Chapter

Applications of Tannins in Industry

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Abstract

Tannins are water-soluble natural polyphenols mainly present in plant-based materials, including food. Tannins play a very significant role as a raw material for sustainable green industries. Therefore, they are mainly used in diverse types of industries such as leather, feed, fisheries, beverages, etc. They also find application as potential medicinal agents, antioxidants, metal chelators; and cater as inhibitors of harmful pro-oxidative enzymes and of lipid peroxidation process. Recently, several important properties like antiseptics, anticarcinogenic, and anti-inflammatory of tannins have been documented in the human that make them suitable candidates for pharmaceuticals and nutraceutical industries. Because of current concerns related to synthetic compounds used in the human health and food industries, which leave highly adverse effects on the human body and environment, tannins can offer an alternative to these harmful chemicals in recently emerging industries.

Keywords: tannins, nutraceutical, wood, leather, pharmaceuticals industries and antibacterial activity

1. Introduction

Biochemically, tannins are sort of secondary metabolites predominantly available in the plant-based foods and beverages. The name "tannin" is originated from the industrial process of "leather tanning," in which animal hides are converted into leather through downstream processing. It is worthwhile to mention that tannins were used in this process from historic times. On the basis of their presence, various parts of plants such as bark, wood, leaves, seeds, roots, and even the plant galls are the major sources of tannin extractions used for various purposes (**Table 1**). Algae is also rich source of tannin-based compounds such as phlorotannins which comprise of antioxidant, antidiabetic, anti-inflammatory, and antitumor properties evaluated in the case of human [1, 2]. In addition to health benefits, phlorotannins isolated from brown seaweeds have been used in the cosmetics also [3]. Some researchers have defined tannins as "Any phenolic compound of sufficiently high molecular weight containing sufficient hydroxyls and other suitable groups (i.e., carboxyls) to form effectively strong complexes with protein and other macromolecules under the particular environmental conditions being studied" [4].

Plant tannins are a large group of natural phenolic compounds which contain a range of molecular weight between 500 and 3000 Da. Currently, they have been divided into three main subgroups: (1) hydrolysable tannins, (2) condensed tannins, and (3) phlorotannins. Hydrolysable tannins are highly soluble in water; biochemically, they consist of a central core of a carbohydrate (D-glucose) with

S. no.	Name of plant species	Plant parts	Major components	Medicinal use
1.	*Krameria triandra* L.	Root	Tannic acid, rhataniatannic acid, peculiar acid principle, krameric acid, phlobaphene, phloroglucin, and proanthocyanidins	Chronic diarrhea, menorrhagia, urinary diseases, bleeding from the bowels, bad throat, and antibacterial agents for the eyes, nose, and gums
2.	*Potentilla erecta* (L.) Rauschal	Roots	Pentadigalloylglucose, pedunculagin, epigallocatechin, catechins, and proanthocyanidins	Inflammations, wound healings, diarrhea, inflammation of bowel bacterial, fungal, and viral infections
3.	*Sanguisorba officinalis* L.	Root	Sanguiin H-6	Dysentery and insect bites
4.	*Potentilla kleiniana*	Aerial parts	Agrimoniin and potentillin	Diarrhea, cough, lymphadenitis, and hepatitis
5.	*Syzygium cumini*	Bark	Corilagin and related ellagitannins	Bad throat, asthma, dysentery, and ulcers
6.	*Quercus robur* L.	Bark	Grandinin, castalagin, and glucogallin	Diarrhea, itching, and burning
7.	*Phyllanthus muellerianus* (Kuntze) Exell	Leaves, stem, and bark	Geraniin, phenazine derivative of geraniin, Corilagin, and furosin.	Wound healing
8.	*Geranium thunbergii* Siebold exLindl. & Paxt.	Leaves	Geraniin	Intestinal disorders
9.	*Mouriri pusa* Gardn. (Melastomataceae)	Leaves	Catechins and other condensed tannins	Gastritis and ulcers
10.	*Acacia nilotica* (L.) Willd. exDelile.	Pod	Gallocatechin-gallate, methyl gallate, catechin, catechin gallate, galloylglucose, and epicatechin	Fever, diabetes, and gum diseases
11.	*Diospyros kaki* Thunb.	Fruit	Proanthocyanidin oligomers based on catechin, gallocatechin, catechin-3-O-gallate, and gallocatechin-3-O-gallate	Antiseptic and cardiovascular diseases
12.	*Quercus infectoria* Oliv.	Gall	Tannic acid	Bacterial, fungal, and viral infection

Note: Table indicates that tannin and its components are present in most of the parts of the plants which offered great level of medicinal sources or pharmaceutical agents [59].

Table 1.
Plant species containing tannins and their medicinal use.

its hydroxyl groups or polyol esterified with phenolic compounds such as gallic acid (3,4,5-trihydroxybenzoic acid) or hexahydroxydiphenic acid, which also known as ellagic acid (ellagitannin). Hydrolysable tannins mainly originated from Pentagalloylglucose (2-O-digalloyl-1, 3, 4, 6-tetra-O-galoyl-α-D-glucopyranose), which is a basic structural unit of hydrolysable tannins. The main source of structural diversity among the hydrolysable tannins is the presence of diverse types of oxidative linkages that give rise to oligomeric compounds with molecular weight between 2000 and 5000 Da [5]. Characteristic examples of hydrolysable tannins are (1) gallic acid; (2) hexahydroxydiphenic acid; (3) ellagic acid; and (4) pentagalloylglucose, which contain a central glucose molecule as the core attached with multiple gallic acid units, while ellagitannins are associated to hexahydroxydiphenic acid. Hydrolysable tannins are mainly present in angiosperm and dicotyledons. Both gallotannins and ellagitannins may synthesize individually or in the form of a mixture in plants. Gallic acid has been extracted from plant families, for example, Ericaceae, Geraniaceae, or Fagaceae; whereas, ellagic acid is available in Hamamelidae, Dilleniidae, and Rosidae species [6].

