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RECENT ADVANCES IN STUDYING TANNIC ACID AND ITS INTERACTION WITH PROTEINS AND POLYSACCHARIDES

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Abstract. The purpose of this review was to gain a deeper understanding of tannic acid (TA) and its properties, which could be important for improving the technology of gluten-free food. TA is widely used in agriculture, food, medicine, and other fields due to its unique physiological functions (anti-tumor, anti-oxidation, antibacterial, anti-viral, etc.). It can closely interact with proteins and polysaccharides, which can significantly influence the structure, function, and nutritional properties of compounds. In this article, TA is chosen as a polyphenol model, and the structure of tannins and the degree of their extraction have been considered systematically. Prospective application of interaction between TA and common biological macromolecules have been presented. In this review, different classes of tannins are summarized. Advantages and disadvantages of different methods of extracting tannins have also been described. This review provides detailed information about the mechanisms of interaction of TA with biological macromolecules such as proteins and polysaccharides. Maize, buckwheat, rice flour and starch should be introduced as non-traditional raw materials in production of pasta for people ill with coeliac disease. Pasta dough from unconventional raw materials has non-standard rheological characteristics, and it is difficult to impart good plastic properties to it. That is why, studying the properties of tannins is necessary to improve the technology of gluten-free pasta. However, due to the different nature and composition of proteins, gluten-free foods do not have a network structure. So, they can hold neither water nor starch granules, their prepared dough is loose, with low viscosity, and is not easily moulded. That is why, the use of tannin to form a strong structure when developing a gluten-free pasta technology has become the main purpose of the research. Some potential problems of gluten-free dough processing can be solved by using new technical means. In view of this, the authors put forward the idea of using TA to form cross-links and a strong gluten-free dough structure.

Keywords: tannic acid, classification, extraction, interaction mechanism, protein, polysaccharide.

Introduction. Formulation of the problem

Tannins are polyphenolic compounds widely occurring in tissues of plants such as persimmon, tea, coffee, pomegranate, sorghum, etc. Tannins are usually divided into 2 classes according to their structure: hydrolysable tannins and condensed tannins (also known as proanthocyanidins). The former are glucose monosaccharide esters connected to gallic (gallotannins) or ellagic (ellagitannins) acid. Hydrolysable tannins are subdivided into ellagitannin and gallotannin, such as punicalagin, pomegranate-rind tannins, aleppo galls tannins, etc. Tannic acid (TA) is a typical representative of hydrolysable tannins. Condensed tannins are catechin polymers such as propelargonidins, prodelphinidins, and profisetinidins. It is believed that TA exhibit strong antioxidant and α-amylase inhibitory activity, which is useful for obese people and type II diabetes patients [1-3]. To some extent, these functions are related to

polyphenol-protein interactions due to the functionality provided by phenolic and aliphatic hydroxyl groups. However, sediments and astringency in some fruit juices are also related to the cross-links among polyphenols, proteins, and polysaccharides [4-6].

Production of pasta from non-traditional raw materials (maize, buckwheat, rice flour and starch) should be improved for patients with coeliac disease. Pasta dough from unconventional raw materials has non-standard rheological characteristics, and it is difficult to impart good plastic properties to it. That is why, studying the properties of tannins is necessary to improve the technology of gluten-free pasta. Coeliac disease (CD) is chronic intestinal malabsorption caused by the intake of gluten from products made from raw materials like wheat. Nowadays, CD is identified as a common life-long disease, and 1% of the world population is diagnosed with this it [7-8]. The solution to the problem can only be a lifelong gluten-free diet (GFD). However, due to the different nature and composition of proteins, gluten-free foods do not have a network structure. So, they can hold neither water nor starch granules, their prepared dough is loose, with low viscosity, and is not easily moulded. That is why, the use of tannin to form a strong structure when developing a gluten-free pasta technology has become the main purpose of the research. Some potential problems of gluten-free dough processing can be solved by using new technical means. In view of this, the authors put forward the idea of using TA to form cross-links and a strong gluten-free dough structure.

