

Review

Anti-cariogenic effects of polyphenols from plant stimulant beverages (cocoa, coffee, tea)

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ABSTRACT

Polyphenols occurring in cocoa, coffee and tea can have a role in the prevention of cariogenic processes, due to their antibacterial action. Cocoa polyphenol pentamers significantly reduce biofilm formation and acid production by *Streptococcus mutans* and *S. sanguinis*. In the same way, trigonelline, caffeine and chlorogenic acid occurring in green and roasted coffee interfere with *S. mutans* adsorption to saliva-coated hydroxyapatite beads. Studies carried out on green, oolong and black tea indicate that tea polyphenols exert an anti-caries effect via an antimicrobial mode-of-action, and galloyl esters of (–)-epicatechin, (–)-epigallocatechin and (–)-gallocatechin show increasing antibacterial activities. The anti-cariogenic effects against α -haemolytic streptococci showed by polyphenols from cocoa, coffee, and tea suggest further studies to a possible application of these beverages in the prevention of pathogenesis of dental caries.

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1. Introduction

Dental caries is a common chronic disease which affects from 60 to 90% of young population [1]. During the past few decades, changes have been observed in prevalence, distribution and pattern of dental caries in the population.

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A significant decrease of the onset of tooth decay has been observed, especially in the western part of the world, in nations like Germany [2], England, USA, Scandinavia, Scotland [3], Norway [4] and Australia [5].

This diminution of dental caries levels could be due to the use of different fluoride-releasing vehicles and other preventive systems [3,4,6].

However, recent research demonstrated that dental caries distribution was non-homogeneous through different geographical areas, and there were many variation inside each nation too. In fact, several population groups still have a high caries incidence and a need for dental care [7–9].

In particular, an Italian cross-sectional study highlighted that in a sample of 1333 students, 59.11% had caries experience (DMFT>0) (mean of decayed teeth) [10]. Furthermore, a recent survey examined oral health situation through mean value of DMFT and Significant Caries Index (SiC) in a young-population sample in Campania (Italy) and determined the possible relationship between oral health behaviour, socioeconomic factors and caries experience. The study demonstrated a caries prevalence of 81%, a sample mean values of 3.5 for DMFT and that the variables influencing statistically DMFT values in the sample are the following: family socio-economic level, level of educational attainment of children mothers and use of the school canteen service [11].

Therefore, dental caries yet remain a widespread public disease that highlight an urgent need to find new effective strategies. If some remedies will not initiated, there could be a serious negative impact upon the future oral health (and systemic health) of the global community, with a major increase in the cost of dental services [12].

In terms of treatment, the data indicate that expenditure on dental care represents a large part of health expenditure and that it weighs almost entirely on household budgets. The

average annual expenditure for dental care per household in 2002 was to 740 Euro [13].

The multifactorial aetiology of caries allows several interpretations to explain prevalence disease changes. They could be variously ascribed to the different in dietary habits, especially the consumption of sugar, variations in the patterns of oral hygiene, changes in the virulence of oral and dental plaque microflora and alterations in the oral protective mechanisms including the immune status.

The formation of dental plaque, which plays an important role in the development of caries and periodontal disease in humans, could be initiated by several strains of oral streptococci [14,15]. The major aetiological players are thought to be the two α -haemolytic streptococci, *Streptococcus mutans* and *S. sobrinus*, potent cariogenic, although several other types of bacteria (notably lactobacilli and actinomyces) may also be involved. The carbohydrate substrates can become available either directly (sugar ingested in food or drink) or be derived from dietary starch by the action of bacterial or salivary amylases, or both.

Mutans streptococci produce 3 types of glucosyltransferase (GTFB, GTFC, and GTFD), and synthesize an adherent and water-insoluble glucan from appropriate carbohydrate substrates, most favourably sucrose at low pH values, which causes the organisms to adhere firmly to the tooth surface [16,17]. For many oral streptococci, glucans comprise an extracellular slime layer produced in the presence of sucrose that promotes adhesion and the formation of a dental plaque biofilm.

The formation of dental plaque leads to localized demineralization due to the accumulation of acids. (Fig. 1)

Theoretically, the inhibition of each step in the process of caries formation contributes to the prevention of dental caries [18].

