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ROLE OF POLYPHENOL IN DENTISTRY AND GENERAL HEALTH

Dentistry

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ABSTRACT

Polyphenols have gained much interest recently due to its anti-oxidant capacity and possible benefits to human health such as anti-carcinogenic, anti-atherogenic, anti-ulcer, anti-thrombotic, anti-inflammatory, immune modulating, anti-microbial, vasodilator and analgesic effects. Polyphenols constitute one of the most common groups of substance in plants. Polyphenol compounds have been reported to have wide range of biological activities, many of which are related to their conventional antioxidant action; however increasing scientific knowledge has highlighted their potential activity in preventing oral disease, including the prevention of tooth decay, oral ulcers, oral cancers, gingivitis, periodontitis and halitosis.

KEYWORDS

Polyphenols, anti-oxidant, biological activity

Review of Polyphenol in Dentistry and General health:

1. Polyphenols are regular components of human diet and are associated with several beneficial health effects. [1] Many polyphenols have been identified in plants which are classified as flavonoids, phenolic acids, stilbenes and lignans depending on their chemical structures. They possess several biological activities including **antioxidant, antibacterial, antiviral, immunomodulatory**, **antiinflammatory, antiallergic, antimutagenic, antiviral, antineoplastic**, **antithrombotic,** and **vasodilatory** activities. The most prominent activity of polyphenols is expressed to be their antioxidant activities against oxidative stress related with their ability to scavenge hydroxyl radicals, superoxide anions, and lipid peroxy radicals.[2]

2. Epidemiological studies have revealed that there are strong associations between the consumption of polyphenols and prevention of certain **metabolic diseases.** Oxidative damage is implicated in a number of diseases including **cancer**, **cardiovascular** and **neurodegenerative diseases** and polyphenols act in these cases as antioxidants with different mechanisms of actions. The role of free radicals, including the superoxide radical (O2 −), hydroxyl radical (.OH), hydrogen peroxide (H2O2), and lipid peroxide radicals have been implicated in **cancer**, **cardiovascular disease**, **diabetes**, **gastrointestinal inflammatory diseases**, **liver disease**, and also in **aging**. [3]

3. Catechin and its derivatives, oligomeric proanthocyanidins, quercetin and quercetin chalcone, ginkgo polyphenols, silymarin, and others can be utilized in preventative and treatment protocols for **cardiovascular disease, cancer, and liver diseases.** Regular consumption of isoflavones such as genistein found in soy reduced **arteriosclerosis** and certain cancers since they have the capability to act as phytoestrogens.[4]

4. The prevalence of **obesity** and related **metabolic complications** with morbidity has increased dramatically in recent years. **Diabetes and obesity** are major risk factors for **cardiovascular diseases**, several forms of **cancer** (such as colon and prostate) and **metabolic diseases**. High polyphenol and selectively-restricted probiotic diet is proposed as a regimen by nutritionists for maintaining normal body weight and this type of diet has attracted great attention recently. The anti-obesity effect of green tea catechins is particularly attributed to Epigallocatechin Gallate (EGCG), which exhibits its antiobesity effects through suppression of adipocyte differentiation and proliferation, inhibition of fat absorption from the gut, and suppression of catechol-o-methyltransferase (COMT) enzyme that inhibits fatty acid oxidation in brown adipose tissue.[5]

5. The administration of purified anthocyanins from blueberries were reported to lower serum triglycerides, cholesterol and leptin levels. Different mechanisms were suggested to explain the effects of polyphenols on the **lipid metabolism** however the exact mechanisms are still unknown [6]

6. Dietary polyphenols, have **antioxidant** and **anti-inflammatory** properties via modulating different pathways, such as NF-κB-, mitogen activated protein kinase-dependent signaling pathways and thereby regulating metabolism, stress resistance, cellular survival, cellular senescence/aging, inflammation-immune function.[7]

7. Resveratrol has been suggested to **increase glucose uptake** through up-regulation of estrogen receptor-α, and increase GLUT 4 expression through phosphatidylinositol-3 kinase and AKT pathway. Through up-regulation of SIRT 1, resveratrol is denoted to help mitochondrial biogenesis, oxidative phosphorylation, and suppress lipid accumulation. [8]

8. Inflammation is a free radical involved process. The enzymes cyclooxygenase and lipoxygenase which oxidize arachidonic acid in cell membranes form potent pro-inflammatory metabolites, including prostaglandins, leukotrienes, and thromboxanes. Polyphenols quercetin, rutin, kaempferol, curcumin, and silymarin exhibit inhibition of cyclooxygenase and lipoxygenase *in vitro*. In addition, polyphenols can induce antioxidant enzymes such as glutathione peroxidase, catalase and superoxide dismutase which protect the cells by decomposing hydroperoxides, hydrogen peroxide and superoxide anions, respectively. They can also inhibit the expression of enzymes such as xanthine oxidase. [9]

