Geriatrics Gerontology INTERNATIONAL Medline Indexed

Geriatr Gerontol Int 2014; **14:** *238–250*

REVIEW ARTICLE: EPIDEMIOLOGY, CLINICAL PRACTICE AND HEALTH

Green tea: A novel functional food for the oral health of older adults

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Functional foods are foods with positive health effects that extend beyond their nutritional value. They affect the function of the body and help in the management of specific health conditions. Green tea, a time-honoured Chinese herb, might be regarded as a functional food because of its inherent anti-oxidant, anti-inflammatory, antimicrobial and antimutagenic properties. They are attributed to its reservoir of polyphenols, particularly the catechin, epigallocatechin-3-gallate. Owing to these beneficial actions, this traditional beverage was used in the management of chronic systemic diseases including cancer. Recently, it has been emphasized that the host immuno-inflammatory reactions destroy the oral tissues to a greater extent than the microbial activity alone. Green tea with its wide spectrum of activities could be a healthy alternative for controlling these damaging reactions seen in oral diseases, specifically, chronic periodontitis, dental caries and oral cancer, which are a common occurrence in the elderly population. **Geriatr Gerontol Int 2014; 14: 238–250.**

Keywords: chronic periodontitis, dental caries, functional food, green tea, oral cancer.

Introduction

Functional foods are usually defined as "*healthful foods or food ingredients that have a potential health benefit beyond their nutrient content when consumed regularly in typical quantities as part of a varied diet*".[1] A variety of foods including whole grains, garlic (allyl compound), soybeans, carrots (carotenoids), tomatoes (lycopene), tea (polyphenols), fiber, vegetables and fruits are included in this group.[2] They play an important role in healthy aging. As part of a routine diet, they might prevent chronic diseases in older adults.[3]

Periodontitis and caries are the most frequent dental problems in older individuals.[4] Altered host response in association with virulent plaque biofilm, increased oxidative stress, immunosenescence and inflammaging cause degenerative changes in the cells and tissues, which increases the risk for oral diseases.[5] Besides the aforementioned two conditions, oral cancer, halitosis and tooth erosion are also seen in this age group.

Accepted for publication 15 October 2013.

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Tea is the most common functional beverage consumed worldwide. It is derived from the leaves of *Camellia sinensis*, which is processed in different ways to produce either green, black or oolong tea. Of the total tea produced, 20% is green tea, consumed commonly in Asia, parts of North America and the Middle East, whereas 78% is black tea popular in Western and Asian countries.[5] Less than 2% is oolong tea, consumed mainly in southern China and Taiwan.[5]

Green tea, technically known as *Camellia sinensis* Theaceae, is the richest source of polyphenols, specifically epigallocatechin-3-gallate (EGCG). It is a non-fermented form of tea produced by drying and steaming the fresh leaves to inactivate the polyphenol oxidase.[6] Black tea contains thearubigins and theaflavins, which are produced from the enzymatic oxidation ("fermentation") of polyphenols in the crushed leaves of *Camellia sinensis*.[6] Oolong tea is manufactured by partial oxidation of these leaves.[6]

Studies have shown that green tea has better health effects over black tea.[7,8] The polyphenol concentration in green tea is approximately 30–40% as compared with 3–10% in black tea, resulting in the highest anti-oxidant activity.[9] Besides, it has potent anti-inflammatory, antibacterial, antiviral, antimutagenic and anti-aging properties.[10–12] With this background, the present review focuses on the role of green tea as a functional food for healthy oral cavity of older adults.

 doi: 10.1111/ggi.12194

Need for functional foods in older adults

It has long been a quest for the scientific community to identify food substances with benefits that extend beyond their basic nutritional properties. Some of these have been listed in Table 1. The literature shows that the physical, chemical, and physiological properties of food substances affect the oral tissues and organs. A diet rich in fermentable carbohydrates, acidic and soft foods is detrimental to oral health.[13]

Recent advances have led to the development of foods and beverages with "*functional ingredients*" that prevent the development or progression of oral diseases.[13] These include non-fermentable sugars (polyols), anti-oxidant rich beverages, probiotics, prebiotics and foods with remineralizing properties.[13] They are specifically useful in dental caries, chronic periodontitis and tooth erosion.

In older adults, there is an increased risk of nutritional deficiencies specifically as a result of an unbalanced diet. They have a slower metabolic rate, reduced physical activity, and altered hunger, thirst, satiety, smell and taste sensations.[14] Furthermore, older adults develop systemic problems (e.g. diabetes, obesity, atherosclerosis, arthritis, cardiovascular diseases, lung and degenerative diseases of the central nervous system) as a result of increased inflammaging (a chronic low-grade inflammation) and immunosenescence. These subsequently result in impaired mobility, feeding problems, tooth loss from poor oral health, alterations in salivary flow (as a result of medications) and swallowing difficulties. As a consequence, the elderly develop a preference for soft and micronutrient deficient foods.[14] Thus, there is an urgent need to identify the functional foods that would enhance their oral and systemic health by overcoming the effects of aging.