The purpose of this review was to gain a deeper understanding of tannic acid (TA) and its properties, which could be important for improving the technology of gluten-free food. To this end, the following has been done: different classes of tannins have been summarized, and advantages and disadvantages of different methods of extracting tannins have been described; more detailed information is provided about the mechanisms of interaction of TA with biological macromolecules, such as proteins and polysaccharides.

Analysis of recent research and publications

Definition and categories of tannins. Tannins widely occurring in the roots, stems, leaves, and fruit of plants are natural polyphenolic compounds. They were originally defined by Bate-Smith as water-soluble phenolic compounds with molecular masses between 500 and 3000 Da, displaying typical phenolic reactions (e. g., the blue colour with iron (III) chloride) and precipitating alkaloids, gelatines, and other proteins [9-10]. However, this definition does not include all tannins [11]. Plant polyphenols having a molecular weight of less than 500 Da can hardly produce effective cross-links among the fibres of hidden collagen, while those with over 3000 Da can hardly penetrate into hidden fibres. Tannins are a group of plant polyphenols capable of binding with animal skin proteins and turning them into leather. Condensed tannins are formed from flavan 3.4-diols (proanthocyanidin). Polyphenols of food products have different functional properties like the ability of forming the colour and astringency of food [12].

Nowadays, the range of TA application has gradually expanded to household chemicals, food, medicine, printing, and dyeing, leather industry, etc. Some researchers, basing on the chemical structure of tannins, suggested naming plant tannins for plant polyphenols or complex phenols [13], but it was not recognized. As a rule, tannins are considered to be part of polyphenols, and are divided into two classes according to their structure [14]. Condensed tanning agents, also known as proanthocyanidins, are oligomers or polymers of catechin and gallocatechin monomers that are cross-linked by flavonoids C_4–C_8 and C_4–C_6, and cannot easily be broken down by acids and alkalis, nor by endoenzymes or microorganisms of animals' intestines [15]. The chemical structure of tannins is complex because of the differences in the quantity and location of phenolic hydroxyl groups and the differences in the cross-linking mode and the quantity of flavonoid monomers [16]. Condensed tannins are widely found in the pips and skins of grapes, where they are contained in the quantity 2.2–8.0%.

Hydrolysable tannins are formed by esterification of acids and their derivatives (gallic acid, ellagic acid, etc.) with carbohydrates (glucose or polyol) generally divided into two types: gallic tanning agents and ellagitannins. In medical literature, gallic tannins (gallotannins, Chinese tannins) are called tannic acid. Ellagitannins contain chebulic acid formed from pomegranate rind tannins. Gallotannin forms gallic acid that is associated with glucose. Ellagitannin is formed by gallic acid and ellagic acid, which is attached to C_3–C_6 glucose [12]. Polyphenolic groups in hydrolysable tannins can be esterified or oxidatively crosslinked to form more complex hydrolysed tannins. Hydrolysable tannins are easily hydrolysed by acid or tanninacylhydrolase, and the products include gallic acid, ellagic acid, pyrogallol, and resorcinol [17]. TA is often considered as a typical representative of hydrolysable tannins in the laboratory. With the progress of plant tannin research, the so-called complex tannins with the above two tannins types have been discovered. The classification of tannins is shown in Table 1.

The ability of tannins to form complexes with proteins reduces the biological value of protein foods. The astringency of a tannin solution is due to the interaction with the oral mucosa proteins. The nature of a tea depends, to a large extent, on the content of tannins able to form a tea film with caffeine. Polyphenols are easily oxidized by oxidative enzymes. The transformation of tea leaves into tea is based on the enzymatic oxidation of tea leaf polyphenols. For green tea, these enzymes are inactivated by blanching. By controlling the degree of oxidation, you can get black or red-coloured tea [12].

