Chapter 13
Green Tea and Its Role in Cancer Prevention and Therapy

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Abstract Cancer is one of the major causes of mortality worldwide, and despite desperate attempts, many patients still suffer from poor prognosis. Hence, efforts for discovering and developing more potent and effective anticancer agents continue. A growing body of research and experiments indicates the potential of some medicinal plants as a possible source of anticancer agents. In recent years, the health benefits of consuming green tea (derived from the plant *Camellia sinensis*) have been extensively documented. The ailments which can be treated and/or prevented include different types of cancer, heart and liver diseases, and neuroprotective and antioxidant activities. Many of these beneficial effects are related to tea catechins, particularly (-)-epigallocatechin-3-gallate (EGCG) content. Green tea consumption is also linked to the prevention of many types of cancer including breast, prostate, lung, colon, and stomach cancers. Moreover, cancer rates in Asian countries such as Japan and China where green tea is consumed in large quantities are significantly low according to epidemiological studies. These associations are confirmed by experiments with animals as well as cultured cancer cells. The use of EGCG instead of crude green tea extracts permitted studies to elucidate the mode of anticancer of green tea. Clinical studies demonstrating the prevention of cancer by green tea or by EGCG were recently questioned. The use of the nontoxic green tea or EGCG as anticancer agent is highly recommended.

Keywords Apoptosis • Cancer prevention • Cancer therapy • EGCG • Green tea • Oncogene • Signal transduction

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Fig. 13.1 *Camellia sinensis* branch and flower (Wikipedia)

Abbreviations

EGCG	(-)-Epigallocatechin-3-gallate
MAPKs	Mitogen-activated protein kinases
ODC	Ornithine decarboxylase
PSA	Prostate-specific antigen

13.1 Introduction

Natural products, mainly plants and their constituents, have been used in the cure of diseases from ancient times. In the Bible, we find that Adam and Eve ate the fruits of the "Tree of Wisdom," which grew in Paradise. It resulted in "opening their eyes" and realizing that they were naked. So, it is clear that medicinal plants grew in Paradise. Tea is derived from the leaf of the plant *Camellia sinensis* (Fig. 13.1). Chinese people had become aware, as early as 4000–5000 years ago, that tea could cure and prevent some human diseases (Mair and Hoh 2009). Today, hundreds of millions of people around the world drink tea. It appears that one type of tea, in particular, green tea, has many health benefits. Green tea is processed by steaming fresh tea leaves immediately after harvest. The result is minimal oxidation of the naturally occurring polyphenols in the tea leaves. Black tea is processed by drying tea leaves and by crushing upon harvesting to encourage oxidation, which converts

Fig. 13.2 Various tea leaves (contribution of Zohara Yaniv)

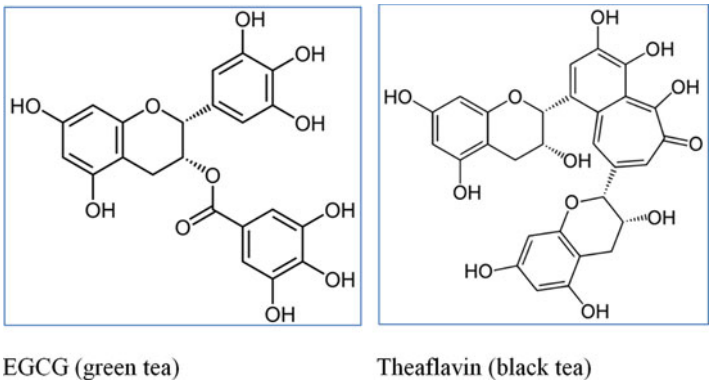

Fig. 13.3 Tea polyphenols

indigenous tea polyphenols to inactive oxidation products. This results in the appearance of the typical red-brown color and aroma of black tea (Fig. 13.2). It is generally accepted that next to water, tea is the most consumed beverage in the world, with a per capita consumption of 120 ml/day (Katiyar and Mukhtar 1996). Of the total amount of tea produced in the world, 78 % is black, and 20 % is green. Black tea is used primarily in the West, whereas green tea is mainly consumed in Asian countries (Mukhtar and Ahmad 2000). Botanical evidence indicates that leaves of green tea contain polyphenols (Fig. 13.3) including (-)-epigallocatechin-3-gallate (EGCG), which amount to 8–12 % of the dried green tea leaves. One cup of green tea will contain approximately 30–40 mg of EGCG, which is claimed to possess many therapeutic activities. These include anticancer activities, cardiovascular therapies, antioxidant activities, and anti-inflammatory behaviors (Rahmani et al. 2015).