Naturally occurring condensed tannins are polyphenolic bioflavonoids, are polymers of polyhydroxy flavan-3-ol units, for example, (+)-catechin and (−)-epicatechin-2, (+)-gallocatechin, and flavan-3, 4-diols. They are also known as proanthocyanidins (PA) that ascribed to their hydrolysis to anthocyanidins in heated ethanol treatment. Due to presence of stereoisomerisms in hydroxylation patterns at three chiral centers, bond positions, and type of interflavan bond; proanthocyanidins are present in variety of active forms, for example, (1) (+)-catechin; (2) (−)-epicatechin; (3) (+)-gallocatechin; (4) (−)-epigallocatechin; and (5) (−)-epigallocatechin gallate. Among them, (+) catechin and (−) epicatechin are predominantly present in nature [7]. There are several plant species which offer rich source of proanthocyanidins (see **Table 1**). Proanthocyanidins can be obtained from red wine, green tea, cocoa, and chocolate. However, condensed tannins can further be classified on the basis of reaction rate like, slow reacting tannins like quebracho and mimosa and fast reacting tannins like pine and pecan (*Carya illinoensis*) [5, 7, 8]. Furthermore, some researcher also classified tannins into four different classes based on their structural properties, namely, (1) gallotannins, (2) ellagitannins, (3) complex tannins, and (4) condensed tannins.

After the industrial revolution, most of the synthetic chemicals were used in the diverse types of industries including food, pharma, beverage, leather, and other industries. But prolonged applications of synthetic chemicals in the area of health and other industries left a myriad of adverse effects on environment and human health. Therefore, current focus has been shifted on alternative natural compounds like tannins that can be exploited in the form of functional food, nutraceutical, cosmetology, and pharmaceutical industries.

The global tannin market is expanding very rapidly; according to estimation, 1076.3 kilotons tannin was required in 2015 which expected to rise with CAGR of 5.8% from 2016 to 2025. The demand was mainly in the wine, leather, pharmaceuticals, and wood industries. In case of USA, approximately 282.4 kilotons tannins were produced; its 62.3% is used in leather industries alone. Europe is another emerging market for tannins and tannin-based products. It is due to large scale wine production, which is accounted for 38% revenue generations in Europe. Hence, global market size for tannin related industries may increase up to $3.3 billion by 2025. The applications of condensed tannins are expected to increase up to 424.8 kilotons by 2025 in comparison of 242.9 kilotons in 2015 [9].

But, there are several unresolved issues linked with applications of tannins such as antinutrient effect, resistance to enzymatic hydrolysis, and lack of complete information about their interactions with other biomolecules and mode of actions in human and animals. The aim of this chapter is to present a brief discussion on the application of tannins in modern industries and to review their positive and negative aspects. It also shows that tannins are being used as sustainable raw material with other green materials in new emerging industries.

2. Application of tannins in various industry

Currently, hydrocarbon-based raw materials are exploited in different petrochemical industries ranging from fuel to cosmetology. It leads to the widespread deficiency of raw material eventually that creates high inflations, environmental degradation, and adverse effects on human and animal health. This necessitates to explore new alternative natural biopolymers such as polylactic acid, chitosan, lignin, and tannins for replacing with currently used hydrocarbon based polymers. Tannins can be the best natural raw material for emerging and traditional industries. This is attributed to tannin's unique natural properties, chemical structure, and commercial properties [10]. Tannins provide several advantages like being as good biomaterial, antimicrobial, antioxidant, pharmaceutical, biopesticide, and nutraceutical agent. Tannins can be tapped for their applications in food, wood, leather, pharma, and other industries as possible raw material, as given below.

2.1 Food industry

Tannins are the secondary metabolites present in a substantial amount in plant-based food products. Due to their positive effects on the food as antibacterial and antioxidants, they are the major constituent of foods. Tannins are used as food preservatives, packaging materials, and food enhancements which owe to their protective nature.

2.1.1 Food packaging

Currently, most of the food items available in the market are wrapped in the packing materials which are plastic, polyethylene, and low-density polyethylene (LDPE) and linear low-density polyethylene (LLDPE) due to their lightness, inertness, and easy availability. In fact, packaging increases the shelf-life and prevents physical damage, contamination, and deterioration in view of environmental contaminants. But these synthetic materials pose great level of environmental and health hazards. Hence, the concept of natural and active packaging has been introduced and there being continuous efforts to make packing materials from biological sources like, chitosan, starch, gelatin, tannins, and methylcellulose [11, 12]. In view of consumer awareness and knowledge, it becomes essential to develop new wrapping material for food items. However, nitrocellulose-based package are already in use in food industry, but currently the "active packaging" also introduced. Active packaging is a better option which protects the food material, simultaneously it also acts as an additive to improve antioxidant properties of foods and absorb unwanted substances such as heavy-metals or exhausted oils and to protect against oxidation, UV, and moisture-based degradation.