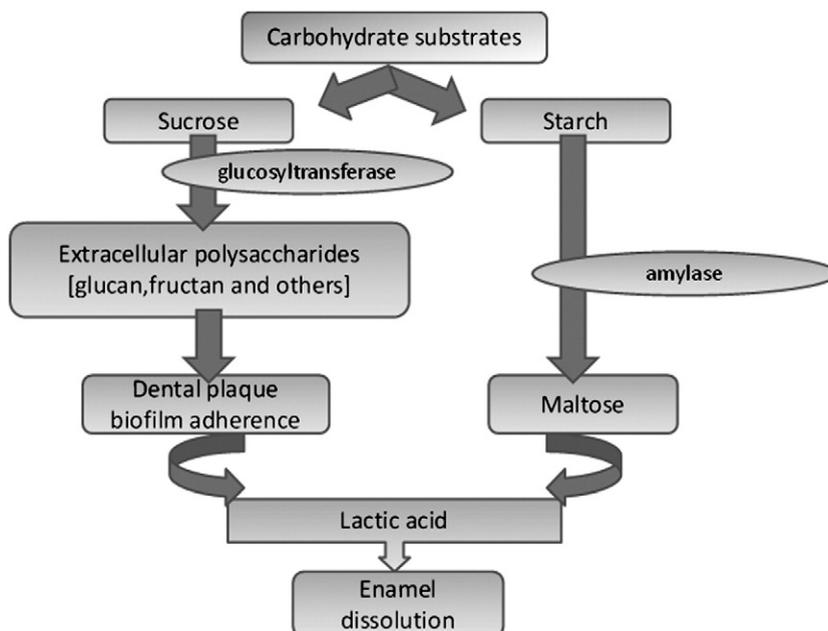


Fig. 1. Pathogenesis of dental caries.

The insurgence of caries is generally prevented by cleaning teeth, but at least two different methods have been developed: in Western Countries, the practice of cleaning teeth with toothbrush devices is largely diffused. Very frequently active principles extracted by plants are included in the preparation of dentifrices as abrasive, and also to ensure a stronger antibacterial action [19,20]. On the other hand, many African, Asiatic and American communities use chewing sticks made by different part of a plant (root or stem short branches). As far as concerns chewing sticks, about 141 species have been listed [19]. Generally, they are flowering plant belonging to Dicotyledonae, and are also used in the treatment of different kinds of diseases.

Some of these plants have been investigated in detail for their effectiveness in the control of dental plaque [21,22]. However, although many compounds from natural products capable of controlling dental caries have been extensively surveyed [23,24], only a very restricted number of these is available for clinical applications because of effectiveness, stability, odor, taste and economic feasibility.

In the last years, there has been an increased interest on the properties of some plant stimulant beverages, particularly chocolate coffee and tea, which have demonstrated anti-cariogenic *in vitro* and *in vivo* activity. Although folk medicinal uses have been reported for chocolate (*Theobroma cacao* L.), coffee (*Coffea arabica* L., *C. canephora* Pierre) and tea (*Camellia sinensis* (L.) O. Kuntze), (Table 1), their universal diffusion is due to the stimulant action on nervous system of caffeine [25], an alkaloid occurring in coffee and tea, and, to a minor extent, also in cocoa.

T. cacao L. is a member of Bromeliaceae native to forests of Central and South America. Two subspecies are cultivated: calabacillo (*T. cacao* L. subsp. *sphaerocarpum* (A. Chev.) Cuatrec.), from South American rain forests, and criollo (*T. cacao* L. subsp. *cacao*) from Mexico. The two subspecies are interfertiles [26,27]. The use of cacao seeds to prepare drink was diffused among Aztecs, and Spanish introduced this use in Europe, during the XVII century [28]. Today, the seeds of *T. cacao* are used to prepare both cocoa powder and chocolate tablets. Seeds are fermented and during this

Table 1
Folk medicinal uses.

