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REVIEW ARTICLE

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## Pharmacological and Therapeutic Applications of Novel Tannins

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### ABSTRACT

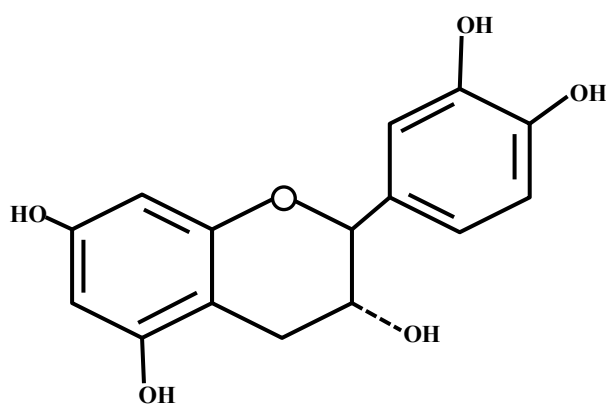
*Tannins are hydrophilic compounds that are commonly present in the dietary compound and several types of plants. Synthetic tannins are utilized as a barrier against some infections and diseases such as itchy, inflamed, weeping, cancer, diabetes, and other fatal diseases. Tea polyphenols and several types of tannins work as a barrier against carcinogens so they showed the anti-carcinogenic activities. On the other hand, consuming the high dose of tannins believed to cause cancer that's mean tannins can show the activities as carcinogens. In this article, we focus on metabolic pathways by different types of tannins and their medicinal or industrial benefits. Review also focuses on the medical importance of tannins including anti-microbial, anti-viral, anti-inflammatory, anti-cancer, anti-mutagenic, and anti-oxidant, etc. Despite their beneficial activity, tannins show some harmful activities such as they work as a carcinogenic factor.*

**Key Word:** Hydrophilic, Polyphenols, Carcinogenic, Dietary compound and Synthetic tannins.

### INTRODUCTION

"Tannin" was coined by Seguin to clarify the substances present in vegetable extracts, they are the type of 'astringent, and polyphenols of sour plants that answerable for the bind and precipitate the proteins (Praveen et al. 2012). The name of tannins is taken from the French word 'tannin' that designates the mean the chain of natural polyphenols. Tannins unit originated brownness power type and were seen like sponge. It's a marvel that the tannins square measure created from each sort of plants in several ambiances worldwide. Tannins square measure typically found in huge quantities at intervals the bark of trees where they act as a barrier for micro-organisms and defend the tree. They're put together used in coloring, photography, process brewing, and wine furthermore as an astringent in medicines. Significantly, tannins blood group major factor of tea (Nonaka et al. 1981). They're put together used as refinement materials to precipitate proteins in wines and brew. As tannins usually minor the absorption of many provides into the body, tannins are typically noted as anti-nutrients (Ricardo et al. 1991).

Tannic acid analysis thus started, applying new analytical ways in which have disclosed the distribution of varied polyphenolic compounds of varied chemical structures contained in several species of healthful plants (Okuda et al., 1989). At intervals, the new approach tannins square measure divided keep with their structural characteristics into four most vital groups: gallotannins, ellagitannins, advanced tannins and condensed tannins (Khanbabaei et al. 2001). There square measure tons of drug information that advocate that tannins unit useful in external treatment of skin inflammation and injuries that intake of tannins may stop the onset of chronic diseases (Serrano et al. 2009). Tannins square measure known to inhibit lipid per chemical effect in vitro and contain the facility to scavenge free radicals important in cellular prooxidant states. Most of the actions of tannins, along with their free radical-scavenging capability, principally rely on their structure and degree of activity (Okuda et al. 2005; Jerez et al. 2007). The astringent like tannins is because they'll precipitate proteins and render them proof against accelerator attack. Once applied on a wound or injury, tannins blood group protective coating so on stop external irritation and then promote healing. In this literature specifically shown that potential biological activity together with anti-microbial, anti-oxidant, medication, anti-cancer, anti-diabetic, anti-nuclear, anti-hyperglycemic, anti-pruritic, anti-mutagens, and anti-nutrients and conjointly effects on human. In this review, within the different hand exposed those industrial approaches like prescription drugs, lather, and beverages.



