

## ANTI-CARIOGENIC EFFECTS OF POLYPHENOL PLANT PRODUCTS-A REVIEW

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### ABSTRACT

Polyphenols occurring in Grape seeds, 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 tea and black tea indicate that tea polyphenols exert an anti-caries effect via an anti-microbial mode-of-action, and galloyl esters of epicatechin, epigallocatechin and galocatechin showed increasing antibacterial activities. The anti-cariogenic effects against 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.

**KEYWORDS:** Grapes, Tea, Cocoa, Coffee, *S. mutans*, Dental caries, Polyphenols

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### INTRODUCTION

Dental caries is the most common disease with high prevalence among human population. It is a multifactorial infectious disease that depends on diet and nutrition, microbial infection, and host response. The prevalence of these diseases is continuously increasing with change in dietary habit of peoples and increased consumption of sugar.<sup>1</sup> It is crucial to control the disease by many ways including reduction of sucrose diet, proper brushing, and use of fluoride topical and systemic and visiting the dentist at a regular intervals. Although the introduction of fluoride has resulted in the reduction of dental caries, the latter is still the most common infectious disease in humans and is especially prevalent in children and people with xerostomia (dry mouth).

However, recent research demonstrated that dental caries distribution was non-homogeneous through different geographical areas, and there were many variations inside each nation too. In India, nearly 60-70 % of the child population is affected by dental caries.<sup>2</sup>

Risk factors for dental caries in rich communities is associated with factors such as frequent intake of carbohydrate-rich or sugary foods enables the cariogenic bacteria to maintain a low pH on the surfaces of the teeth. Children who already have one or more dental cavities are considered high risk for developing more. A

low fluoride level on the surface of the teeth reduces the remineralization process and increases the risk for caries. First, the most important component in the treatment of the caries disease is prevention.

In fact, several population groups still have a high caries incidence and a need for dental care.<sup>2-4</sup> 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. In the recent past, there has been an increased interest in the therapeutic properties of some medicinal plants and natural compounds which have demonstrated anticariogenic activities in vitro and in vivo. Among these phytoconstituents, several polyphenolic compounds like tannins (catechins) and flavonoids seem to be the most promising biomolecules. Remarkable anticariogenic potency has been observed for alkaloids.

Bioactive constituents play a very important role in multiple mechanisms, which may be responsible for many pharmacological effects. Numerous synthetic substances and antibiotics have been used in the control of dental plaque. However, these compounds cause many unexpected side-effects. It has been claimed that the use

of medicinal plant and natural products, incorporated in food and beverages (juices, fruits), offers potential candidates for anticariogenic agents. Although folk medicinal uses have been reported for *Vitis vinifera* (Grapes), chocolate (*Theobroma cacao* L.), coffee (*Coffea arabica* L., *C. canephora* Pierre) and tea (*Camellia sinensis* (L.) O. Kuntze), considering the traditional use of the *Potentilla* species, it would be meaningful to investigate its phytochemical profile and biological properties in the dental field for the first time. (Table I)

### **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.<sup>4</sup> A polyphenol antioxidant is a type of antioxidant containing a polyphenolic substructure. 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 (Figure1). The main groups of polyphenols are: flavonoids, phenolic acids, phenolic alcohols, stilbenes and lignans.<sup>4</sup> Flavonoids constitute the largest and most diverse family of polyphenols. More than 4000 flavonoids species have been identified in plants these compounds have antioxidant activity and the list is constantly growing.<sup>5</sup> 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.<sup>6</sup> Fruit represent the main sources of polyphenols, but vegetables, leguminous plants, and cereals are also important sources.<sup>7</sup> The grape seed extracts are industrial derivatives from whole grape seeds. There has been a special debate on the health benefits of antioxidants, the polyphenols in wine red anthocyanidins and resveratrol.

