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Review Paper

Tannins: An Antinutrient with Positive Effect to Manage Diabetes

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Abstract

Plant tannins, including hydrolysable and condensed varieties, are well known antioxidants in medicinal plants, foods, and edible fruits. Phenolic compounds and flavonoids are a unique category of plant phytochemicals especially in terms of their vast potential health-benefiting properties. Tannins are potential antioxidants. They have been considered to be cardio-protective, anti-inflammatory, anti-carcinogenic and anti-mutagenic, among others. Tannins enhance glucose uptake and inhibit adipogenesis, thus being potential drugs for the treatment of NIDDM. Tannins can improve the pathological oxidative state of a diabetic situation. Many earlier studies suggested that phenolic compounds and flavonoids protect against many types of cancer. In particular, phenolic compounds have been reported to modulate intracellular signalling through PI3K and p38 MAPK pathways, modulating the activity of target enzymes and modulating gene expression. Condensed Tannins have a wide range of biological and pharmacological activities including antioxidative, cardio-protective, antitumor, antibacterial, antiviral, anti-inflammatory and immune-modulatory. These specific phytochemicals provide a promising area of research for future human studies and potential nutraceutical for disease prevention and treatment.

Keywords: Tannin, phenol, phytochemicals, antioxidants, nutraceutical.

Introduction

Plant tannins, one of the major groups of antioxidant polyphenols found in food and beverages, have attracted a lot of attention in recent years because of their multifunctional properties beneficial to human health. Deriving its name from the technical word 'tanning' that meant converting animal hides to leather through chemical processes; tannin is basically used for this function. It is found in abundance in the tree bark, wood, fruit, fruit pod, leaves, and roots and also in plant gall. Tannin is defined as "Any phenolic compound of sufficiently high molecular weight containing sufficient hydroxyls and other suitable groups (i.e. carboxyls) to form effectively strong complexes with protein and other macromolecules under the particular environmental conditions being studied"[1]. Tannins can be classified into two broad groups - hydrolysable tannins and condensed tannins/ Proanthocyanidins (PA). Hydrolysable tannins (HT) are molecules with a polyol (D-glucose) as a central core. The hydroxyl groups of these carbohydrates are partially or totally esterified with phenolic groups like gallic acid (gallotannin) or ellagic acid (ellagitannin). Hydrolysable tannins are usually present in low amounts in plants. HT are easily hydrolysed by mild acids and bases to yield carbohydrate and phenolic acids. Condensed tannins (PA) are a group of naturally occurring polyphenolic bioflavonoids, specifically taking the form of oligomers or polymers of polyhydroxy flavan-3-ol units, such as (+)-catechin and (-)-epicatechin[2] and flavan-3,4-diols, such as leucoanthocyanidins or a mixture of the two. Catechin has two symmetric carbon atoms resulting in 4 optical isomers (+) catechin, (-) catechin,(+) epicatechin and (-) epicatechin. Of these, (+) catechin and (-) epicatechin occur in nature.

Consumption

Condensed tannins/PA are more widespread in the plant kingdom than hydrolysable tannins. Consumption of tannin-containing food products varies from region to region. Legumes and beans, staples in many countries, contain large quantities of condensed tannins[3,4]. Sorghum, which contains between 0.13-7.2% condensed tannin, is a common food staple in Asia, Africa, and countries in the Near and Middle East[5]. The North American diet, which is relatively poor in grains, legumes and fruits contain much less tannin. It has been reported that tannin consumption in India ranges from 1.5- 2.5 g/day, depending on the region, and about 1g/day within the USA[6]. Of the two types of tannins, condensed tannins are also more resistant to microbial decomposition than hydrolysable tannins. The daily intake of catechin and proanthocyanidin dimers and trimers has been estimated to be 18–50 mg/d, with the main sources being tea, chocolate, apples, pears, grapes and red wine[7].

Sources: Condensed Tannin: Coffee, tea, wine, grapes, craneberries, strawberries, blueberries, kathaa (Acacia catechu), supari (Areca catechu), apples, apricots, barley, peaches, dry fruits, mint, basil, rosemary etc.

Hydrolysable Tannin: Pomegranate, strawberries, raspberries, aonla (Emblica officinalis), clove, barley, rice, oat, rye etc.