**Figure 1: Molecular structure of Tannins**

### **Classifications of Tannins**

Tannins are substances employing high molecular mass and are hydrophilic polyphenols capable to precipitate proteins. Tannins were classified for the initial time in 1922 via Freudenberg, depending on their chemical structures. They can be classified into three groups as well as hydrolyzable tannins, condensed tannins, and pseudo tannins.

### Hydrolyzable tannins

Hydrolysable tannins, in conjunction with *Castanea sativa*, *Terminalia* and *Phyllanthus tree selection*, *Caesalpinia coriaria*, *tara*, *algarroba*, *valonea*, *oak* alternative|and many different} other industrial tannin extracts are purported to be combination of simple phenols like gallic and ellagic acids and primarily glucose, through gallic and digallic acids(Pizzi et al.2008). Those tannins are hydrolyzed via acids, or catalyst and manufacture ellagic acid and gallic acid. Chemically, these are esters of polymer acid-like ellagic acid. The tannins derivative as of gallic acid is referred to as gallic tannins and from of ellagic acid are noted as Ellagitannins. The acid is originated in rhubarb, clove and ellagic acid is originated in eucalyptus leave and myrobalans and pomegranate bark. These tannins treated with metal chloride to created blue or black color.

**Table 1. Medicinal plants and their application.**

| Local name   | Botanical name                           | Family         | Utilized of parts | Medicinal Applications                                                   |
|--------------|------------------------------------------|----------------|-------------------|--------------------------------------------------------------------------|
| Amaltas      | <i>Cassia fistula</i> Linn.              | Caesalpinaceae | Bark              | Cancer, glandular tumors, diarrhea                                       |
| Anwal        | <i>Cassia auriculata</i> Linn.           | Caesalpinaceae | Bark              | Eye infections, diabetes, rheumatism                                     |
| Arjuna       | <i>Terminalia arjuna</i> Wight. & Ara.   | Combretaceae   | Bark              | Asthma, bile duct disorder                                               |
| Arunj        | <i>Acacia nilotica</i> Willd.            | Mimosaceae     | Bark              | Anti-malaria, anti-diabetic                                              |
| Baheda       | <i>Terminalia bellirica</i> Roxb         | Combretaceae   | Fruit             | Asthma, hepatitis, bronchitis                                            |
| Bulbul       | <i>Acecia leucophloea</i> Willd.         | Mimosaceae     | Bark              | Bronchitis, cough, ulcers                                                |
| Dhawra       | <i>Anogeissus latifolia</i> Wall.        | Combretaceae   | Leaves            | Diabetes, liver complaints                                               |
| Dhokra       | <i>Anogeissus pendula</i> Edgew          | Combretaceae   | Leaves            | Skin disease, diarrhea, gastric disorder                                 |
| Farash       | <i>Tamarix aphylla</i> Karst.            | tamaticaeae    | Bark              | Skin disorder, astringent                                                |
| Ghatbor      | <i>Zizyphus xylopyrus</i> (Retz.) Willd. | Rhamnaceae     | Fruit             | Stress ulcers, liver and bladder disease                                 |
| Godal        | <i>Lannea coromandelica</i> Merrill.     | Anacardiaceae  | Bark              | Ayurveda and Siddha medicines (ulcers, swellings)                        |
| Sadad        | <i>Terminalia alata</i> Heyne            | Combretaceae   | Bark              | Anemia, heart diseases, diarrhea                                         |
| Bodho-okhati | <i>Astilbe rivularis</i>                 | Saxifragaceae, | Rhizome           | Infectious and other diseases, Anti cancerous, Anti-diabetic, Anti-ulcer |

### **Condensed tannins**

These tannins are immune to hydrolysis and that they derived from the flavonols, catechins and flavan-3, 4-diols. On treatment with acids or enzymes, they're rotten into phlobaphenes. On dry distillation condensed tannin manufacture catechol. These tannins are referred to as catechol tannins. These tannins are found in bark, male fern, feather palm seeds, tea leaves and wild cherry bark, bahera fruits, Amla, etc. they manufacture green color with ferrous chlorides. Whereas hydrolyzable tannins and most condensed tannins are water-soluble however few giant condensed kinds of tannins are insoluble (Wheeler et al. 1979).

