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Review on Tannic Acid: Potensial Sources, Isolation Methods, Aplication and Bibliometric Analysis

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ABSTRACT

Tannic acid is the simplest form of astringent hydrolysable tannin in which naturally occurring in practically all aerial plant tissues and regarded as the most famous tanning material. Tannic acid having various types of pharmacological activities including anti-viral, anti-cancer, anti-oxidant, anti-microbial, anti-helminthic, anti- haemorrhoids, and anti-diarrhea. Tannic acid can be isolated from various parts of herbaceous and woody plants via different methods such as maceration, soxhletation, micro-channeling and solvent distillation. Tannic acid also found other prospective use in numerous fields such as in textile, leather, corrosion prevention and in rubber based epoxy resin. Bibliometric analysis shows research on tannic acid application trend is move towards the application of tannic in hydrogel formulations and incorporation.

Keywords: tannic acid, application, sources, pharmacological activities, bibliometric

1. INTRODUCTION

In 1796, Seguin initially introduced "tannin" term which is originates from the ancient Celtic word for oak to define a substance isolated form oaks bark that can convert animal skin into leather [1][4]. The history of the identification of tannic acid (TA) is somewhat long, started from in the middle of 19th century, where TA formula is identified as $C_{27}H_{22}O_{17}$ by Adolf Strecker [1]. Today, TA is defined as penta-m-digalloyl glucose where the glucose molecule core is connected to 10 galloyls by aliphatic ester bonds and given the empirical formula $C_{76}H_{52}O_{46}$ with average molecular weight of 1701.19 g/mol [5][7]. The molecular structure of TA is depicted at **Figure 1** [8].

Tannic acid is a weak acid with pKa range from 2.5 to 8.5 [1]. It is decomposed above 200°C and its flash point and auto ignition temperature are 199°C and 527 °C, respectively. Tannic acid is soluble in water, alcohol and acetone. Furthermore, it is insoluble in ether, benzene and chloroform [9][10]. Tannic acid which is hygroscopic is getting darkens when come to expose with air and light. In the presence of mild oxidizing agents, TA is oxidized [10]. It was mentioned that α-hydroxy-ortho-quinones is formed during TA oxidation [1]. Meanwhile, the products of acids, alkalis or enzymatic hydrolysis of TA are gallic acid and glucose or quinic acid [11][12]. The unique structure of TA in which have multiple catechol and galloyl groups linked to a glucose core allows it to form manifold interaction modes with a diverse compounds and materials [13].

2. SOURCES AND ITS ISOLATION

TA can be found in various parts of herbaceous and woody plants such as tara pods, wallnut husk and shell, galls of Quercus species, leaves or nutgalls of Rhus species, and galls on the R. chinensis [14][16]. Tara (Caesalpinia spinosa), a leguminous tree indigenous to Peru and widely distributed in South America, is having 8–10 cm long oblong indehiscent orange pods which is rich of TA [14][15]. Tara pod's TA is widely applied in numerous industries including pharmaceutical, chemicals, and tanneries. Furthermore, walnut husk and shells also reported as source of tannic acid. It was mentioned that 120.4 ± 4.19 mg GAEs/L extract is obtained from walnut shell extraction [17].

Quercus genus which is belongs to the Fagaceae family and comprises of many species is also stated as rich sources of tannic acid. Three different solvents including ethanol, acetone, and mixture of diethylether:ethanol:water (25:3:1) are applied in TA extraction from two Turkey oak galls i.e. Q.infectoria subsp. infectoria and subsp. boissieri. It was found that 8 hours of maceration with 80% of ethanol gave the highest TA extract which was up to 127.683 mg/g [16].