13.2 Anticancer Activities

Cancer is a multifunctional disease including genetic and metabolic alterations. This disease is still one of the major causes of mortality worldwide. Therefore, the effort for developing new and better anticancer agents has never been stopped. According to the tradition and experimental studies, a great number of medicinal plants have been reported to have anticancer properties (Bachrach 2012). Green tea extracts showed beneficial effects on cancer-related diseases and quality of life of individuals suffering from different forms of cancer. It has been demonstrated in in vitro and in vivo studies. Clinical trials supported the use of green tea extracts in treating cancer patients, and the results of the clinical studies became so popular that even the BBC stated on December 5, 2005, that:

> Green tea extract may help patients with a form of leukemia. It is exciting that research is now demonstrating that this agent may provide new hopes for chronic lymphocytic leukemia (CLL) patients.

Green tea or its active polyphenol-EGCG inhibits the growth of various cancers such as breast, prostate, colorectal, and bladder cancers. The following is a review of the latest literature dealing with these aspects.

13.2.1 Breast Cancer

Breast cancer is the most common malignancy in women in the world, and its rate is increasing in both developing and developed countries. Significant studies conducted in Asia, where green tea is consumed in large quantities, tend to show a low onset of breast cancer. The rate of breast cancer in China is 28.7 per 100,000 women per year, which is four- to fivefold lower than rates in developed countries (Bray et al. 2004). A case-control study conducted in Southeast China included more than 1000 women with confirmed breast cancer. These patients drank between 249 and 750 g of dried green tea leaves per annum. A significant inverse relationship between the severity of the disease and the amount of green tea consumed was established (Zhang et al. 2007). Epidemiological studies showed a strong negative correlation between consumption of green tea and the onset and frequency of many types of cancer. Thus, the onset of breast cancer in Japan was delayed by 8.7 years after daily drinking ten cups of tea, compared to a delay of 3.0 years after drinking only three cups of tea per day (Fujiki et al. 1998). The inverse association between risk of breast cancer and green tea intake was also observed among Japanese hospitalized patients (Inoue et al. 2001). These findings were not limited to people drinking green tea, as similar results were obtained when EGCG, and no crude green tea was consumed. Studies with Japanese breast cancer patients revealed (Nakachi et al. 1998) that increased consumption of EGCG decreased the recurrence of stage I and II breast cancer. No improvement in prognosis was observed in stage III breast cancer. Suganuma et al. (1999) also reported that high daily

consumption of green tea was associated with a lower recurrence rate among stage I and II breast cancer patients.

Kumar et al. (2009) studied the effect of tea consumption on the risk of breast cancer in 5082 women in Wisconsin. They found a 37 % reduction in breast cancer risk among women who consumed at least three cups of green tea per day. Clement (2009) also observed that habitual green tea consumption attenuates the risk associated with breast cancer.

The reduced rate of cancer incidence among people in Asia, who consume green tea, cannot be attributed to genetic factors. Foreign-born Asian Americans who reside in North America and who consume Western food have an increased risk of cancer, based on the years of residence in North America (Shimizu et al. 1991). The rate for breast cancer was substantially higher when migration took place early in life. These findings suggest that lifestyle in the young rather than in later life is important in the etiology of breast cancer (Shimizu et al. 1991). Similarly, cancer rates for Korean American immigrants have increased for prostate, colon, and rectal cancers, based on the years of residence in the United States (Lee et al. 2007). Many authors agreed that green tea reduced the risk of breast cancer. However, recent studies conducted in Japan (Iwasaki et al. 2010a, b; Iwasaki and Tsugane 2011) showed that there was no correlation between breast cancer risk and drinking of green tea. These studies should be repeated and extended.