### **Pseudotannins**

This is not a special cluster of tannins, however, it is also treated as a sub-cluster. As a product of they are doing not adjust to Goldbeater's diagnostic experiment and are low down relative molecular mass compounds. Ipecacuanha acid in ipecacuanha and Chlorogenic acid in low and nux vomica and catechins in cocoa are samples of pseudo tannins. The recognition takes a look at for chlorogenic acid is disbursed by extracting the drug with water and treating this extract with ammonia resolution, followed by exposure to air, which leads slowly to the formation of green color.

### **Dietary source and Properties**

Tannins are freely soluble in glycerol, water, acetone, and alcohol, and dilute alkalies. They're meagerly soluble in chloroform, ester and alternative organic solvents. They have purple, violet or black impetuous with iron compounds. They're precipitated by a variety of bimetal lead acetate, salts notably potassium dichromate, and subacetate. They join with skin as well as conceal making animal skin Associate in Nursingd with gelatin and mineral to make an insoluble compound. They mix with alkaloids to make tannates, most of that is insoluble in water.

### **Tannins as potential Biological Activities**

#### **Anti-Microbial**

Tannins appear to have produce microorganism growth in many ways that, like inhibition of living thing microbic enzymes, deprivation of the substrates needed for microbic growth or protest on microbic metabolism through inhibition of organic process (De Bruyne et al.1999). Complexation of metal ions within the microorganism growth atmosphere by tannins might even be a mechanism of their antimicrobial action (Scalbert et al. 1991). *Acacia mearnsii* bark contains water-soluble tannins that have strong Anti-microbial activities against *E.coli* that are adhered to and under the biofilm of lettuce leaves. They also have strong inhibition activity against *S.aures* but show weak inhibition against *A.niger* and *Candidia*. (Dos et al. 2017)

#### **Anti-Nutrients**

Tannins are usually considered to be nutritionally objectionable. Tannins kind complexes with proteins, starch, and digestive enzymes to cause a reduction in nutritional standards of foods. Most of the first reports associated with the antinutritional property of tannins were targeted on phenol and alternative chemical reaction tannins.

Tannins are reported to be to blame for reducing feed intake, rate of growth, feed potency, net metabolizable energy, and macromolecule edibility. Tannins embrace damages to membrane lining of canal, alteration of excretion of sure cations, and raised excretion of proteins and essential amino acids (Singleton et al. 1969).

#### **Anti-Cancer**

Maplexins A-I is a sequence of structurally connected gallotannins in recent times inaccessible from the scarlet maple (*Acer rubrum*) class in a very investigation, maplexins A-I was classified for anticarcinoma property in opposition to human tumorigenic (colon, HCT-116; breast, MCF-7) and non-tumorigenic (colon, CCD-18Co) cell lines. Consequently, maplexin has antitumor property (14). Cuphiin D1 (CD1) is novel macrocyclic hydrolyzable tannin, it had been inaccessible from *Cuphea hyssopifolia* (Lythraceae) and it's been exposed to exert anticancer commotion aligned with to HL-60 cells (Wang et al. 2000). Ellitannin isolated from the *C. ladanifer* (Cistaceae) showed to reduce the production of M220 pancreatic carcinoma cells and MCF7/HER2 and JIMT-1 breast cancer cells (Barrajon et al. 2010).

