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Condensed Tannins: Its Various Perspectives as a Vital Bio-Metabolite

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ABSTRACT

Tannins are maximally available phytoconstituents in the plant kingdom, where they function as a protective and regulate plant growth. Different types of condensed tannins carry a huge potential as pharmaceutical agents as well as pharmaceutical aid. The tannins are important and efficacious chemicals for tanning, absorption of minerals, and precipitation of proteins. These are also used for the production of ink and adhesives. Presently, tannins are being considered as important nutritives. The solicitation of tannins as medicine is another new dimension. These paper frameworks are the general evidences about tannins, different condensed tannins, the other multiple benefits and utilization of tannins. The potential world supply of tannins is huge. Pharmaceutical procedures of tannins are successfully adopted. Applying tannins in the beverage industries including beer, fruit juice, or wine is more functional. Tannin-based foams, more developed phenolic type, is a fast-moving research field. A substantial amount of research is still continuing in this area and some trials, too.

Keywords: *Tannins, Catechins, Applications, Astringents, Potential*

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INTRODUCTION

Tannins are a class of polyphenolic phyto-metabolite, with the eminence to bind and precipitate proteins, and alkaloids. Tannin term is derived from the tanning procedure of hides to provide leather, by this secondary metabolite. Tannins are heterogeneous, high molecular weight, water-soluble, polyphenolics in seeds of legumes, fruits and vegetables, where they protect against biotic and abiotic stressors. They are white to buff colored amorphous powders, or glossy, pasty substances, to reddish-brown powders. Tannins are in the form of powder, flakes, or masses, used mainly as antimicrobial, antioxidant, and in form of neutraceuticals (McDonald *et al.*, 1996). Tannins, readily complexes with alkaloids, polysaccharides, and proteins. Tannins display antioxidant properties, in free radical scavenging activity as well as possess antimicrobial, and cardio-protective potential (Ding *et al.*, 2001). They also seem to cure metabolic disorders and prevent several stress-related diseases. Tannins also suggest multiple applications in food, wood, leather industries as possible raw material for tanning leather, dyeing fabric, making ink, apart from core pharmaceutical uses Tannins are known as bactericides because they complex within bacterial membranes, killing their activity (McDonald *et al.*, 1996). Tannin-based medicinally important derivatives are used to cure intestine infections. Its solutions are acidic in nature with astringent taste. Tannins are, widely distributed in plants, providing particular astringency, aroma in different species of Tea (Ding *et al.*, 2001). They do occur normally in the roots, wood, bark, leaves, fruits, particularly in the bark of oak species as in **Figure 1**.

Figure 1. Bark of Oak Species

They occur as pathological growths resulting from attack of insects. Tannins are flavonoid category polymers, reserved in vacuoles. Many tannin enriched powders as in **Figure 2**; decrease the mutagenic activity caused by mutagens (Manosroi *et al.*, 2010).

Figure 2. Tannin Powder

Tannins are valuable secondary metabolites, required for the well-being of human beings. The growth of many microbes is inhibited by tannins, therefore is used as vital anti-microbial agent. Tannic acid and propyl gallate were found cidal for different species of bacteria (Aneja *et al.*, 2012). They may exert their biological effects in many manners as in **Figure 3**, as non-absorbable, which helps it to act in the gastrointestinal tract in the form of antioxidants, anti-microbial, and as an anti-mutagenic (Ogawa & Yazaki, 2018).

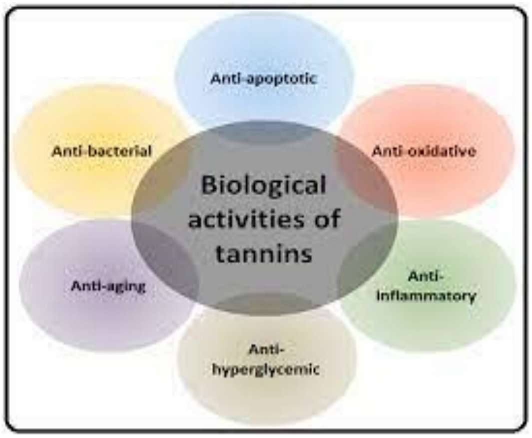

Figure 3. Activities of Tannins

MATERIALS AND METHODS

Literature was reviewed in a narrative manner in order to pertain the information about active tannins present in the different plants and their different aspects. The search was done on Google scholar, MEDSCAPE, BMC, Science Direct, MEDLINE database, SCOPEMED and other relevant databases, using keywords Tannins, Catechins, Applications, Astringents, Potential, with the help of reviews, researches, findings of seminars, conferences, symposiums etc.