Recently, a packaging material was prepared by introducing tannins into cellulose nanofibrils in a single step process of mechanical fibrillation. This newly developed packaging film offers high density, and enhanced surface hydrophobicity which resulted in almost six times improvement in air-barrier and antioxidants properties. Simultaneously, nanocellulose-tannin-based films are active packaging materials which also provide a green, sustainable, nontoxic packaging source for food and pharmaceutical products [11, 12].

Two perishable food items, Cherry tomatoes (*Solanum lycopersicum var. cerasiforme*) and grapes (*Vitis vinifera*), were effectively preserved from *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*) for 14 days by tannin-based film that was produced by introducing 15% (w/w) tannin into chitosan, gelatin, and methylcellulose films. Hence, tannins improve the physiochemical properties of biopolymer films, consequently improvement in overall ability to preserve fruits and vegetables. In addition, it reduced the weight loss and improved the browning index of fruits during storage. Another oligomeric procyanidins (OPCs)-based membrane in combination of flaxseed gum (FG) and lauric acid (LA) had more water vapor permeability (WVP), mechanical properties, and peroxide value (POV) of packaging film [13]. The film was evaluated for oil, salt, and vegetable preservation for 75 days. The results indicate that membrane can be used as promising packaging material.

Generally, chitin is used as packing material, but its poor antibacterial and antioxidant abilities make it unsuitable for food packaging; therefore, tannic acid was introduced in the chitin film via single step process of interfacial assembly. Tannins addition to packaging has significantly improved the antibacterial and antioxidant properties of chitin-based packaging film. Improved quality of chitin-based film is mainly attributed to hydrogen and hydrophobic bond formation between chitin and tannins [14].

Protein is a major component of food, and its protection is of utmost significance in packed foods. So far, tannin- and carbohydrate-based packaging films were prepared. But, a soluble dietary fiber (SDF) and tannin-based nanocluster assembly is prepared by introducing calcium ions that creates a cross-linking nucleus in membrane. Linkage between nanoassembly and proteins offer additional advantages such as high level of antimicrobial properties and excellent cell biocompatibility which was proved by FT-IR, XRD, and DSC tests [15]. Tannin-based packing materials thus offer green, sustainable, and ecofriendly alternative that can be used in the food preservation and biomedical fields.

2.1.2 Food preservation

Microorganism, fungus, yeasts, virus, pollens, and chemicals are the biggest threat to food's shelf-life in home as well as in food markets. Biochemically, proanthocyanidins and gallic acid are flavonoid monomers by nature and are major food constituents isolated from pomegranate, strawberry, blackberry, raspberry, walnuts, almonds, and seeds. Various studies have proved that tannins prevent growth of microorganisms. Tannins are quite effective against the resistant methicillin-resistant *Staphylococcus aureus* (MRSA) [16, 17]. Moreover, Punicalagin, an ellagitannin, isolated form pomegranate peel show very strong antibacterial properties against *Staphylococcus aureus* and can be used to control *S. aureus* contamination in food industry.

Food-based viral infection is another major health problem in human and animals. Currently, blueberry proanthocyanidins were tested against human norovirus growth in apple juice (AJ) and milk with 2% fat tannin-rich fraction from pomegranate rind (TFPR) inhibited the growth of human norovirus [18]. Hence, hydrolysable tannins are potential antiviral agents that used can be used in the food preservation to make food items more safe and preserve for prolonged period by using natural compounds.

Guava is a major tropical fruit which is also considered as a model system to study climacteric and non-climacteric fruit ripening process. Hence, it provides enough opportunities to understand post-harvest management of perishable fruits. In order to improve the shelf-life of fruits, various types of wax films, coating, and chemical treatments are used for long time. Tannins isolated from various natural sources act as preservatives due to their antibacterial and antioxidant properties. A coating material of tannic acid cross-linked with zein protein was used for coating on the guava fruit. Actually, zein is a prolamin (protein) isolated from aqueous alcohol-soluble fraction of corn (*Zea mays* L.) that earlier used to improve the shelf-life of guava fruit [19]. The coated guava fruits showed reduced ripening process and improved shelf-life compared with uncoated fruits. The coated fruits also showed more positive biochemical parameters associated with better fruit shelf-life, such as total soluble solids, respiration rate, and chlorophyll contents. Moreover, ethylene, ROS production, less water loss, and gas exchanges are also observed, which are attributed to cross-linking between tannic acid and zein [19]. Hence, tannin-based package and coating material may prove more effective and ecofriendly in food industry.

2.1.3 Functional foods or nutraceuticals industry

Normal food components mainly provide the energy and essential nutrients for the growth and development for animals including human, but food also consist of bioactive molecules or phytochemicals and their inclusion in the appropriate quantity can act as possible therapeutically active agents also known as nutraceuticals, for example, (poly) phenol-rich tannins [20]. Currently, study of molecular mechanisms and pathways such as cell proliferation, apoptosis, inflammation, differentiation, angiogenesis, DNA repair pathway, and carcinogens activation offer new therapeutic targets. The application of tannins has great potential as a nutraceuticals in order to prevent various diseases such as cancer, cardiovascular, kidney diseases, and diabetes. Major sources of tannins are fruits, vegetables, bark, wood, leaves, and seeds such as green tea, apples, cocoa, chocolate, grapes, apricots, and cherries. Among them, role of tannins present in the tea and coffee to prevent the cancers have been studied by large number of scientists. The green tea contains condensed tannin namely epigallocatechin gallate (EGCG) and epicatechin gallate (ECG), which have shown anticancerous activity in terms of inflammatory and antioxidant properties both in vivo and in vitro experimental systems [21]. Actually, EGCG decrease activation of NF-kB and (AP-1) TNF-α pathways simultaneously which ultimately reduced the production of IFN-γ. It can also enhance the apoptosis process through suppression of COX-2 enzyme that leads to the production of PGE2 (prostaglandins) in various types of cell lines of colon cancer cells, such as SW837, HT-29, and HCA-7 cells. Being a polyphenol, EGCG is a strong antioxidant that reduces the activity of nitric oxide (NO) and malondialdehyde (MDA) and conversely increases superoxide dismutase (SOD) activity in case of colonic mucosa. Hence, EGCG can improve the effect of cancer chemopreventive potency by preventing the cell proliferation, migration, and invasion of tumor in cancer patients [20].

