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Chapter

Tea Polyphenols Chemistry for Pharmaceutical Applications

Ponnusamy Ponmurugan, Shivaji Kavitha, Mani Suganya and Balasubramanian Mythili Gnanamangai

Abstract

Tea is one of the most ancient popular beverages and extensively used dietary supplement in the western world. Tea leaves are rich in polyphenols and also well known for its antioxidant properties. In addition, green tea extract contains several polyphenols with antioxidant compounds. The predominant effective antioxidant components are epigallocatechin 3-gallate and epicatechin 3-gallate (monomers). Tea polyphenols have an additional role to induce aroma and taste in beverages. Furthermore, tea polyphenols have multiple applications in food industry and biomedical applications. This chapter will summarise the origin of tea leaves and its beneficial account on antioxidant, food industry (meat products, plant products and fish products) and therapeutic applications against many diseases such as lowering of blood pressure, diabetes, Parkinson's disease and anticancer properties. Mainly tea polyphenols have potential to inhibit the cancer proliferation of skin, prostate, lung and breast cancer.

Keywords: nanoparticles, quantum dots, tea polyphenols, tea chemistry

1. Origin of tea leaves

'*Camellia sinensis*' is the botanical name of tea plant and was originated from Southeast Asia [1]. Tea was introduced by Portuguese and Chinese during the sixteenth century [2]. During the seventeenth century, drinking of tea became popular in Britain [3]. In the current scenario, tea is one of the most ancient and popular beverages around the world followed by water. Tea is grown primarily in tropical and temperate regions which include China, India, Japan and Sri Lanka [5]. Tea plants were cultivated in several African and American countries. Primarily it has two varieties such as *Camellia sinensis* and *Camellia assamica*, and it belongs to the *Camelliaece* family. Tea plant is an evergreen shrub with optimal range from 15 to 20°C. The *sinensis* strain has originated from China and it produces different categories based on processing [4], such as black tea (wilted and fully oxidized), green tea (unwilted and unoxidized) and oolong tea (wilted, bruised and partially oxidized). Furthermore, *assamica* strain is originated from Assam region, especially in Northern India. Due to its enormous growth, it is a favour for India, Sri Lanka and African countries. But this strain is not used for producing black, white and oolong teas [5].

2. Types of tea

a. Green tea (non-fermented)

b. Black tea (fermented)

c. Oolong tea (partly fermented)

d. White tea (least processing)

All the four types of tea are made from same (*Camellia sinensis*) plant, but it differs from processing methods. Green tea is made by crushing tea leaves—and then steaming, rolling and drying them. It undergoes minimal processing and contains 80–90% catechins and flavanols (10% of total flavonoids). The infused leaf is green, and the liquor is mild, pale green or lemon-yellow. Black tea involves additional processing steps such as aeration and withering. Specifically, it contains 20–30% of catechin, 50–60% of total flavonoid and theaflavins and thearubigins representing 10%, respectively. Black tea is the most common type of tea produced and consumed. The infused leaf has a dark brown colour and a sweet aroma. Oolong tea is a partially or semi-fermented tea. A full-bodied tea with a fragrant flavour and a sweet fruity aroma has some qualities of both black tea and green tea due to its manufacturing process. It is more suitable for people who prefer a low caffeine option. White tea is appreciated by tea connoisseurs for its unmatched subtlety, complexity and natural sweetness. It is also considered to be a far greater source of antioxidants than green tea because the tea leaves undergo minimum processing [6]. During the black tea manufacturing process, tea leaves are crushed and subjected for enzymatic oxidation process/fermentation process. Subsequent fermentation of catechins is condensed and it leads to produce the theaflavins (TFs) and thearubigins (TRs). These constituents are responsible for specific taste and colour of black tea [7]. Furthermore, during the fermentation process, monomeric polymers are converted to polymeric polyphenols (theaflavins and thearubigins). The polymeric polyphenols (theaflavins and thearubigins) are higher molecular weight and they are not absorbed by the gastrointestinal tract, but monomeric polyphenols (catechins) are very smaller in size [8]. The black tea contains 3–10% of monomeric polyphenols, higher concentration of polymers and gallic acid than the green tea [9]. Oolong tea is produced by partially oxidization process with fewer amounts of polymeric polyphenols and it contains higher amount of EGCG than the black tea.