### **Polyphenols of grape, cocoa, coffee and tea**

Grape Seed is rich in polyphenols such as resveratrol call that may affect the growth and development of cancer cells and as a result leads to apoptosis. Resveratrol grape seeds are a very potent extract. This is one of the varieties of potential chemopreventive effects.

The polyphenolic content of cocoa seeds represent 6-8% of their dry weight<sup>8</sup> The main polyphenols found are catechins: catechin and epigallocatechin. Moreover,

also L1-L4 and polymeric cyanidins have been found, along with 3-a-Larabinosidyl and 3-B-D galactosidyl cyanidins.<sup>8,9</sup> 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<sup>9</sup>.

Phenolic acid content of green coffee is 5.5% in *C. arabica*, and about 12% in *C. canephora*<sup>10</sup> Caffeic and ferulic acids are the major components, and can occur almost entirely as diester of quinic acid (chlorogenic acid).<sup>11</sup> 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.<sup>12,13</sup>

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<sup>4</sup>. These constituents are oxidized during fermentation to yield a complex mixture of secondary polyphenols including theaflavins, theasinensins and oolongtheanins<sup>14</sup>. 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.<sup>15</sup>

### **Polyphenols in human diet and bioavailability**

PPs are common in all human diets wherever fruit and vegetables are consumed. However, available information on quantitative PP intake is incomplete and comprehensive reference food composition tables are not available, because of the wide range of PPs and the considerable number of factors that modify their concentration in foods. For example, flavonoids and phenolic acids in apples vary by a factor of 1:4; flavonols, which are found in the peel of apples, are not found in pulp; and PP composition and level vary in time and space within the same fruit according to sun exposure and maturation degree.<sup>16,17</sup>

PP intake and bioavailability are generally assessed using the total antioxidant capacity of plasma, which is based on the characteristic antioxidant activity of PPs. However, this method is not free from flaws, because there are many other micronutrients, such as vitamins E and C, with greater antioxidant activity and because

antioxidant capacity is not directly correlated to the in vivo mechanisms of defence, which are mainly enzymatic.<sup>18</sup> A list of total antioxidant capacity of plant foods and beverages is displayed in Table II<sup>19</sup>

More recently, PP intake has been assessed using dietary diaries. The mean daily PP intake among Finnish adults is 863 mg, with phenolic acids representing 75% of total intake, followed by proanthocyanidins (14%), anthocyanidins and other flavonoids (10%). The main PP sources in this sample were coffee, cereals, fruits, mostly berries and berry products.<sup>20</sup> The mean daily PP intake from fruits and vegetables among French adults is 219 mg (males), 193 mg (females) from fruit and 78 mg (males), 67 mg (females) from vegetables.<sup>21</sup>

Little is known about PP absorption, bioavailability, bio distribution and metabolism, although there is probably a common pathway. The aglycones, that is, the non conjugated forms, are generally absorbed intact from the digestive tract, while esters, glycosides, or polymers must be

hydrolyzed before being absorbed. Oral and intestinal microorganisms also are responsible for PP degradation into aglycones and, occasionally, production of various simple aromatic acids. Absorbed PPs are conjugated into methylated, glucuronidated or sulphated derivatives, a metabolic detoxication process common to many xenobiotics. Such mechanisms are so efficient, that aglycones are generally absent or present at low concentrations in blood after consumption of nutritional doses. PPs are detected in many tissues, but mainly in the mucosae of the digestive tract and, principally, the oral mucosa. The best absorbed PPs are isoflavones and gallic acid, followed by flavanones, catechins and quercetin glycosides. The least well absorbed PPs are proanthocyanidins, anthocyanins and galloylated catechins. All PPs are excreted chiefly in the urine and bile.<sup>7, 22-26</sup>

### **Biological properties of polyphenols**

Proanthocyanidin (PA) is a naturally occurring plant metabolite widely available in fruits, vegetables, nuts, seeds, flowers and barks.<sup>27</sup> As a bioflavonoid, it contains a benzene pyranphenolic acid molecular nucleus (referred to as flavin) as part of its much larger molecular structure. PA are a mixture of monomers, oligomers, and polymers of flavan-3-ols (known as catechins), which are ubiquitous in plants. Widely used as natural antioxidants and free-radical scavengers, PAs have been proven to be safe in various clinical applications and as dietary supplements. PA from fruits and herbs has been thought to prevent ischemia/reperfusion damage caused by reactive oxygen species such as superoxides and

peroxynitrites activities, and the acid production by *Streptococcus mutans*.