There are three categories of functional foods: basic foods with natural bioactives (e.g. carrots that contain beta carotenes), processed foods with added bioactives (e.g. milk supplemented with omega-3 fatty acids) and foods that are enhanced to have more bioactives (e.g. tomatoes with increased levels of lycopenes).[15]

Green tea might be regarded as a basic functional food, as it is naturally rich in active anti-oxidants. It could be incorporated into the diet in the form of a beverage for favorable oral and systemic health of older adults.

Green tea as a functional food for oral health in older adults

Green tea is a functional food loaded with beneficial components, such as proteins, enzymes, carbohydrates,

Table 1 Functional foods and their actions in oral cavities

Functional foods	Active component	Properties	Oral condition
Fruits and vegetables			
Carrots	β-Carotenoids	Anti-oxidants	Chronic periodontitis
Tomatoes	Lycopene	Anti-inflammatory	Mucosal lesions
Cranberries	Procyanidins, proanthocyanidins		
Citrus fruits	Flavanones, vitamin C		
Berries, Cherries, Red grapes	Anthocyanins		
Broccoli	Flavanols		
Onion	Thiols		
Nuts			
Walnuts	Omega-3-fatty acids	Anti-inflammatory	Chronic periodontitis
Beverages			
Green tea	Epigallocatechin-3-gallate	Anti-oxidant	Chronic periodontitis
Black tea	Theaflavins	Anti-inflammatory	Dental caries
Cocoa	Flavanols	Antimicrobial	
Chocolate	Flavanols	Antimutagenic	
Sugars			
Xylitol, sorbitol	Polyols	Antimicrobial	Dental caries
Whole grains			
Wheat	Sterols	Antimicrobial	Chronic periodontitis
Oats	Prebiotics	Anti-inflammatory	
Dairy products			
Yoghurt	Fluorides	Antimicrobial	Dental caries
Milk/fortified milk	Calcium/probiotics		Chronic periodontitis

Table 2 Composition of green tea

Components	Concentration
Proteins	• 15–20% dry weight • Mainly enzymes
Carbohydrates	• 5–7% dry weight • Cellulose, pectins, glucose, fructose, sucrose
Lipids	• Linoleic and linolenic acids
Sterols	• Stigmasterol
Vitamins	• Vitamins B,C,E
Xanthic bases	• Caffeine • Theophylline
Pigments	• Chlorophyll • Carotenoids
Volatile compounds	• Aldehydes, alcohols, esters, lactones, hydrocarbons
Minerals and trace elements	• 5% dry weight • Calcium, magnesium, chromium, manganese, iron, copper, zinc, molybdenum, selenium, sodium, phosphorus, cobalt, strontium, nickel, potassium, fluoride and aluminium
Polyphenols	• Catechins: Epigallocatechin-3-gallate (59% of the total of catechins), epigallocatechin (19%), epicatechin-3-gallate (13.6%), epicatechin (6.4%)
Other components	• Gallic, chlorogenic and caffeic acids, kaempferol, myricetin, quercetin

lipids, sterols, polyphenols, vitamins, caffeine, theophylline, pigments, volatile compounds and trace elements (Table 2).[16] Among these, polyphenols including catechins (flavan-3-ols) are the key therapeutic ingredients. There are four major catechins present in green tea: EGCG, epigallocatechin (EGC), epicatechin-3-gallate (ECG) and epicatechin (EC). They comprise of 3-phenolic rings A, B and C, with a double ring attached by a single bond to a third ring (Fig. 1). Multiple hydroxyl groups are attached to these rings. EGCG is an ester derivative of EGC, resulting from esterification at the third hydroxyl position of the C ring with a gallate moiety.[17] Besides the aforementioned catechins, green tea also contains gallic and phenolic acids, such as chlorogenic and caffeic acids, and flavonols, such as kaempferol, myricetin and quercetin.[16]

The concentration of catechins in green tea depends on its processing and geographical location, as well as the growing conditions.[16] It has been suggested that a bag of green tea contains 80–100 mg of polyphenols, of which EGCG is approximately 25–30 mg.

The various properties of green tea that make it a valuable functional food, specifically EGCG, its most abundant catechin, are as follows (Fig. 2):

1 Anti-inflammatory

Injury to the tissues or exposure to bacterial endotoxins, pro-inflamamtory cytokines, mitogens and viral proteins triggers the immune-inflammatory reactions, such as the arachidonic acid (AA) pathway. Furthermore, there is activation of nuclear factor kappa-B (NF-κB), which regulates the chronic inflammatory reactions and pro-inflammatory cytokine production (Fig. 2).[18] It plays an important role in inflammaging as well.

EGCG, the most abundant catechin in green tea, acts either directly or indirectly on NF-κB. It efficiently blocks lipopolysaccharide-induced inducible nitric oxide synthase (iNOS) expression by disrupting the binding of NF-κB to the iNOS promoter. This reduces the production of nitric oxide (NO), an important mediator of inflammation.[19] EGCG also reduces tumor necrosis factor-α-mediated degradation of the inhibitor of NF-κB.[20] Furthermore, the reactive oxygen species (ROS) formed during the inflammatory process from the damaged cells are scavenged by EGCG, thereby downregulating the NF-κB. These anti-oxidant effects have been explained later.