2.1 Chemical composition of tea leaves

Tea leaves contain a number of chemical compounds. When they are processed, these compounds break down and form new compounds. The tea leaves are rich in polyphenols [10], caffeine (approximately 3.5%), theobromine (0.15–0.2%), theophylline (0.02–0.04%), lignin (6.5%), organic acids (1.5%), chlorophyll (0.5%), thiamine (4%), free amino acids (1–5.5%) and numerous flavonoid compounds. In addition, they consist of other compounds including flavones, phenolic acids and depsides, carbohydrates, alkaloids, minerals, vitamins and enzymes [11]. Tea leaves also contain flavanols—quercetin, kaempferol, myricetin, and their glycosides. The most favourable effects of tea are accredited to the polyphenols and 3–6% of caffeine [12].

In addition to this, several polyphenolic catechins are available in green tea, which include (−) epicatechin (EC), (−) epicatechin-3-gallate (ECG), (−) epigallocatechin-3-gallate (EGCG) and (−) epigallocatechin (EGC) (**Figure 1**). In green tea, it has some other compounds with interest of human health like caffeine,

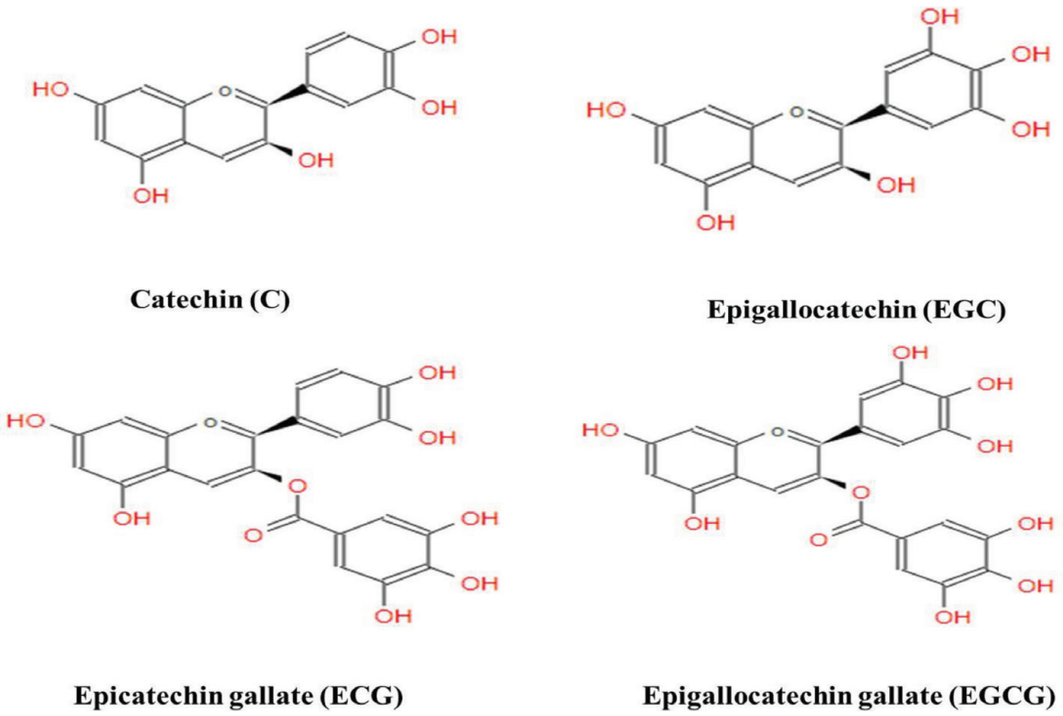

Figure 1.
Structure of catechins (EC, EGC, ECG and EGCG).

fluoride, minerals and trace elements (chromium and manganese) [13, 14]. In green tea, catechins are present in high amount because it is produced by young leaves. It is noteworthy for its highest content of catechins and it is closely related to influence the quality [15, 16].