13.2.2 Prostate Cancer

Every year nearly 200,000 men in the United States are diagnosed with prostate cancer, and the other 29,000 succumb to the disease (Johnson et al. 2010). Genetic backgrounds may contribute to prostate cancer risk. Men who have a first-degree relative (father or brother) with prostate cancer have twice the risk of developing prostate cancer, and those with two first-degree relatives affected have a fivefold greater risk compared with men with no family history. About 99 % of cases occur in those over the age of 50 years (Johnson et al. 2010). Prostate cancer incidence in China, where green tea is consumed in large quantities, is the lowest in the world. Gupta et al. (2001) and Adhami et al. (2004) reported that tea polyphenols could inhibit the development of prostate cancer in animals. The chemopreventive effect of green tea was studied by Henning et al. (2011), who found that green tea extracts were more effective than black tea extracts. Bettuzzi et al. (2006) reported that in humans, a high dose of green tea catechins (200 mg catechin – given three times per day) prevented prostate cancers. The incidence of cancer in men in the treated group was 3 %, while it was 30 % in the control group. It implies that a chemopreventive effect of 90 % was achieved. A larger cohort study involving 49,000 Japanese men who were followed up for 14 years showed a marked reduction in the risk of advanced prostate cancer in those with habitual consumption of green tea (Kurahashi et al. 2008; McLarty et al. 2009) and reported that patients with prostate cancer, who received a daily dose of 800 mg of EGCG, showed a significant reduction of

the prostate-specific antigen (PSA), with no elevation of liver enzymes. They concluded that EGCG could play a potential role in the treatment or prevention of prostate cancer. Kurahashi et al. (2008) studied the effect of green tea consumption on 404 cancer patients in Japan and found a dose-dependent decrease in the risk of advanced prostate cancer. In China, the effect of drinking more than three cups of green tea on the development of prostate cancer was also studied (Jian et al. 2004). Again, it was found that prostate cancer risk declined with increasing frequency, duration, and quantity of green tea consumed. Henning et al. (2011) studied the chemopreventive effects of tea on prostate cancer and found that the effect of black tea was much weaker than green tea.

On the other hand, recent studies (Kumar et al. 2015) raised some questions whether EGCG, 200 mg per day, could reduce the likelihood of prostate cancer diagnosis and whether green tea could be used for the prevention of prostate cancer. These studies should be repeated and confirmed.

13.2.3 Other Types of Cancer

Chronic Lymphocytic Leukemia (CLL) In 2013, 42 patients with chronic lymphocytic leukemia were treated with EGCG at a dose of 2000 mg, twice daily for 6 months. This treatment resulted in the reduction of absolute lymphocyte count in 29 (69 %) of the patients (Shanafelt et al. 2013).

Colorectal Cancer This cancer represents the third most common and the second deadliest type of cancer for both men and women in the United States claiming over 50,000 lives in 2014 (Pabla et al. 2015). Yang et al. (2007) evaluated the association between green tea consumption and colorectal cancer risk in a cohort of 67,710 Chinese women. They found an inverse association between green tea drinkers and cancer for both colon and rectal cancers. Kumar et al. (2007) and Larsen and Dashwood (2009) reported that EGCG might be a beneficial therapeutic agent in treating colon cancer. A cohort study in Singapore (Sun et al. 2007) found that, for men, green tea, but not black tea, consumption affected the risk of the advanced stage of colon cancer.

Stomach Cancer It was shown that among 711 green tea drinkers in Shanghai, the incidence of stomach cancer was low (Yu et al. 1995). Wang et al. (2015) studied the effect of green tea extracts on 160 stomach cancer patients. They found that larger amount of consumption, lower temperature, and longer interval were strongly associated with a lower risk of stomach cancer.