EGCG inhibits the pro-inflammatory cytokines, such as interleukin (IL)-1β, which plays an important role in inflammaging.[21] This property has been specifically utilized in the management of arthritic joint disease.[22] IL-1β is produced by activated inflammatory cells. It induces the production of matrix metalloproteinases (MMP), and downregulates the levels of their inhibitors. It even hinders the production of proteoglycans and type II collagen. Additionally, it activates cell signaling pathways, such as activator protein-1 (AP-1), which control the gene expression for several MMP. EGCG prevents this by inhibiting the key signal transduction pathways. It specifically inhibits MMP-1, -2 and -7 with the help of its gallolyl group.[22] This prevents the degradation of the extracellular matrix in various chronic diseases.

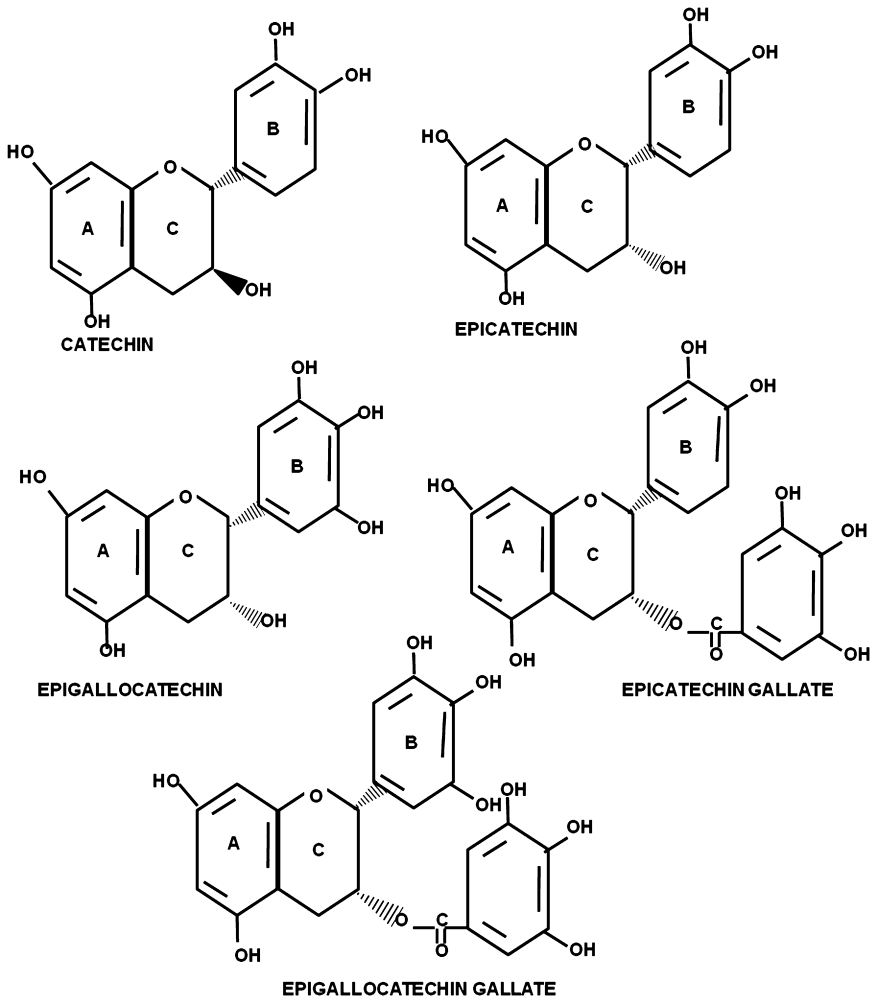

Figure 1 Structure of green tea catechins.

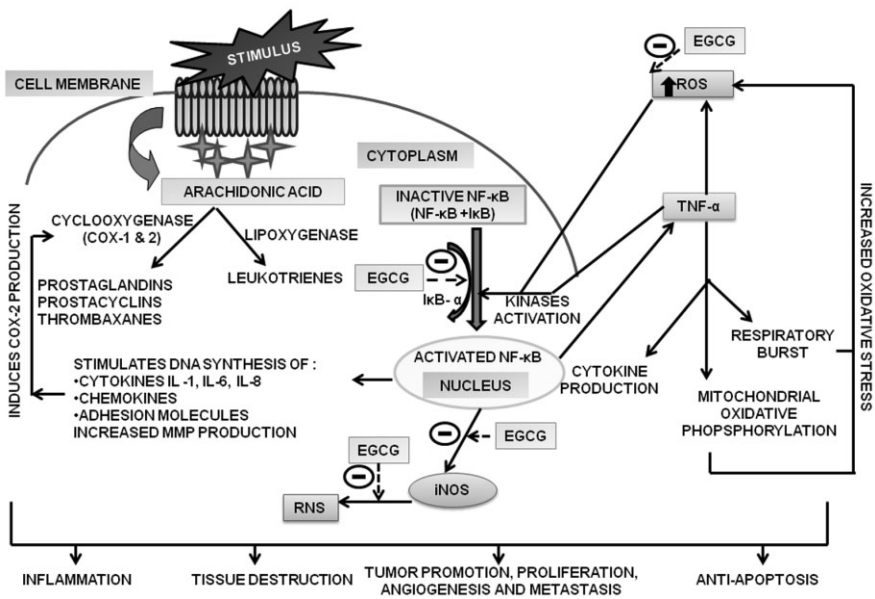

Figure 2 Mechanism of action of green tea catechins. EGCG, epigallocatechin-3-gallate; IL, interleukin; iNOS, inducible nitric oxide synthase; IκB, nuclear factor kappa-B-inhibitor; NF-κB, nuclear factor kappa-B; ROS, reactive oxygen species; TNF, tumor necrosis factor.