3. Flavour constituents

The taste and the flavour of tea are enhanced by chemical compounds, which are polyphenols, caffeine, organic acids and volatile terpenes [17]. The characteristic taste of green tea is a mixture of bitterness, umami taste, sweetness and slight sourness. Furthermore, it has been detected that the tea taste is influenced by polyphenols, amino acids and caffeine [18]. The aroma of tea is enhanced by volatile organic compounds such as terpenoids, alcohol and carbonyl compounds.

4. Antioxidant mechanism

In a food manufacturing company, lipid oxidation and development of rancidity is a major issue. Lipid oxidation reduces shelf-life, quality and nutritional value of their products. Autoxidation causes oxidative deterioration of food lipids as a chain reaction of free radical generation through initiation, propagation and termination. Oxidation initiators such as heat, light, ionizing radiation, transition metals, metalloproteins and enzymes facilitate the generation of these primary free radicals. In the primary oxidation, lipid hydroperoxides are identified to reduce the taste and odour. Disintegration of hydroperoxides yields aldehydes, alcohols, ketones, hydrocarbons and acids that are considered as the secondary oxidation products of lipids.

In a food industry, antioxidant is expected to delay the development of rancidity in food. Antioxidant is a substance that detains lipid oxidation by inhibiting the

free radical formation or which can diffuse the oxidation reaction. This substance helps to preserve the foods by delaying development of rancidity and discoloration due to lipid oxidation. There are two different categories of antioxidants which are involved for their mechanisms are divided into primary and secondary antioxidants. Primary antioxidants inhibit and disrupt the initiation phase and the propagation stage of antioxidants. Secondary antioxidant are involved in the deactivation process of singlet oxygen, chelate the metal ions, UV-rays absorption, scavenge oxygen and helps to regenerate the primary antioxidants. Primary antioxidants in combination with secondary antioxidants are used for better health benefits.

Tea polyphenols are well known for their antioxidant properties and these are primarily attributed to the combination of hydroxyl groups and aromatic rings. The above said primary constituents (hydroxyl groups and aromatic rings) aid in assembling their chemical structure with binding, which lead to the hydroxyl groups that lead to neutralization of lipid free radicals. Many studies report that tea polyphenols and tea catechins are exceptional electron donors with effective scavengers of physiologically relevant reactive oxygen species and superoxide anions [19–23]. Catechins also exhibit antioxidant activity through redox potential of the transition metal ions. Mainly polyphenolic compounds have hydroxyl and carboxyl groups and they have the ability to bind with iron and copper [20].

Green tea catechins exhibit antioxidant activity via inhibition of pro-oxidant enzymes and they induce antioxidant enzymes [23]. Catechins and their derivatives are used as a substrate in food products, and they show high antioxidant activity [24]. Green tea catechins have active antioxidants in bulk oils and give similar performance to other hydroprofile antioxidants such as redox and ascorbic acid [25, 26]. Catechins are also used as an emulsifying agent, and they show delaying oxidation of polyunsaturated fatty acids that are rich in marine and vegetable oils [27]. In corn oil, dry glycerol system was oxidized at 50°C and the antioxidant activity of epigallocatechin gallate showed superior activity than the epicatechin [27]. Zhong and Shahidi [28] conducted the study of structural modification of epigallocatechin to improve lipophilicity by esterification of epigallocatechin gallate with selected fatty acids such as stearic acid, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The lipophilized derivatives produced greater antioxidant activity than the original epigallocatechin molecule.

Radical scavenging activities of catechin, epicatechin and epicatechin gallate were higher than those of L-ascorbate and beta-carotene [29]. In another study, Nanjo et al. [22] reported that DPPH radical scavenging activities of catechin and epicatechin were less than epigallocatechin, epicatechin and epigallocatechin gallates. Epicatechin is another monomeric flavonol from green tea. Few reports suggested that epicatechin is capable of scavenging hydroxyl radicals, peroxy radicals and superoxide radicals [30–33]. The antioxidant activity is rich in green tea followed by oolong, black and pu'erh tea [5]. Chan et al. evaluated the role of non-polymeric phenolic (NP) and polymeric tannin (PT) constituents in the antibacterial and antioxidant activities of different brands of tea such as green, black and herbal teas. All the six types of tea were examined and revealed that PT constituents have shown strong antibacterial and anticancer activity [5]. Another advantage of tea catechins possesses anti-discolouring effect on beverages and margarine containing beta-carotene [34–37]. Hence, tea polyphenols act as antioxidants by delaying the process of β-carotene degradation. The individual tea polyphenols were examined separately; epigallocatechin showed strong anti-discolouring effect, whereas epicatechin and catechin showed no activity, and gallic acid had moderate activity.

