy, as the crude drug and its constituents have themselves anti-cancer actions [158].

In a research, extracts (methanol) of the leaves, stem and rhizome of *Boesenbergia* species (*Boesenbergia rotunda*, *Boesenbergia pulchella* var *attenuate* and *Boesenbergia armeniaca*) were studied. In the cytotoxicity assay, *B. rotunda* showed the most prominent and promising result as anticancer medicinal plant. It showed positive antiproliferative effect against five cancer cell lines: ovarian (CaOV3), breast (MDA-MB-231 and MCF-7), cervical (HeLa) and colon (HT-29) cancer cell lines. In addition, the rhizome



of *B. pulchella* var *attenuata* and *B. armeniaca* shown positive result in cytotoxicity assay tested against breast cancer (MCF-7). Thus, the *Boesenbergia* species investigated would be a promising anticancer remedy for breast cancer [159].

**Table 6. Natural anticancer agents from natural products.**

Common name	Scientific name	Anticancer agent
Watermelon	<i>Citrullus vulgaris</i>	Lycopene
Mango	<i>Mangifera indica</i>	Lupeol
Pineapple	<i>Ananas comosus</i>	Bromelain
Cherry	<i>Prunus avium</i>	Perillyl alcohol
Papaya	<i>Carica papaya</i>	Lycopene
Guava	<i>Psidium</i>	Lupeol

## Conclusion

Significant part of drug discovery has been focused on agents to prevent or treat cancer and it was concluded that natural products are still an important source of new drugs, especially in the anti-cancer therapeutic areas. Plant derived natural products have received considerable attention in recent years due to their diverse pharmacological properties including antioxidant and antitumor activity. This review presents that agents derived from plants can be used not only to prevent cancer, but also to treat cancer and such plants may be sources of drugs for cancer treatment in the future (Table 6).

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