Botanical name	Country	Uses description	Part used	Preparations	Authors
<i>Coffea arabica</i> L.	Brazil	Taken orally for influenza	Seed	Decoction	[37]
	Cuba	Orally by males as an anaphrodisiac	Seed	Hot water extract	[38]
	Haiti	1) Is taken orally for anemia, edema, asthenia, and rage; 2) orally for hepatitis and liver troubles. 3) used externally for nervous shock; 4) is taken orally or the leaf is applied to the head for headache.	1) Grilled fruit and leaf; 2) fruits; 3) soaked fruit; 4) leaf	1) 4) Decoction; 2) internal use; 4) fresh applied	[39]
	Mexico	1) Used to treat fever; 2) taken orally by nursing mothers to increase milk production.	1) Leaves; 2) roasted seed	1) Poultice; 2) hot water extract	1) [40] 2) [41]
	Nicaragua	1) For headache, stomach pain; 2) taken orally for fever and used externally for cuts and hemorrhage	1) Leaves; 2) seed	1) Used externally; 1) hot water extract; 2) decoction	1) [42] 2) [43]
	Peru	1) Is taken orally as a stimulant for sleepiness and drunkenness; 2) is taken orally to induce labor, and the hot water extract is taken orally as an antitussive in flu and lung ailments	1) Dried fruit; 2) leaf	1) Hot water extract; 2) infusion	1) [44] 2) [45]
	Thailand West Indies	Is taken orally as a cardiotoxic and neurotonic 1) Is taken orally for asthma; 2) is taken orally for scorpion sting	Dried seed 1) Seed; 2) root	Hot water extract 1) Hot water extract; 2) juice	[46] [44]
<i>Camellia sinensis</i> L.	India	1) Taken orally for headache and fever; 2) applied to teeth to prevent tooth decay; 3) is taken orally for abortion; 4) contraceptive and hemostatic.	1) Dried and fresh buds and leaves; 2) dried leaf; 3) 4) fresh leaf	1) 2) Decoction; 2) powder; 3) 4) juice	1) [47] 2) [48] 3) [49] 4) [50]
	Mexico	Taken orally by nursing mothers to increase milk production	Leaf	Hot water extract	[41]
	Turkey	To treat diarrhea	Leaves	Are taken orally	[51]
	China	Taken orally as a sedative, an antihypertensive, and anti-inflammatory	Dried leaf	Hot water extract	[52]
	Guatemala	Used as eyewash for conjunctivitis	Dried leaf	Hot water extract	[53]
	Kenya	1) Applied ophthalmically to treat corneal opacities; 2) used for chalazion and conjunctivitis	1) Dried leaf; 2) not indicated	1) Water extract; 2) infusion	1) [54] 2) [55]
	Thailand	1) Taken orally as a cardiotoxic and neurotonic; 2) taken orally as an antifungal	1) Dried leaf; 2) dried seed	1) 2) Hot water extract	1) [46] 2) [56]
<i>Theobroma cacao</i> L.	Mexico	Aphrodisiac	Seed	Not indicate	[57]
	Venezuela	For kidney and other urinary problems	Not indicate	Not indicate	[58]
	Latin America	Is applied to wrinkles in the hope of correcting them	Cocoa butter	Not indicate	[59]
	Latin America	Remedy for alopecia, burns, cough, dry lips, eyes, fever, listlessness, malaria, nephrosis, parturition, pregnancy, rheumatism, snakebite, and wounds	Not indicate	Not indicate	[60]

process they change colour, while the typical chocolate flavour develops. After being dried, the seeds of *T. cacao* are grinded, and from this material is obtained the cocoa powder, which serve to prepare chocolate drinks [29].

The genus *Coffea* (Rubiaceae) is represented by more than 20 species, but only *C. arabica* L., and to a much lesser extent, *C. canephora* Pierre are cultivated to produce coffee seeds. *C. arabica* is an evergreen shrub or small tree native to Ethiopia [30]. Its cultivation was introduced in Arabia before the 15th century, and subsequently was extended to other Countries of Asia, America and Africa [31]. All the cultivated *C. arabica* plants spread throughout Continents show a remarkable genetic homogeneity, which make them particularly sensitive to pest attack [32,33]. The plant has some medicinal uses, against respiratory and renal affections, and in the cure of jaundice and malaria, and as pain-killer, but it has been highly valued since Ancient times for its stimulant action [34].

