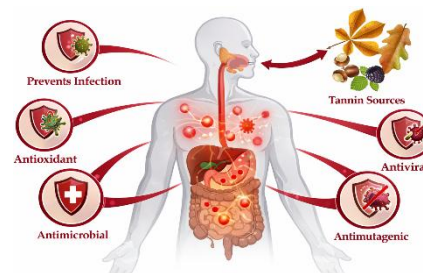


CHAPTER 12

Tannins and Their Biomedical Potential



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ABSTRACT: Tannins are a diverse class of naturally occurring polyphenolic compounds widely distributed across different plant species, where they play key structural and defensive roles. These bioactive metabolites have gained considerable scientific interest due to their broad spectrum of therapeutic properties, including antimicrobial, anticancer, antiviral, antidiabetic, antioxidant, anti-inflammatory, and antimutagenic activities. Based on their chemical structure, tannins are primarily classified into two major groups: hydrolysable tannins and condensed tannins, each exhibiting distinct biological functions and pharmacological significance. Derived from a variety of medicinal plants, tannins have demonstrated remarkable efficacy against numerous diseases and physiological disorders, highlighting their relevance in traditional medicine and modern biomedical research. However, despite their promising health benefits, excessive intake of tannins may lead to adverse effects, emphasizing the need for careful evaluation of safety limits and dose-dependent toxicity. This chapter provides a comprehensive overview of tannins, encompassing their sources, classification, mechanisms of action, and therapeutic applications.

Plants are the ones that produce a wide variety of metabolites that not only benefit the plants but also humans and other animals. These include primary metabolites like carbohydrates, vitamins, lipids and proteins and they play a vital role in the survival of humans. Unlike primary metabolites, secondary metabolites are synthesized primarily as a defense mechanism against environmental stressors (Singh et al., 2020). Secondary metabolites can be broadly categorized into three major classes, namely phenolic compounds, terpenoid compounds, and nitrogenous compounds. Tannins are one of the most common phenolic compounds, or polyphenols, which are structurally differentiated into hydrolysable and condensed tannins (De-Melo et al., 2023).

Tannins are taken by more than eighty percent of the global population in different forms. Tannins are present in many food and drink items that are obtained from plants, and these compounds play a major role in the overall flavor, astringency, and

health benefits of the product (Fig.1). Due to this reason, they are frequently used by children as well as adults. Moreover, they are reported to enhance the mood and lower fatigue. In America and Brazil, Guarana seeds are incorporated into soft drinks, which is a major source of tannins (Kumar et al., 2018).

Tannins are highly valued secondary plant metabolites, characterized by their extensive health-promoting properties and broad pharmacological potential, rendering them significant candidates for therapeutic applications. These phenolic essentials are utilized in internal and external applications in the nutraceutical, pharmaceutical and herbal remedial sectors. Tannins may also be used externally on swollen or damaged skin, as well as in the mouth to prevent several chronic diseases. Moreover, they have potent pharmacological properties such as antioxidants, antimicrobials, antivirals, anti-mutagenic, anti-carcinogen, and anthelmintic activities (Smeriglio et al., 2017;

Hossain et al., 2021). The regular intake of tannins is associated with a reduced risk of chronic illnesses, such as cardiovascular disease, cancer and diabetes (Cosme et al., 2025). The current chapter discusses the sources, mechanism of action and medicinal potential of tannins.

CLASSIFICATION

Tannins can be largely divided into two major groups, one of them being hydrolysable tannins (HT) and the other is condensed tannins (CT). Hydrolysable tannins have a glucose-like central polyhydric alcohol that is esterified with either gallic acid or gallic acid derivatives (Nishira & Joslyn, 1968). These tannins can be further subclassified into groups such as gallotannins, which hydrolyze to produce sugars and phenolic

acids—predominantly gallic acid. Prominent examples include Chinese gallotannin (derived from *Rhus semilata*) and sumac tannin (from *R. coriaria*). The Ellagitannins on the other hand degrade to give glucose, ellagic acid, gallic acid and at times other structurally similar acids. They are myrobolan (*Terminalia chebula*) and divi-divi (*Caesalpinia coriaria*) tannins (Haslam et al., 1961). The second principal group, Condensed tannins, are made of flavan-3-ol subunits that are joined together chemically to form oligomers and polymers. Although HT and CT differ structurally, they can be characterized as astringent, medium-to-high molecular weight polyphenolic molecules, which have the most important attribute of binding and precipitating soluble proteins (Naumann et al., 2017).