Table 1 – Classification of tannins [18]

Name	Classification criteria and chemical structure	Examples
1. Hydrolysable tannins	Gallic acid and its oxidative fixation product are formed by an ester bond or a hydrazone bond, can be hydrolysed by an acid, alkali, or enzyme to form polyol and phenolic acid.	tannic acid
a) gallotannins	Phenolic carboxylic acid produced by hydrolysis is gallic acid	chinese gallotannin
b) ellagitannins	Phenolic carboxylic acid produced by hydrolysis is ellagic acid or another substance biogenetically related to hexahydroxybiphenylic acid.	eugenin
2. Condensed tannins	A condensate composed of hydroxyflavanoids, which does not produce significant low molecular weight compounds, but, instead, tends to polymerize into an amorphous compound (often red) in the acid.	cinnamon tannins
3. Complex tannins	Contains both hydrolysable and condensed tannins, with two types of tannins	cyclobalanopsis, glycoside, ellagic acid

Extraction, separation, and purification of tannins. The storage, drying, and extraction conditions of the sample can result in changes in the extraction rate and the tannin structure, thereby changing its chemical, physical, and physiological activities. The degree of fineness, the ratio of the materials, the type of the solvent, the temperature, and the duration of the extraction can affect the extraction rate. At present, the methods of extracting tannin mainly include leaching, supercritical fluid extraction, ultrasonic extraction, semi-bionic extraction, microwave-assisted extraction, and enzyme conversion [19–23]. The advantages and disadvantages of these methods are shown in Table 2.

Table 2 – Comparison of tannin extraction methods

Method	Advantages	Disadvantages
Leaching	Energy saving, easy operation; the complex system of organic solvents and water has a strong ability to dissolve tannin, can break down the tannin-protein bond	The extraction rate is low, the tannin crushing takes too long, easy oxidation
Supercritical fluid extraction	Strong extraction ability and high extraction rate	Rigid extraction conditions (temperature, pressure, etc.); long extraction time; high cost; decreasing biological activity of tannin.
Ultrasonic extraction	Is time-saving, increases the extraction rate, saves energy, is widely adaptable	It is easy to form an ultrasonic empty region
Semi-bionic extraction	Strong selectivity and high extraction rate	Is similar to the high-temperature boiling method that easily affects the effective active ingredients.
Microwave-assisted extraction	Accelerates the rapid dissolution of active ingredients in the cells, improves their reactivity, selectivity, and low solvent consumption	Does not help separation and purification, is susceptible to extraction by solvents
Enzyme conversion extraction	The intracellular substances are more soluble and diffusive, and thus make the extraction effective, with mild conditions, high biological activity of extracts, environmental friendliness, and safety	The operation needs a low temperature, and after precipitation, separation should be carried out as soon as possible to prevent the organic solvent from affecting the enzyme activity.
Purification	Simple, easy to operate; short cycle; the extraction solvent can be reused	Low extraction rate, low purity, other extraction methods are needed

The crude extract of tannin contains a lot of impurities such as sugar, protein, lipids, etc. Tannin itself is a mixture of components similar in their structure and physical and chemical properties. This mixture needs separation and purification. It is usually purified by stepwise extraction with an organic solvent. Methanol can cause alcoholysis of depsipeptide bonds in hydrolyzed tannins. Ethyl acetate can dissolve a variety of hydrolysable tannins and oligomeric condensed tannins. Ether only dissolves polyatomic phenols with a small molecular weight. Chen [24] purified Chinese gallotannin from activated carbon adsorption, which increased the tannin weight by about 1%, and the colour and transmittance were obviously improved [25-27]. This can be used as a purification technology for tannic ink.