In last two decades, a great interest has been emerged in the protective role of tannins against free radicals and reactive oxygen species produced inside cells, which caused degenerations and diseases such as cancer, atherosclerosis, and cardiovascular ailments. Proanthocyanidins have cardiovascular protective effect due to their antioxidant activity, inhibition of LDL oxidation, ability of vasodilation, antiplatelet activity, and protection against ischemia-reperfusion injury. Another tannin-based compound, gallic acid (3,4,5-trihydroxybenzoic acid), a naturally occurring with low molecular weight, plays very important in the protection of cardiovascular health through rejuvenating the antioxidant system which include large number of enzymes such as SOD, CAT, GPx, GRx, and GST which constitutes a scavenging system against the free radicals [22].

Diabetes mellitus, associated with high level of glucose concentration in the blood, is harmful for whole tissues in human body. Several investigations have shown that it can be reduced or managed by adding the appropriate amount of tannins in the nutrition or supplements of patients [23]. Because, tannins improve the glucose uptakes in body cell and simultaneously reduce the synthesis of adipocytes, hence act as the potential therapeutic agents. In a highly significant study, it shows that epigallocatechin gallate increases the glucose uptake by regulating insulin-signaling pathways, such as PI3K (phosphoinositide 3-kinase) and p38 MAPK (mitogen-activated protein kinase) activation and GLUT-4 translocation [24]. Tannins help reduction of blood glucose levels and offer antioxidants effects [23]. Therefore, it can be concluded that tannin-based foods are potential agents used as either nutraceutical or supplementary agents in food or medicine. A dimer of proanthocyanidin acts against the hyperglycemia that was created by sucrose feeding and by inhibiting the activity of α-glucosidase enzyme. The efficacy of proanthocyanidin has also been proved by molecular docking and strong inhibitory activity experiments.

It is already mentioned that nutraceuticals or functional foods have the health promoting effect on the human and animal health. Several epidemiological studies have clearly established a relationship between (poly) phenol-rich food items and human health. It has substantially enhanced consumer awareness about the tannin-rich diet, and their disease prevention capability; therefore, there is high demand of functional foods. A large number of tannin-based compounds are isolated and characterized from fruits and vegetables (**Table 1**). But, despite high cost incurred on extraction and separation of tannin, it offer only low yield which is a major cause of concern [25]. Additionally, it does not provide the pure content which hindered to test the efficacy and absorption of tannin-based foods in human subject. Grape-seed proanthocyanidins (GSP) were lyophilized to improve their in vivo absorbability. It was achieved by esterification of the water-soluble GSP and immobilized lipase. Lipophilicity was tested by 1-octanol/water partition coefficient as the absorbability parameter. Further, it was observed that GSP derivatives, 3′,5′-2-O-lauroyl epigallocatechin, 3′-O-lauroyl catechin, 3′-O-lauroyl epicatechin, and 3′,3″,5″-3-O-lauroyl epicatechin gallate show high level of radical scavenging activity; hence, it can be used as the strong antioxidant in food to prevent the major degenerative diseases and aging, which are generally caused by the free radicals in the tissues [25]. Recently, B-type proanthocyanidins were isolated and purified from fruits of elephant apple (*Dillenia indica* Linn.), their structural and bioactive properties were examined by using NMR, electron spray ionization, and matrix-assisted laser desorption ionization time of flight mass (MALDI-TOF) spectra. In this experiment, yield of 0.23% was achieved that is far greater than commercial grape-seed proanthocyanidins [26]. Hence, the EAPs may be used as promising functional food agents. In view of above health benefits provided by tannin-based compounds; they are now available in the dietary supplements. These contain biological extracts packed with both types of tannins and their consumption may provide health benefits. Recently, a concoction of ellagitannins, punicalagins, and polyphenols was commercialized by brand name, that is, Healing America Ellagitannin capsules and Ellagic Active Tablets.

2.2 Wood industry

Wood is the inseparable part of the furniture and several important industries. Wood contains organic acids, tannins, and lignocellulosic material which are most susceptible to biological, chemical, and physical decaying agents. Therefore, wood requires a large number of synthetic adhesives, glues, antitermite chemicals, and other coating materials in order to protect it. However, these materials have tremendously benefitted the wood industry, but they adversely affect the environment conditions. Because synthetic phenolics, amino resins, and formaldehyde used in wood industries are generally carcinogenic in nature. To overcome this problem, scientists are investigating natural materials of herbal or animal origins, such as tannins, that can be the best option or alternative material to be used in the wood industries [27].