2 Anti-oxidant effect

Oxidative stress is the key factor in immunosenescence and inflammaging.[23] It initiates the development and progression of chronic oral diseases including periodontitis, dental caries and oral cancer. Under normal physiological conditions, the oxidants are scavenged by anti-oxidants, such as vitamin E, catalase, glutathione peroxidase and superoxide dismutase. However, their excessive production damages the biological molecules, such as nucleic acids, lipids, proteins and carbohydrates.[24]

Green tea catechins are potent anti-oxidants. They directly scavenge ROS, inhibit the redox sensitive transition metal ions and transcription factors, pro-oxidant enzymes, and induce the anti-oxidant enzymes.[25]

The anti-oxidant action of green tea can be explained as follows:

i) Effect on NO and iNOS:

NO exerts oxidative stress by either directly reacting with the macromolecules to initiate lipid peroxidation or by reacting with superoxide radicals to form the peroxynitrite anion.[26] Lipid peroxidation reduces the fluidity of the cell membrane, increases its permeability, inactivates the membrane receptors and enzymes, and generates toxic degradation products.[27]

The production of NO is controlled by the iNOS gene which is expressed after the activation of the NF-κB pathway.[28] Thus, the inhibition of NF-κB by EGCG prevents excessive generation of NO.

ii) Effect on ROS and anti-oxidant enzymes:

EGCG scavenges a wide variety of ROS including superoxide, hydroxyl radical and hydrogen peroxide.[24] This process involves the delocalization of electrons, formation of intra- and intermolecular hydrogen bonds, rearrangements of molecules, and chelation of metal ions.[29,30] The phenolic hydroxyl groups in catechins act as electron donors.[25] Their scavenging capacity is directly proportional to the number and arrangement of ortho-dihydroxyl and ortho-hydroxyketol groups, the C2-C3 double bonds, concentration and solubility, accessibility of the active group to the oxidant, and the stability of the reaction product. The number of hydroxyl groups on the B ring governs the anti-oxidant capacity.[25]

The 3, 4 catechol structures on the B ring have an affinity for peroxyl, superoxide and peroxynitrite radicals. The ROS attach to the ortho-dihydroxy site on the B ring. The hydroxyl groups inhibit lipid peroxidation.[25]

The ortho-trihydroxyl group and 3-gallate esters in EGCG chelate iron and copper, thereby preventing the Fenton and Haber–Weiss reactions responsible for free radical formation.

EGCG modulates the ROS-generating enzymes, such as iNOS and xanthine oxidase (XO). The effect of ECGG on the former has already been explained. The latter mediates the oxidative damage to the tissues by reacting with oxygen molecules to form superoxide.[25] EGCG strongly inhibits XO, and even upregulates the anti-oxidant enzymes in plasma.[31]

3 Antimutagenic effect

It has long been proposed that the molecular, cellular and physiological changes during aging influence cancer cell growth.[32] There are three major hypotheses proposed to explain this association. First, the prolonged duration of exposure to carcinogens increases the prevalence of cancer. Second, the age-related changes in the immune-inflammatory system increase the induction of new neoplasms and the growth of already existent, but latent, tumor cells. The senescent cells lose their ability to undergo apoptosis and produce some factors that stimulate epithelial cells with oncogenic mutations. Finally, with aging, the combined effects of mutational load, telomere dysfunction and altered stromal milieu increases.[32]

Studies have shown the chemopreventive potential of EGCG.[33–36] Various molecular targets of EGCG in cancer therapy are the molecules and pathways involved in cell survival and growth. These include the growth factors, cell cycle, apoptosis, telomerase, oxidative stress, NF-κB signaling, AA pathway products, pro-inflammatory cytokines, cellular proliferation factors, oncogenes, metastasis related enzymes and angiogenesis.

The antimutagenic properties of EGCG have shown beneficial effects in cancers of the skin, lung, colon, pancreas, prostate and mammary glands, as reported in several epidemiological and animal studies, as well as human cell line studies.[37–42] These form the basis for its application in the management of oral cancer, as explained later.

4 Antimicrobial activity

Aging is associated with changes in the microbial environment of the body. The combined effects of immunosenscence, inflammaging and altered microflora increase the susceptibility to infections, including oral diseases.

