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An Insight on Mechanism of Hepatoprotective Herbs Containing Tannins

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Abstract: Tannins are polyphenolic compounds that secondary metabolties of the plants. Tannins play a prominent role in general defense strategies of plants. Tannins are known to have hepato-protective activity. Some of the common tannins that exhibit hepato- protective activity include tannic acid, ellagic acid, gallic acid, ellagitannin, gallotannin, proanthocynidines etc. The present chapter includes the review of hepatoprotective action of some of the herbs. It can be concluded from the exhaustive study that tannins are majorly found in family like myrtaceae, mimosaceae, combretaceae, rosaceae, anacardiaceae etc. The common mechanism of actions of tannin containing herbs exhibits hepato- protective action includes free radical scavenging. The tannin containing drugs supress or inhibit the formation of free radicals generated due to the metabolism of hepato-toxins. Tannins are widely used in marketed formulations that are used in the treatment of hepato-toxicity. The chapter also includes the compilation of herbal marketed formulations available for the treatment of liver toxicity and liver diseases.

Keywords: Tannins, hepato-toxicity, free radical scavenging, liver disease

1. Introduction

Tannins are phenolic molecules that have been adsorbed to tannic acids and can be effective herbivore deterrents for a variety of industries [1]. Tannic acid is another name for tannins. Tannins are secondary metabolites found in plant mobility components. Tannins are non-nitrogen natural compounds with an intricate hub and convergent migration [2]. It is found in many plants' roots, arbours, bark, leaves, and fruit, particularly in oak (Quercus) coats and Rhus and Terminalia chebula inner surface coatings. The term tannin was first applied to a class of chemicals that combine with animal skin and form animal pores in 1796 [3]. The majority of real tannins are composed of complex polyphenols with a medium molecular weight that can be formed by polymerization of soft polyphenols. The hydrolysis of ordinary mineral acid, including enzymes, may result in the formation of complex glycosides [4].

Tannins are plant-derived soluble, astringent complex phenolic chemicals used in the tanning of animal skins or the precipitation of proteins. Tannins are phenylpropanoid compounds that are typically condensed into polymers of various lengths. Phenolic compounds have hydroxylated aromatic rings with the hydroxy group directly attached to the phenyl, substituted phenyl, or another aryl group [5]. Tannins and phenolic compounds are widely distributed secondary metabolites in plants that contribute significantly to plant defence systems and food quality. The terms "hydrolysable" and "condensed" tannins distinguish two forms of vegetable tannins: gallic acid-derived tannins and flavan-3,4-diol-derived tannins [6].

Tannins are water-soluble phenol derivatives produced spontaneously by higher plants and preserved as secondary metabolic products. Tannins are polyphenols with chemical molecular weights ranging from 500 to 3000 Da [6]. In complexes with saccharides, alkaloids, and proteins, its molecular weight can reach 20,000 Da, exhibiting phenol-like reactions. The chemical structure of tannic acid is determined by the plant species that produces it. Currently, over 8000 different tannins have been found and chemically described. There are certainly many more tannins whose chemical structures have not yet been found [7].

All tannins share some characteristics that allow them to be classified into two main groups: hydrolysable tannins (gallotannins, ellagitannins, and complex tannins—mainly glucose, gallic acid, and ellagic derivatives) and condensed tannins (non-hydrolysable) called procyanidins, which contain the condensed carbon chain typical of flavonoids. Condensed tannins have better antibacterial, antiviral, and antifungal properties than hydrolyzable tannins. Hydrolyzable tannins can be hydrolyzed by weak acids or bases to produce glucose and phenolic acids. Proanthocyanidins, also known as condensed tannins, are abundant in plants and have a substantial impact on food quality. These are hydrolysis-resistant flavonoid polymers with 2-50 (or more) flavonoid units [8]. Some very large condensed tannins are insoluble in water, although the bulk of condensed tannins and hydrolyzable tannins are.

The chemical structure of tannins determines their biological activity. Tannins, depending on their concentration, can also be utilised as a metal ion chelating agent, a biological antioxidant, or a complexing or precipitating agent (in low concentrations as a complexing, and in high as a precipitating agent). Because of the diverse tannin structures and biological effects, it is hard to predict the effects of tannins on every living organism. [9].

Tannins are plant-derived astringent-tasting polyphenols that can bind to and precipitate proteins. When plant cells are destroyed (for example, during food preparation), all phenolic compounds are swiftly converted into diverse reaction products, adding to the complexity of dietary polyphenol compounds. This explains the complexities of polyphenols in food [10].

Holding tannins in the mouth causes a strong astringent sensation. Tannins are thought to attach to proteins in the tongue and mucous membranes in the oral cavity, causing them to denature. A shrinking effect occurs when tannins denaturate proteins in the oral mucosa. Astringency is thought to be closely related to the pain and tactile sensations caused by protein denaturation [11]. Tannins must be dissolved in saliva to have an astringent effect. As a result of tannin insolubility, a rise in molecular weight caused by polymerization results in a lack of astringency. Because of the presence of soluble tannins, certain persimmons are highly astringent and thus inedible. Yet, because to tannin insolubility, the astringency fades after they are dried or matured. These condensed tannins are made up of a polymer with a high molecular weight (15 000) derived from catechins. Because they have high protein coagulation activity, they are utilised to clarify Japanese sake as well as a preservative [12].

According to research, there are around 8000 different tannins. Plant cells were shown to contain both unbound and bound tannins [13]. Tannins, gallotannins, ellagitannins, proanthocyanidins (condensed tannins), and complex tannins are the four main tannins found in terrestrial plants. Phlorotannins are marine plant tannins that include phloroglucinol polymers or chains. The concentration of tannins can range from 0.2 to 25% DW depending on numerous factors such as plant species, harvest season, habitat, and extraction techniques. [14]. Tannins have been proven to contain antioxidants, antimicrobials, antimicrobials, chemotherapies, and other biological actions. The biological activity of tannins controls the quantity of hydroxy and aromatic rings it contains. Ortho-dihydroxyl groups are a distinguishing feature of orthopaedic metal ions [15].