Cervical Lesions Ahn et al. (2003) investigated the clinical efficacy of green tea extracts given to 27 patients with cervical lesions caused by human papillomavirus (HPV). These patients received 200 mg of EGCG for 12 weeks. A 69 % response

rate was noted in patients treated with green tea extracts compared with a 10 % response rate in untreated controls.

Biliary Tract Cancer Consumption of 120 ml green tea extracts per day decreased the risk of biliary tract cancer (Makiuchi et al. 2016).

Liver Cancer The influence of drinking green tea on 3694 liver cancer patients from China, Japan, and Singapore was tested (Huang et al. 2016). A significant association between highest green tea consumption and reduced risk of liver cancer was reported. No association was observed when patients drank only one cup of green tea per day. The protective effect of green tea consumption on the risk of liver cancer was observed only for the group of Asian women, but not for men.

Gastric Cancer Five gastric cancer cell lines were found to be sensitive to EGCG treatment and induced apoptosis (Onoda et al. 2011).

13.2.4 Brain Functions

The loss of cognitive function due to the structure and function damage of neuronal cells is a common process including Parkinson's and Alzheimer's diseases. A study conducted in the United States demonstrated a decrease in Parkinson's disease in the population who consumed two cups or more of green tea per day (Hu et al. 2007). Similar results were obtained by studying how green tea drinking affected cognition of people in Malta (Caruana and Vassallo 2015). A slower progression of Alzheimer's disease was observed in humans treated with EGCG and conducting voluntary exercise (Walker et al. 2015). Green tea and the EGCG compound, in particular, could boost memory and could even be of benefit in the prevention of various neurodegenerative diseases (Winreb et al. 2008).

13.3 Modifications of the Active Components

13.3.1 Nanoparticles

The possibility of nanotechnology was put forward to improve the bioavailability of the active components of green tea. Siddiqui et al. (2009) proposed to control cancer by using polylactic acid-polyethylene glycol nanoparticles that encapsulated EGCG. Results indicated that the effect of the new formulations on prostate cancer was ten times higher than that of the formulations with non-nanomaterials after 24 h of administration. In inhibition of apoptosis, 3 μg nano-EGCG showed 57 % inhibition, whereas 30 μg ordinary EGCG showed a 35 % inhibition (Siddiqui et al. 2010).

dePace et al. (2013) synthesized EGCG-encapsulated chitosan-coated nanoliposomes. The stability of EGCG was significantly enhanced, and the inhibition of proliferation of breast cancer cells was improved.

13.3.2 Structure Modification

Lambert et al. (2006) improved the activity of EGCG in the human body by structural chemical modification of the drug. They substituted eight OH groups of EGCG by OAc groups. This new molecule was termed "a prodrug." When the new compound entered the cells, a new EGCG drug was formed by the activity of the enzyme esterase. The amount of the new EGCG was increased up to 30 times. When pro-EGCG was orally administered to rats, the anticancer activity was increased by twofold (Landis-Piwowar et al. 2007). Dou et al. (2008) and Dou (2009) also prepared a peracetate-protected EGCG and demonstrated its potential use in cancer prevention and treatment. Two novel fluoro-substituted EGCG analogs increased the anticancer activity of green tea polyphenols (Yang et al. 2010). Gelatin-based 200 nm nanoparticles (Shutava et al. 2009) and colloidal mesoporous silica-encapsulated EGCG greatly promoted the efficacy of EGCG on breast tumors (Ding et al. 2015). Other chemical modifications of EGCG were proposed by Yi et al. (2014). These studies opened new possibilities for improving the biological activities of EGCG.

13.3.3 Safety

Along with the use of green tea as a therapeutic agent, its toxicity was also investigated. Mazzanti et al. (2015) found that liver diseases resulted if high concentrations of green tea extracts were used as antiobesity agents (containing 25 % catechins). If the amounts of daily green tea extracts are controlled (daily dose of 30 g tea polyphenols), no toxicity was observed. However, they recommended that green tea extracts should not be taken on an empty stomach for the safety of the consumers. It was concluded that the consumption of highly concentrated green tea extracts in the empty stomach was more likely to lead to adverse effects (Sarma et al. 2008). Pregnant women should also avoid drinking green tea extracts at high concentrations. Lambert et al. (2010) administered 1500 mg/kg EGCG orally to mice and found that the activity of alanine aminotransferases increased by 138 times and the survival was decreased by 85 %. These studies implied that high dosages of EGCG were toxic to the liver. It has been suggested that the equivalent of seven to eight cups, three times daily, can be taken safely for at least 6 months (Pisters et al. 2001).