Column chromatography is currently the most important method to prepare pure tannins and related compounds. Silica gel, cellulose, polyamide, polystyrene gel (such as MCI-gelCHP-20), polyethylene gel, dextran gel, etc. were chosen as available stationary phases, of which the sephadex gel sePhadex LH-20 was the most commonly used. Other chromatographic methods such as paper chromatography, thin-layer chromatography, countercurrent chromatography, and centrifugal partition chromatography have also been reported to be used to extract tannins [18].

Properties of tannins. The physiological activity of TA is the ultimate manifestation of its interaction with proteins, polysaccharides, nucleic acids, etc., which, on the contrary, depend on tannins' molecular structure. TA has proved their excellent antioxidant, antinutritional, anti-microbial, anti-bacterial, anti-mutation, anti-mutation, anti-aging, anti-tumour activity, unique bioactivity, ability to capture free radicals, and other functions that are due to phenolic hydroxyl groups (Fig. 1, 2).

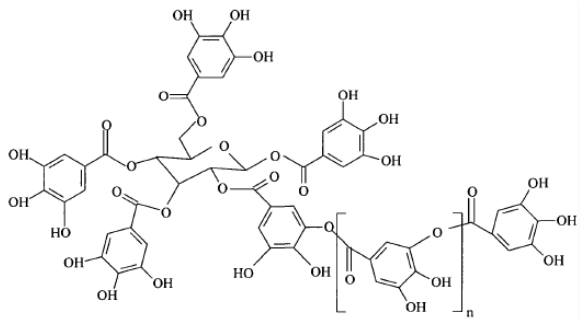

Fig. 1. Molecular structure of tannins [36]

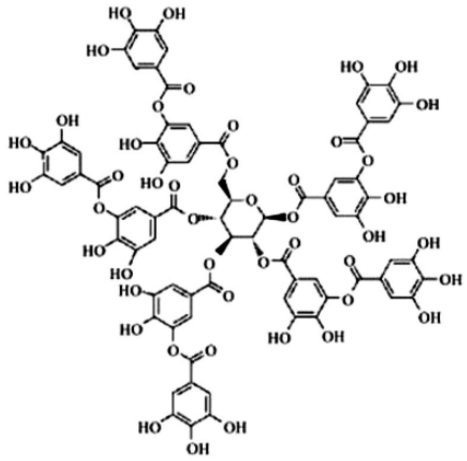

Fig. 2. Molecular structure of TA [37]

Now scientists are paying attention to TA in various fields. The anti-nutritional properties of TA allow developing functional products like hypoglycemic products and diet pills that are very effective in preventing diseases and promoting health. Plant protection experts use these properties of TA to reduce the damage from insects to crops. However, TA has its unfavourable aspects, too. It has a certain degree of biological toxicity [28-29]. If the amount of TA in the food is excessive, it will inhibit the activity of digestive enzymes, reduce absorption of vitamins, minerals, and proteins by the human body, which can result in gastroenteritis, digestive tract congestion, and liver damage [30]. The presence of phenolic hydroxyl groups, especially ortho-phenolic groups, allows TA to be linked to water-soluble proteins (such as salivary proteins). This makes saliva lose its lubricating properties, causes epithelial tissue contraction, dryness, and astringency. Over the years, condensed tannins have been the ones mostly associated with astringency. Although some sensory experiments with people have revealed that ellagitannins can have an effect on the astringent action, there is still little information about the interaction of hydrolysable tannins and salivary proteins (SP) [31-32]. Besides, studies have shown that a lot of phenolic hydroxyl groups in TA can be oxidized by polyphenol oxidase into coloured ortho-quinones. This makes the colour of persimmon juice products unstable during their shelf life. Besides, self-condensation forms macromolecular insoluble precipitate when treated with acid, thereby affecting the clarity of persimmon juice. Also, persimmon tannin affects the action of pepsin in the digestive tract, and the complexes with minerals such as calcium and iron, thus causing solidification of persimmon in the stomach [33-35]. Therefore, dehydrating treatment is a key step in manufacturing persimmon juice.