### **Potential anti-cariogenic actions of grapes, cocoa, coffee and tea beverages and role of their flavonoids**

Proanthocyanidin (PA) is a naturally occurring plant metabolite widely available in fruits, vegetables, nuts, seeds, flowers and barks.<sup>28</sup> As a bioflavonoid, it contains a benzene-pyranphenolic acid molecular nucleus (referred to as flavin) as part of its much larger molecular structure. PA are a mixture of monomers, oligomers, and polymers of flavan-3-ols (known as catechins), which are ubiquitous in plants. Widely used as natural antioxidants and free-radical scavengers, PAs have been proven to be safe in various clinical applications and as dietary supplements.

**Grape Seeds:** Raisins are dried grapes, fruits of *Vitis vinifera* L. (Vitaceae).<sup>29</sup> Today, most raisins are produced from Thompson seedless grapes, which were introduced to California in 1862 by William Thompson.<sup>30</sup> This variety is classified as a raisin-type grape that produces a green, seedless fruit. While dominating raisin production, it is also widely used for fresh consumption and for making juice concentrate and wine as well.<sup>29, 31</sup> The antimicrobial compounds present in raisins capable of suppressing growth and/or virulence properties of oral pathogens have been fractionated and identified.<sup>30</sup> Thompson seedless raisins were chosen in the study because the hexane-soluble fraction of the crude methanol extracts demonstrated growth inhibitory activity against two oral pathogens, the cariogenic *S. mutans* and the periodontopathic *Porphyromonas gingivalis*. PA from grape seed extract (GSE) have been thought to prevent ischemia/reperfusion damage caused by reactive oxygen species such as superoxides and peroxynitrites activities, and the acid production by *Streptococcus mutans*.

**Cocoa:** This is a plant product in the form of a bean. It has three main components such as cocoa liquor, cocoa butter and cocoa powder. The protective effect of cocoa on dental caries is receiving a great concern. The possible protective effect of cocoa on dental caries is receiving attention, but previously published data concerning the anti-cariogenic effects of constituents of chocolate are conflicting.

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. Subsequently it was suggested the possibility that phenolic substances could be responsible of the observed anti-caries effect of cocoa powder.<sup>32</sup>

Moreover it was showed that a water soluble extract of

cocoa 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.<sup>5</sup>

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 significantly reduced biofilm formation and acid production by *S. mutans* and *S. sanguinis*.

**Coffee:** Roasted coffee possesses antibacterial activity against Gram positive and Gram negative bacteria, including *S. mutans*.<sup>33, 34</sup> Moreover *C. arabica* and *C. canephora* extracts interfere with *S. mutans* adsorption to saliva-coated hydroxyapatite beads. Green coffee and roasted coffee showed comparable anti-adsorption 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.<sup>35</sup> 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 hypothesized that this effect could be due to the synergistic action of more chemicals occurring in coffee powder.<sup>36,37</sup>

**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.<sup>38</sup>

Extract obtained from different teas effect 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 glucosyl transferase. Polyphenol (designated Sunphenon) compound 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 was studied in both in vitro and in vivo. Thus feeding of the drinking water containing 0.1% Sunphenon reduced caries incidence in *S. mutans* infected animals.<sup>39</sup>

## CONCLUSION

The studies carried out in these last decades have supported the antibacterial role of polyphenols from grapes, 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* species 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.