C. sinensis (L.) O. Kuntze is a perennial shrub, or small tree belonging to Theaceae, native to Southwest Asia. Different morphological varieties have been described. However, in the case of Assamese and Chinese varieties their genetic homogeneity has been demonstrated despite of the observed morphological differences [35]. For millennia, tea was used as a medicinal beverage in China, its native country, where the cultivation began, about 4000 years ago. Now the plant is cultivated in large areas of Asia, Africa and Latin America [36]. Tea is classified into three types, green tea, oolong tea and black tea, on the basis of the manufacturing process. All of these tea are prepared from leaves of *C. sinensis* and its varieties. Green tea is prepared from fresh tea leaves that are pan-fried or steamed and dried to inactivate enzymes. Black tea is prepared by crushing withered tea leaves and allowing enzyme-mediated oxidation, commonly referred to as fermentation. During the fermentation process, the constituents of the leaves are converted to numerous secondary products that contribute to the characteristic color and flavor of black tea. Finally, oolong tea is a partially fermented product, manufactured in China and Taiwan, and highly valued in Asia [36].

In this review are presented the most important results which have been obtained on the beneficial effects of the consumption of chocolate, coffee and tea on oral health, and particularly on the anti-cariogenic activity of the polyphenols, mainly flavonoids, occurring in these plants.

2. Chemistry and occurrence of plant polyphenols

Polyphenols constitute one of the most widespread groups of substances in plants, including a wide variety of molecules that contain at least one aromatic ring with one or more hydroxyl groups in addition to other substituents [61]. Polyphenols can be divided into several classes according to the number of phenol rings that they contain and to the structural elements that bind these rings to one another. The main groups of polyphenols are: flavonoids, phenolic acids, phenolic alcohols, stilbenes and lignans [61].

Flavonoids constitute the largest and most diverse family of polyphenols. More than 4000 flavonoids have been identified in plants and the list is constantly growing [62]. The common structure consists of two aromatic rings linked by 3 carbons, most often forming a heterocyclic ring. There are two branches of the flavonoid family: 3-desoxyflavonoids

and 3-hydroxyflavonoids. Variations in position, number, and nature of substituents give rise to a huge number of different flavonoids. Flavones, which are desoxyflavonoids, and flavonols (3-hydroxyflavonoids) are the most common flavonoids, and they can occur either as aglycones or as glycosides [63].

Fruit represent the main sources of polyphenols, but vegetables, leguminous plants, and cereals are also important sources [64].

3. Polyphenols of cocoa, coffee and tea

The polyphenolic content of cocoa seeds represent 6–8% of their dry weight [65]. The main polyphenols found are catechins: (+) chatechin and (+)-epigallocatechin. Moreover, also L1–L4 and polymeric cyanidins have been found, along with 3- α -L-arabinosidyl and 3- β -D-galactosidyl cyanidins [65,66]. Both fermentation of seeds and their subsequent roasting affect polyphenol content and composition and their final concentration in cocoa powder depends on the variety of *T. cacao*, as well as the degree of fermentation [66].

Phenolic acid content of green coffee is 5.5% in *C. arabica*, and about 12% in *C. canephora* [67]. Caffeic and ferulic acids are the major components, and can occur almost entirely as diester of quinic acid (chlorogenic acid) [68].

Coffee is generally processed in many ways which include fermentation of berries and roasting of seeds. These processes, along with the presence of defective seeds, influence the final concentration of polyphenols in coffee beverages. However, independently of manufacture process, the final beverage contains consistently high concentration of chlorogenic acids [69,70].

Tea is characterized by the presence of the polyphenolic catechins including: epigallocatechin-3-gallate (EGCG), epigallocatechin (EGC), epicatechin-3-gallate (ECG), and epicatechin. The tea catechins, in particular, are major constituents of fresh tea leaves [36]. These constituents are oxidized during fermentation to yield a complex mixture of secondary polyphenols including theaflavins, theasinensins and oolongtheanins [71]. However, most of the secondary polyphenols in black tea have not yet been chemically characterized because of their complexity and the difficulties associated with their separation and purification. Also oolong tea contains considerable amounts of catechins and oligomerized catechins [72].