5. Application in food industry

5.1 Incorporation method in food industry

The appropriate incorporation of green tea extract is essential in food products, and to ensure tea, antioxidants components are thoroughly mixed in the food matrix. For adequate shelf-life extension in food, small amount of tea extract is required and it may determine the achievement of the antioxidant benefits. Commercially available green tea in a grained powder form and tea extract can be solubilized in water. Water soluble green tea extract has low viscosity which makes it essential for spraying and homogenous distribution. Green tea extract can be dispersed into food grade solvent to produce oil-soluble liquid product. The liquid form of green tea extract is directly added into oils and fats. The oil may be heated at 40–60°C temperature under stirring condition; during the process, tea extract is slowly added to oil. The above said process is extended for an additional period to aid their uniform distribution of green tea extracts in oils (**Figure 2**).

5.2 Green tea application in food products

In recent years, green tea extract supplemented products are ever growing of consumer interest. Green tea extract is used for many food products including bread [38] biscuits, dehydrated apple [39] and meat products [40]. In a food industry, the major problem is lipid oxidation and it induces the potential toxicity

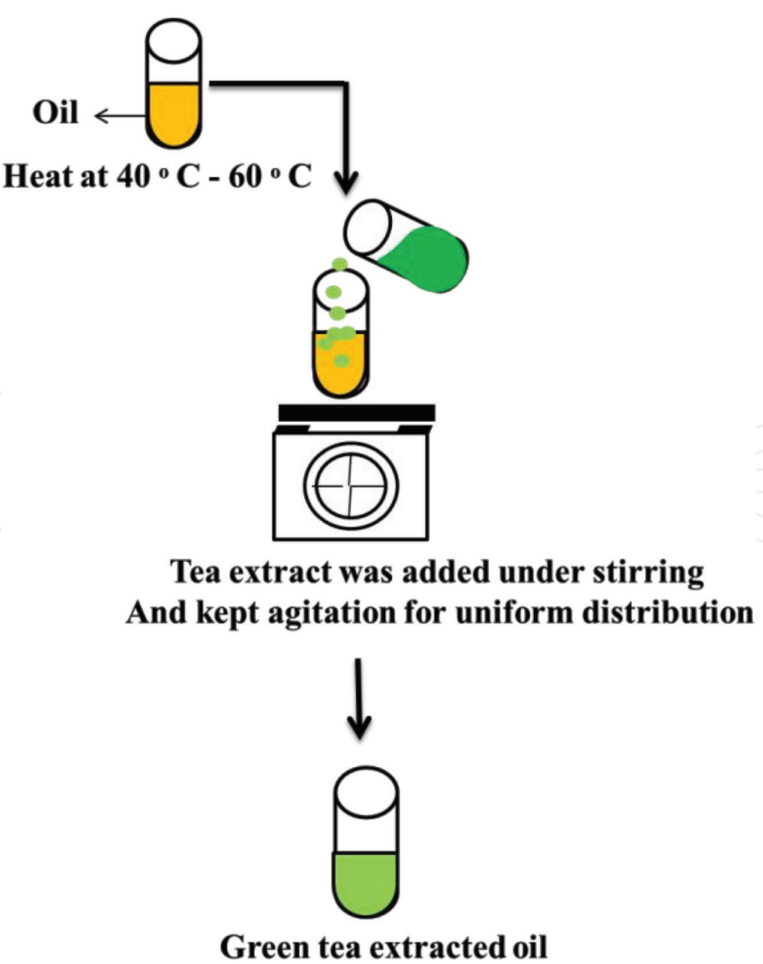

Figure 2.
Schematic representation of green tea extracts incorporation in food industry.

in food products [33]. The main application of green tea extract is spraying in many food products and it showed comparable antioxidant performance to conventional synthetic antioxidant tert-butylhydroquinone (TBHQ). Furthermore, green tea extract is more cost-effective than other natural sources. Usually, meat and meat products have high lipid content and they range from 4.5 to 11%, and thus they are vulnerable to lipid oxidation [41]. Fish tissues are composed of highly unsaturated fatty acids and they are even more susceptible for lipid oxidation than meat and meat products [33].