Extracts of green tea possess antimicrobial activity against the bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), *Helicobacter pylori*, α-haemolytic *Streptococci*, viruses (e.g. hepatitis, HIV, rota-, entero- and influenza virus), yeasts, filamentous fungi, *Chlamydia*, mycoplasmas and parasites.[43]

The direct antimicrobial effects have been attributed to EGCG, whereas the indirect effects are as a result of modification of antibiotic sensitivity and bacterial virulence factors.[43] EGCG has the capacity to reverse methicillin resistance in MRSA isolates.[44] It produces synergistic effects with conventional antibiotics, and modifies the expression of key proteins from both Gram-positive and -negative bacteria.[45] Additionally, it prevents the transfer of drug-resistant plasmids in a dose-dependent manner.[46] The sub-inhibitory

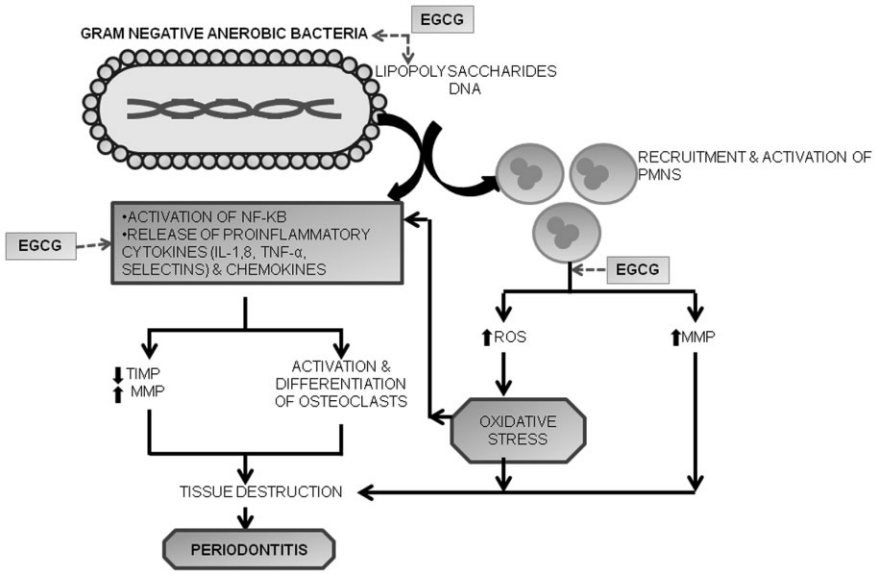

Figure 3 Green tea in the management of chronic periodontitis. EGCG, epigallocatechin-3-gallate; IL, interleukin; MMP, matrix metalloproteinases; PMNS, polymorphoneutrophils; ROS, reactive oxygen species; TIMP tissue inhibitor of matrix metalloproteinases; TNF, tumor necrosis factor.

concentrations of EGCG reversed tetracycline resistance in *Staphylococci* by inhibiting the Tet (K) efflux pump.[47]

High EGCG concentrations irreversibly damage the bacterial cytoplasmic membrane by generating hydrogen peroxide within the bilayer or by inhibiting the cytoplasmic enzymes and type II fatty acid synthesis system.[48–50] It affects the architecture of the bacterial cell wall, including its thickness, turnover and separation, by reducing the autolysin production and activity.[51,52] It degrades the phospholipid palisade.[53,54] The membrane interactions of catechins are governed by the degree of hydroxylation of the B ring, the presence of gallate moiety and the stereochemistry of the C ring.[43] These antimicrobial properties of EGCG make it an ideal agent for targeting the microbial complexes involved in periodontal disease and dental caries.

The preventive role of green tea in the development and progression of oral diseases can be explained as follows:

A. Chronic periodontitis

Immunosenescence has long been regarded a risk factor for chronic periodontitis.[5] This has been attributed to changes in periodontium, increased oxidative stress, inflammaging, complex interactions between multiple genetic traits, infectious agents and lifestyle factors (e.g. diet and smoking) in older adults.[55,56]

Epidemiological studies have shown that regular intake of green tea prevents the development and progression of chronic periodontitis.[10,11] In a study on 940 Japanese males aged 49–59 years, the relationship between the daily dietary administration of green tea and chronic periodontitis was evaluated. It showed that every one cup per day increase in green tea intake resulted in a 0.023-mm decrease in the mean probing depth, a 0.028-mm decrease in the mean clinical attachment level and a 0.63% decrease in bleeding on probing. Thus, green tea intake was inversely correlated with the clinical parameters of chronic periodontitis.[10]

In another report, the cross-sectional data from the Ohsaki Cohort 2006 study was analyzed to determine the association between tooth loss as a result of chronic periodontitis or dental caries and green tea consumption. The study included 25 078 participants (12 019 men and 13 059 women; aged 40–64 years) who were questioned about green tea consumption and tooth loss. It was shown that in men there was a progressive reduction in the odds for tooth loss (cut-off point of ≤20 teeth) with increase in consumption of green tea (1.00 for ≤1 cup/day, 0.82 for 1–4 cups/day, and 0.77 for ≥ or 5 cups/day). Almost similar results were reported in women.[11]

Some studies on older adults have reported beneficial effects of green tea gels or chips placed directly into the periodontal pockets after scaling and root planing. It was postulated in these reports that pockets treated with green tea showed a significant reduction in the levels of periodontopathogens, as well as mean probing depths.[57,58]

The beneficial effects of green tea in the prevention of chronic periodontitis can be explained as follows (Fig. 3):

1 Effect on periodontopathogens

In addition to the antibacterial effects described earlier, green tea specifically acts on the periodontopathogen, *Porphyromonas gingivalis*.[59,60] *In vitro* studies have shown that EGCG and EGC inhibit gingipains (cysteine proteases of *P. gingivalis*), and binding of fimbriae to the oral epithelial cells.[59,61] Furthermore, they inactivate bacterial collagenases and protein tyrosine

phosphatase enzymes.[60,62] These actions have been attributed to their gallolyl moieties with ester linkage at third hydroxyl positions.[59–62]