Mechanism for Lowering Blood Glucose levels

Condensed tannins are widely distributed in fruits, vegetables, forage, plants, cocoa, red wine, and certain food grains, such as sorghum, finger millets, and legume. Most of the early reports related to the anti-nutritional effects of tannins were centered on tannic acid and other hydrolysable tannins. However, as hydrolysable tannins are present only in trace amounts in commonly consumed foods, the more predominant condensed tannins are of more concern due to their anti-nutritional effects of tannins. The implication of food tannins on human health is a public concern, but it has preventive benefits to health also, some tannins are antioxidants. They have been considered to be cardio-protective, anti-inflammatory, anti-carcinogenic and anti-mutagenic, among others. These protective effects are related to their capacity to: (a) act as free radical scavengers; (b) activate antioxidant enzymes. They have been observed to enhance the glucose uptake through mediators of the insulin-signaling pathways, such as PI3K (Phosphoinositide 3-Kinase) and p38 MAPK (Mitogen-Activated Protein Kinase) activation and GLUT-4 translocation. The reduction in glycemia (blood glucose levels) caused by phenolic compounds has been attributed to such actions as a reduction in the absorption of nutrients (*i.e.* tea catechins inhibit intestinal glucose absorption[8]), reduction in food intake (*i.e.* green tea epigallocatechin gallate significantly reduces food intake[9]), induction of β cell regeneration[10] and a direct action on adipose cells that enhances insulin activity[11]. Tannins have also been described as anti-hyperglycemic agents in diabetic rats[12]. Phenolic compounds also modify enzymatic and transcriptional activities. However, the ability of nuclear receptors to modulate a wide variety of genes reveals them to be targets in the treatment of such disorders as diabetes or dyslipemia. Nuclear receptors are implicated in the control of lipid homeostasis. They establish a coordinated net of metabolic sensors which integrates lipid metabolism, inflammation, drug metabolism, bile acid synthesis and glucose homeostasis among other processes[13,14].

Health Benefits

PAs have been reported to have a wide range of biological and pharmacological activities including antioxidative, cardioprotective, antitumor, antibacterial, antiviral, anti-inflammatory and immune-modulatory effects[15,16]. Experimental and clinical studies have shown that proanthocyanidin has an antioxidant effect, antinociceptive and cardioprotective properties, without inducing significant toxicological effects[17,18,19]. While sharing some antioxidant activities with other phenolics, recent works[20, 21] have described the capacity of tannins to enhance glucose uptake and inhibit adipogenesis, thus being potential drugs for the treatment of non-insulin dependent diabetes mellitus. One of the therapeutic approaches for decreasing postprandial hyperglycemia is to prevent or delay absorption of glucose by the inhibition of carbohydrate hydrolyzing enzymes, α-amylase and α-glucosidase, in the digestive organs[2]. Recent studies showed that phenolic phytochemicals from botanical sources are natural inhibitors of α-amylase and α-glucosidase[3-6] with a strong inhibitory effect on α-glucosidase, but a mild inhibitory effect on α-amylase and thus can be used as an effective measure to prevent postprandial hyperglycemia with minimal side effects[4-6]. Therefore, phenolic antioxidant-mediated inhibition of these enzymes can significantly decrease the postprandial hyperglycemia after ingestion of a mixed carbohydrate diet and could be an effective strategy in the control of type 2 diabetes[7].