The process of tanning has been the main application of them, which means that their name comes from leather. They have sometimes been ignored in terms of their potential but recently scientists have unveiled their properties, which include antimicrobial, antioxidant, anticancer and anti-inflammatory effects, as well as their role in cardiovascular, neuroprotective and general metabolic diseases prevention (Maugeri et al., 2022).

SOURCES OF TANNINS

The natural products, such as fruits, vegetables, cereals, seeds and other foods are rich and diverse sources of medicinal compounds, and tannins are among them (Ahmed et al., 2025). Tannins are broadly used in the context of human health, protection of plants, farm management, and growth. Another important property that determines their activity is that they are capable of binding and denaturing vertebrate herbivores. Many of their advantages are based on this unique property, such as their astringent taste, their ability to react with ROS and reduce them, their antimutagenic, antiviral, and antibacterial properties (Erb & Kliebenstein, 2020; Fraga et al., 2019; Kashi et al., 2019; Smeriglio et al., 2017). Shikimic acid pathway is identified as one of the primary biosynthetic pathways to core plant phenolic compounds, which usually collaborates with malonic acid to form the required precursors (Sogvar et al., 2020).

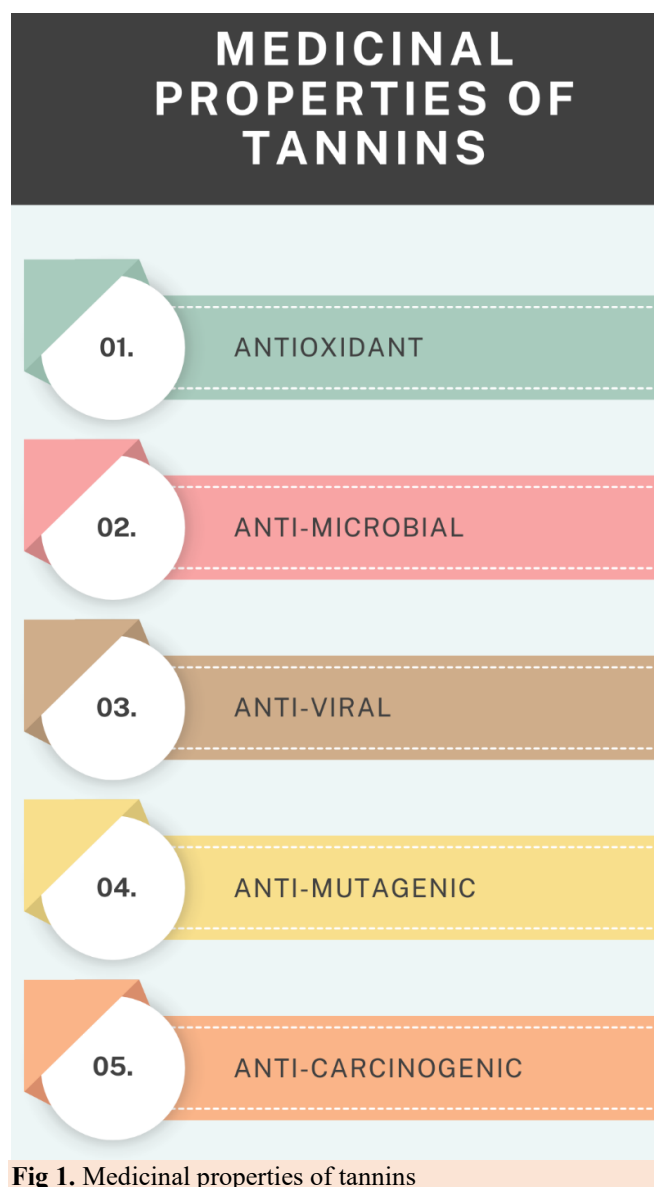


Fig 1. Medicinal properties of tannins

Tannins are very reactive and strong binding oligomers, or polymers, and they found in various plants. They can form both intramolecular and intermolecular hydrogen bonds. Tannins have a wide range of attachments to macromolecules (Smeriglio et al., 2017). Chung et al., (1998) categorized these substances into two main types: condensed or hydrolysable. Hydrolysable tannins composed of a certain number of phenolic acid molecules are split into two established groups named 'gallotannins' and 'ellagitannins' based on the acids produced upon hydrolysis gallic acid and ellagic acid, respectively. The term hydrolysable is used for these substances because acids and high temperatures can easily cleave their ester bonds (Durazzo et al., 2019; Li & Duan, 2019).

Tannins can hardly be isolated from the plants that produce them because the interaction between procyanidins and prodelphinidins takes place within the plants (Del Bianco et al., 2021). The whole range of plants including broad beans, beans, barley, blackcurrant, cinnamon, and black tea can be viewed as potential tannin sources, since they produce either procyanidins or prodelphinidins selectively in different parts of the plants like roots, bark, shoots, flowers, and seeds (Smeriglio et al., 2017; Del Bianco et al., 2021).