In a food industry to prevent the lipid oxidation, synthetic antioxidants are used as preservatives, such as butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA) and tert-butylhydroquinone (TBHQ), because they are inexpensive and effective [33]. Therefore, these synthetic antioxidants are found to be highly toxic at higher concentrations [42] and thus natural antioxidants are suitable for preventing the lipid peroxidation. Hence tea catechin has high potential for the inhibition of lipid peroxidation in foods [43, 44]. Specifically, EGCG is more efficient for inhibition of lipid peroxidation than the α-tocopherol and BHA. The plausible mechanism of catechins has been found effectively to chelate metal ions and it initiates the lipid peroxidation chain reaction [45].

5.3 Tea catechins role in meat and meat products

Each species of meat differs in the level of fatty acid and iron, thus its susceptibility to lipid oxidation also differs [46]. For instance, beef has been found to be more susceptible to lipid oxidation followed by duck, ostrich, pork and chicken. The green tea catechins are highly efficient to prevent the lipid oxidation when supplemented with meat and meat products. For example, 300 mg/kg of tea catechin is minced with red meat (beef and pork) and poultry (chicken, duck, ostrich) meat to prevent the lipid oxidation under refrigeration storage. Similarly, catechin (200 mg/kg) is also being used in plastic package of cooked and raw beef under modified storage conditions (80% O_2 and 20% CO_2) with 4°C refrigeration for 7 days to inhibit lipid [39]. Hence, tea catechins have been shown to have high potential against lipid oxidation in meat and meat products. The catechins are used to prevent the lipid oxidation in meats by chelating iron, which is the major active catalyst for oxidative rancidity in meat [47]. Furthermore, tea catechins trap the peroxy radicals and suppress the free radical chain reactions; finally, it prevents the lipid oxidation in meat products.

Several studies reported that catechins are not effective against the discolouration of meat and meat products, while using 200 mg/kg of catechin minced at 2°C for 20 days in the atmosphere of 80% O_2 and 20% CO_2 [39, 48]. By contrast, Tang et al. [49] noticed that the addition of catechins improved colour stability under modified atmosphere packaging (MAP) condition with 80% O_2 and 20% CO_2 under refrigeration for 7 days. Banon et al. reported combinatorial (catechins with sulphite) treatment showed delaying in discolouration with of raw sulphite beef patties packed under alcoholic condition during refrigeration for 9 days [50]. The beneficial effect of catechins minced with meat and meat products improved their quality and enhanced shelf-life with additional antioxidant potentials to consumers. Furthermore, catechins in meat and meat products are rich in iron, because catechins can bind with iron to reduce its absorption in the body [51].

5.4 Tea catechins role in fish and fish products

Oxidative deterioration is the major problem of fish and fish products, and it causes degradation and off-flavour development. Commercially available catechins are applied in salmon fillets at a concentration of 0.5% (w/w) and it is

found to extend the shelf-life of the fillets compared to untreated samples [52]. The catechin concentration will vary from fish to fish, e.g. silver carp 0.2% (w/w) and mackerel patties (300 mg/kg). Tea catechins are also additionally used in fish oils (@250 ppm) to prevent oxidative deterioration. Oxidative deterioration was significantly delayed in fish and fish products during storage [36, 43, 53]. The tea catechins have high potential to prevent the lipid peroxidation than tocopherol, BHA, BHT and TBHQ [53, 54]. Therefore, tea catechins have wide applications in fish and fish products in order to enhance the shelf-life and health benefits.