Proanthocyanidins

Condensed tannins as proanthocyanidins, poly-flavonoid catechol-based tannins, designed by the compression of diverse flavones joined by carbon-carbon non hydrolyzable bonds. Its extract comprises of flavonoid oligomers, in form of flavan-3-ols, flavan-3,4-diols (Choubey *et al.*, 2018). Due to the occurrence of a bigger quantity of phenolic rings, are soluble in water, alcohol, and acetone and can coalesce proteins (Shi *et al.*, 2020). They are principally initiated by water extraction from wood and bark (Sieniawska, 2015). Proanthocyanidins, exist in seeds, nuts, fruits, bark, and flowers as a resistance alongside abiotic and biotic stressors. Their astringency prevents from predators and pathogens. Tannins, mostly proanthocyanidins, are one of the mostly present ingredients in daily ingested food. Epi-catechin is the most profuse, trailed by catechins and type B-procyanidin. The building elements of proanthocyanidins are catechins and epi-catechin (Kim *et al.*, 2014). Phenolic compounds complement to the quality of substances, due to organoleptic qualities and oxidative stability. They in the form of Flavonoids, like anthocyanins and flavan-3-ols all play important role in the Wine Industry. Anthocyanins are pigments found in the skin of grapes, responsible for red wine colour (Kamiloglu *et al.*, 2016). Astringency is a composite development concerning many mechanisms as an upsurge in connection amongst tannins and proteins of epithelium. Proanthocyanidins dimers are common, often convoyed by oligomer condensed tannins (Motta *et al.*, 2020). These compounds break in acidic alcoholic settings to give red pigments called Phlobaphenes. Proanthocyanidins show free-radical scavenging and antioxidant activities (Fraga & Oteiza, 2011). Catechins and epi-catechin are mainly, responsible for astringency. Procyanides, as oligomer of catechins and epi-catechin monomers, are prevalent in foods as significant medicinal derivatives (Fathima & Rao, 2016). Proanthocyanidins are known to impede lipid peroxidation and lipoxygenases to reestablish the oxidative balance of the body (Brenes *et al.*, 2016). Some procyanidins such as procyanidin B1 and procyanidin B3 are tougher antioxidants than ascorbic acid or α-tocopherol (Okuda & Ito, 2011; Xie *et al.*, 2018).

Catechins

Catechins are type of phenolics present in foods comprising antioxidants, as in **Table 1**. Eighty percent of all polyphenols of green tea are backed by catechins. It is a naturally occurring Flavonol, which is the tannic juice or boiled extract of Acacia catechu (Takemoto & Takemoto, 2018). They are constituent of Ficus mucuso, Ficus gnaphalocarpa, Ficus cordata, and Khaya grandifoliola, and are very abundant in tea, cocoa, and berries, especially as epigallocatechin-3-gallate (Mazzanti *et al.*, 2015). The four main catechins that occur in green tea are (-)-epi-catechin (EC), (-)-epicatechin-3-gallate, (-)-epigallocatechin, and (-)-epigallocatechin-3-gallate (Ozdal *et al.*, 2016). Catechins help to prevent cell damage and suspends free radical formation in the body, shielding cells and molecules from damage. These free radicals play an important role in aging and many types of diseases (Cao *et al.*, 2020). Tea polyphenols and catechins are influential chemical agents of reactive oxygen varieties in vitro and act mediately as oxygen inhibitors via affecting the transcription. Catechins have proven to modulate apoptosis, by modifying the expression of pro-apoptotic genes (Giovando *et al.*, 2019; Kuriya *et al.*, 2020). Catechins, as kinds of polyphenols, are free radical chemical agents due to the usual phenolic hydroxyl groups' chemical composition in polyphenols, in which catechin effectively liberate the radical scavenger. Many act as powerful oxygen inhibiting functions in the cardiovascular system. The impacts of green tea on cancer chemoprevention have been related to its oxygen inhibiting functions (Liao *et al.*, 2020).

The consumption foods rich in catechins with the anticipation of chronic diseases, such as inflammatory bowel diseases are validated in several studies (Choi & Shin, 2016). Catechins affect the molecular mechanisms involved in angiogenesis, multidrug resistance in cancers, etc. present majorly in green tea as crude medicine and daily beverage in Asia, specifically in Japan and China (Choi & Shin, 2016). Blackberries, broad beans, apples, cherries, black grapes and raspberries are rich in them (Nagle *et al.*, 2006). Cumulative studies specified that the catechins that belong to polyphenols influenced the antimicrobial ability as could remarkably kill specific pathogenic bacteria, including Pseudomonas, Xanthomonas, Agrobacterium spp. and Clostridium perfringens (Singh *et al.*, 2011; Romero *et al.*, 2020).