The high molecular weight and degree of polymerization of tannin antioxidants are regulated. The proteins are firmly linked to the tannins' phenolic group via a hydrogen connection with the peptide-NH group [16]. Hydrogen bonds cannot be broken by digestive enzymes or microbial attack. Tannins are used in a range of applications, including medicine, foods, beverages, printing inks and adhesives, the tealing and tanning industries, plastic perch, water filtration, and area coating. Its efficacy as a complexing or precipitating agent is related to its concentration [17].

The liver and its function in the body

The liver is the body's primary site of metabolism and excretion. The human liver's metabolic processes for metabolising chemicals include oxidation, reduction, hydration, condensation, hydrolysis, conjugation, and isomérization. Any of the processes outlined above could be disrupted, resulting in liver or hepatotoxicity damage, which could lead to a variety of disorders [18]. These diseases are linked to a rise in global mortality rates. Hepatotoxins can induce liver injury through drugs, chemicals, dietary changes, and herbal remedies. Ayurveda has a variety of herbal and herbal formulae that have been studied for their ability to hepatoprotect various sorts of liver diseases [19].

Several critical metabolic functions are regulated by the liver. Hepatic damage causes a disruption in metabolic function. Because of its strategic location in the organism, it is sensitive to xenobiotics. Toxins from the gut are the first to reach the liver, where they cause a variety of liver disorders. As a result, liver illnesses remain one of the most serious public health issues. Current treatment for hepatic illness improvement has very little to offer, and plant-based medicines are usually used to address hepatic concerns [20, 21].

Hepatitis and living circumstances Hepatotoxicity

One of the most common global health challenges, particularly in developing nations, is liver disease. There are three types of hepatitis: non-inflammatory hepatitis, acute hepatitis, and chronic hepatitis. Cirrhosis or inflammatory fibrosis, as well as chronic hepatitis (degenerative). Heavy metals, pollution, starvation, and the

use of over-the-counter medications are all variables. These are frequently caused by people who do not have a doctor's prescription.
As a result of the aforementioned circumstances, the hepatocytes are damaged and rendered useless. The long-term consequences include hepatitis, jaundice, liver fibrosis, and alcoholic liver disease. One of the most common causes of heart disease is an increase in cholesterol in blood circulation, which indicates liver illness/insult. Low-density zones house a sizable part of the population. LDL cholesterol (LDL C) and triacylglycerols (TAGs) are the two types of lipids linked to an increased risk of cardiovascular disease [22].
Excess alcohol, toxic substances such as thioacetamide (TAA), and drugs such as paracetamol (PCM) can all cause liver cell death [23].
Carbon tetrachloride (CC14) is a chemical substance that is used to make inorganic and organic carbon tetrachloride. Chemical, aflatoxin, bacterial, and viral disorders (for example, hepatitis A, B, C, and D) have all been thoroughly researched [68]. The mitochondrial P450 cytochrome and endoplasmic reticulum metabolism. As a result, Rogue oxygen species CC14 are produced (ROS, CCl3, O). The chain reaction begins, which may result in lipid peroxidation [24].
PCM is used as an analgesic or antipyretic (fever prevention). PCM is commonly used as a pain reliever. High doses of this medicine harm liver cells, causing damage or illness. Furthermore, excessive PCM administration might result in the loss of most liver cells (necrosis), resulting in substantial hepatic damage such as nuclear pyknosis and cytoplasm's. As PCM is metabolised in the liver, it produces N-acetyl p-benzoquinone imine, an oxidative molecule that forms a covalent link with protein sulphide groups (cytochrome P450 enzymes). Glutathione (GSH) is produced as a byproduct of this mechanism, causing hepatocyte necrosis [25].
TAA is another chemical that prevents RNA from freely passing between the nucleus and the cytoplasm and causes membrane damage. This hepatic impairment is caused by the TAA metabolite wound. TAA has the ability to reduce the number of liver cells as well as the frequency with which oxygen is consumed. Also, it reduces the amount of bile salts and deoxycholic acid bile components [26]. Bile excretion is hampered as a result of hepatotoxin-induced liver damage. An increase in blood toxins demonstrates this. As a result, it is critical for human survival to always maintain the integrity of the hepatitis [27]. Despite its enormous regeneration capacity, it is prone to constant degeneration. Moreover, environmental contaminants such as chemotherapeutic drugs' xenobiotics may depress and reduce the body's natural liver defence systems, leading to hepatic dysfunction and hence liver injury [28].

Many studies have found that oxidative stress caused by free radicals is the primary cause of liver damage such as hepatocyte degeneration, necrosis, edoema, and apoptosis. Free radicals produce liver lesions or damage due to lipid oxidation or covalent binding, resulting in tissue destruction. ROS is linked to several ageing issues, including atherosclerosis, diabetes, lung and kidney damage, hepatitis, disease, cancer, inflammatory diseases, and heart disease, and includes peroxylics, hydroxyls, alcohol radicals and super-oxides, as well as the degradation of membrane fibres, proteins, and nucleic acid [29, 30]. Lipid peroxidation affects cell membranes, impairing their functionality and structural integrity. The cell's ability to maintain consistent ion gradients and transport is significantly harmed. Hepatic damage can be caused by high-dose usage and exposure to particular toxins [31].