In recent years, a lot of attempts have been made to improve the bio-durability and commercial properties of wood and wood-based furniture by using tannin-based preservatives. Although both condensed and hydrolysable tannins are used as adhesive, but mimosa tannin is proved to be the most effective wood glue, which attributed to good cross-linking, auto-condensation, poly condensations reactions, and hyper activity. Tannin-based adhesive is proved to be harder than pure synthetic adhesive due to great level of bonding with other aldehydes or different non aldehyde hardeners (glyoxal, furfuryl alcohol, hexamine, etc.) and lignocellulosic materials. Several industries in South Africa and America are using the mimosa and quebracho-based tannins that could reduce the formaldehyde-based emission from the industries. A similar technology has been used to produce the interior and exterior grade particle board largely used in the furniture industry [28]. Apart from this, catechin and gallic acid-based epoxide adhesives and starch-based adhesives from tannins were also produced. Epoxy adhesives are produced by reactions between catechin and epichloridrin via alkylation in the presence of unsaturated halogenated compound that leads to the oxidation. Tannin-based adhesives have been used for grinding wheels, angle grinder disks, and automotive brake pads matrices also.

Coating material is extremely useful to prevent wood surface from biotic and abiotic adversities like, rain, winter, and summer, and insects and microorganisms. Generally, coating material comprises of polyurethane and isocyanates. The urethane-based coating material is prepared by using the lignin and lignosulfonate/hydroxypropylate. Recently, Pinus tannins and di-isocyanates were used to prepare more effective coating material by exploiting hydroxypropylation and hydroxybutylation reactions which enhanced the bonding patterns between hydroxyl groups provided by tannins (flavonoids) and isocyanates [29]. However, tannins and isocyanate-based adhesives are good and environmental friendly, but these should be replaced with more bio-based material like tannins because they are naturally designed to protect wood against fungal attacks and natural decaying process of wood.

2.3 Medicine and pharmaceuticals

After the industrial revolution, large numbers of synthetic chemicals were used as drug molecules to treat numerous diseases but they left several adverse effects on the human and environment. Therefore, attention has been shifted to identify new alternative natural compounds that are to be clinically effective and create minimum adverse effects. A large number of natural compounds such as polyphenolic-based secondary metabolites, for example, tannins, are isolated and characterized as preventive therapeutic agents, which can be isolated from fruits, vegetables, or plants or expressed in the microorganism by metabolic engineering. Many studies have clearly shown that tannins are natural antioxidants linked with the prevention of degenerative diseases such as atherosclerosis, cardiovascular diseases, neurodegenerative diseases, and certain types of cancers by acting as antioxidants and antibacterial.

2.3.1 Tannins as preventive medicine

Reactive oxygen species such as, hydroxyl radical (HO•), superoxide anion ($O_2{\bullet}^-$), and peroxyl radical (ROO•) and the non-radicals like, hydrogen peroxide (H_2O_2) and hypochlorous acid (HOCl) are produced in biological systems. They adversely affect cellular protective systems which are responsible for many degenerative diseases in human. In order to overcome toxic effects of reactive oxygen species (ROS), tannins can be used as ROS scavenging agents. Actually, tannins have the ability to donate electron to a free radical or ROS and make them more stable compounds therefore, render less harmful effects on cellular environment [22, 30, 31]. Tannins also help by supporting antioxidant enzymes involved in the ROS scavenging activities, simultaneously inactivating the metal ions produced by free radicals. Many tannin-based products such as gallic acid (GA) (3,4,5-trihydroxybenzoic acid), proanthocyanidins, epigallocatechin gallate (EGCG), and ellagic acid-4-O-α-D-xylopyranoside have been tested and found highly effective as antioxidants. Gallic acid, isolated from many plant extracts, shows strong antioxidant properties responsible for the antioxidant and anticancer activities. Moreover, gallic acid derivatives (GADs) are present in large number of herbal medicines and formulations used for variety of diseases. Tannin derivatives like mucic acid gallate, mucic acid lactone gallate, monogalloylglucose, gallic acid, digalloylglucose, putranjivain A, galloyl-HHDP-glucose, elaeocarpusin, and chebulagic acid isolated from fruits of *Phyllanthus emblica* exhibit antioxidant activities that are already proved by the study of animals models. Currently, researchers have shifted their focus on the role of individual tannin molecules rather than group of compounds in the biological system for example, gallic acid, and epigallocatechin gallate (EGCG) from fruits and teas, respectively, are widely studied [22, 32].

2.3.2 Antibacterial properties of tannins

Synthetic antibiotics are being used as antibacterial agents for a long time in medical and animal sciences. But prolonged application of antibiotics lead to the development of resistance against the antimicrobial agents among the bacterial species attributed to selective evolutionary processes, a problem being faced by researcher world over. Nowadays, methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug-resistant pathogenic microorganisms are great health problems responsible for large number of morbidity and mortality in human population. Moreover, development of resistance to virtually all currently available antibiotics make situation more worsen. Therefore, it is of urgent need to discover new natural antimicrobial agents or antibiotics to cope with the development of antibiotics resistance [31].

However, many antibiotic resistance mechanisms are prevailed in the resilient microbial strains, but the mechanisms studied in *Staphylococcus aureus* RN4220 and IS-58 strains show that these particular strains have the capability to drain out the antibiotics from cytoplasm through proteinous membrane pumps. In a highly significant study, sub-concentration of pump inhibitors and tannins was used which significantly inhibited pump functions in both RN4220 and IS-58 strains [33].