13.3.4 Selective Toxicity

Selective toxicity means that the drug must be effective against the target but have minimal or no toxicity to humans or normal counterparts. In general, the efficacy of the treatment of cancer is directly proportional to the ability of the drug to selectively target the cancer cell, thus improving the life of the patients. Green tea has been used for many years without observing disturbing side effects. The selective anticancer toxicity of green tea and/or EGCG was also confirmed experimentally.

Chen et al. (1998) studied the effect of EGCG on breast cancer cells and their respective normal counterparts. After exposure to EGCG at 200 μM, for 8 h, more than 50 % of the cancer cells became apoptotic. In contrast, less than 1 % of the normal counterpart was affected. Wang and Bachrach (2002) tested the effect of EGCG on fibroblasts in which transformation by H-*ras* was controlled. It has been demonstrated that EGCG did not affect the growth of normal fibroblast, whereas the transformed cells became apoptotic.

13.4 Clinical Studies

The first clinical trials on the effects of tea polyphenols on humans were conducted at the MD Anderson Cancer Center in collaboration with the Memorial Sloan Kettering Cancer Center. To examine the safety and possible efficacy of consuming the equivalent of >10 cups of green tea per day, 30 cancer patients suffering from advanced solid tumors were treated with green tea for >6 months. The treatment appeared to be beneficial (Mukhtar and Ahmad 2000).

Bettuzzi et al. (2006) tested 60 volunteers with the predominant premalignant lesion of prostate cancer. The patients received 600 mg of green tea extracts daily. One year later, only 3 % of the patients who received the green tea extract developed prostate cancer, compared with 30 % in the placebo group. Choan et al. (2005) treated 19 patients with prostate cancer with green tea extracts (250 mg twice daily) for 2 months. This treatment reduced the levels of prostate-specific antigens (PSAs). A clinical trial with 60 volunteers who received 600 mg of green tea extracts per day for 1 year revealed that in the treated patient, only one developed prostate cancer, while nine cancers were found in the placebo controls Brausi et al. (2008). If the green tea extracts contain caffeine in high concentrations, gastrointestinal effects were observed.

13.5 Mode of Action

After establishing the biological activities of green tea and of EGCG, it was of great importance to find out the mode of their actions. It could provide some information whether toxic side effects could be avoided.

13.5.1 Tyrosine Kinase

The scheme of signal transduction pathways is illustrated in Fig. 13.4a. Membrane-associated receptors for tyrosine kinase which appear on the top of the scheme demonstrated an important role in signal transduction and malignant transformation processes. Increased tyrosine phosphorylation of a 130 kD protein has been implicated in cell transformation by c-H-*ras* and by Src family tyrosine kinase (Wang and Bachrach 2002). The phosphorylation of the 130 kD protein in the transformed cells was twofold higher than those of the normal cells. Adding 20 μM EGCG to those transformed cells caused a 50 % inhibition of tyrosine phosphorylation. However, no decrease in phosphorylation was observed in the neutral counterpart kinase (Wang and Bachrach 2002). These findings suggest that EGCG elicited a specific and a preferred anticancer effect. Similar results were obtained by Larsen et al. (2010), Shirakami et al. (2012), and Colomer et al. (2016), who confirmed that the anticancer activity of EGCG could be linked to the inhibition of tyrosine phosphorylation.