Radical Peroxidation and Lipid
Free radicals prevent lipid peroxidation, in part through the free radical scavenging mechanism [32]. Ethanol metabolism results in lipid peroxidation, which can lead to cirrhosis and hepatitis. In recent years, fewer harmful plant chemicals have been used as Hepatoprotective agents are substances that protect the liver. It is consequently critical to do ongoing research on plant varieties. The search for novel hepatoprotective compounds in the area has been substantial. Yet, previous research has shown that oxidative stress, which causes damage, is increased by the overproduction of reactive oxygen species (ROS). Diabetes, for example, has a mechanism that is linked to several clinical diseases. Nide and liver damage, as well as cancer and heart disease, are all risks. Glutathione Peroxidase (GSHPx) and other antioxidant-dismutase-like enzymes SODs Catalase (CAT) is an oxidative stress-protecting enzyme for cells [33]. Cu-Zn, Mn-SOD, and Cu-Zn-SO D are examples of enzyme antioxidant defence systems. Natural peroxidants like as CAT and GSH are reductases that are employed to eliminate ROS either directly or sequentially to stop or slow the process. ROS can thus be eliminated. It is critical to avoid lipid peroxidation. Being an essential antioxidant in the cytoplasm, GSH should be kept at a constant level. Xenobiotics deletion and detoxification. When it comes to xenobiotics, CCl_4 is regarded as a major source of acute liver cell injury. Generation of free radicals (trichloromethyl radicals) [34]. Compounds that boost the activity of glutathione S-transferase, which can convert harmful substances into innocuous ones, are becoming increasingly difficult to find.

The liver has a defence mechanism. Plants and their components have been claimed to be effective in the prevention and treatment of a variety of ailments. Disease therapy is more successful since they have fewer negative effects on the body's systems. Excessive alcohol use is now one of the leading causes of liver disease worldwide [33]. Because alcohol metabolism occurs in the liver, there is a link between ethanol use and alcoholic liver disease because this process impacts lipoprotein and lipid metabolism. Alcohol dehydrogenase also converts ethanol to acetate, which produces reactive oxygen species via cytochrome P4502E1 (ROS). [35,36]. The liver process causes oxidative stress, which causes liver damage and changes the structural stiffness of the hepatic cell membrane, allowing cyto sanitary enzymes to enter the circulation. As a result, an increase in blood-stream cytosolic enzymes is a common biochemical indicator of liver injury [37]. The quantities of aspartate transaminase (AST) and alanine transaminase (ALT) in injured liver cells' cytoplasm and mitochondria are elevated. Because of the altered liver cell membrane shape, cell membrane leakage causes a rise in serum hepatospecific enzymes. Also, a high level of bilirubin in the blood indicates a high rate of erythrocyte breakdown. As a result, maintaining a working liver is critical for human health [38].

Hepatoprotective actions of some tannin containing herbs Tannic Acid

Tannic acid is a polyphenol that has a negative impact on oxidative stress. Tannic acid's hepatoprotective function is not widely recognised, however it is a novel topic being researched. Tannic acid is a natural molecule found in a variety of fruits and vegetables, including strawberries, beans, grapes, cacao, and tea. Tannic acid protects the liver from damage caused by excessive alcohol consumption. Furthermore, TA was reported to lower the mutagenicity of polycyclic aromatic hydrocarbons in salmonella typhimurium and Chinese hamster V79 cells, as well as to limit the tumorigenicity of polycyclic aromatic hydrocarbons and N-methyl N-nitrosourea cells in mouse skin, lung, and forestomach. The anticarcinogenic and antimutagenic properties of TA may be due to its antioxidant properties, which reduce reactive metabolic production and its negative downstream repercussions [39].

Based on its antioxidant properties, we anticipated that TA could protect the liver from APAP overdose-induced damage to reactive oxygen species [40].

Nonetheless, at high levels, TA was investigated as a liver toxin. Acute TA poisoning revealed that, independent of the liver's origin or source, the highest TA concentrations (1500 mg/kg) caused significant tissue damage, followed by mild 1000 mg/kg and nil damage (500 mg/kg) [41]. Tannic acid's structure is depicted in Figure 1.

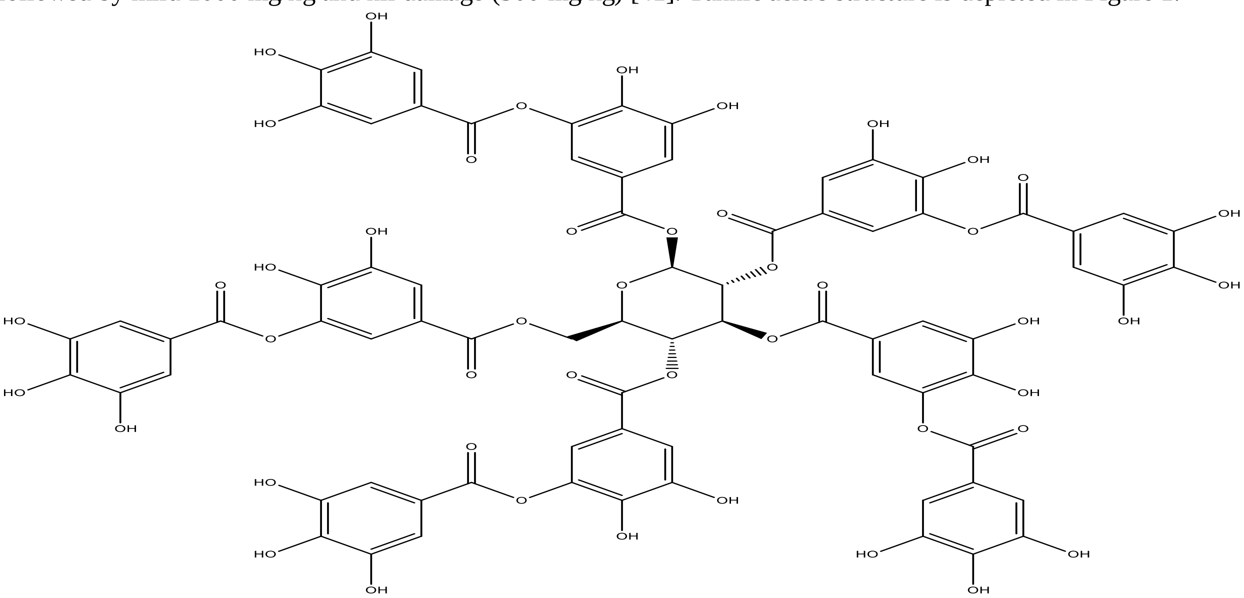

Figure 1: Structure of Tannic Acid

Mechanism of Action

Tannic acid can treat hepatotoxicity caused by medication. Medical medicines such as acetaminophen emit substances such as nitrous oxide, which cause hepatotoxicity. Tannic acid, as an antioxidant, suppresses the formation of these chemicals, preventing damage and toxicity in liver cells. Control of oxidative stress, suppression of inflammatory responses, and reduction of hepatocyte death are all likely associated to TA hepatoprotective effects [42, 43]. Tannic acid-containing plants are listed in Table 1