It was also informed that the highest concentration of TA and other form of gallotannins (gallic acid) are found in gallnuts from Rhus semialata and Quercus infectoria. The TA and gallic acid concentration are to 50–75% gallotannins, with extraction rate of TA is up to 99–100%[5]. Isolation methods as well as their process yield of TA from different materials are tabulated in **Table 1.**

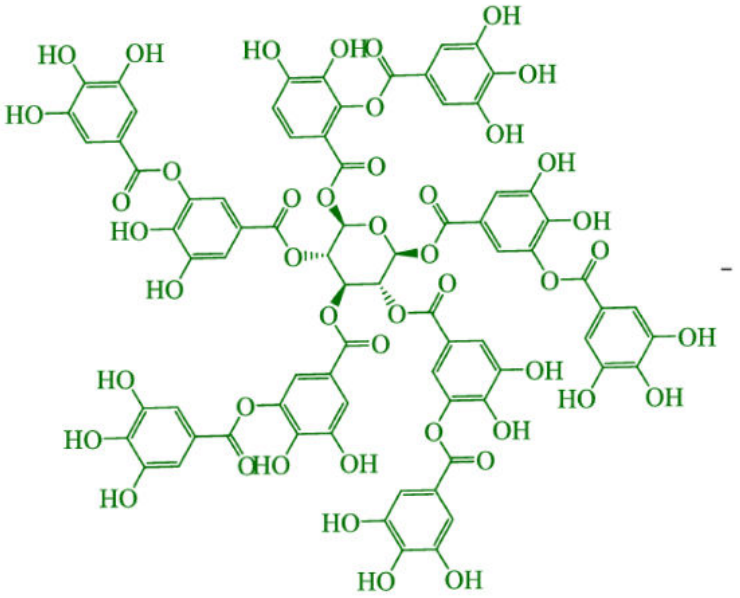


Figure 1. Molecular structure of tannic acid [8]

Table 1. Tannic acid plant sources and its separation

No	Sources	Isolation	Yield	Refferences
1	Q.infectoria subsp. Infectoria and subsp. Boissieri	Maceration; Solvent: 80% of ethanol, solid liquid ratio 1:20, t = 8 hours, room temperature	127.683 mg/g	[16]
		Maceration; Solvent: 96% of ethanol, solid liquid ratio 1:20, t = 8 hours, room temperature	81.012 mg/g	[16]
		Maceration; Solvent: acetone, solid liquid ratio 1:20, t = 8 hours, room temperature	67.2 mg/g	[16]
		Maceration; Solvent: diethylether:ethanol:water (25:3:1); solid liquid ratio 1:20, t = 8 hours, room temperature	0.112 mg/g	[16]

No	Sources	Isolation	Yield	Refferences
2	Quercus leaves	Microchannel; solvents: ethylacetate as organic solvent and ethanol 10 % (water 90 % + ethanol 10 %) as aqueous phase; Extraction condition: pH of 2, temperature=33.1°C, volumetric flow ratio=1.2, and contact time of 25.35 s	96.76±1.97%	[18]
3	Grape seeds	soxhlet distillation; Solvent: ethanol; Extraction condition: 40-60°C for 24 hours	4.1 g/100g(dry weight),	[19]
	Pomegranate peels	soxhlet distillation; Solvent: ethanol; Extraction condition: 40-60°C for 24 hours	27.6 g/100g(dry weight)	[19]
4	Walnut shell	-	120.4 ± 4.19 mg GAEs/L extract [7,21].	[17]
5	Walnut pellicle	Soxhletation Solvent: methanol; Extraction condition: 60°C for 30 min, solid liquid ratio: 1.5:25	18.0 ± 1.39 mg/100 g	[20]
	Walnut hull	Soxhletation Solvent: methanol; Extraction condition: 60°C for 30 min, solid liquid ratio: 1.5:25	70.5 ± 8.75 mg/100 g	[20]

3. PHARMACOLOGICAL PROPERTIES AND POTENTIAL APPLICATION

Tannic acid found numerous positive effects toward human health. Ethanolic extract of D. falcata leaves in which comprised of tannin as much as 55.77 ± 1.55 mg/g, equivalent to tannic acid, shows a positive effect in haemorrhoids treatment [21]. Combination of aluminum potassium sulfate and TA also applied for internal hemorrhoids treatment [22]. Some studies found that post-weaning diarrhea could be effectively alleviated by dietary supplementation of 0.2% or 1.0% TA. It was also mentioned that appropriate doses of TA have a beneficial effect on the diarrheal prevention on animals [23][24].