#### **Anti-Oxidant**

Tannins don't operate entirely as primary antioxidants (i.e., they present hydrogen atom or electrons), they conjointly operate as secondary antioxidants. Tannins have the power to chelate metal ions like Fe (II) and interfere with one in all the reaction steps within the Fenton effect and thereby retard oxidization (Karamac et al., 2006). Presently used ways to embrace the DPPH (1, 1-diphenyl-2-picrylhydrazyl) assay, that measures the power of a substance to scavenge the DPPH radical, reducing it to reductant (Solis et al. 1997). Higher antioxidant activity was conjointly found for *P. carthagenensis* with the  $\beta$ -carotene bleaching methodology compared to quercetin and BHT. This higher activity wasn't ascertained for antioxidant that has comparatively high polarity. We tend to propose that this extract contains lipotropic compounds that act by inhibiting or retarding oxidization of  $\beta$ -carotene. *P. recta* herb extract was prepared using different solvents with different polarities and the maximum scavenging activity was of Ethyl acetate against DPPH,  $H_2O_2$ , HClO. The extract with diethyl ether has stronger  $O^{2-}$  scavenging activity (Agnieszka et al. 2013).

#### **Anti-Viral**

Tannins are widespread in humans, significantly kids or immuno-compromised patients (Solis et al. 1997). When a prime disease, HSV tends to act the somatic cell of the ganglia and its reactivation could cause continual herpetic infection (Whitley et al. 1998). When a primary infection, tannins tend to act the somatic cell of the ganglia and its reactivation could cause continual herpetic infection (Baringer et al. 1973). Studied five nonahydroxyterphenoyl- (NHTP) consist of C-glycosidic ETs (castalagin, vescalagin, grandinin, roburin B, and roburin D, all originate in *Quercus* spp. and *Castanea* spp.). The authors tested the activity of those compounds towards cells infected by four HSV strains, 2 of that were immune to medication (ACV), the foremost effective drug on the market against HSV mediated diseases. The mode of anti-HIV activity of HTs has additionally been studied. Complimentary and biphenyl pyrogallol-type patterns are shown to be helpful pharmacophores for the reticence of HIV-RT (Lee et al. 1992).

### **Anti-Inflammatory**

The impact of corilagin on lung injury caused by bleomycin exposure was investigated in Associate in nursing animal model of pulmonic pathology. Corilagin abrogated bleomycin-induced respiratory organ pathology, reduced the amount of apoptotic respiratory organ cells and prevented respiratory organ animal tissue cells from membrane breakdown. Anti-inflammatory actions to tannins isolated from the bark of *Anacardium occidentale* L. While not appearing to act by the release of adrenal hormones, tannins may produce effects in a non-specific manner by their astringent properties on cell membranes thus affecting cell function. Anti- Hyaluronidase activity and anti lipoxidase activity was observed maximum in ethyl acetate extract of the herb (Dos et al. 2017).

### **Anti-Diabetic**

The oral organization of *Syzygium cumini* bark extracts daily for forty-five days (300 mg/kg of body weight) considerably faded blood sugar levels and exaggerated levels of plasma endocrine and C-peptide of each traditional and diabetic rat (Matsumoto K et al. 2012). Kaki-tannin prevented an increase in plasma total cholesterol, non-HDL cholesterol, triglycerides, and endocrine in kind two diabetic mice fed a high-fat diet. Moreover, the intake of kaki-tannin prevented liver disease and iatrogenic the genes associated with cholesterol metabolism (Saravanan G et al. 2006). The lowering of glucose levels is obtained by the inhibition of  $\alpha$ -amylase and  $\alpha$ -glucosidase activity. Hydrolyzable tannins acutissimin A/B, vescalagin, grandinin/roburin E, epiacutissimin A/B, heptagalloyl glucose and hexagalloyl glucose are according to inhibit  $\alpha$ amylase within the in vitro human (Ubillas R. et al. 1994).