Table 1. Catechins and Epi-catechin Concentrations in Foods

S.No	Source	Flavonol content
1.	Chocolate	460-610
2.	Beans	350-550
3.	green tea	100-800
4.	Apricots	100-250
5.	Red wine	80-300
6.	Black tea	60-500
7.	Cherries	50-220
8.	Apple	20-120
9.	Peach	50-140

Epi-Catechins

The Flavonol epi-catechin, is the most profuse flavonoid present in various fruits such as blackberries, cherries, grapes, apples, etc. Catechins hold two benzene rings and a dihydropyran heterocyclic ring (Spennati *et al.*, 2019). There are two isomers in Trans configuration that are called catechins and there are other two isomers in cis configuration, namely epi-catechin (Filgueira *et al.*, 2017). Epi-catechin is one of the most profuse flavonoid in pears, cocoa, and tea leaves. High contents of epigallocatechin, epi-catechin gallate, and epigallocatechin gallate exist in green and black tea (Borisova *et al.*, 2019). Catechins metabolites are accountable for this effect on blood vessels. Epi-catechin can mend numerous constraints of visceral fat inflammation (Arina & Harisun, 2019).

Gallocatechin

Gallo-catechins is catechin, substituted by hydroxyl groups at positions 3, 3', 4', 5, 5' and 7, the trans isomer, from *Acacia mearnsii*. It is a catechin and a flavan-3, 3’, 4’, 5, 5’, 7-hexol, or a flavan-3-ol, with the gallate residue as an isomeric substitution. Epi gallocatechin is another type of catechin, with the gallate residue as an isomeric cis position (Aguerre *et al.*, 2020). The anthocyanidin from catechins or epicatechin is cyanidin so that the equivalent polymers are selected as procyanidins and prodelphinidins, respectively (Rajput *et al.*, 2018). Tea catechins, had positive effects on bone metabolism (Grenda *et al.*, 2020).

Epi gallocatechin

Epigallocatechin gallate, that is called epigallocatechin-3-gallate, too, is a type of the ester of epigallocatechin and gallic acid and catechin. EGCG, is the highly ample catechins in tea. Epigallocatechin is a flavan-3,3',4',5,5',7-hexol (Santos-Buelga et al, 2019). It is an antioxidant, a plant metabolite, and a food component. It is an enantiomer of a (+)-epi gallocatechin, as a powerful compound that may benefit health by reducing inflammation and averting definite long-lasting ailments (Fazio *et al.*, 2018). It is a plentiful polyphenol extracted from green tea (Sharma, 2019). Various catechins exist in green tea that the most profuse of them is EGCG , responsible for above 50% of the catechins, in addition to (−)-epigallocatechin (EGC), (−)-epi-catechin (EC), epicatechin-3-gallate (ECG), and (+)-catechins (Sharma, 2019).

Catechin gallate

Catechin-3-O-gallate is a gallate ester obtained by formal condensation of the carboxyl group of gallic acid with catechins. It is a polyphenol, and a member of flavans. It derives from Gallic acid and a (+)-catechins. It is a flavan-3-ol, a kind of flavonoid, existing in green tea, buckwheat and grape**.** These compounds are antioxidants. Beneficial effects of green tea polyphenols are in the preclusion or conduct of cardiovascular, hepatic, pulmonary, and intestinal diseases, cancer due to its antioxidant and anti-inflammatory stuffs. Catechins disable proteins and affect the membrane of the target cell, and are much more active against Gram-positive than Gram-negative bacteria (Ogawa *et al.*, 2018).

Gallocatechin gallate

The catechin EGCG is the main flavonoid compound of green tea**.** It is the ester of Gallic acid and gallocatechin, epimer of epigallocatechin gallate. Its epimer gallocatechin gallate is more firm and bioactive, even when minimum contained in green tea. They are commonly found in chocolate, cocoa, coffee, cranberries, legumes, nuts, green grapes, and tea. It is the highly plentiful and influential antioxidant existing in green tea (Nardeli *et al.*, 2019).