There are numerous studies on investigating the anti-cancer activities of TA. Several solid malignancies such as liver, breast, prostate, mouth and throat, colon, glioma, lung, pancreatic, colorectal and ovarian cancers have been reported to be inhibited by TA [5][25]. The exact mechanism of TA anti-cancer is not known. The anti-oxidant effect of TA is correlated in the altering of the gene expression of the associated cancer as well as in the disruption of cancer cell signaling [5]. TA in combination with other cancer treatment was also investigated. Combination of TA with conventional chemotherapeutic drugs (doxorubixin) demonstrated a synergistic effect i.e reduction in cardiotoxicity as well as significant increase in its anti-cancer efficacy [26].

Tannic acid represents anti-oxidant capacities as compared to others types of anti-oxidant agents such as BHA, BHT, a-tocopherol and trolox; TA shows as an effective natural antioxidant component [27]. TA purified from e seeds of Sumac (Rhus coriaria L.) also show a higher anti-oxidant capacities compared to BHT [28]. Anti-helminthic of TA was in vitro assessed against the Neoechinorhynchus buttnerae [29]. They compared three different compounds consist of eugenol, thymol and tannic acid. It was found that TA ranks the lowest activities than the other two compounds.

Anti-microbial properties of TA are reported in many literatures. Tannic acid has been reported to present the activity against Methicillin Resistant *Staphylococcus aureus* (MRSA) pathogen. It has been reported that TA has the ability to inhibit the MRSA

adaptive resistance [30]. The inhibition activity of TA to influenza A virus and thus tannic application in filter functionalization is reported [13]. Moreover, TA incorporation on nano-silver particles due to its antiviral activities against Herpes simplex virus 2 (HSV-2) is investigated [31].

Table 2. Tabulation of tannic acid pharmacological activities

No	Activities	References
1	Anti-haemorrhoids	[21] [22]
2	Anti-diarrheal	[23] [24]
3	Anti-cancer	[5] [25] [26]
4	Anti-oxidant	[27] [28]
5	Anti-helminthic	[29]
6	Anti-viral and anti-bacterial	[13] [30] [31]

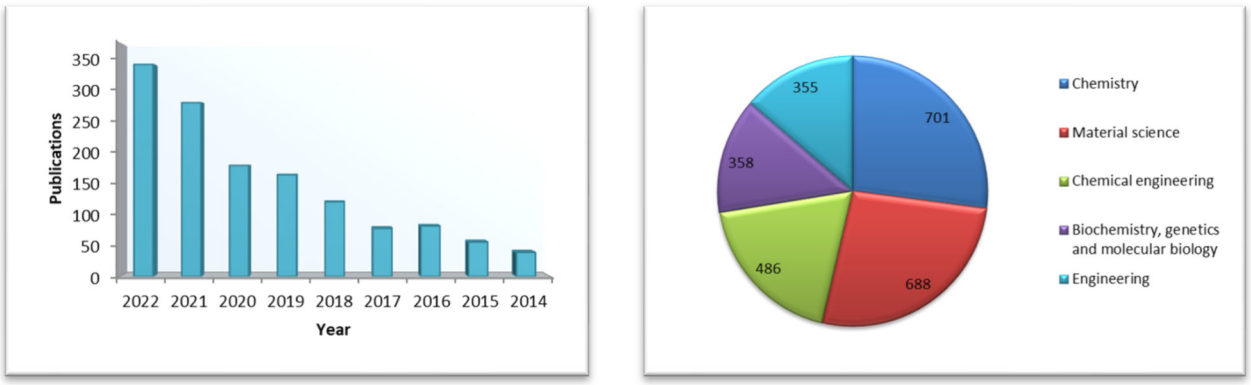
Besides of potential application of TA in human health purposes, TA found other prospective use in numerous fields such as in textile, leather, corrosion prevention and in rubber based epoxy resin. Tannic acid is one of main mordant agent in leather and textile industry [24]. It was reported that complexes of TA and iron ions are applied as iron-gall inks [32]. Tannic acid is reacted with iron (II) sulfate in an aqueous solution to produce black pigment upon oxygen exposure. Tannic acid is also developed to be used as coating materials for metals corrosion prevention. Research showed that layer by layer coating comprised of tannic acid and polyethylenimine can prevent carbon steel from getting corroded when immersed in deionized water for 1 month [33]. Tannic acid is also utilized as hardener agent in rubber based epoxy resin. It was reported that the addition of TA can improve the physicochemical properties of the rubber epoxy resin. The gel content are glass transition are improved with TA addition [34].