9. Polyphenols can also contribute to health by **inhibiting the platelet aggregation** where the 3,4-dihydroxyphenylacetic and 4-hydroxyphenylacetic acid metabolites were found to be more active than their precursors rutin or quercitin. [10]

10. Polyphenols concentrations in plasma are low as usually less than 1 μmol/L in part because of rapid metabolism by human tissues so the activities of the metabolites gain important attention to reveal the beneficial effects of polyphenols. Understanding the mechanisms of actions of polyphenols and their metabolites either as antioxidants or modulators of cell signaling will help to evaluate the modulators in metabolic diseases. The metabolites formed in the small intestine and hepatic cells, and low molecular weight catabolic products produced by the colonic microflora carries critical interest for drug discovery and also for dietary prevention of disease including metabolic diseases. [11]

11. Interestingly, using an aged mouse model of accelerated senescence (SAMP10 mice). It was demonstrated that green tea catechins, when administered in drinking water, have a protective effect on cognitive dysfunction and suppresses cerebral atrophy in these animals. Furthermore, green tea also decreases the levels of 8-oxo-deoxyguanosine (8-oxodG), a marker of oxidative DNA damage, in the kidney, liver and cerebrum, suggesting that green tea polyphenols may have a beneficial effect on the damage from the **aging process**. [12]

12. Oxidative stress is believed to be a major contributor to the pathogenesis of **Parkinson's disease**, especially the death of dopaminergic neurons. Recently, misregulated iron metabolism in the brain has been shown to be involved in the generation of the pathological Lewy bodies in Parkinson's disease through iron-induced

aggregation of alphasynuclein. In well-established animal models of Parkinson's disease, neurotoxins 1-methyl-4- phenyl-1,2,3,4-tetrahydropyridine (MPTP) and 6-hydroxydopamine (6-OHDA) induce dopaminergic cell death and accumulation of Lewy bodies, mediated through several mechanisms involving oxidative stress. Various studies have shown that green tea and EGCG significantly prevent these pathologies in animal models. EGCG, administered orally in doses as low as 25 mg/kg, prevented loss of dopaminergic neurons in the substantia nigra and preserved striatal levels of dopamine. Recently, it is also showed that EGCG prevented the accumulation of iron and alpha-synuclein in MPTP-treated mice. These effects have been attributed to the antioxidant activity and iron-chelating properties of EGCG, respectively.[13]

13. Although there is no epidemiological evidence in human studies of the benefit of green tea for Alzheimer's disease, several studies in animal and cell culture models suggest that EGCG from green tea may affect several potential targets associated with **Alzheimer's disease** progression. It was showed that EGCG protects against beta-amyloid induced neurotoxicity in cultured hippocampal neurons, an effect attributed to its antioxidant properties. In addition, studies recently showed that EGCG regulates the processing of APP, through PKC activation, to the nonamyloidogenic soluble APP (sAPP), thus preventing the formation of the neurotoxic beta-amyloid.

EGCG and other green tea catechins have also been shown to inhibit the betasecretase enzyme (BACE1) that is responsible for processing sAPP to beta-amyloid, thus having a potentially synergistic inhibitory effect on the production of beta-amyloid. Thus, the inhibitory effect of green tea catechins on Alzheimer's disease targets and the neuroprotective effect of their antioxidative activity strongly suggest that these catechins have potential application in the treatment of Alzheimer's disease. [13]

14. Stroke - EGCG show to afford protection against neuronal damage after ischemia in gerbils, when administered systemically at 50 mg/kg immediately after excitotoxic ischemic insult. At this dose, EGCG also exhibits a significant antioxidant effect in rats and protected against neurological deficit and infarction due to the focal ischemia, when administered 24 h after a transient cerebral occlusion. When administered in drinking water days before ischemic damage in rats, green tea extract also has an antioxidant effect and protects against neurologic deficits suggesting that drinking green tea can have neuroprotective benefits, and that EGCG may also have application as a neuroprotective agent against acute ischemic damage. [12]

Since the evidence of therapeutic effects of dietary polyphenols continues to accumulate, it is becoming more and more important to understand the nature of absorption and metabolism *in vivo*. Moreover the identification and measurement of the physiologic polyphenol metabolites represent a key prerequisite for the understanding of the role of dietary polyphenols in human health.

- Regular consumption of foods/ beverages containing polyphenols may help prevent oral cancer effectively.
- With regard to dental diseases, studies on humans are needed to confirm the promising results provided by many experimental studies.
- Better knowledge of structure, dose and bioavailability of dietary polyphenols will be essential in the future to properly evaluate their role in the prevention of oral diseases.

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