5.5 Tea catechins role in plant food products

The green tea catechins are supplemented with plant food products to extend the shelf-life and health benefits. For example, catechins are added in vegetables, oils, cakes, starch, bread and juice to extend their shelf-life and health benefits of their products. To prevent the lipid oxidation, 200 ppm of catechins were added in canola oil (**Figure 3**) [55]. Tea catechins were also added in apple juice to prevent from bacteria, and have many applications in other plant food products [56]. In another study, dry apple product was enriched with green tea extract. The changes in the antioxidant activity and colour were analysed. The antioxidant content and the antioxidant capacity of dry apple were increased by addition of green tea extract, but the colour changes were observed only slightly, meanwhile no difference was observed in aroma and taste [38].

5.6 Health benefits of green tea

Green tea catechins are associated with number of diseases due to its reactive oxygen species against cancer, cardiovascular and neurodegenerative diseases. Several studies are reported for the anticancer activity of green tea catechins, especially in animal models of skin, breast, prostate and lung cancer [57, 58]. In addition, green tea catechins have several properties such as anti-angiogenic [59, 60], anti-mutagenic [61, 62] and hypocholesterolemic [63]. Furthermore, green tea

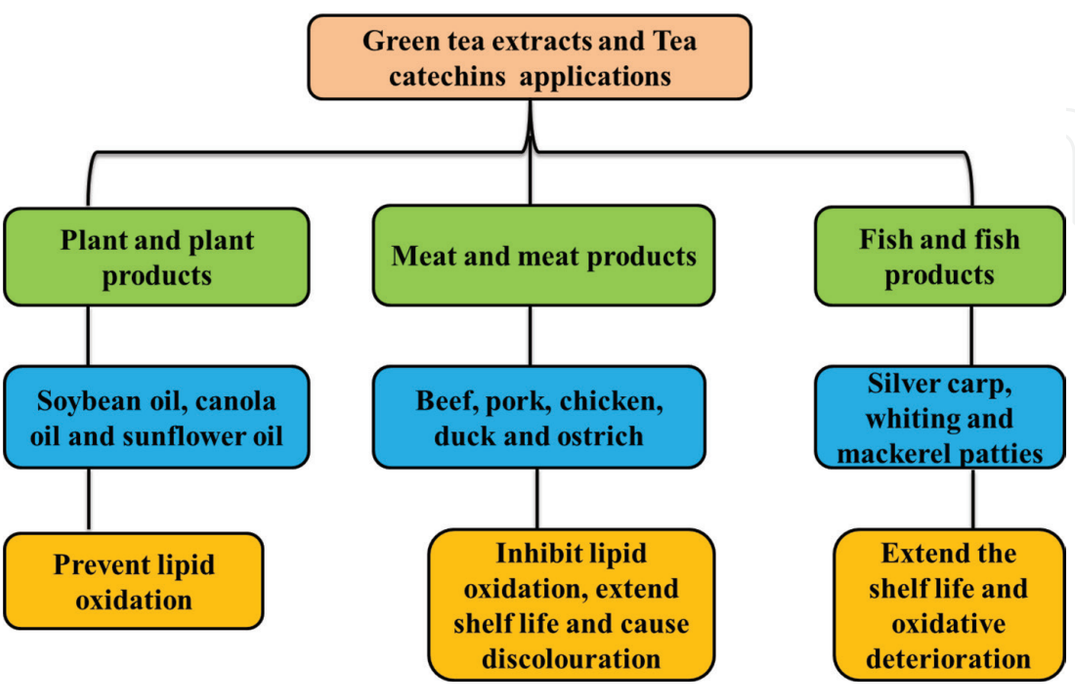

Figure 3.
Green tea extract and catechins' applications in food industry.

has shown significant protection against neurodegenerative diseases (Parkinson's disease, Alzheimer's disease and Ischemic damage) [64]. Tea polyphenols are extensively studied against various medicinal properties like anti-diabetic activity in mice model [65], antibacterial [66], anti-HIV [67], anti-aging [68] and anti-inflammatory activity [69].