### **Anti- Hypoglycemic**

Pharmaceutical firms have introduced a range of hypoglycemia and/or anti-hyperglycemic medicine to treat diabetes, however, most of that is radiogenic or promoting weight gain (Klein et al. 2007). Varied meditative plant extracts are tested to treat DM and showed insulin-like properties (Simlai et al. 2013). Since tannins are known because of the active antidiabetic and antiadipogenic parts of *Lagerstroemia speciosa*, we tend to explore the marine member of Lythraceae, the mangrove tree species *Sonneratia Alba* Sm., that is made in tannin which will show hypoglycemic property (Shi S et al. 2000 and Watson L et al. 1992) . hyperglycemia was elicited in healthy mice that were fasted for six hours by one intraperitoneal injection of streptozotocin (STZ) (Sigma-Aldrich Co., Missouri, USA), that was dissolved in three-millimeter turn buffer with pH 4.5 at a dose of 50 mg/kg weight. Streptozotocin acts as an associate alkylating agent of DNA in  $\beta$  cells of the Islets of Langerhans within the pancreas and maybe a higher different in inducing hyperglycemia in mice (Eleazu C et al. 2013).

### **Anti-Pruritic**

Antipruritics, conjointly referred to as anti-itch medication, are medications that inhibit the itch usually related to sunburns, allergies, eczema, psoriasis, and chickenpox. Jewelweed is void of any anti-itch activity in many controlled studies (Eleazu C et al. 1997). Artificial tannins are established adjuvants within the medical aid of fretful, inflamed, weeping, superficial skin diseases. The therapeutic effects of artificial tannins area unit supported their tanning action similarly as on local anesthetic effects. In terms of pharmacology and clinical relevancy, artificial tannins are significantly versatile substances. They need conjointly been used as steroid-free (Foelster-Holst et al. 2007). Tests of the local anesthetic properties of artificial tannins were dispensed victimization experimental and in vitro take a look at ways.

Puschmann and Matthies were ready to prove the antipruritic result of tamol via the aminoalkane wale and lip stimulation ways (Puschmann M). The aminoalkane wale technique was dispensed on healthy volunteers. The antipruritic result of a shower additive and a suspension, every containing artificial tannin in numerous concentrations, was tested. An aminoalkane answer was applied on scarified skin before and once treatment. The reddened wale areas were measured planimetrically.

### Anti-mutagens

The antimutagenic activity of various elements of tannins was additionally reported showed that tannin strangled the agent activity. Antimutagens are the agents that interfere with the mutagenicity of a substance. The interference is within the kind of interference of the transformation of a mutagenic compound into mutagen, inactivation, or otherwise the interference of mutagen-DNA reaction. Gichner incontestable that tannic and gallic acid strangled the mutagenicity of MNU and MNNG in *S. typhimurium* TA100. The antimutagenic effects of those acids were mostly ensuing from interactions between MNU and MNNG with these tannins outside the microorganism cell (Gichner T et al. 1987). Horikawa additionally incontestable that epigallocatechin, EGCG, epicatechin gallate, and tannin isolated from extracts of Chinese medicative herbs *Prunella Spica*, *rheum palmatum*, genus *Polygonum multiflorum*, *agrimonia pilosa*, *Ephedea sinica*, and *Teitoutou* powerfully strangled the mutagenicity of B[a]P (2.5 µg/ plate) in *S. typhimurium* TA98 with S9 mix (Horikawa K et al. 1994). EGCG was shown to be a potent anti mutagen against direct-acting mutagens (Okuda et al. 1984).