Tannins have been used against the ATCC 43300 and MRSA clinical strains as membrane pump inhibitors and their mode of action was studied by using next-generation sequencing (NGS) in order to get deep understanding of antibacterial mechanisms at genome, transcriptome, and protein synthesis level. This investigation indicates that tannins mainly disrupt protein synthesis mechanisms by bringing major changes in ribosome pathways, which further caused a change in the translation processes in MRSA cells eventually leading to reduction in bacterial growth. Hence, tannins can be used as potential tools against the anti-MRSA agents in clinical application particularly, in antiseptic body solutions and antibacterial cream [31]. More recently, three ellagitannin-based tannins and isorugosin-A extracted in acetone from the fresh leaves of *Liquidambar formosana* showed high level of antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa* that attributed to tannins binding with membrane proteins, by polyphenolic acyl groups [30].

Tannin and its derivatives show great antibacterial properties which are used against a large number of bacterial species such as *Aeromanas*, *Bacillus*, *Clostridium*, *Enterobacter*, *Helicobacter*, *Klebsiella*, *Proteus*, *Pseudomonas*, *Shigella*, *Escherichia*, *Staphylococcus*, or *Streptococcus* and fungal species like *Aspergillus*, *Coniophora*, or *Penicillium*. Antibacterial activity of tannins particularly, polymeric proanthocyanidins proved highly effective against *Escherichia coli* and *Staphylococcus aureus*. It is attribute to binding of tannins with urinary tract epithelium and intestinal epithelium that prevent binding of disease causing organisms. In view of above findings, tannic acid is used as an inhibitor and immunomodulatory against multidrug resistant bacteria (MDR) [28, 33].

The antibacterial properties of tannins are not only studied in animals but in plants too. Several microorganisms cause the substantial loss in the fruit, vegetable, and plant species resulting in great economic loss. After the green revolution, huge amount of pesticides were used to prevent the bacterial and insect attacks in crops which lead to the environmental pollution and soil contamination. But bio-based pesticides or natural products can be the best option of chemical-based antibacterial agents. Recently, crude methanol extract of *Sapium baccatum* was used against the *Ralstonia solanacearum*, a causal agent of bacterial wilt of tomato. The extract mainly contains gallic acid, methyl gallate, corilagin, tercatain, chebulagic acid, chebulinic acid, and quercetin 3-O-α-L-arabinopyranoside which all show strong antibacterial activity except one tannin-based product, that is, quercetin 3-O-α-L-arabinopyranoside. In in vivo studies, the concentration of 2000 and 1000 μg/mL of crude extract reduced the development of tomato bacterial wilt by 83 and 63%, respectively [34].

2.3.3 Antifungal properties of tannins

The growth of fungi such as *Fusarium semitectum*, *F. fusiformis*, and *Alternaria altternata* can be hindered by gallic acid [22, 35]. The ethyl acetate extract and its sub-fraction from red raspberry (*Rubus idaeus*) fruit have high level of antifungal activities against the *Candida albicans*, *C. glabrata*, and *C. parapsilosis* strains of fungi due to their antimicrobial activities of tannins. These fungal strains form drug-resistant biofilms inside the oral cavity responsible for dental caries, periodontal disease, and denture stomatitis. However, the activity of extract was dose dependent, and 25 and 12.5 μg/mL of 80% ripe fruit extract was more effective as antiadherence or antibacterial agents against the microbial films formations [35].

2.3.4 Immunomodulatory activities of tannins

Immune system plays a very significant role to cope up with infectious agents like bacteria, virus, fungus, pollens, and parasites. Some experiments show that tannins modulate human immune system in a highly positive manner, thus tannins act as immunomodulatory agents in the battle against infectious diseases. Leishmaniosis, a disease that caused by parasitic protozoan's complex, comprise of more than 20 different species of *Leishmania* genus. Its conventional treatments are highly expensive, and lead to many side effects; moreover, protozoan resistance to treatments has been reported. Two most important tannins, gallic acid (GA) and ellagic acid (EA), were tested for antileishmania, cytotoxic, and immunomodulatory activities. Both GA and EA significantly reduced the infection and infectivity of macrophages infected by *L. major*. Moreover, both GA and EA induced high immunomodulatory activity of macrophage cells that proved by enhanced phagocytic capability, lysosomal volume, nitrite release, and intracellular calcium in macrophages. Therefore, tannins can be used as potential therapeutic agents against the leishmaniosis [36].

2.4 Role of tannins in animal husbandry

Bacterial and fungal infection is also a threat to the poultry, livestock, and animal husbandry which is responsible for high level of mortality. To overcome this problem, several antibiotics have been used for decades that proved to be very effective; consequently, it improves animal and poultry production in the world. But it is well known that extreme application of antibiotics promotes the antibiotic-resistant among the microorganisms in cattle [37–39]. Therefore, in-feed antibiotics and plant-based antibacterial agents, such as phytogenic compounds (e.g., tannin), have been discovered and promoted, which have great promises in future. In recent past, great attention has been given to antibacterial activities of tannins and their effects as dietary source in animal [37]. It has been concluded that tannins with saponins and essential oils can be used as in-feed antibiotics against bacteria, fungi, and yeasts. Because, tannins are toxic to bacteria and potentially inhibit growth of *Salmonella*, *Shigella*, *Staphylococcus*, *Pseudomonas*, and *Helicobacter pylori*, but it would be noteworthy that they show species specific antibacterial activity. Moreover, tannin-containing forage in cattle diets helps to control animal pasture bloating, intestinal parasite, and disease causing bacteria in ruins of animals. Tannins can hinder microbial growth by using several mechanisms including lack of nutrient to bacterial cell, inactivate vital extracellular enzymes, inhibition of oxidative phosphorylation, chelation of metal ions, and complex formation with membrane and proteins [38]. It has been seen that condensed type of tannins are mainly present in forage legumes, trees, shrubs, tree leaves, and browse shrubs, but their concentration vary from species to species that influenced by environmental conditions also [40]. Tannins from mimosa (HT), chestnut (HT), and quebracho (CT) have been used as in-feed antibiotics in animals [41]. But the major challenge for tannins as antibiotics is the lack of systematic and comprehensive studies on the various aspects such as doses, side effects on digestions simultaneously prolong use can develop resistance against the in-feed antibiotics as in case of normal antibiotics [40]. Moreover, tannins are antinutrient factors for monogastric animals and poultry.