Table 1: Plants containing Tannic acid [44]

S. No.	Name of the plant	Biological Name	Family
1	Babul	Acacia nilotica (L.) Willd.	Mimosaceae
2	Arunj	Acacia leucophloea Willd.	Mimosaceae
3	Sadad	Terminalia alata Heyne.	Combretaceae
4	Arjuna	Terminalia arjuna (Roxb.) Wight. & Ara.	Combretaceae
5	Amaltas	Cassia fistula Linn.	Caesalpiniaceae
6	Anwal	Cassia auriculata Linn.	Caesalpiniaceae
7	Godal	Lannea coromandelica (Houtt.) Merrill.	Anacardiaceae
8	Dansara	Rhus mysurensis Heyne.	Anacardiaceae
9	Farash	Tamarix aphylla (L.) Karst.	Tamaricaceae
10	Jangaljalbi	Pithecellobium dulce Benth.	Mimosaceae
11	Khair	Acacia catechu Willd.	Mimosaceae
12	Ghatbor	Zizyphus glaberrima Santapau.	Rhamnaceae
13	Baheda	Terminalia bellirica Roxb.	Combretaceae
14	Anonla	Emblica officinalis Gaertn.	Euphorbiaceae
15	Dhokra	Anogeissus pendula Edgew.	Combretaceae
16	Dhawra	Anogeissus latifolia Wall.	Combretaceae

Gallic acid

Gallic acid is a well-known phenolic acid found in gallnuts, grapes, grenades, tea, and oak bark. It is antibacterial, antifungal, antidepressant, anti-asthmatic, and anti-obesity. Gallic acid has been shown to have a hepatoprotective effect against N′-nitrodiethylamine-induced liver damage. Gallic acid supplementation has been found to be a promising bioagent for hepatic damage management. Gallic acid can potentially cause liver fibrosis due to its CCl_4 hepatoprotective effect. Throughout the Asian subcontinent, at least 30 Ayurvedic plants and their formulations are used to cure and control a variety of ailments. The outcomes are approximations [45]. The synthetic pharmaceutical may be effective for the treatment of numerous human ailments, including liver fibrosis, but extended exposure to these treatments may be fatal because the ultimate objective of drug metabolism and detoxification is the burden of the liver. As a result, research into appropriate and friendly alternative drugs has become a priority today, since they demonstrate extraordinary, side-effect-free therapeutic efficacy. These excellent treatment options exert their protective effect through one or more combinations of processes that influence apoptosis and cell proliferation, such as the activation of detoxification enzymes, the prevention of the synthesis of reactive carcinogenic metabolites, and the scaling of ROS. Its multiple healing properties, including as antioxidants, anti-inflammatory, and anti-carcinogenic properties, are gaining interest as potential therapies for naturally occurring physiologically active polyphenols acquired from common dietary sources. Gallic acid has been proven to be effective in the therapy of such liver damage [46]. The structure of gallic acid is depicted in Figure 2.

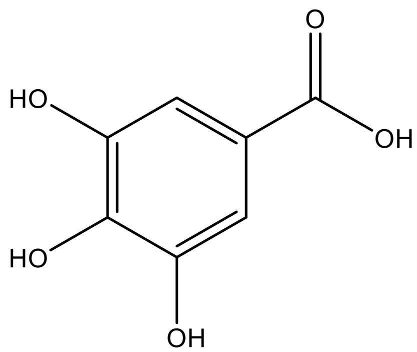

Figure 2: Structure of Gallic Acid

Mechanism of Action

Hepatic function in NDEA-wounded rats is expected to be restored by activating Nrf2-medicated antioxidant enzymes and suppressing inflammatory mediators COX-2 via the NF-B pathway. [47]. the many plants that contain gallic acid are listed in Table 2.

Table 2: Plants containing Gallic Acid [48]

S. No.	Name of the plant	Biological Name	Family
1	Babool	*Acacia Arabica*	Mimosaceae
2	Khair	*Acacia catechu*	Fabaceae
3	Jamun	*Eugenia jambolana*	Myrtaceae
4	Hirda	*Terminalia chebula*	Combretaceae
5	Behda	*Terminalia belerica*	Combretaceae
6	Dalimb	*Punica granatum*	Punicaceae
7	Amla	*Phyllanthus emblica*	Phyllanthaceae

Ellagic Acid

Ellagic acid is a well-studied plant-based polyphenol found in blackberries, raspberries, strawberries, cranberries, walnuts, pecan trees, grans, wolfberries, and other vegetable foods. There are antioxidant, antimutagenic, and anticarcinogenic activities present. Ellagic acid has been shown to reduce hepatic cholera, free fatty acids, and phospholipids while increasing aminotransferases, lipid peroxides, and hydroperoxides in the blood. Elagic acid alleviated alcohol-induced toxicity in rats by increasing body weight and restoring normal body weight ellagic acid in rats with ethanol-induced hepatotoxicity [49].