4. Biological properties of polyphenols

Despite their wide distribution, the healthy effects of dietary polyphenols have come to the attention of nutritionists only in the last years. The health benefits of polyphenols include antioxidant, anticancer, and anti-inflammatory effects [73–75]. Moreover, experimental studies, strongly support a role of polyphenols in the prevention of cardiovascular disease. In particular, it has been shown that the consumption of polyphenols limits the development of atheromatous lesions, inhibiting the oxidation of low density lipoprotein [76–79].

Increasing epidemiological evidence supports the view that fruits and vegetables have protective role in oral diseases, including cancer, presumably mediated by their content of polyphenols, particularly flavonoids [80,81]. Furthermore, tea

polyphenols have been shown to have anticancer activity *in vitro* and oral cancer preventive activity in animal models [82,83]. Recently, preliminary results from an intervention study have shown that oral and topical administration of a tea preparation significantly reduced the size of oral lesions and the incidence of micro-nucleated oral mucosa cells in leukoplakia patients compared with a non-treated group [84].

5. Potential anti-cariogenic actions of cacao, coffee and tea beverages and role of their flavonoids

5.1. Cocoa

The possible protective effect of cocoa on dental caries is receiving increasing attention, but previously published data concerning the anti-cariogenic effects of constituents of chocolate are conflicting. An early study indicated that a high sucrose diet was equally cariogenic in the presence or absence of cocoa bean ash [85], while the incorporation of cocoa powder or chocolate into hamster diets was reported to reduce caries [86] and another *in vivo* study has shown that the cariogenic potential indices (CPI) of chocolate with high cocoa levels was less than 40% that of sucrose (10% w/v) and also lower than chocolates containing low cocoa levels [87].

More recently it has been found that cocoa products contain inhibitors of the enzyme dextranucrase, responsible for the formation of the plaque extracellular polysaccharides from sucrose [88].

Subsequently it was suggested the possibility that phenolic substances could be responsible of the observed anti-caries effect of cocoa powder [89].

Moreover it was showed that a water soluble extract of cacao powder significantly reduced caries scores in rats infected with *S. sobrinus*. According to the authors, the observed effect could be due to the inhibitory action of cocoa water extract on the synthesis of water-insoluble glucans [90].

A following study has demonstrated that cocoa polyphenols inhibit the growth of *S. sanguinis*, but not that of *S. mutans*. On the other hand, the pre-treatment of artificial saliva-coated wells with cocoa polyphenol pentamer (the most active component from MIC studies) significantly reduced biofilm formation and acid production by *S. mutans* and *S. sanguinis*. So, although *S. mutans* appeared to be refractory to the growth-inhibitory or lethal effects of the cocoa polyphenol pentamer in MIC/MBC studies, acid production from sucrose was significantly inhibited [91].

Recently it has been reported that the ground husk of cocoa beans, a product of cocoa manufacture, were used to prepare a mouth-rinse for children. The regular use of the mouth-rinse has given a 20.9 reduction of mutans streptococci counts, and was even more effective in decreasing plaque scores [92].

5.2. Coffee

Roasted coffee possesses antibacterial activity against Gram positive and Gram negative bacteria, including *S. mutans* [93,94]. Moreover *C. arabica* and *C. canephora* extracts interfere with *S. mutans* adsorption to saliva-coated hydroxyapatite beads [95]. Green coffee and roasted coffee showed comparable antiadsorption properties. The components which exhibited

the highest anti-adhesive activity were trigonelline, caffeine and chlorogenic acid. These findings have been partially confirmed by another study conducted on Brazilian coffee powders. Water extracts prepared with these products showed no effect on *S. mutans* growth, but significantly reduced the adherence of the bacterial cell to glass bead surface [96].

In a following paper the same authors have evaluated the effect of boiled and non-boiled coffee water solutions on the adherence of dental enamel and dentine. Both the solutions of commercial coffee had significant effect, reducing the adherence of *S. mutans* to dental surface. The authors hypotheses is that this effect could be due to the synergistic action of more chemicals occurring in coffee powder [97,98].