5.7 Tea polyphenols and their anticancer properties

Green tea extract rich in catechins has been subjected to numerous studies and shown to modulate cancer growth, metastasis, angiogenesis and other aspects of cancer progression by affecting different mechanisms [52, 57, 70–73]. Green tea consumption has beneficial effect of carcinogenesis in the digestive tract, which is postulated, and it induces the inhibition by EGCG [74]. Banon et al. [50] reported combinatorial (catechins with sulphite) treatment showed delayed discolouration in raw beef patties packed under alcoholic condition with 9 days refrigeration period [72]. Epigallocatechin-3-gallate (EGCG) potentially induced apoptosis and suppressed cell growth by modulating expression of cell cycle regulatory proteins, activating killer caspases and suppressing activation of NF-KB cells [75]. Tea polyphenols have potential to inhibit the growth of stomach cancer cells and also inhibit the proliferation of stomach cancer cells (KATO III), and specifically, they inhibit the tumour necrosis factor-α (TNF-α) of stomach cancer cells [76]. In addition, tea polyphenols have shown inhibitory effects against gastrointestinal cancer and also they are efficient to inhibit the proliferation of various other cancer cells. Epigallocatechin-3-gallate (EGCG) was reported to control and promote IL-23-dependent DNA repair which will enhance cytotoxic T-cell activities and block cancer development by inhibiting carcinogenic signal transduction pathways [77]. Epigallocatechin-3-gallate (EGCG) was also shown to modulate several biological pathways including growth factor-mediated pathway, mitogen-activated protein kinase pathway and ubiquitin/proteasome degradation pathway [78]. In a clinical study, regular green tea consumption was demonstrated and it expressed delayed cancer onset. Furthermore, breast cancer patients experienced lower recurrence rate and longer remissions [78]. In another clinical study, it is proven that 200 mg of EGCG by oral administration was more effective to patients with human papilloma virus-infected cervical lesion [79]. Epigallocatechin-3-gallate (EGCG) is the most studied catechin in cancer research, but under in vitro analysis, ECG and EG catechins are treated with pancreatic ductal adenocarcinoma cells where they exhibited stronger anti-proliferative and anti-inflammatory effects including inhibition of NF-KB, IL-8 and UPA than EGC. Breast cancer is the most common cancer in women around the world. In western countries, breast cancer is more prevalent compared to Japan. In Japan, regular tea consumption, as part of the diet, and also green tea consumption are most believed to reduce the risk of breast cancer [80]. It is reported that 10–40 μM of EGCG inhibit tumour formation and downregulate ER-α36 expression in 24 h, which is consistent with downregulation of the epidermal growth factor receptor (EGFR). Epigallocatechin-3-gallate (EGCG) inhibits the growth of ER-negative human breast cancer stem cells through downregulation of ER-α36 expression and it indicates that EGCG treatment will lead to longer survival of patients with mammary cancers [81]. Green tea polyphenols have various health benefits of cancer prevention and also used as an adjuvant in chemotherapy. Few studies suggest that the use of combinatorial drugs (green tea with chemotherapeutic drugs) has shown reduced risk of cancer, improved survival rate among cancer patients and decreased chemotherapy-mediated side effects [82]. In addition, mice were treated with EGCG, anticancer drugs alone and combinatorial drugs, and an average reduction of tumour volume size to 73.5% (EGCG), 66.3% (anticancer

drugs) and 29.7% (EGCG combinatorial drugs) was reported respectively. This report strongly suggests that combinations of EGCG show effective results than the treatment with EGCG and anticancer drugs while treating alone. Furthermore, calculations for complete elimination of tumour in mice are converted to that for humans which would be intake of 6–9 (1.37–2.05 g of EGCG) cups of green tea per day [83].

6. Conclusion

This study enlightens about the green tea and its bioactive components (EGCG, ECG, EGC and EC). These bioactive components are rich in antioxidants and supplemented with various food products to inhibit the lipid peroxidation. In addition, it extends the shelf-life and health benefits of food products by their antioxidants. Furthermore, it has great potential applications in various diseases such as diabetic, anti-obesity and anticancer. Many reports suggest the use of tea polyphenols to kill the cancer cells and also show various combinations with other similar compounds. This study suggested the use of green tea supplemented food products to promote health benefits. It prevents the cancer and these products can be included as dietary supplement for cancer fighters. This study clearly defines a big platform of tea constituents for food industries and theranostic applications.

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