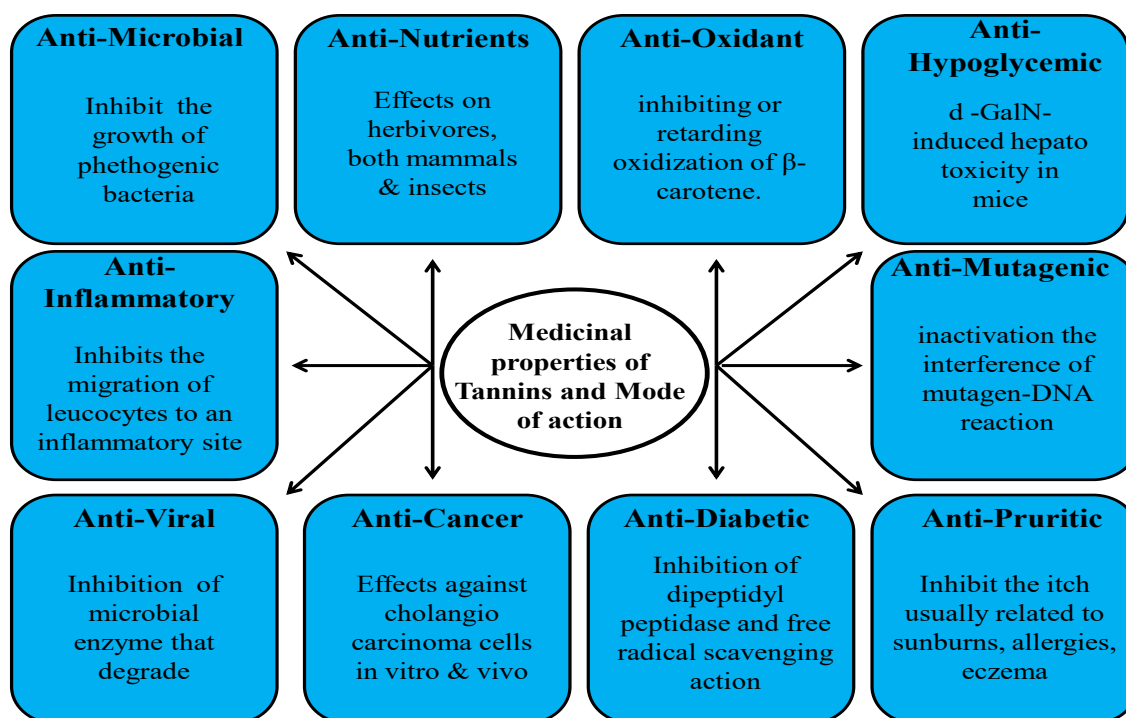


Figure 2. Medicinal properties of Tannins and their mode of action.

### **Effects on Human health (Carcinogenic effect of Tannins)**

A carcinogen is any substance, radionuclide, or radiation that promotes carcinogenesis, the formation of cancer. This might result in the power to wreck the genome or to the disruption of cellular metabolic processes. Carcinogens don't seem to be essential now toxic; therefore, their impact will be insidious. Polyphenols of tea are according to promote carcinoma in mice. Morton supported results of medical specialty studies, conjointly associated plant tannins with human cancers (Morton et al. 1972). Tannins applied to burns or injected subcutaneously were according to cause tumors in experimental animals as a result of tannin is hepatocarcinogenic to rat; it's been involved because of the etiology of human liver cancer inbound geographic areas (Korpass B et al. 1961). Many studies have shown that the two- to threefold will increase of the danger of muscular structure cancer with the uptake of very popular tea was because of the new temperature instead of the tea itself (Victoria et al. 1987).

### **Industrial Approaches**

#### **Pharmaceuticals**

Tannins are standard to own associate antimicrobial activity. this is often logical as their capability to tan proteins implies that they'll advance irreversibly conjointly with the proteins in microorganism membranes, so inhibiting any activity they could have. It follows that prescription drugs containing tannins and aimed toward set microorganism enteric infections are around already for a few times. Some studies on their anticavity effectiveness have conjointly been conducted (Mitsunaga T. et al. 1994). To boot, the utilization of tannins in alternative pharmaceutical medical applications, are according, notably regarding their antitumor and antitumor activity.