Tannins can also act as the antinutrients in rumens of livestock due to their binding to vital biomolecules in biological systems. Several adverse effects such as availability of nutrients, metal ions chelation, binding with proteins and hinder the growth of beneficial microflora have been observed in the cattle gut. To test the adverse effect of tannin as diet component on lamb gut microflora and fermentation was studied. Both types of tannins, that is, hydrolysable and condensed with 4% extract of chestnut (*Castanea sativa*, *Caesalpinia spinosa*), *mimosa* (*Acacia negra*), and *gambier* (*Uncaria gambir*) feed to lamb. The results show that tannins meagerly affect gut microflora including fungi in the lamb gut for 45 days. Simultaneously, it also shows that high level of tannin inclusion in diet proved as antimicrobial agent against the harmful methanogens and protozoa without affecting ruminal fermentation [42].

3. Nanotechnology and tannin

Cancer is a fatal disease and its occurrence in the human population is the major cause of concern. However, the role of tannins as chemopreservants in the cure of cancer has been widely discussed by many researchers [42]. The chemoprevention "is a means of cancer management by which the occurrence of the disease can be entirely prevented, slowed, or reversed via administration of one or more naturally occurring and/or synthetic compounds" [43]. Currently, target-based delivery of anticancer agents to the site of cancer or tumor is major challenge. In order to target tumor at nanolevel, cancer nanotechnology has made tremendous progress in last one decade. It is assumed that, if drug is delivered at nanolevel at site of tumor with a high level of specificity so that cancer can be better managed. Nanoparticles of various tannin-based compounds are also prepared but their toxicity to normal body cells left major side effects. Therefore, encapsulation of many types of tannin like, epigallocatechin-3-gallate in chitosan-tripolyphosphate nanoparticles was investigated for target-based delivery to tumor. It is well known that (−)-epigallocatechin-3-gallate, (−)-epigallocatechin, (−)-epicatechin-3-gallate and (−)-epicatechin act as anticancer and antioxidant agents. The nanoemulsions and liposomes of tannins have proven highly effective in target-based delivery of anticancer drugs in case of HepG2 cells [44]. So far, nanoencapsulation method is proved only in in vitro studies and animal models but it is rarely proved effective in normal and cancerous cells.

3.1 Antiviral activity of tannin

In current era, viral infection is the major threat to the human and animal population. Tannins also show antiviral activity in case of several diseases such as HIV, herpes simplex virus 2 (HSV-2). In case of herpes simplex virus 2 silver nanoparticles with tannic acid (TA-AgNPs) act as microbicide by preventing adsorption of viral particle in the body. Additionally, tannins also provide the better adjutant properties for example, substantial improvement of production of IFN-gamma+ CD8+ T-cells, activated B cells, and plasma cells. In case of spleen also, tannins promotes production of higher amount of IFN-gamma+ NK cells and effector-memory CD8+ T-cells particularly, in case of second challenge against HSV-2 immune response [45].

Free-living protozoa species of *Acanthamoeba* genus generally cause significant infections of keratitis and encephalitis in human. Acanthamoeba keratitis is a cornea related infection that adversely affected eye vision. It is resistance to current available therapy. To overcome this problem, both pure silver and gold nanoparticle and tannic acid-modified of nanoparticles of silver and gold were prepared and their activities were tested against the clinical strains of *Acanthamoeba* spp. The tannic acid-modified nanoparticles proved more effective and less toxic to eye infection. Moreover, tannic acid-modified silver nanoparticles were well absorbed by the trophozoites eventually inhibits germination of cyst which is a major stage of life cycle of amoebae parasite [46]. So that it can be concluded that tannin-based nanoparticles are more effective than pure silver and gold particle.

4. Leather industry

In leather industry, tannins are generally used to convert animal hide into leather. Here, the main role of tannins is to protect leather from microorganism and heat related deterioration [47]. Tanning industry is thought to be the oldest industry and was started in north western regions of Europe after the Roman conquest [48]. Tannins bind with the skin proteins and protect it from petrification, which is owed to the antibacterial property of tannins. This is due to the chemical bonds established between collagen, the main constitutive protein of skin, for example, collagens, and the tannins present in the vegetable materials. It is estimated that about 15–45% tannins binds with collagens per dry weight. After the industrial revolution, chromium-based tanning was introduced to achieve fast and speedy leather production. But chromium is a potentially carcinogenic and creates high level of pollution and soil contamination. Additionally, it limits recovery and reuse of wastes from leather industries. Water from leather industry creates more pollution, and increase biological oxygen demand (BOD) and chemical oxygen demand (COD) in polluted water. In order to overcome this problem, plant-based tannins can be substitute for chromium in leather processing. It is already mentioned that vegetable tannins were used in the leather industry since historical times. But now, tannins from different parts of plants have been utilized in leather productions [49]. Plant tannins offer many benefits such as high quality and thermal stable leather products.