5.3. Tea

The effect of tea polyphenol (TP) on mineralization behavior of enamel in two sterile *in vitro* systems was also investigated. The data from this *in vitro* study suggest that TP has no effect on de/remineralization of enamel blocks and there is no synergetic action of TP and fluoride in a sterile system. This finding supports the proposition that tea polyphenols exert an anti-caries effect via an anti-microbial mode-of-action [99].

Extracts obtained from different teas affect caries development, as their polyphenol components reduce the production of acidic compounds and the ability of streptococci to synthesize adherent water-insoluble glucan from sucrose with the cooperative action of glucosyltransferase [100,101].

Polyphenol compound (designated Sunphenon) from leaf of *C. sinensis* has been partially purified by extraction of the boiling water with ethyl acetate. The effect of Sunphenon on cariogenic *S. mutans* groups (serotype c and g) was studied in both *in vitro* and *in vivo*. The summary of results was described as follows. 1) Addition of Sunphenon to *S. mutans* JC-2 (c) caused a decrease in cell viability. The activity of Sunphenon showed that multiple application are required for killing cells and the maximum effect was seen between 60 and 90 min treatment. However, treatment of *S. mutans* with Sunphenon did not induce complete cell death after 90 min incubation. 2) When *S. mutans* JC-2 (c) was pretreated with Sunphenon, the cellular attachment on saliva-treated hydroxyapatite surface was significantly reduced. 3) When saliva-treated hydroxyapatite surface was pretreated with Sunphenon, the cellular attachment of *S. mutans* JC-2 (c) was also markedly inhibited. 4) Sunphenon had no inhibitory effect on lactic acid production by *S. mutans* JC-2 (c). 5) Sunphenon showed a strong inhibitory effect against water-insoluble glucan synthesis by glucosyltransferase from *S. mutans* JC-2 (c) or *S. sobrinus* 6715 (g). 6) Specific pathogen-free rats infected with *S. mutans* JC-2 (c) and fed a cariogenic diet containing 0.5% Sunphenon developed significantly fewer carious lesions than controls infected with *S. mutans* and fed the same diet without Sunphenon. Furthermore, feeding of the drinking water containing 0.1% Sunphenon reduced caries incidence in *S. mutans* infected animals [102].

A study indicated that the oolong tea polyphenolic compounds could be useful for controlling dental caries. It was examined an extract of oolong tea and its chromatographically isolated polyphenolic compound for *in vitro* inhibitory effects on glucosyltransferases (GTases) of mutans

streptococci and on caries development in Sprague–Dawley rats infected with mutans streptococci. The samples showed no detectable effect on the growth of mutans streptococci. However, insoluble glucan synthesis from sucrose by the GTases of *S. mutans* MT8148R and *S. sobrinus* 6715 was markedly inhibited, as was sucrose-dependent cell adherence of these mutans streptococci. The addition of the oolong tea extract and the isolated polyphenol compound into diet and drinking water resulted in significant reductions in caries development and plaque accumulation in the rats infected with mutans streptococci [103].

The inhibitory effects of oolong tea extract (OTE) on the caries-inducing properties of mutans streptococci were examined *in vitro*. OTE reduced the rate of acid production by mutans streptococci accompanied with the retardation of growth rate of mutans streptococci, while the action by chromatographically isolated oolong tea polyphenol (OTF6) was weak. On the other hand, both oolong tea products decreased cell surface hydrophobicity of almost all the oral streptococci examined in the study, and also induced cellular aggregation of *S. mutans*, *S. oralis*, *S. sanguinis* or *S. gordonii*. In these reactions, OTF6 showed a more pronounced activity than OTE. Furthermore, the oolong tea products inhibited the adherence of mutans streptococci to saliva-coated hydroxyapatite. These results suggest that OTF6 may inhibit bacterial adherence to the tooth surfaces by reducing the hydrophobicity of mutans streptococci, and OTE may inhibit caries-inducing activity of mutans streptococci by reducing the rate of acid production [104].