Ellagic Acid is also well known for its hepatoprotection against carbon tetra chloride-induced liver injury. The activity of liver enzymes such as alanine transaminase, aspartate transaminase, and alkali phosphatase, malondialdehyde levels, and a reduction in glutathione and catalase activity on liver tissues all contribute to CCl_4-induced hepatotoxicity. Research support the use of these active phytochemicals against toxic hepatocysis by avoiding lipid peroxidation, enhancing the antioxidant defence system, or repairing hepatocytes. The structure of ellagic acid is seen in Figure 3.

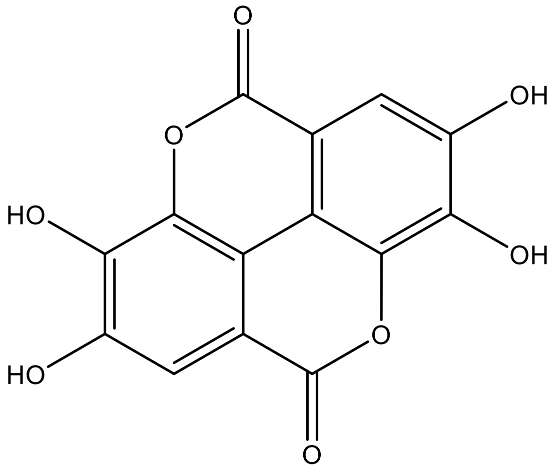

Figure 3: Structure of Ellagic Acid

Mechanism of Action

Ellagic acid has also been found to reduce ethanol-induced hepatotoxicity by research in moderating ethanol-induced changes in the production of matrix metalloproteinases and matrix-metalloproteinase tissue inhibitors (s). Furthermore, ellagic acid has been shown to have antifibrotic properties, making it useful in the prevention of hepato-lipid disease.

Ellagic acid is an antioxidant that protects the liver. It has the same result. The reported ellagic acid also reduced the formation of hydroxyproline and fibrous connective tissues, indicating its antifibrotic properties. Ellagic acid has also been shown to inhibit the conversion of hepatic stellate (HSC) cells into activated types that create extracellular matrix and cause liver fibrosis [50]. The list of plants that contain ellagic acid is shown in Table 3.

Table 3: Plants containing Ellagic Acid [48]

S. No.	Name of the plant	Biological Name	Family
1	Acai	*Euterpe oleracea*	Arecaceae
2	Apple	*Malus domestica*	Rosaceae
3	Arctic bramble	*Rubus arcticus*	Rosaceae
4	Black raspberry	*Rubus occidentalis*	Rosaceae

5	Blackberry	*Rubus spp.*	Rosaceae
6	Blackberry	*Rubus glacus*	Rosaceae
7	Blackberry	*Rubus fruiticosus*	Rosaceae
8	Blackberry	*Rubus adenotrichus*	Rosaceae
9	Cambuci	*Campomanesia phaea*	Myrtaceae
10	Chestnut	*Castania sativa*	Fagaceae
11	Cloudberry	*Rubus chamamorus*	Rosaceae
12	Cranberry	*Vaccinium macrocarpon*	Ericaceae
13	Grape	*Vitis vinifera*	Vitaceae
14	Grumixama	*Eugenia brasiliensis*	Myrtaceae
15	Jabuticaba	*Myrciaria jaboticaba*	Myrtaceae

Gallotannins

Gallotannins are natural polymers formed by repeated esterification of hydroxyl groups of D-glucose and gallic acid in polymer chains in the so-called "depside." The term depside refers to a diverse group of chemicals made up of polyphenols made up of two or more mono-aromatic units linked by an ester linkage. Another kind of gallotannin is formed via the esterification of shikymium acid and quinic acid with gallic acid [51].

Compounds such as methyl gallate, gallic-3, 4-galloylgallic acid, 1.2, 3, 4, 6-penta-O-galloyl—d-glucose and gallic acid esters, as well as gallic acid, have been shown to have hepatoprotective properties. These compounds are found in Galla Rhois, a plant whose extracts are used by the Korean medical system to treat liver damage. Rhus Javanica L., from the Anacardiaceae family, has been studied as a natural product having excellent ethno-pharmacological properties. Galla Rhois is an excrescence on the sumac leaf caused by parasitic aphids, specifically Schlechtendalia chinensis Bell. As a traditional medicine, GR has long been used to treat diarrhoea, seminal discharges, intense sweating, bleeding, and chronic cough in Korea. Galla Rhois, which is high in gallotannins, has been shown to be hepatoprotective against the liver damage caused by carbon tetra chloride [52].

The development of various diseases, such as atherosclerosis, liver dysfunction, lung and kidney damage, ageing, and diabetes, is thought to be an important factor in reactive oxygen species. Numerous natural antioxidants, despite their diverse origins, can protect against and treat ROS-induced liver damage. Gallotannin has received a lot of attention as a new therapeutic medicine candidate due to its strong antioxidant activity. Several studies are currently being conducted on its new role and mechanism. To develop treatments for oxidative stress-inducing illnesses, we investigated the protective effect of gallotannin on hepatic damage in ICR mice after CCl4 exposure. Several studies have found that pretreatment with Gallotannin is associated with the prevention of hepatocyte apoptosis, inflammation, and fibrosis by decreasing oxidative stress generated by carbon tetrachloride treatment [53]. The structure of gallotannin is seen in Figure 4.