5. Other industrial applications

In addition to above mentioned applications, tannins are also used in diverse types of industries, such as paper industry where high pressure mimosa tannin impregnated alpha cellulose paper is prepared. This impregnated paper offer more abrasive resistance, adhesion properties, water vapor resistance, and staining properties [50]. Recently, natural tannin-based foam without any formaldehyde is prepared that used as acoustic absorbers, metal ion adsorption, panels crash protection, packaging, etc., but low mechanical strength of tannin foams is major impediment in its further applications [51].

Beverage industry is well known for tannins applications particularly, in case of the wine making. Like leather industry, wine making is also very old industry since historic time. Tannins are used in wine to provide color formations, antioxidants, aroma, proteins precipitations, and flavor development. The source of tannins in the wine is grapes skin, seeds, and addition of oak flakes which add market values to wine [52].

6. Future prospectus

Tannins are phenolic-based secondary metabolites that are present in the plant kingdom, including algae. Actually, tannins produced in the plant body and involved in the plant protections and act as antimicrobial, antiparasitic, anthelmintic, antiviral, antioxidant, and deferred cattle. Hence, they help plants to fight various types' infections. In addition to biological roles, they also play very important roles in industrial sector, animal feeding, mining, chemical industry, and tanning industry. But there are several limitations associated with the tannins. The main negative effect of tannins as food is their absorptions and binding with various types of biomolecules such as proteins, starch, and metal ions in the digestive system, hence hinders their nutritional availability to human and animals, for example, proanthocyanidins. Some experiments show that complex of tannins and proteins are resistant to various types of proteases in animal digestive system that make proteins unavailable for livestock nutrition. Dietary tannins bind with the proline-rich proteins and as result two types of soluble and insoluble complexes formed which is responsible for astringent sensation [53]. The astringency feeling is perceived by the tongue in the form of diffuse feeling associated with extreme dryness and roughness in mouth [54]. Some experiments also show that tannins also decrease activities of intestinal microflora, consequently less absorption of organic matter and soluble fiber that attributed to damage the mucosal lining of the digestive system. Moreover, high dose of tannins like catechin used in supplements can cause renal failure, hepatitis, fever, hemolytic anemia, thrombocytopenia, and skin disorders. Due to the structural complexities, tannins are also considered as potential pollutants in industries, where tannins are used as the major substrate.

Single-meal bioavailability studies have shown major antinutrient activity of tannins is metal ions chelation that cause severe deficiency of essential minerals in human. In this series iron deficiency is most prevalent in population particularly in the developing countries. Recently, single-meal studies in case of hydrolysable and oligomeric catechin and epicatechin tannins (tea and tannic acid) have conducted. It shows reduced iron bioavailability in diet particularly in long term, but it needs more investigation by using appropriate animal model systems in order to study antinutritional role of tannins [55]. Moreover, tannins not only affect iron availability, but also iron metabolism; the ferritin, an iron transport protein, is adversely affected by tannin binding in soybean seed ferritin (SSF) and consequently changes the tertiary/quaternary structure of the protein.

In view of current scientific investigation, it has now become possible that tannins can be exploited in a better way because they are major sustainable raw materials for green chemistry in future. Recently, several tannase or tannin acyl hydrolase enzymes have isolated, characterized, and classified from microorganism and fungi, hence toxic effect of tannins is reduced through hydrolysis and oxidation [56, 57]. Various species of filamentous fungi that produced tannase are used for bioremediation in leather tannin industries.

Several studies have been conducted to overcome the adverse effect of tannins in the food item like, fruit and vegetable. In a major breakthrough, lactic acid bacteria fermentation-like incubation is exploited in *Xuan Mugua* fruits, as a result up to 70% tannin content reduced with substantially reduced astringency, hence that method can be used in the food industry [58].

7. Conclusions

Tannins are phenolic-based secondary metabolites that are present in the plant kingdom, including algae. Actually, tannins produced in the plant body involved in the plant protections and act as antimicrobial, antiparasitic, anthelmintic, antiviral, antioxidant, and deferred cattle. Hence, they help plants to fight various types of infections. In addition to biological roles, they also play very important roles in industrial sector, animal feeding, mining, chemical industry, and tanning industry. But there are several limitations associated with the tannins applications. The main negative effect of tannins as food are their absorptions and binding with various types of biomolecules such as, proteins, starch, and metal ions in the digestive system; hence, they hinder their nutritional availability to human and animals.

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Conflict of interest

Authors declare no conflict of interest.

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Acronyms and abbreviations

PA	proanthocyanidins
LDPE	polyethylene and low-density polyethylene
LLDPE	linear low-density polyethylene
WVP	water vapor permeability
SDF	soluble dietary fiber
MRSA	methicillin-resistant *Staphylococcus aureus*
TFPR	tannin-rich fraction from pomegranate rind
EGCG	epigallocatechin gallate
MALDI-TOF	electron spray ionization and matrix-assisted laser desorption ionization time of flight mass
TA-AgNPs	silver nanoparticles with tannic acid
HSV-2	herpes simplex virus 2

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