TA-protein interaction. The interaction between polyphenols and proteins mainly includes covalent form of binding and non-covalent form of binding. Non-covalent form mainly includes hydrophobic bonds, hydrogen bonds, ionic bonds, and van der Waals forces, among which hydrophobic bonds and hydrogen bonds are the main forces (Fig. 3). Polyphenols interact with proteins closely related to their structure, concentration, and solution parameters (pH, ionic strength, temperature, and alcohol concentration) [38]. Generally, the affinity of polyphenols for proteins decreases with an increase in the temperature. However, polyphenol has a stronger affinity for protein when the pH of the solution is close to the isoelectric point. Binding with polyphenols induces changes in the secondary structure of protein, which mainly include an increase or decrease of α-helix, β-sheet, β-turn, and accidental curl. Besides, the solubility of many non-covalent protein-TA complexes is reduced compared to that of free proteins. There is often turbidity observed in polyphenol-rich beverages such as apple juice, wine, and beer. It is probably due to interaction of TA and proteins [39-42]. For example, turbidity is supposed to result from interaction of cereal protein (hordein) in ethanol [43] with isoprene polyphenols in hops or other polyphenols from grains [44]. Other functional properties of proteins (such as increasing or reducing the thermal stability, improving the emulsifying properties, changing the gelation point of proteins, and inhibiting the cleavage and absorption of proteins) can also be changed by binding to polyphenols [45-46]. Pan et al. conducted an experiment involving mixing and adding TA and gelatine and demonstrated turbid precipitation of pineapple juice formed by TA and proteins with mixed activity. In our previous study, we established static fluorescence cancellation of a-amylase in the presence of TA caused by their binding interaction. Audrey L. Girard et al. studied the effect of proanthocyanidins (PA) and TA on the rheological properties and stability of a wheat gluten film. They

have found that, unlike catechins, both PA and TA can significantly improve the dough stability, which may be explained by their extensive cross-linking with gluten [45]. Spectroscopic studies have also demonstrated that hydrogen binding is the main interaction between zein and TA. We consider that this property of TA can improve the quality of gluten-free foods. However, the effect of TA on the physicochemical properties and structural mechanism of gluten-free dough needs further study.

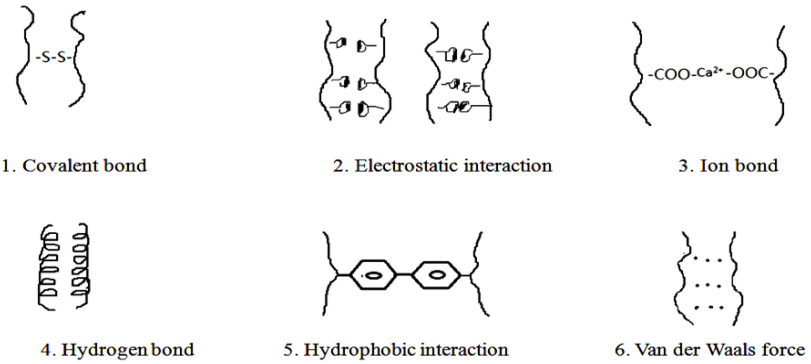

Fig. 3. Schematic diagram of the interaction between polyphenols and proteins [47]

TA-polysaccharide interaction. The interaction between polysaccharides and polyphenols mainly forms non-covalent complexes through hydrogen bonds and hydrophobic bonds [48-50]. By studying the effects of fruit polyphenols and pectins on the properties of bread, Sun-Waterhouse et al. found that polyphenols are mainly combined with pectin by non-covalent interactions such as hydrogen binding [51]. Elsa Brandão et al. studied the effect of two wine polysaccharides (arabinogalactan proteins-AGPs and rhamnogalacturonan II-RGII) on the interactionof salivary proteins SP and polyphenols. They believed that both polysaccharides were effective to inhibit or reduce SP-polyphenol interaction and aggregation. Audrey L. Girard et al. found that TA could break the disulphide bond in gluten protein and form a new intersection network with gluten protein, which improved the flour quality. It is possibly due to the presence of non-covalent interactions between starch and TA. Like interactions with protein, some polysaccharide-polyphenol complexes can also cause solution turbidity. For example, studies by Mercedes Lataza Rovaletti et al. have shown that polysaccharides in beer can interact with TA, which in turn causes turbidity in beer [52]. This interaction also increases the turbidity caused by the interaction of proteins and TA in juice.