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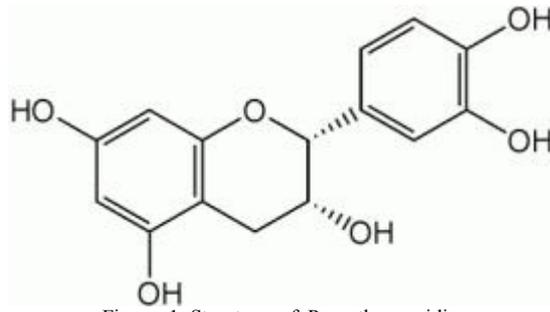
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Table I. Folk medicinal uses

Botanical name	Country	Uses description	Part used	Preparations
Vitis vinifera (Grapes)	European grapes (Vitis vinifera)	used as natural color ,food , treat diarrhea, heavy menstrual bleeding and uterine hemorrhage, anti oxidant activity. reduce the risk of coronary heart disease, vascular complications in <u>diabetic</u> patients, anticancer phytochemicals and antibacterial and antiviral activities	Grape skin extract Grape seed extract	Fermented extracts used to prepare wine.
	North American grapes (Vitis labrusca and Vitis rotundifolia)		Grape skin extract Grape seed extract	Used to prepare decoction , dried seeds powder used in capsules
Theobroma cacao L. (Cocoa)	Thailand	1) Taken orally as a cardiotonic & neurotoni; 2) taken orally as an antifungal	Crushed seeds	1) 2) Hot water extract
	Mexico	Aphrodisiac	Seed	Not indicate
	Venezuela	For kidney and other urinary problems	Not indicate	Not indicate
Coffea arabica L. (Coffee)	Latin	Is applied to wrinkles in the hope of correcting them	Cocoa butter	Not indicate
	America	Preparing aerated drinks	Dried seeds	Easy preparation with CO <sub>2</sub>
	Latin	Remedy for alopecia, burns, cough, dry lips	Not indicate	Not indicate
	America	eyes, fever, listlessness, malaria, nephrosis, parturition, pregnancy, rheumatism, snakebite, and wounds	Not indicate	Not indicate
	West Indies	1)is taken orally for a asthma; 2) is taken orally for scorpion sting	1) Seed; 2) root	1) Hot water extract; 2) Juice
Camellia sinensis L. (Tea)	India	1) Taken orally for headache & 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
	Mexico	Taken orally by nursing mothers to increase milk production	Leaf	Hot water extract
	Turkey	To treat diarrhea	Leaves	Are taken orally
	China	Taken orally as a sedative, an antihypertensive, & anti-inflammatory	Dried leaf	Hot water extract
	Guatemala	Used as eyewash for conjunctivitis	Dried leaf	Hot water extract
	Kenya	1) Applied ophthalmically to treat Corneal opacities; 2) used for chalzion and conjunctivitis.	1) Dried leaf; 2) not indicated	1) Water extract; 2) infusion

Table II – Total antioxidant capacity of various plant foods and beverages, assessed as Trolox – a water soluble vitamin E analogue – equivalent antioxidant capacity (mmol Trolox per kg of food or l of beverage). <sup>19</sup>			
Food/beverage	Trolox/kg or l	Food/beverage	Trolox/kg or l
Spinach	8.5	Cola	0.1
Pepper	7.6–8.4	Black tea	3.6
Broccoli	3.0	Green tea	6.0
Carrot	0.4	Coffee (espresso)	36.5
Potato	0.8	Coffee (soluble)	32.5
Tomato	1.7	Beer (lager)	1.0
Blackberry	20.2	Cognac	1.3
Grape	2.5–3.9	Whiskey	1.7
Olive	10.4–14.7	Rum	<0.1
Pineapple	9.9	White wine	1.6–1.9
Strawberry	10.9–11.3	Rose' wine	1.5–2.4
Orange juice	3.0	Red wine	9.0–12.1



Figure\_1\_Structure\_of\_Proanthocyanidin