THERAPEUTIC ACTIVITIES OF TANNINS

Antiviral Activity

Naturally occurring and synthetic tannins exhibit antiviral activities that are broad-spectrum in a high number of pathogens (Lin et al., 2013; Ajala et al., 2014). They consist of such important viruses like human immunodeficiency virus, enteroviruses, caliciviruses, rotavirus, influenza virus A, vesicular stomatitis virus, paramyxoviruses, and herpes simplex virus (HSV) (Fukuchi et al., 1989; Cheng et al., 2002). The antiviral mechanisms of action are multifaceted, involving the inhibition of viral adsorption, penetration, nuclear entry, and reverse transcription. Particularly, the ability of hydrolysable tannins and galloylated condensed tannins to affect viruses is mainly explained by the possibility to inhibit the adsorption of the virus (Isenburg et al., 2005; Rauf et al., 2019).

The activity of the hydrolysable tannins as antiherpetic agents is proportional to the number of galloyl or hexahydroxy-diphenyl groups available,

whereas the activity of the condensed tannin against the herpes virus is proportional to the level of condensation (Beretta et al., 2009). Dimeric ellagitannins (oenothein B, coriariin A, and agrimoniin), which have been shown to strongly inhibit viral adsorption, have been observed to have potent anti-HIV activities. This effect is attributed to tannins binding to the viral envelope, thereby preventing the virus from attaching to the host cell and entering through the plasma membrane (Xie et al., 2007). Furthermore, the ellagitannin casuarinin has been reported to exhibit anti-herpes activity by inhibiting viral attachment and penetration, as well as disrupting late stages of the viral replication cycle (Flesch et al., 1998).

At micromolar concentrations and in dose-dependent ways, human cytomegalovirus (HCMV), hepatitis C virus (HCV), measles virus (MV), and respiratory syncytial virus (RSV) infections were successfully cured by other hydrolysable tannins, chebulagic acid, and punicalagin (Ubillas et al., 1994) without causing appreciable cytotoxicity. Furthermore, each virus has varying degrees of viral attachment, penetration, and transmission due to these natural chemicals. In particular, the tannins prevented HCMV, HCV, and MV from completing all of these stages of infection (Lee et al., 2010). The HCV protease is remarkably inhibited by hydrolysable tannins. HCV protease is inhibited by casuarinin and chebulagic acid, which are non-protein and non-peptidomimetic (Magos et al., 2008).

Antiulcerant Activity

Infection of the stomach or duodenum is one of the most common and widely spread gastrointestinal disorders called ulcers (Fig. 2). In a way, it is an inflammation that leads to the breaking down of the mucous membrane or skin that covers the digestive tract. If the normal balance of acid and alkaline mucosal defense activity gets upset, ulceration follows (Zhang et al., 2009). This condition might be related to certain factors like frequent use of drugs, changes in diet, and stress. The presence of acid and pepsin in gastric juice together with infection caused by the gram-negative bacterium *H. pylori* is indispensable for the occurrence of peptic ulcers.