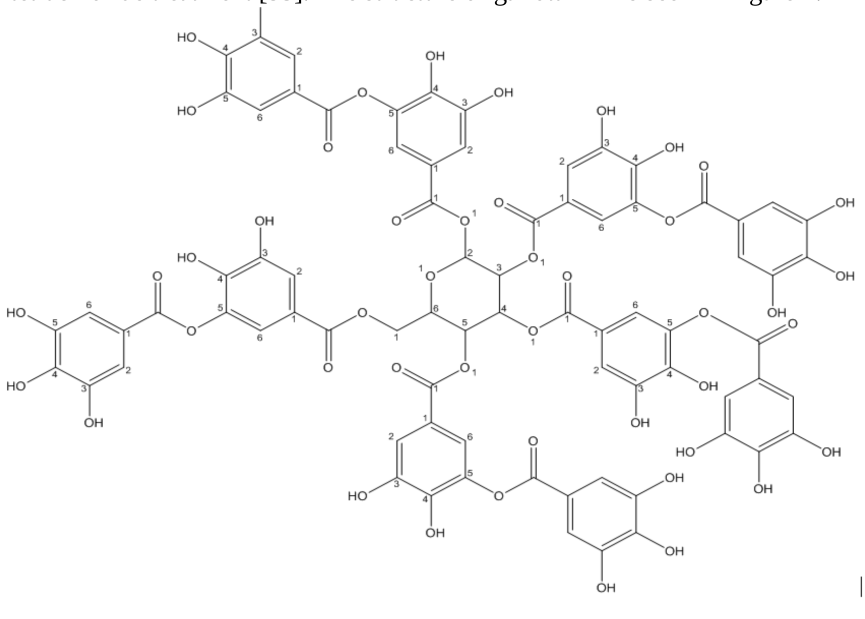

Figure 4: Structure of Gallotannin

Mechanism of Action

By oxidative stress removal and overregulation of antioxidant enzymes, gallotannin-enriched Galla Rhois extracts significantly reduce the increase of serum indicators of liver toxicity, historic damage, induction of apoptosis, and hepatic fibrosis [54]. Table 4 lists the plants that contain gallotannins.

Table 4: Plants containing gallotannins [55]

S. No.	Name of the plant	Biological Name	Family
1	Sumac	Rhus typhinia	Anacardiaceae
2	Sumac	Rhus coriaria	Anacardiaceae
3	Sumac	Rhus semialata	Anacardiaceae
4	Aleppo	Quercus infectoria	Fagaceae
5	Tara	Caesalpinia spinosa	Leguminoseae

Ellagitannins

Ellagitannins are bioactive polyphenols found in a variety of fruits, vegetables, and seeds, including grenadines, black frames, peaches, strawberries, walnuts, and almonds. ETs are complex ellagic acid (EA) derivatives that belong to the hydrolyzable polyphenol tannin class. The hydrolysis of ETs with acids or bases causes the spontaneous lactonization of hexahydroxydiphenic acid (HHDP). After acid hydrolysis, the ETs were employed as EA equivalents for food samples for detection and quantification. ETs are the most abundant tannin group. They also play an important role in human food and have numerous biological properties, including antioxidants.

ETs and EAs as antioxidant compounds rely greatly on their chemical structure. The occurrence of multiple hydroxide functions at position ortho in ETs is due to a strong capacity to donate a hydrogen atom and sustain the unpaired electron. ET and EA antioxidant activity is tightly related to hydroxylation levels and decreases with sugar transport.

ETs, AE, and their related metabolites exhibit a wide range of biological actions that have positive implications for human health. ET, EA, and associated metabolites' antioxidant activities, oestrogens and/or anti-estrogens, anti-inflammatory and prerebiotic properties. Ellagitannins have a high antioxidant effect and can prevent free radical-induced liver damage [56]. The structure of ellagitannin is seen in Figure 5.

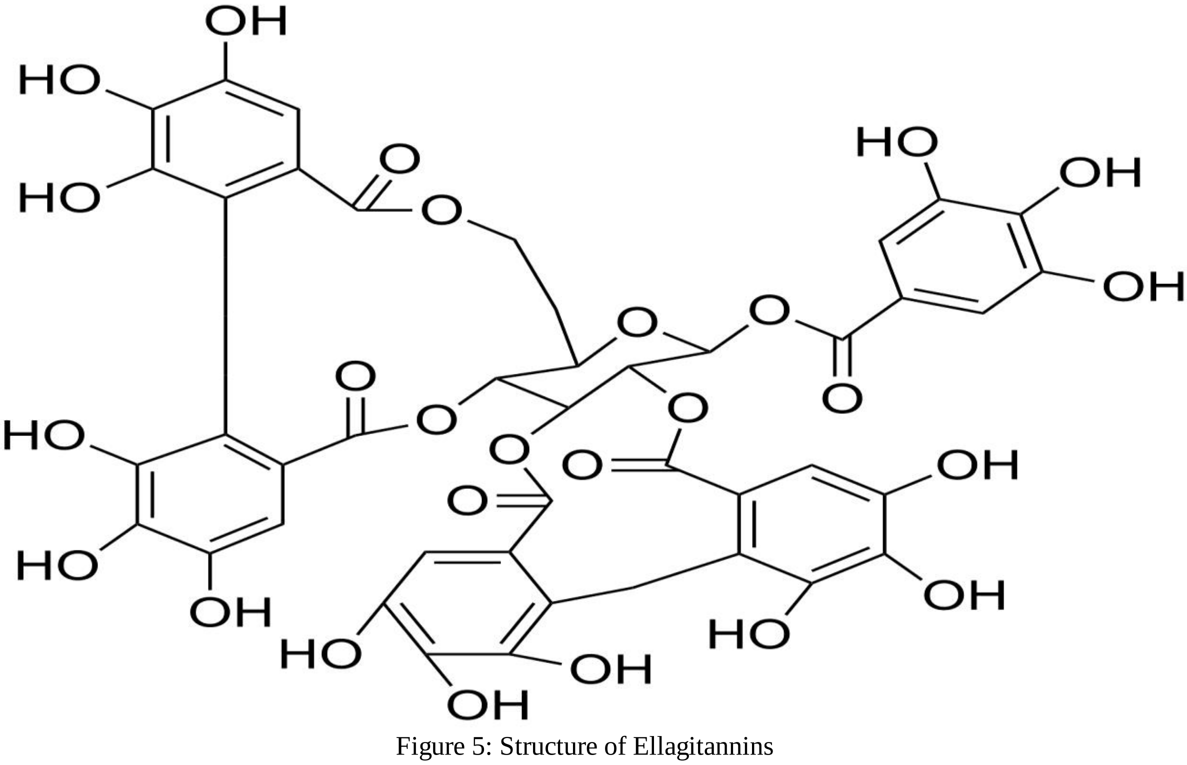

Figure 5: Structure of Ellagitannins

Mechanism of Action

The significant relationship between anti-radical measurement and ETs revealed that high molecular weight polyphenols were the key contributors to antioxidant capacity. ET-structures form as a result of multiple hydroxy-functions in ortho, which have a greater ability to donate a hydrogen atom and support a low molecular weight electron.