TA-polysaccharide-protein interaction. TA-polysaccharide-protein interaction exists in many food systems. Studies have shown that polysaccharides can affect aggregation of proteins and polyphenols. The disappearance of astringency during ripening is thought to be a fragment of water dissolved in the cell wall after depolymerization of pectin interferes with binding of salivary protein to polyphenols, thereby weakening the astringency [53–55]. The same theory is applied to the sensory qualities of wine. These changes in the astringency are related to polysaccharides, indicating that the polysaccharide prevents aggregation of salivary proline-rich proteins and TA. The combination of polyphenols with high molecular polymers imparts a unique interfacial structure to the compounds. Patel et al. [52] showed that the emulsification and strength of interfacial gel of the colloidal complex formed by TA and methyl cellulose were increased. As Madhan et al. [56] noted, gelatine and catechin complexes can transform hydrophilic gelatine proteins into hydrophilic-lipophilic balance compounds, thereby the emulsion interface structure can be stabilized better. Jockson reported [57] that in fruit juices, polysaccharides can be absorbed on the surface of water-soluble colloids, such as gelatine, to prevent binding of water-soluble colloidal polyphenols, thus inhibiting juice turbidity. Studies have shown that different types of polysaccharides have different effects on the interaction of proteins and polyphenols. Polysaccharides due to their different structures can be divided into anionic polysaccharides and neutral polysaccharides. Anionic polysaccharide, such as linseed gum, xanthan gum, carrageenan, pectin, acacia, and dextran sulphate, can inhibit the interaction of protein and polyphenols in juice, thus effectively preventing the turbidity and sedimentation. However polysaccharides such as carob gum, guar gum, arabinogalactan, and dextran have no obvious inhibitory effect on the formation of protein-polyphenol complexes. Susana Soares believes that gum arabic and polygalacturonic acid mainly inhibit the precipitation caused by salivary proteins and concentrated tannins by the competitive mechanism, while pectin forms a protein-polyphenol-polysaccharide ternary complex with salivary proteins and concentrated tannins [58]. Besides, monosaccharides and disaccharides can affect the solubility of protein-TA complexes. Harbertson et al. found that high concentrations of glucose, fructose, and sucrose increased the solubility of protein-TA complexes [59-60].

Conclusion

At present, studies of the interaction of protein, polyphenol, and polysaccharide mainly focus on two aspects. The first is studying (based on the non-covalent interaction of protein and polyphenol) the problem of turbidity and precipitation in beer, in wine, and in fruit and vegetable juice-containing beverages when mixing them, and researching the special effect of polyphenol on important digestive enzymes in the human body. The second is studying the effect of polyphenols on the protein-polysaccharide interaction to solve the problem of strengthening polyphenols in the food system [60]. Despite a comprehensive study of the botanical and nutritional aspects of tannins, studies of the interaction of TA with components in natural plants, food, and even in the human body are still few. For example, the interaction between proteins, polyphenols, and polysaccharides in foods and beverages greatly affects their structural and functional properties. However, there are still few studies devoted to the effect of TA on gluten-free protein as well as to changes in the turbidity, rheological properties, and bioavailability of polyphenolic compounds due to interactions among proteins, tannins, and polysaccharides. That is why further studies of the structure and functional properties of the protein-TA-polysaccharide ternary complex will help develop and use the complex that improves the stability and bioavailability of polyphenolic compounds.

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