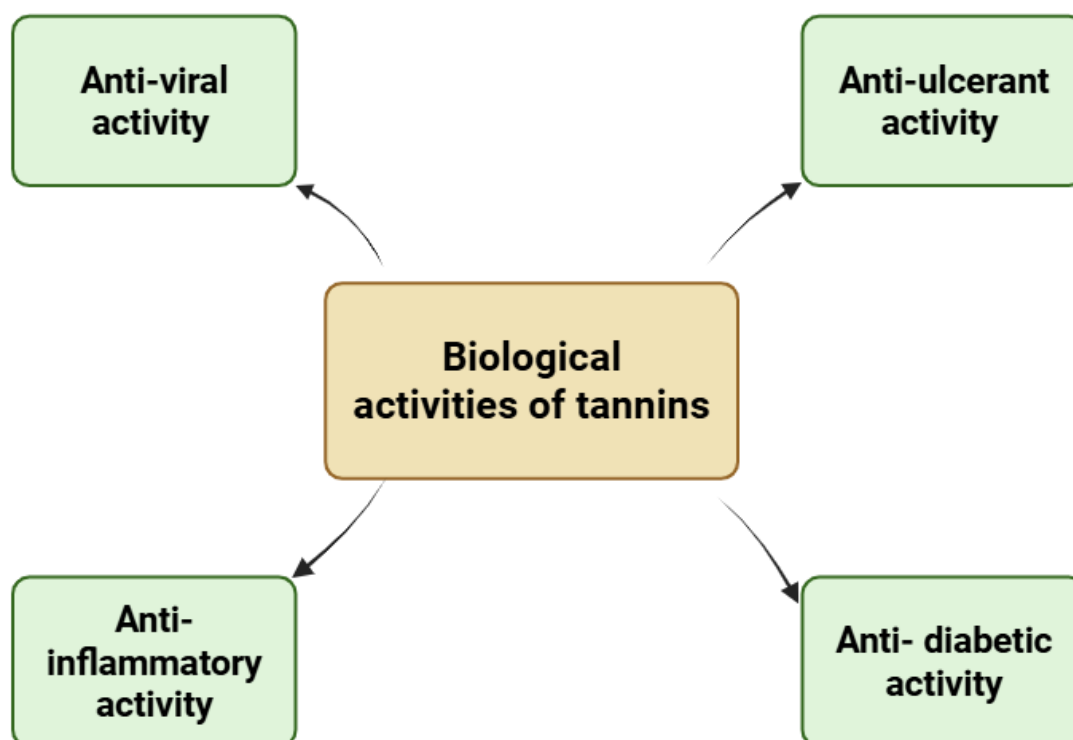


Fig 2. The biological activities of tannins

Tannins, due to their astringent ability, are the main component in the formation of the tannin-protein complex, which is responsible for the interaction of tannins with the tissues and thus the creation of the barrier. This barrier of the tannin-protein complex increases the resistance of the stomach to mechanical and chemical damage or irritation and thus protects it from gastric ulcers. In addition, numerous research studies have indicated that tannins not only possess anti-*H. pylori* property but also facilitate tissue repair and are antioxidants (Vasconcelos et al., 2010).

Antioxidant Activities

Tannins exhibit marvelous antioxidant activities and are used in the fields of food as well as medicine. Tuyen et al. (2017) reported that tannins are present in Japanese chestnut (*Castanea crenata*), which possess significant free radical scavenging activities. Tannins present in plants are documented to improve antioxidant status in ruminants. Grape pomace inclusion in the diets of lambs have shown to improve muscle antioxidants, lower ROS reactive oxygen species and elevate superoxide dismutase activity (Zhao et al., 2018). It was also reported that condensed tannins extracted from *Ficus altissima* exhibit superior antioxidant activities.

Procyanidins, which are a class of tannins, exhibit significant free radical quenching properties. However, their scavenging activities depend upon the degree of polymerization (Serrano et al., 2009). Grape seed proanthocyanidin-rich extract, a type of condensed tannin, has shown protective efficacy against steroid instigated oxidative stress and lowered the levels of MDA, NADPH oxidase, and ROS (Tousson et al., 2018). Moreover, *Cassia abbreviata* root extract, which is also a tannin, lowered oxidative stress and lipid peroxidation while increasing GSH (Sobeh et al., 2018).

Pentagalloylglucose is another tannin with remarkable antioxidant properties. It is documented that this compound lowered ROS and JAK/STAT signaling and improved Nrf2/HO-1 signaling in mesangial cells. These activities show that pentagalloylglucose exhibit anti-apoptotic and antioxidant properties (Tong et al., 2014). Furthermore, procyanidins (tannins) lower the risk of cardiovascular diseases by reducing the levels of cholesterol and creatinine kinase. Moreover, their free radical quenching properties prevent the stimulation of NF- κ B associated inflammation in cardiac tissues (Barszcz et al., 2018). Therefore, tannins exhibit remarkable antioxidant properties.

Anti-Inflammatory Effects

A study on animal models found that different ellagitannin extracts (geraniin, corilagin, and furosin) preserved the lung epithelial membranes, reduced the amount of lung cell death, and even cured the lungs fibrosis caused by bleomycin (Zhang et al., 2009). In addition, the research was directed towards the wound-healing properties of trigalloylglucose and gallic acid from *Terminalia chebula* and pentagalloyl-glucose, the main ingredient of *Paeonia suffruticosa*. Moreover, *Lythri herba* turned out to be a potent anti-inflammatory agent because of its anti-hyaluronidase and anti-elastase activities (Piwowarski et al., 2011).

Proanthocyanidin also exhibits anti-inflammatory activities. It lowers NF- κ B/TLR-4 pathway and reduces the levels of inflammatory cytokines (TNF- α , COX-2, IL-6 and IL-1 β) as well as ROS and nitric oxide (El-Shitany & Eid, 2017). Tannins also improve cardiac function via inhibiting Smad 2/3 and JAK/STAT signaling along with cardiac inflammation and fibrosis (Gao et al., 2020).