Most of the active compounds in black tea are tannins which are 90% catechins. Epicatechin is the major component of natural tannin in grapes. The hydrolyzable tannins in aged wines come from the oak barrels, and are mainly composed of gallic acid and ellagic acid esters. Some monomers also lower blood glucose levels and have insulin-like effects[22,23:9,10]. Several mechanisms, depending on the structure studied, have been suggested to explain this effect. Epicatechin prevents hyperglycemia by inducing *β* cell regeneration[10] Epigallocatechin-gallate does so possibly by reducing food intake[9] and in hepatocytes it shares insulin signaling pathways possibly by modulation of the redox state of cell[25]. Tea catechins inhibit intestinal glucose absorption[8]. And finally, another explanation for the effects of some monomers in modulating glucose concentration is (like the demonstrated effects of grape seed procyanidins) direct action on adipose cells, since epicatechin gallate and especially epigallocatechin-gallate, enhance insulin activity in rat epididymal adipocytes[11]. As it was said to flavonoids, the antioxidant properties of tannins are equally responsible for other interesting biological properties. Flavan-3-ols are thought to interfere in the pathogenesis of cardiovascular disease *via* several mechanisms: antioxidative, antithrombogenic, and antiinflammatory. In particular, PAs and flavan-3-ol monomers aid in lowering plasma cholesterol levels, inhibit LDL oxidation, and activate endothelial nitric oxide synthase to prevent platelet adhesion and aggregation that contribute to blood clot formation[24,25]. Daily intake of Green tea polyphenols appears to have multiple health benefits summarized below, including reduced risk of cancer and cardiovascular disease: i. Catechins protect against radiation, including increased survival and decreased incidence of radiation-induced tumors. ii. Catechins have antimutagenic activity against both spontaneous and chemically-induced mutations. iii. Catechins have anti-tumor activity, inducing phase I and II metabolic enzymes that increase the formation and excretion of detoxified metabolites of carcinogens, slowing the rate of cell replication and thus the growth and development of neoplasms, and preventing spontaneous and chemically-induced cancers. iv. Catechins are powerful antioxidants that inhibit oxidation of LDL-cholesterol, reduce cholesterol levels, and reduce body fat, resulting in a decreased risk of heart disease. v. Catechins have regulatory effects on blood pressure and high blood-pressure induced strokes. Individuals consuming more than five cups a day having a 500% decrease in stroke incidence. vi. Catechins have antibacterial activity against food borne pathogenic bacteria and cavity-inducing bacteria, modifying the intestinal microflora, reducing undesirable bacteria and increasing beneficial bacteria. vii. Catechins have an anti-hyperglycemic action, lowering both blood-glucose and normalizing insulin release. viii. Catechins show antiviral effects, inhibiting reproduction of numerous viruses including influenza and human immunodeficiency virus.

Procyanidins are flavonoids with an oligomeric structure, and it has been shown that they can improve the pathological oxidative state of a diabetic situation. The study was conducted on an extract of grape seed procyanidins (PE) which was given orally to streptozotocin-induced diabetic rats. This had an antihyperglycemic effect, which was significantly increased if PE administration was accompanied by a low insulin dose. The antihyperglycemic effect of PE may be partially due to the insulinomimetic activity of procyanidins on insulin-sensitive cell lines. In summary, procyanidins have insulin-like effects in insulin-sensitive cells that could help to explain their antihyperglycemic effect *in vivo.* These effects must be added to their antioxidant activity to explain why they can improve diabetic situations[12]. Increasing interest in the health benefits of tea has led to the inclusion of tea extracts in dietary supplements and functional foods. However, epidemiologic evidence regarding the effects of tea consumption on cancer and cardiovascular disease risk is conflicting. While tea contains a number of bioactive chemicals, it is particularly rich in catechins, of which epigallocatechin gallate (EGCG) is the most abundant accounting for approximately half of the total catechins and also the most powerful of all the catechins with an antioxidant activity about 25–100 times more potent than that of vitamins C and E[26].

Catechins and their derivatives are thought to contribute to the beneficial effects ascribed to tea. Tea catechins and polyphenols are effective scavengers of reactive oxygen species in vitro and may also function indirectly as antioxidants through their effects on transcription factors and enzyme activities. The fact that catechins are rapidly and extensively metabolized emphasizes the importance of demonstrating their antioxidant activity in vivo.. In humans, modest transient increases in plasma antioxidant capacity have been demonstrated following the consumption of tea and green tea catechins. The effects of tea and green tea catechins on biomarkers of oxidative stress, especially oxidative DNA damage, appear very promising in animal models, but data on biomarkers of *in vivo* oxidative stress in humans are limited. Larger human studies examining the effects of tea and tea catechin intake on biomarkers of oxidative damage to lipids, proteins, and DNA are needed[27].

Conclusion

Phenolic compounds and flavonoids are a unique category of plant phytochemicals especially in terms of their vast potential health-benefiting properties. They are widely present in plant foods, and research in the last decade has increased dramatically. The existing literature on cell constituents through direct scavenging of free radicals due to their antioxidant properties. However recent data indicate that the protective effect of flavonoids wine and cocoa products may have positive effects on human health. Many earlier studies suggested that phenolic compounds and flavonoids protect against many types of cancer. In summary, phenolic compounds have been reported to (a) modulate intracellular signalling through PI3K and p38 MAPK pathways; (b) modulating the activity of target enzymes (*e.g.* nitric oxide synthase); and (c) modulating gene expression. Therefore these specific phytochemicals provide a promising area of research for future human studies and potential utility for disease prevention and treatment.

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