ETs and EA have a direct relationship with hydroxylation in terms of antioxidant efficacy. Ellagitannins reduce free radical-induced liver injury by a variety of mechanisms, including direct radical-scavenging activity, metal chelation, and enhanced antioxidant cellular defences such as superoxide dismutase (SOD) and glutathione [57]. Table 5 includes the medications that contain ellagitannins.

Table 5: Drugs containing ellagitannins [58]

S. No.	Name of the plant	Biological Name	Family
1	Cashew nut	Anacardium occidentale	Anacardiaceae
2	Pistachio	Pistacio vera	Anacardiaceae
3	Mango	Mangifera indica	Anacardiaceae
4	Hazelnut	Corylus avellana	Betulaceae
5	Persimmon	Diospyros kaki	Ebenaceae
6	Chestnut	Castanea sativa	Fagaceae
7	Walnut	Juglans regia	Juglandaceae
8	Guava	Psidium guajava	Myrtaceae
9	Cloves	Eugenia caryophyllata	Myrtaceae
10	Pimento	Pimenta officinalis	Myrtaceae
11	Pomegranate	Punica granatum	Punicaceae
12	Plum	Prunus domestica	Rosaceae
13	Apricot	Prunus armeniaca	Rosaceae
14	Peach	Prunus persica	Rosaceae
15	Bird cherry	Prunus avium	Rosaceae
16	Strawberry	Fragaria spp	Rosaceae
17	Raspberry	Rubus idaeus	Rosaceae
18	Blackberry	Rubus fruticosus	Rosaceae
19	Blackcurrant	Ribes nigrum	Saxifragaceae
20	Redcurrant	Ribes rubrum	Saxifragaceae
21	Gooseberry	Ribes grossularia	Saxifragaceae
22	Tea	Camelia sinensis	Theaceae
23	Grape	Vitis vinifera	Vitaceae
24	Muscadine grape	Vitis rotundifolia	Vitaceae

Proanthocynidines

Proanthocyanidines are monomeric flavan-3-ol oligo- or polymers produced as a byproduct of the flavonoid biosynthesis process. Food processing and waste farming Proanthocynidines

Proanthocyanidines are monomeric flavan-3-ol oligo- and polymers generated as a byproduct of flavonoids production. Agricultural and food waste contain a massive amount of proanthocyanidines, which can be used to create a sustainable supply of dietary supplements and functional components. Proanthocyanidines are condensed tannins with a variety of pharmacological actions. Antioxidants, anticancer, anti-diabetic, neuroprotective, and antibacterial properties are among the health benefits of these phytochemicals, which are referred to as "offensive and defence molecules." Proanthocyanidines are found in flowers, nuts, fruit, bark, and plant seeds of several plants as a defence against biotic and abiotic stressors. Its astringency protects the plants from infections and disease predators. These are oligomeric and polymeric flavonoid biosynthetic chemicals. Proanthocyanidine is composed of catechin and epicatechin. Catechin synthesis catalyses the initial step in the manufacture of proanthocyanidine, leucoanthocyanidin reductase.

Proanthocyanidines with high antioxidant activity have been approved. It protects against oxidation and cellular damage caused by hydrogen peroxide [59]. The structure of proanthocynidines is seen in Figure 6.

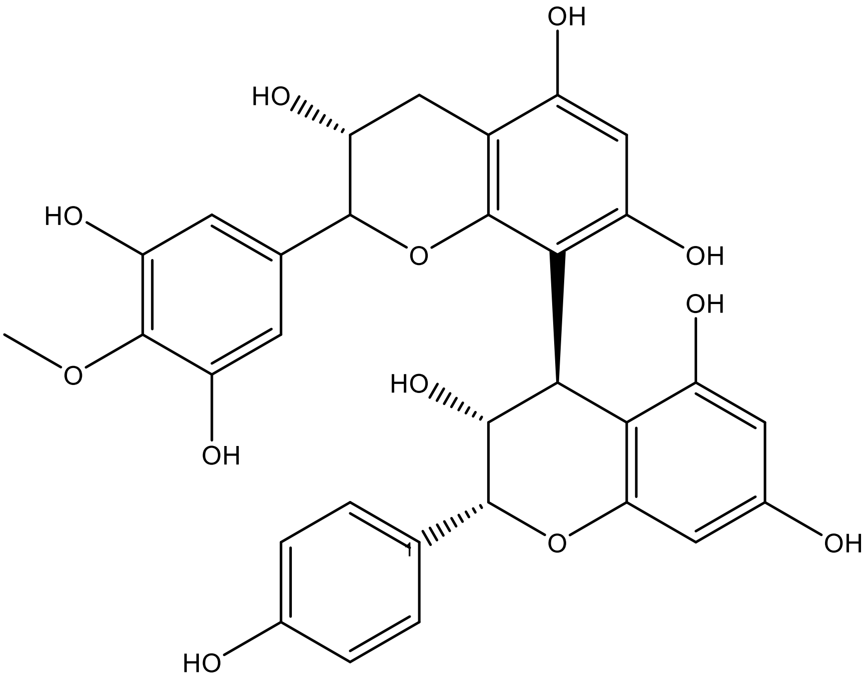

Figure 6: Structure of Proanthocynidines

Mechanism of Action

The proanthocyanidine extract reduces the alteration of glutathione in the liver. The Silent Information Regulator 1 / SiRT1 gene, which regulates the apoptotic response to DNA damage, is improved by proanthocyanidine expression to reduce oxidative loss. It also significantly reduces epigastric discomfort, pain severity, episode frequency, and the need for narcotic pain relievers. One of the various proanthocyanidine pain-relieving medicines is inflammatory suppression in macrophages.