Anti-Mutagenic Effects

Tannins exhibit remarkable anti-mutagenic and anti-cancer properties. Dolara et al. (2005) reported that tannin administration lowered the tumor proliferation by 50%. *In vitro* studies have reported that tannins inhibited the development of cancer via preventing EGFR (epidermal growth factor receptors) phosphorylation (Fridrich et al., 2007). In addition to this, proanthocyanidins reduce tumor progression via increasing ROS and lowering cell viability as well as migration (Kaplum et al., 2018). Moreover, tannins block cell cycle in G2/M phase, lower cdc25 and cyclin B1 expressions, while increasing apoptosis as well as cleavage of caspase-8 and caspase-3 in human hepatic cancer (HepG2) cells (Upanan et al., 2019).

Anti-Diabetic Activity

Tannins are extremely potent phytochemicals holding health benefits that especially concern chronic diseases in a very large range. They are highlighted as potential for Type 2 Diabetes (NIDDM) because of their effects on glucose uptake and prevention of fat cell formation (adipogenesis). Also, they can be instrumental in

neutralizing the diabetic-vulnerable oxidative stress (Ajebli & Eddouks, 2019). These compounds, particularly condensed tannins, and their related phenolic compounds have got the strong association with cancer prevention, even besides metabolic health. They exert their effects by modulating the intrinsic pathways, i.e., the PI3K and p38 MAPK signaling cascades, which in turn allows them to alter the expression of genes and the activity of corresponding enzymes (Kumari & Jain, 2012). Tannins delay the absorption of glucose from the intestine. Tannins exhibit similar activities as of some synthetic drugs i.e., acarbose and voglibose, and reduce α -amylase as well as α -glucosidase activities (Matsui et al., 2001). They also delay insulin dependent diabetes mellitus via modulating the antioxidant environment of pancreatic β -cells (Serrano et al., 2009). In addition to this, procyanidins (tannins) also regulate some insulin-signaling transduction pathways via micing or influencing insulin effects (Pinent et al., 2004). Kumari & Jain (2015) reported that tannins improve the uptake of glucose and thereby lower blood glucose concentrations which significantly reduces the risk of diabetes. Hence, these properties confirm the anti-diabetic activities of tannins.

ADVERSE EFFECTS OF TANNINS

Prior studies have revealed that tannins also exhibit some deleterious effects. Tannins exhibit anti-nutritional properties as they form complexes with macromolecules (proteins and carbohydrates) as well as minerals (magnesium, calcium and phosphorous) and make the constituents unavailable for the use of body (Hagerman et al., 1998). In addition to this, they can even enhance the activity of a cancer-causing substance, if it is present in body along with tannins (Mather, 1997). Reportedly, tannic acid in tannins may cause hepatic damage in animals as well as humans (Medugu et al., 2012). Tannins also inhibit the activities of endogenous enzymes via making indigestible complexes (Awad et al., 2001). However, they may be consumed with care due to their diverse health benefits.

SAFE LIMITS FOR TANNIN CONSUMPTION

Tannins should be consumed under safe limits. Consuming 1.5g-2.5g of tannins daily is beneficial

and has no side effects (Rao & Prabhavathi, 1982). Due to fewer threats and significant benefits of tannins, they can be consumed from their common sources, i.e., natural products, cacao, tea and marijuana to live a healthy and disease-free life (Ghosh, 2015). No extensive research has been conducted on the safe limits for tannin consumption and only a few studies have reported the consumption limit of tannins. Tannic acid, a tannin, serves as a nutritional additive which animals can safely consume up to 15 mg per kg of body weight. The FDA has restricted tannin usage to particular food categories but the agency continues to recognize them as Generally Recognized as Safe (GRAS) for their role as food additives. Moreover, they are approved by the Nourishment and Sedate Organization of FDA (Hoque et al., 2025).

CONCLUSION

The various therapeutic aspects of natural tannins have been discussed in this chapter. The excellent antidiabetic activity of tannins, which is based on their ability to raise glucose uptake and reduce oxidative stress, places them in the management of NIDDM. The strong anti-inflammatory capabilities of tannins can also help in the treatment of chronic diseases since they can influence the signaling pathways of the disease. Most importantly, the findings support the case for tannins' considerable antiviral effects, where they disrupt different phases of viral invasion, as well as their remarkable anti-ulcerant activity which is frequently executed through mucosal defensive and killing actions. In conclusion, the various contrastive bioactive properties of tannins e.g., metabolic, protective, and antimicrobial make them one of the most valuable classes of phytochemicals for the development of future nutraceutical and pharmaceutical interventions. The continuation of research will be a necessity to unlock the full potential of these compounds for human health.

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