13.5.2 Mitogen-Activated Protein Kinases (MAPKs)

Growth factors (mitogens) are known to bind to specific receptors which are located on the cellular membrane. The mitogen receptor complexes then trigger a cascade of events, such as the activation of the oncogene Ras. The activation of protein kinases is considered as the next step in signal transduction (Fig. 13.4a). MAPKs are phosphorylated by MAPK/ERK kinases, which in turn are activated by Raf. Human breast cancer cells, exposed to EGCG, revealed a dose-dependent growth inhibition and a decrease in cyclin-dependent kinases (Deguchi et al. 2002). Wang and Bachrach (2002) reported that the concentration of Ras was higher in the fibroblast-transformed cells, as compared to the normal counterpart. The content of Ras in normal cells was hardly affected by EGCG at 5 μM concentration, while the concentration of this protein in the transformed cells was reduced by 35 %. Higher concentrations of EGCG (10 μM) reduced the Ras content of normal cells by 17 % and that of the transformed cells by approximately 50 %. These findings demonstrate that EGCG exerts an inhibitory effect on Ras synthesis. Normal NIH fibroblasts were treated with EGCG for 12 h and then exposed to transforming agents to explore the possibility that EGCG can prevent carcinogenesis. EGCG at 10 μM concentrations inhibited the expression of ERK 1/2 and MAPK (Wang and Bachrach 2002). Similar results were reported by Chen et al. (2008) and Singh et al. (2011). These findings suggest that EGCG can prevent cancer in addition to its therapeutic activity.

Jun is a nuclear proto-oncogene. It constitutes a part of the transcription factor AP-1 and therefore plays an important role in growth processes. The effect of EGCG on the expression of transcription factors was studied in vitro. It was found by Lai

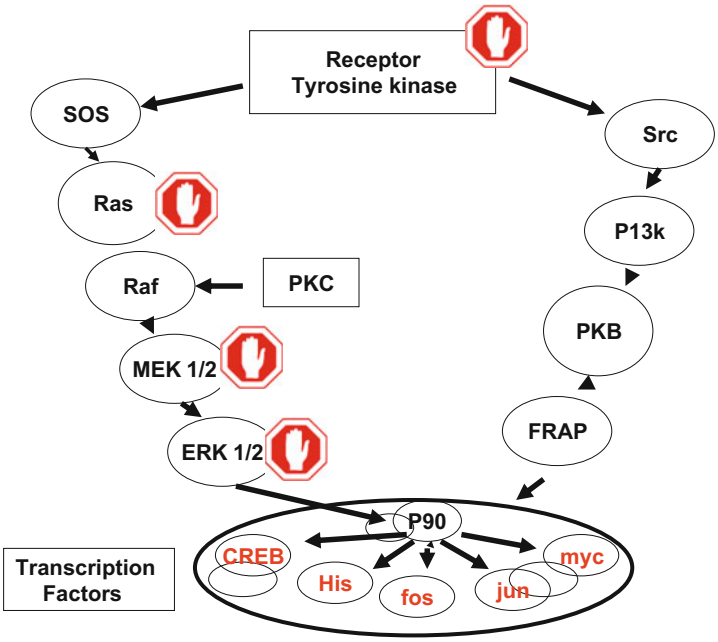

Fig. 13.4a Signal transduction (contribution of the author)

et al. (2004) and by Bachrach and Wang (2002) that green tea EGCG downregulated the expression of c-Fos and c-Jun. The effect of EGCG on the expression of c-Fos and c-Myc was also studied by Chen et al. (1998).

The enzyme ornithine decarboxylase (ODC, EC. 4.1.1.17) catalyzes the conversion of ornithine into putrescine (Fig. 13.4b). It is the most effective rate-limiting step in the biosynthesis of the polyamines: spermidine and spermine. These aliphatic polycations are closely linked with growth processes, and their concentrations increase in cancer cells. Overproduction of ODC is associated with malignant transformation. On the other hand, inhibition of the activity of ODC causes cell apoptosis. It was therefore of interest to find out whether green tea and/or EGCG inhibit ODC activity, prevent growth, and affect carcinogenesis. Wang and Bachrach (2002) showed that the activity of ODC in fibroblast-transformed cells was twofold higher than that in the normal controls. After exposure to 5 μM of EGCG for 12 h, the activity of ODC in the transformed cells was similar to the activity of normal cells (Wang and Bachrach 2002). Similar results were also reported by Stoner and Mukhtar (1995). It can be concluded that EGCG can inhibit the activity of ODC and thus impair growth. If the activity of ODC is inhibited by green tea or by EGCG, then putrescine levels will decline (Fig. 13.4b). It will subsequently lead to the inhibition of the synthesis of spermidine, which in turn will reduce the induction of the oncogenes myc and jun (Fig. 13.4b) and inhibit cellular proliferations. A similar scheme for the effect of green tea on signal transduction processes was also proposed by Rahmani et al. (2015).