Plant-derived proanthocyanidines are abundant and provide a long-term supply of dietary supplements and functional components. Proantho-cyanidine in Plant-Based Food Items Proanthocyanidines are condensed tannins with a variety of pharmacological actions. Antioxidants, anticancer, anti-diabetic, neuroprotective, and antibacterial properties are among the health benefits of these phytochemicals, which are referred to as "offensive and defence molecules." Proanthocyanidines are found in the flowers, fruit, bark, and seeds of many plants as a defence against biological and abiotic stressors. Its astringency protects the plants from infections and disease predators. These are oligomeric and polymeric flavonoid biosynthetic chemicals. Proanthocyanidine is composed of catechin and epicatechin. Catechin synthesis catalyses the initial step in the manufacture of proanthocyanidine, leucoanthocyanidin reductase.

Proanthocyanidines with high antioxidant activity have been approved. It protects against oxidation and cellular damage caused by hydrogen peroxide [60]. Table 6 lists the plants that contain proanthocynidines.

Table 6: Plants containing proanthocynidines [61]

S. No.	Name of the plant	Biological Name	Family
1	Grape seeds	Anacardium occidentale	Anacardiaceae
2	Blueberries	Pistacio vera	Anacardiaceae
3	Apples	Mangifera indica	Anacardiaceae
4	Pears	Corylus avellana	Betulaceae
5	Hazelnuts	Diospyros kaki	Ebenaceae
6	Cinnamon bark	Castanea sativa	Fagaceae
7	Sorghum grains	Juglans regia	Juglandaceae
8	Kiwi fruit	Actinidia chinensis	Actinidiaceae
9	Avocado	Persea americana	Lauraceae
10	Black currant	Ribes nigrum	Grossualariaceae
11	Red currant	Ribes rubrum	Grossualariaceae
12	Chokeberry	Aronia mitschurinii	Rosaceae
13	Gooseberry	Ribes uva-crispa	Grossualariaceae

14	Blueberry	Vaccinium corymbosum	Ericaceae
15	Bilberry	Vaccinium myrtillus	Ericaceae
16	Strawberry	Fragaria ananassa	Rosaceae
17	Cherry	Prunus avium	Rosaceae
18	Plum	Prunus domestica	Rosaceae
19	Peach	Prunus persica	Rosaceae
20	Pear	Pyrus communis	Rosaceae
21	Grape	Vitis vinifera	Vitaceae
22	Apple	Malus domestica	Rosaceae
23	Rhubarb	Rheum rhaponticum	Polygonaceae
24	Peanut	Arachis hypogaea	Fabaceae

Table 7 represents the list herbal marketed formulations which are utilized for their hepatoprotective action.

Table 7: List of herbal marketed formulations used as hepatoprotectives

S. No	Product Name	Dosage Form	Company Name	Indication
1	Punarnavashtak	Kwath	Orient Ayurvedic Pharmacy	Hepatitis. Renal failure. Ascites.
2	Liv 52	Syrup/Tablet	Himalaya drug co.	Protect liver against various hepatotoxins
3	Livergen	Syrup	Standard Pharmaceuticals	Hepatic Regulator
4	Livokin	Syrup	Herbo-med	Hepatic Dysfunctyion
5	Octagen	Syrup	Plethico Pharmaceuticals	Hepatoprotective
6	Stimuliv	Syrup	Franco-Indian	Liver stimulant and liver tonic
7	Tefroliv	Syrup	TTK Pharma	Liver protection
8	Guduchi Satva	Powder	Natur med	Hepatoprotective
9	Liv strong	Syrupp	Yog Rishi	Reduce effect of alcohol on liver
10	LivO MYN	Syrup	Himalaya drug co.	Protect liver against various hepatotoxins
11	Liv 52 HB	Syrup	Himalaya drug co.	Management of Hepatitis B
12	Liver Kidney Care	Syrup	Organic India	Heals and Protect Kidney and Liver
13	Liv On	Syrup	Sri-Sri	Liver tonic
14	Kumaryasava	Syrup	Dabur	Protect Hepatic Enzymes
15	New Livfit	Tablet	Alembic India	Hepatitis B and E
16	Milk Thistle	Capsule	1 mg healthcare solution	Liver Detoxification
17	Liv T	Syrup	SBL	Liver tonic
18	Hepano	Tablet	Dabur	healthy and protects the liver from damage caused by hepatotoxins
19	Hepa Pro	Powder	British Biological	Improves Liver function
20	Silybon 140	Tablet	Micro	Liver disorders
21	Jiva Kutki	Capsule	Jiva Ayurvedic Pharmacy Ltd	enhances liver functioning
22	Liverlil	Tablets	Meyer Vitabiotics	liver health supplements are also useful for patients who are prescribed hepatotoxic drugs to treat and control chronic diseases.
23	Amrutarishta	Liquid	Dhootapapeshwar	enhances liver functioning
24	Diaglinis	Capsule	AN Phaarmaceuticals	acute hepatitis, chronic

				hepatitis, fatty liver, alcoholic hepatitis and cirrhosis
25	Meadbery Liver Detox	Capsule	Meadbery	Supports liver health and improve digestion

2. Conclusion

The current chapter discusses tannin characteristics, structure, and occurrence, as well as tannin involvement in hepatoprotection. Tannins are phenolic chemicals with high molecular weights found in plants, with molecular weights ranging from 500 to over 3000 Da and up to 20,000 Da. Tannin's chemical structure is extremely diversified. Tannins are an essential component of plant cell walls. This chapter focuses on tannin compounds, which have a wide range of effects on hepatic cells. The chapter also includes information on some of the marketed tannin-containing medications that are officially used to treat and control hepatotoxicity.

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