2 Effect on host immune reactions

In response to bacterial infection, host immune reactions are perpetuated, which are more destructive to the periodontal tissues. The bacterial virulence factors stimulate the inflammatory cells to release destructive mediators that perturb the balance with their inhibitors resulting in destruction. The activated osteoclasts destroy bone through the receptor activator of NF-κB ligand (RANKL), RANK, and osteoprotegerin bone destruction pathway. It results in a vicious cycle whereby the accumulation of anerobic plaque biofilm in deep periodontal pockets stimulates the host response and tissue destruction.[63]

EGCG blocks the NF-κB-induced tissue destruction by preventing the production of destructive proteins, MMP and IL-8.[64] Studies have shown the protective effects of EGCG on chondrocytes and bone microarchitecture.[65,66] It even inhibits IL-1-induced osteoclatogenesis.[67]

Another factor to be considered is oxidative stress induced by cigarette smoking, which plays an important role in progression of chronic periodontitis. Cigarette smoke produces direct oxidant burden, as well as stimulating the production of ROS from the inflammatory cells. It is an important source of NO, which induces the NF-κB pathway.[68] The ability of green tea catechins to scavenge ROS has already been discussed.[69,70] Both *in vitro* and *in vivo* administration of green tea in smokers improved the levels of anti-oxidant enzymes in saliva.[68] Recently, the effects of EGCG on the nicotine-induced toxic and inflammatory responses in oral epithelial cells and gingival fibroblasts were investigated.[71] Nicotine was used either alone or in combination with the lipopolysaccharide of Aa. It was found that pretreatment of cells with EGCG neutralized the nicotine-induced toxicity in epithelial cells and fibroblasts.[71] It even inhibited acrolein induced apoptosis in human gingival fibroblasts.[72–74]

B. Dental caries

Dental caries is a dynamic process involving interactions between dental plaque bacteria, host and dietary factors.[75] The World Health Organization has reported that the number of older adults with functional dentition (presence of at least 20 natural teeth) is on the rise.[76] This subsequently would increase the number of aged with dental caries. The latter has been attributed to the increased number of tooth surfaces available for bacterial colonization, bone loss and gingival recession exposing the root surfaces.[77,78] Furthermore, higher morbidity as a result of chronic diseases, use of medications with xerostomic side-effects, poor oral hygiene, frequent carbohydrate intake and heavy restorations might aggravate the problem.[76]

Diet, especially high-sucrose intake, elevates the risk for caries. This led to the development of numerous functional foods, such as fluoridated water, salt and milk; polyol-based sweeteners; and fortified dairy products to reduce the incidence of caries.[79]

Although tea is a significant source of fluoride, studies report that its anticariogenic action is mainly related to a high concentration of polyphenols, such as EGCG.[75,80] It is estimated that a cup of green tea (2.5 g of green tea leaves/200 mL of water) contains approximately 90 mg of EGCG.[81]

The beneficial effects of EGCG were confirmed in an animal study on specific pathogen-free rats infected with *Streptococcus mutans* (strains JC-2, serotype-c), the prime bacteria in dental caries. Rats fed with drinking water containing 0.05% green tea polyphenols showed reduced caries incidence as compared with the controls not receiving these compounds.[79,82] Furthermore, ingestion of sugar-free tea resulted in reduced caries.[83,84]

The virulence of *S. mutans* depends on three aspects; biofilm formation on the tooth surface; acidogenecity, enabling the production of acids from carbohydrates and tolerance to environmental stresses; and particularly low pH (aciduricity).[85] The virulent components of *S. mutans* are its ability to produce glucosyl transferases, bacterial amylases and stress-combating membrane-bound F1Fo-ATPase, agmatine-deiminase, enolase, and lactate dehydrogenase (LDH) systems[75] (Fig. 4).

Several mechanisms have been proposed for the anticariogenic properties of green tea. These effects were seen with tea decoction and chewing gums, as well as mouth rinses. The inhibitory effects of green tea on cariogenesis are as follows:[61,75]

1 Effect on cariogenic enzymes

The streptococcal glucosyl transferase degrades the dietary sucrose, and synthesises extra- and intracellular polysaccharides.[43,75] These polysaccharides help in adherence of bacteria to the tooth surface, formation of plaque biofilm and generate energy during reduced availability of exogenous fermentable carbohydrates in the oral cavity.[75]

EGCG suppresses the salivary and bacterial amylases involved in carbohydrate metabolism. It prevents acid generation by inhibiting LDH enzyme at both the transcriptional and enzymatic levels.[75] Furthermore, it inhibits enolase, a key enzyme for glycolysis, resulting in decreased sugar internalization, glycolysis and acid production by *S. mutans* cells.[75]

2 Effect on bacterial biofilm

In vitro, EGCG inhibited the formation and integrity of bacterial biofilms at concentrations between 156.25 to 625 μg/mL.[75] This was attributed to altered bacterial phenotype through catechin-mediated denaturation or deconformation of protein ligands, such as fimbriae. This subsequently hampered the proliferation and adherence of *Streptococci* to the tooth surface.[74]