#### **Leather**

The leather tanning industry is one in all the foremost ancient processes still operational. Intensive reviews and articles on the utilization of vegetable tannins in leather creating exist (King H et al. 1957 and Roux D.G et al. 1975 and King H.G. et al. 1961 and Clark-Lewis J. et al. 1959). Though the technology of leather manufacture has evolved over centuries, and even in recent years, the essential principles for the production of leather have remained primarily an equivalent. Hide proteins, primarily collagen, are rendered insoluble and dimensionally a lot of stable by treatment with a chemical product able to be part of them and so render them each additional immune to mechanical wear and fewer prone to biological degradation. the most product used these days for animal skin tanning ar (i) acid salts of trivalent chromium, primarily used for the manufacture of sappy leathers for shoe uppers and leather bags; (ii) forestry-derived, natural vegetable tannins, like chestnut and fl flavonoid extracts, primarily used for the manufacture of serious, rigid and arduous leathers for shoe soles, saddles, belts and different implements subject to intensive wear; (iii) aldehydes, specially formaldehyde and glutaraldehyde; (iv) sulfonated artificial polymers, like acid phenol-formaldehyde novolak-type resins and (v) variety of different artificial resins and compounds (acrylics, oxazolidines, aminoplastic organic compound, etc. Conversely, whereas the utilization of artificial amino resin resins is developing within the tanning industry, as they furnish leathers of a particular degree of softness and fl exhibility, and notably appropriate for coloring, their liability is that the excessive and inevitable presence of free formaldehyde and their poor tanning capability because of their low astringency (Marutzky R et al. 1989). Polyphenolic vegetable tannins are accepted to act as powerful free methanal scavengers, as they react quickly and irreversibly with this compound [Pizzi A et al. 1983 and J. Macromol et al. 1980].

## **Beverages**

**Beer:** High amounts of tannins are within the hopes of some beers the quantity of tannins in beer depends on the quality of yeast in conjunction with different factors. The bitterer, a lot of tannic acid, less bitter, the fewer tannins. Tannins in tin are reduced by fining with PVPP, usually sold in inebriant outlets below as PolyClar AT. Ironically, tannin is typically used for fining for proteins in beer. Tannin preferentially binds to haze-forming proteins, however, it doesn't move as powerfully with foam-positive proteins. All brewage contains tannins. Some level of tannins is needed so as for the brewage to style acceptable.

However, if tannins are present in excess, they cause astringency in beer. Astringency could be drying, puckering sensation caused by tannins reacting with salivary proteins on your tongue.

**Wine:** Tannins (mainly condensed tannins) are found in wine, significantly red wine. Tannins in wine will come back from several supplies and also the tactile properties dissent counting on the source. Wine tannins come back from grape skins, stems, and seeds, and their extraction is heavily hooked into the actual trade method concerned. Some tannic acid conjointly comes from barrels, significantly new ones, wherever these are used to age wine. The complicating factor here is that the chemical make-up of the tannins is truly modified throughout the winemaking method. Not solely will the chain length modification, however, the various chemical entities that persist with the sticky bits of the synthetic resin subunits conjointly changes. Recently, a study in wine production and consumption has shown that tannins within the type of proanthocyanidins have a useful impact on tube health. The study showed that tannins suppressed the production of the peptide to blame for hardening arteries.

**Tea:** Teas are another common beverage that contains tannins tea leaf is loaded with tannins which give the bitter style. Once the catechins or antioxidants that are found in tea leaf oxidize, they type tannic acid referred to as thearubigins that is why they're largely found in tea leaf that has been altered. However, there are different tea's that conjointly contain tannins from the reaction method similarly as certain black teas that gain their color from being roast, not alter, therefore there are not any tannins present in them.

In addition to wine and tea, the opposite beverages that contain tannins embrace fruit juice, apple beverage, fruit juice, and beer. This could not be shocking to anyone United Nations agency has styled these four beverages as several have the distinctive bitter taste that comes with the presence of tannins. So, whereas wine could be a common beverage that contains tannins, it's conjointly true of many different beverages similarly.

## **Future Prospects Conclusion**

Tannins are known as the polyphenolic secondary metabolites of plants. The protein interactions of tannins have been researched previously because of their unique features and able to be to apply in various areas. Tannins are of many types of helpful biological activities such as anti-microbial, anti-oxidant, anti-cancer, anti-mutagenic and other many activities but they can be harmful to us. It has been reported that tannins are responsible for decreases in growth rate, net metabolizable energy and protein digestibility in several animals and they can be carcinogenic for humans. Tannins are contributing a role in the industry for beverage, leather, and medicine making so they need some more research. So that we get several benefits by tannins including medicinal compounds, leather material, and beverages like tea, wine, beer, and fruit juice.

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## Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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