A study on black tea has determined the effects of a standardized black tea extract (BTE) on caries formation in inbred hamsters on a regular and a cariogenic diet. It was concluded that a frequent intake of black tea can significantly decrease caries formation, even in the presence of sugars in the diet [105].

Studies on the development of anti-plaque agents for prevention of dental caries have investigated effects of some of tea preparations and their individual components on the glucan synthesis catalyzed by glucosyltransferase (GTF) from *S. mutans*. Extracts of green tea and polyphenol mixtures showed appreciable inhibition in the synthesis of insoluble glucan. Among the components isolated from tea infusions, theaflavin and its mono- and digallates had potent inhibitory activities at concentrations of 1–10 mM against GTF. (+)-Catechin, (–)-epicatechin and their enantiomers had moderate inhibitory activities at these concentrations, while galloyl esters of (–)-epicatechin, (–)-epigallocatechin and (–)-gallocatechin had increased inhibitory activities [106].

Different bacteria were separated from saliva and teeth of cariogenic patients and identified by a variety of morphological and biochemical tests. Extracts of green tea strongly inhibited *Escherichia coli*, *S. salivarius* and *S. mutans* [107].

Experiments also demonstrate the inhibition of salivary amylase activity by extracts of a commercial tea. This effect on salivary amylase may contribute significantly to reduce the cariogenicity of starch-containing foods [108].

6. Conclusions

The studies carried out in these last decades have supported the antibacterial role of polyphenols from cocoa,

coffee and tea, but at the present time their potential use in the control of bacteria responsible of cariogenesis is still under scrutiny. A relatively larger body of evidence has been accumulated on the effects of tea (particularly the green tea) on plaque formation, whereas the data on cocoa and coffee are at a preliminary stage. A first important difference between tea and cocoa is that tea can be considered as a functional food for oral health: drinking tea counteracts the negative effects of *Streptococcus* spp. on teeth integrity. On the other hand, it is necessary to prepare water extracts from cocoa powder or beans, to have a concentrated material which is effective towards oral bacteria proliferation. In the case of coffee, data are scanty and are related only to *in vitro* experiments.

Cocoa and coffee polyphenols seems to be mainly effective against the adhesion of bacteria on the surface of teeth, while tea polyphenols exert different actions: tea infusion can be used as a slow-release source of catechins and theaflavins, which are active towards *Streptococcus* growth, but tea polyphenols can also inhibit the preliminary adherence of *S. mutans* to the tooth surface. The progress of research on the cariogenic effects of tea are indirectly confirmed also by the presence of several patents on this topic. Hara and Hattori [109] first patented an anti-plaque agent composed primarily of a tea-leaf polyphenols. More recently, Sekimoto [110] has developed a food composition for preventing or treating periodontosis which include a green tea extract, and Worrell [111] patented an oral composition made by a *Camellia* extract including about 30% epigallocatechin gallate, at least about 50% total catechins as an antibacterial agent against oral inflammatory conditions as gingivitis and periodontitis.

The effectiveness of polyphenols from these beverages as anti-cariogenic agents needs to be confirmed by larger *in vivo* studies carried out on different age-groups, and in different geographical areas. Further research on anti-cariogenic activity of cocoa, coffee, and tea could open a promising avenue of applications, since they are relatively safe, have taste and odor largely appreciated and could be used at a reasonable cost in the preparation of specific anti-cariogenic remedies.

Another point which need further investigation is the possible role of caffeine and caffeine-like alkaloids contained in the three beverages, which, at the moment, has not received attention. Caffeine reinforces the development of immune-resistance to bacteria and stimulates the activity of lysozyme, which has shown bactericidal activity [112–114]. Moreover, caffeine can directly affect the growth of some Gram-negative bacteria, as *E. coli* and *Pseudomonas fluorescens* [115].

Future studies should focus not only on the potential antibacterial effects of alkaloids contained in cocoa, coffee and tea, but also on the structure–activity relationship of polyphenols from the three plants and on the antagonistic or synergistic effects of mixture of these compounds on plaque formation. These data could represent a first step toward the synthesis of analogues of natural occurring phenols, specifically designed to inhibit both growth and adhesion of bacteria to tooth surface.

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