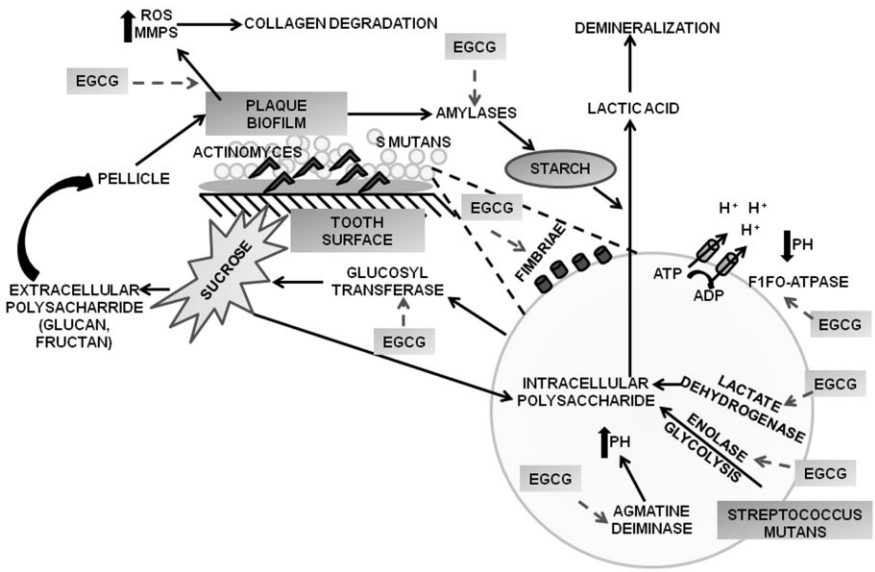

Figure 4 Green tea in the management of dental caries. ADP, adenosine diphosphate; ATP, adenosine triphosphate; EGCG, epigallocatechin-3-gallate.

EGCG at MIC between 50 and 500 μg/mL inhibited *S. mutans*, and was bactericidal at a concentration of 1 mg/mL.[43,61,86]

3 Effect on F1Fo-ATPase and the agmatine deiminase systems

The F1Fo-ATPase and the agmatine deiminase systems are responsible for the aciduric nature of *S. mutans*.[75,85] They help in maintaining an optimal pH across the cell membrane, enabling the glycolysis at low pH within the biofilm.[75]

EGCG suppresses both F1Fo-ATPase and agmatine deiminase systems, leading to energy deficit and disruption of ideal pH across the cell membrane.[75] Subsequently, the glucosyl transferase fails, resulting in decreased production of extra- and intracellular polysaccharides. This disrupts the biofilm integrity and adherence of bacteria to the tooth surface along with increased starvation stress.

Increased cytoplasmic acidity with inhibition of enolase and glycolysis diminishes the ATP pool, further impeding the activity of F1Fo-ATPase.[75] The impairment of LDH decreases the redox potential of the cell, leading to accumulation of glycolytic intermediates toxic to *S. mutans*.[66] This hinders its ability to sustain environmental stresses and even cell death.[75]

A study showed that administration of green tea in the form of a mouth rinse (2 mg/mL of EGCG in 10 mL) inhibited a fall in pH, killed cultured cells of S. *mutans* time dependently and inhibited LDH activity. Thus, green tea mouth rinses could efficiently reduce acid production in dental plaque and S. mutans.[87]

4 Effect on oxidative stress

Besides, the direct role of *S. mutans*, systemic host immune reactions, including oxidative stress, play an important role in caries progression. After the acidic erosion of enamel, a secondary inflammatory reaction is induced in the dentin, which provokes the inflammatory cascade. The bacterial toxins and ROS stimulate release of MMP, which degrade collagen in the dentin.

A recent review on the systemic theory of dental caries hypothesized that high-sugar intake provoked oxidative stress in the body and tooth decay.[88] Normally, the dentinal fluid provides nutrition and anti-oxidants to the cells of the tooth. Its flow is controlled by the endocrine portion of the parotid gland, which receives signals from the hypothalamus. Increased sucrose intake upregulates the free radical levels in the hypothalamus and decreases the parotid hormone production. Anti-oxidant supplementation could thus minimize the effects of ROS on the hypothalamus, and replenish the hormone levels as well as the dentinal fluid flow. This enhances the self-cleansing ability and levels of tissue inhibitors of MMP in dentine, thereby preventing its degradation.[88] This was supported in a recent investigation showing the inhibitory effects of EGCG on MMP, which was more effective than sodium fluoride on acid erosion.[89]

Applications of green tea in other oral conditions

1 Oral cancer

Chronic inflammation and oxidative stress are the major factors involved in the development of malignancies including oral cancer.[90] The prevalence of oral squamous cell carcinoma is very high in older adults.[12,91] Efforts have been made to prevent it by reversal or

suppression, or inhibiting transformation of premalignant cells into a malignant form. Natural agents including phenolics, flavonoids, carotenoids and alkaloids have been tried in this direction.[92] Studies have supported the beneficial role of green tea in the prevention of oral carcinogenesis and conversion of premalignant lesions to malignancy. A phase II randomized, placebo-controlled trial of green tea extract (GTE) was carried out in 41 patients (aged 18–75 years) with high-risk oral premalignant lesions.[93] They received 500, 750 or 1000 mg/m^2 of GTE or a placebo three times daily for 12 weeks. It was reported that GTE suppressed high-risk oral premalignant lesions by reducing angiogenic stimulus. Furthermore, higher doses of GTE improved the short-term (12-week) high-risk oral premalignant lesions outcome.[93]