13.6 Apoptosis

Apoptosis or programmed cell death is the process by which the cells destroy themselves after receiving a signal. When apoptosis does not work, the cells can multiply freely and can be at the root of certain cancers. Apoptosis must be differentiated from necrosis, which is a pathological cell death. Green tea polyphenols induced apoptosis and inhibited the growth of fibroblasts (Bachrach and Wang 2002), human breast cancer cells (Thangapazham et al. 2007a, b), breast cancer (Butt and Sultan 2009; Hu et al. 2014; Zhang et al. 2007, 2012), prostate cancer (Wang et al. 2014), and liver cancer cells (Zhang et al. 2015).

13.7 Discussion

According to the World Health Organization, cancer has been the second leading cause of death in the United States after heart diseases in 2015. However, in the past few years, a slight decline in the number of both cancer incidents and cancer-related deaths is being observed. This decrease is mainly due to cancer prevention and to new approaches for therapy and surgery. Currently, the main treatments for cancer are chemotherapy, radiotherapy, and surgery. Most of the drugs used in chemotherapy are accompanied by several unwanted side effects. Also, patients with poor prognosis are not cured by the drugs. Therefore, a search for new anticancer agents with fewer side effects and higher efficiency and accuracy received high priority. Natural compounds are good sources for the development of new remedies for different disease. A number of phytochemicals isolated from medicinal plants have been shown to decrease cell proliferation and to induce apoptosis. Epidemiologic observations and laboratory studies have indicated that tea consumption may have beneficial effects in reducing certain types of cancer in some populations. One of the key issues in chemoprevention with phytochemicals is to find out whether the activity is due to a single active compound present in the extract. Numerous studies indicated that (-)-epigallocatechin-3-gallate (EGCG) is the active component in green tea but is not found in black tea. There is evidence from in vitro and animal studies that green tea and EGCG are potent antioxidants, inhibit cancer, prevent atherosclerosis, and control blood sugar in the body. Researchers at the University of Kansas feel that EGCG is at least 100 times more effective than vitamin C and 25 times better than vitamin E in protecting cells and their genetic material, DNA, from damage by free radicals. EGCG carries twice the antioxidant of resveratrol found in red wine. In this review, we focus our attention on anticancer activities of green tea and EGCG. We provide evidence that these phytochemicals inhibit the growth of various types of cancer both in vivo and in vitro studies. These remedies, which cause apoptosis, have been used in different countries without reporting any harmful side effects. It appears that they preferentially and selectively attack cancer cells but do not harm healthy counterparts. Therefore, they seem to be an ideal cancer

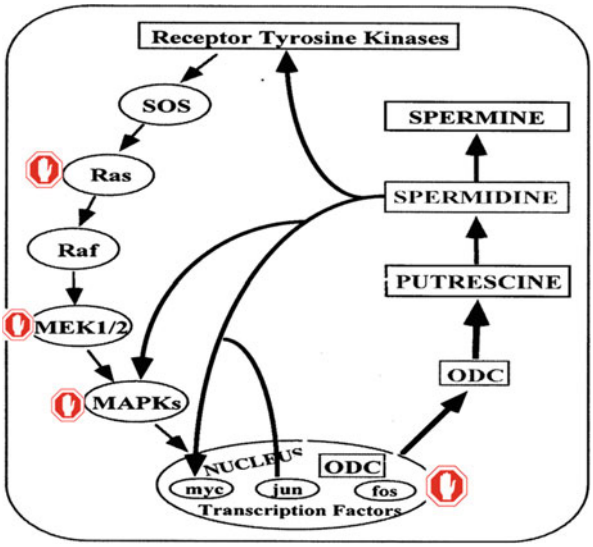

Fig. 13.4b Oncogenes (= inhibition)