Mechanism of action of tannins

Anti-ulcer effect

The astringent action of tannins is the defense mechanism as protective natural predators as healing action in cases of gastritis, treatment of diarrhea which is due to anti-oxidant action, the capability of tannins to chelate metals, and antibacterial actions**.** Phenolic compounds have proved to show vascular protective action thus maintaining the flow in gastric mucosa. Histopathological studies have shown proliferation of fibroblast and epithelization. Tannins have also proved angiogenesis thus healing wounded tissues (Zeng *et al.*, 2019).

Chronic diseases

Many systematic reviews and meta-analysis reports have shown that human and animal studies have noted that proper consumption of tannins prevents the onset of many chronic diseases (Zhang *et al.*, 2019).

Anti-microbial action

The anti-bacterial action of tannins was noted in the case of plasma coagulation by Staphylococcus aureus. Some tannins like methyl gallate, Tannic acid, and propyl gallate were noted to show inhibition in the intestinal bacterial growth of Clostridium clostridiiforme ATCC 25537, C. paraputrificum ATCC 25780, Enterobacter cloacae ATCC 13047, S. typhimurium YG1041, etc. in a culture broth of 100-1000 microg/ml (Zhou *et al.*, 2019).

Radical scavenging and antioxidant activity

Hydrolyzable tannins and Proanthocyanidins tannins show radical scavenging activity which is majorly reliant on on their structure and their anti-radical effect is due to the increased degree of polymerization (Smeriglio *et al.*, 2017).

Antiviral activity

Tannins can attack numerous targets. This effect has been noted when Herpes simplex virus radiolabelled particles showed that galloylated condensed tannins and hydrolyzable tannins worked by inhibiting the absorption of the virus**.** Anti-herpes action was majorly dependent on the hexahydroxydiphenoyl or galloyl groups and its action was significant with the degree of condensation Anti-HIV action was seen in agrimoniin, coriariin A, and dimeric ellagitannins oenothein B. This activity was mediated due to adsorption inhibition of the virus (Lai *et al.*, 2016).

Skin-tumor promotion

Mice-bearing tumors induced by DMBA were treated with epigallocatechin gallate complex tannin. Around 50% reduction in tumors in mice that were treated in combination with EGCG were observed. Anti-tumor action was also noted for C-glucosidal ellagitannin monomer, alienanin B, tenophyllanin A in two stages of carcinoma in mice hence suggesting that other tannins also possess anti-tumor action (Soboleva *et al.*, 2020).

RESULTS AND DISCUSSION

Tannins are being considered as important nutritives. The solicitation of tannins as medicine is another new dimension. Different types of condensed tannins, being rich phytoconstituent, carry unique structural diversity and are known for multiple benefits and utilization. The potential world supply of tannins is huge. Pharmaceutical procedures of tannins are successfully adopted. Applying tannins in the beverage industries including beer, fruit juice, or wine is more functional. being accepted universally is an as anti-oxidant, while in non-pharmaceutical, the major industrial application of vegetable-based tannins is tanning. Many more resarch and exploration about tannins is the need of present era.

CONCLUSION

Condensed tannins and their multiple forms as catechins have the potential for use in anti-bacteria, antioxidative, and anti-inflammatory function. Because of the disequilibrium between the antioxidant system and oxidation system by the direct or indirect anti oxidative impacts, that depend on the condensation, catechins, as oxygen inhibitors, are capable to prevent tissue and cell damage. In addition, they can hinder penetration and growth of immune-related cells and adjust ignition and oxidation contractions through interacting with oxidative stress-related pathways, includingNF-κB,Nrf2, and STAT1/3 pathways, contributing to the decrease of the secretion, and reaction of cytokines, chemokine's, pro-inflammatory cytokines. Through instruction of cell gap junctions, catechines can hinder worsening of gastrointestinal lesions and their turning into cancer. Moreover, they can stabilize intestinal flora. Further researches are required to investigate the exact functions and probable mechanisms, even at the molecular level.

Future prospects

There is enormous potential stored in tannins, as mainly the various forms and application of tannins to carry the dynamic future potential for various possible further advances. Among all the applications, major medicinal application, being accepted universally is an as anti-oxidant, while in non-pharmaceutical, the major industrial application of vegetable-based tannins is tanning. The second highly signifiant use of vegetable tannins is in producing wood adhesives. Synthetic formaldehyde-based resins have shown the desire in applying tannins. The tannin adhesive technology is more advanced. Utilization of tannins in the beverage industry, including fruit juice, beer, and wine is more common and completely functional. The more developed phenolic type that is tannin-based foams, is a reckless-affecting research field. Further studies as well as some industrial trials are still being done in this area . Eventually, ferric inks, the major source of writing inks for past centuries, are considered as phenolic types (Tairova *et al*., 2020).

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