A nationwide large-scale cohort study in Japan evaluated the relationship between green tea consumption (1–5 cups/day for 10.3 years) and oral carcinogenesis.[12] It included 20 550 men and 29 671 women (age 40–79 years), without any history of oral and pharyngeal cancer at baseline survey. The results showed that during a mean follow-up period of 10.3 years, 37 participants developed oral cancer. In women, the hazardous ratio of oral cancer for ≥1 cup of green tea per day was less than for those drinking ≤1 cup per day. However, in males, no such trends were observed. It was concluded that increased green tea consumption was not significantly associated with reduced oral cancer, although there was a decreased risk in women.[12]

Furthermore, local application of green tea mouthwash (containing 800 mg of EGCG) was evaluated in seven participants (6 males and one female) aged 64 years (range 46–74 years).[94] All the participants had at least one recurrent lesion involving the oral mucosa after a complete surgical removal of the initial lesion. Rinsing with EGCG solution for 2 min, once daily before bedtime for a period of 7 days produced beneficial effects on these lesions.[94]

Another study reported that chewing 2 g of green tea leaves for 5 min produced high concentrations of catechins in saliva in the first hour. Thus, tea leaves were a convenient, slow-release source of catechins, and could be used in the prevention of oral cancer and dental caries.[95]

Besides the antimutagenic effects reported earlier, EGCG modulates *HER-2* and *RECK* genes associated with poor prognosis of oral cancer. It inhibits the phosphorylation of *HER-2* and hypermethylation of the *RECK* gene, enhances the expression of *RECK* mRNA and suppresses MMP-2,-9 and urokinase plasminogen activator expression in a dose-dependent manner.[96–98] Additionally, its combination with curcumin, lactoferrin, erlotinib, chemotherapy, and radiotherapy produced synergistic effects on cell cycle arrest and signal transduction inhibition.[99–102] It reduced phase I enzymes (cytochrome B5, P450, B5 reductase, P450 reductase, aryl hydrocarbon hydroxylase and DT-diaphorase), prevented lipid peroxidation, and increased the levels of anti-oxidants and phase II enzymes (glutathione-S-transferase) as shown in *in vivo* models of carcinogenesis.[103,104]

Recently, green tea has been utilized in nanochemoprevention to improve the outcome of chemotherapy. Nano devices, such as injectable nanovectors including liposomes; biologically targeted nanosized magnetic resonance imaging contrast agents; and novel, nanoparticle-based methods, have been used in cancer therapy.[105] EGCG encapsulated in polylactic acid-polyethylene glycol nanoparticles was tested in mice injected with human prostate cancer cells. It was found that nano EGCG retained its biological efficacy with over a 10-fold dose advantage both in cell culture systems and in *in vivo* settings.[105] Similar drug delivery systems might be helpful in targeting cells in oral cancer as well.

2 Dental erosion

Dental erosion is the loss of tooth substance as a result of chronic exposure to exogenous or endogenous acids without bacterial involvement, but with histological evidence of changes in tooth structure.[106] It is frequently seen in older adults with gastro-esophageal reflux disease.

The acidic challenge causes irreversible loss of enamel, uncovering the organic matrix of dentin.[106,107] The MMP, specifically 2, 8 and 9, are involved in the destruction of the extracellular matrix of dentin.[108,109] EGCG and ECG inhibit MMP. They form an organic layer and induce new collagen cross-linking.[110] The proanthocyanidins in green tea react with the organic portion of dentin, thereby increasing its microhardness and microstructure.[111]

3 Halitosis

Halitosis is the emanation of disagreeable odor from the oral cavity as a result of intra- or extra-oral factors.[112] Intra-oral halitosis is primarily caused by the action of proteolytic anerobic Gram-negative bacteria on the amino acids (e.g. methionine, cystine and cysteine). They produce sulphur-containing gases, known as volatile sulphur compounds (VSC). The latter include hydrogen sulphides and methyl mercaptans.[113] In older adultd, reduced salivary flow and impending oral and systemic health is one of the major causes for halitosis.

Various antimicrobial chemicals have been used in conjunction with routine oral hygiene measures to prevent halitosis, but they are associated with numerous side-effects.[112] The antimicrobial actions of EGCG justify its role in the treatment of halitosis. Both *in vitro* and *in vivo* studies have shown its usefulness in the inhibition of bacterial and fungal growth, thereby preventing the production of VSC.[112–115] Hence, green tea might serve as a useful natural alternative in the treatment of halitosis.

Conclusion

Green tea is a potent functional food for older adults. Recent scientific evidence explaining its mechanism of action and biological activities suggest its promising role in the management of periodontitis, dental caries, dentinal erosion, and halitosis in older adults. Furthermore, its antimutagenic property provides an insight into its plausible affects on oral cancer. Future scientific research is required to elucidate the benefits of this functional food in the management of oral diseases, especially in the aged.

Disclosure statement

The authors declare no conflict of interest.

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