agent. Moreover, as EGCG is a single pure and defined reagent, its stability and its mode of action can be monitored easily. Green tea or EGCG can arrest growth of cancer by different mechanisms which include antioxidant action and apoptosis. However, it appears that cell cycle arrest by modulating signal transduction processes can explain the biological activities of green tea and EGCG. Figures 13.4a and 13.4b clearly shows that these phytochemicals interfere with the phosphorylation of tyrosine and protein kinases like ERK1/2 and also suppress the expression of Jun and Fos oncogenes. The synthesis of polyamines, which promote growth, is also inhibited by green tea, due to the reduction of ornithine decarboxylase (ODC) activity (Fig. 13.4b). Therefore, green tea has been shown to exert its chemopreventive effect by targeting various intracellular signaling cascades.

Green tea and EGCG inhibit the proliferation of various cancer cells without affecting normal counterparts. Therefore, green tea can prevent cancer before the onset of the disease or block the progress of the syndrome in sick patients (Fig. 13.5). As EGCG can be obtained from commercial sources, it can serve as an important tool to combat cancer.

13.8 Conclusions

As previously stated, cancer is a major cause of mortality worldwide. Currently, the main treatments for cancer are chemotherapy, radiotherapy, and surgery. Most of the drugs used in chemotherapy are accompanied by several unwanted side effects. Therefore, a search for new anticancer agents with fewer side effects and higher efficiency and accuracy received high priority. Dietary habits influence the risk of

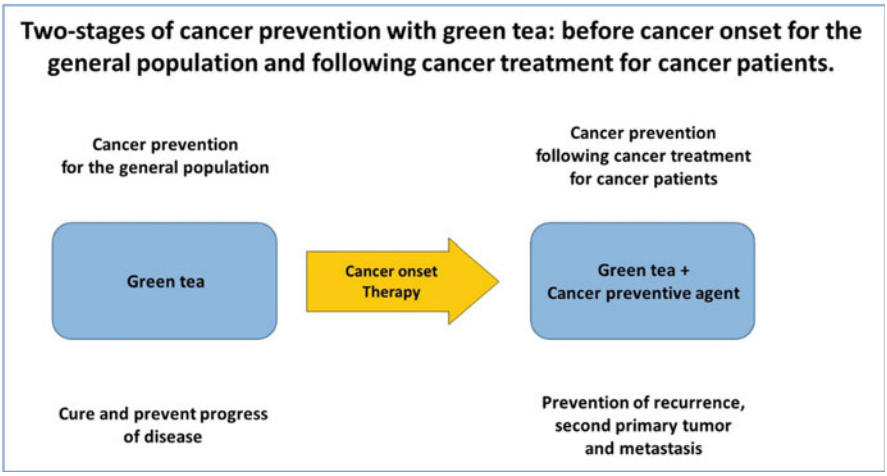

Fig. 13.5 Cure and prevent progress of disease

developing a variety of diseases, especially cancer. Tea derived from the leaf of the plant *Camellia sinensis* is, next to water, the most consumed beverage in the world. When the leaves of *Camellia sinensis* are steamed, green tea is produced. Epidemiologic observations and laboratory studies indicated that green tea consumption might have beneficial effects in reducing certain types of cancers and in preventing its outbreak. Thus, the incidence of cancer is very low in Asian countries like China and Japan, where green tea is consumed in large quantities. Numerous studies suggested that the polyphenol (-)-epigallocatechin-3-gallate (EGCG) is the active component of green tea. The use of EGCG instead of crude green tea extracts permitted studies to elucidate the mode of anticancer of green tea. Green tea or EGCG can arrest the growth of cancer by different mechanisms which include antioxidant actions and apoptosis. They also regulate oncogene activities and modulate signal transduction processes. As green tea and EGCG inhibit the proliferation of cancer cells without affecting normal counterparts, their use as anticancer agents is highly recommended.

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