4. BIBLIOMETRIC ANALYSIS

Bibliometric in which belong to the scientometrics can be applied in evaluating the trends of a certain research field as well as analysing the scientific activities on that research area [35]. In this paper, bibliometris analysis was applied in order to evaluate the trend in tannic acid research. The data based used for bibliometric analysis was scopus-indexed publications. The keywords are “tannic acid application”. As much as 1680 publications are obtained from the search with the mentioned keywords.

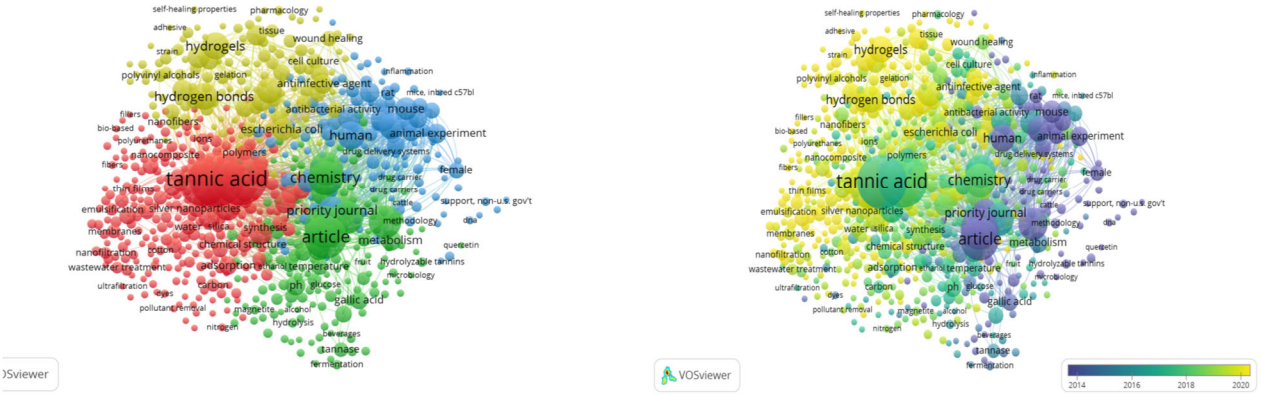
The annual distribution of the publications is shown on Figure 2a and the major area of the publications is represented on **Figure 2b.** It was shown that the number of publication having “tannic acid application” keywords increased along with time **(Figure 2a**). In 2014, there was 39 papers with tannic acid application keywords while in 2022, there are now 344 papers published. It seems that research on tannic acid application is getting more attention from scientists. Moreover, **Figure 2b** shows that chemistry, material science and chemical engineering are the big three of the area of publication with tannic acid application keywords. It seems that tannic acid is tend to developed for material purposes with its chemistry as the subject of the investigation. Chemical engineering took place on its synthesis.

Furthermore, the trend and occurrence of keywords in those 1680 papers are presented by network and overlay visualization as presented in Figure 3a and Figure 3b, respectively. It was showed that there are 4 classes of clusters in Figure 3a with different colours. The main modes of each cluster are tannic acid, article, human and hydrogen bonds. The correlation of TA and hydrogen bonds is might be due to fact that the basis of TA utilization is based on its ability to form hydrogen bond with various molecules. Tannic acid is having many hydroxyl groups with high affinity for hydrogen bonding interaction [5] [36]. The overlay visualization as depicted on Figure 3b shows that the research trend on tannic acid application shift towards tannic acid-based hydrogel development. One example of tannic acid incorporation into hydrogels is the synthesis of nanosheets of CuTA which is produced by applied chelating process of tannic acid and cuprum divalent ions followed by the hydrogels formulation by addition of sodium alginate. The hydrogels are intended for treating bacteria-infected diabetic wounds [37]



(a) (b)

Figure 2. (a) Annual distribution and (b) five major area of the publications with "tannic acid application" keywords



(a) (b)

Figure 3. The network (a) and overlay (b) visualization of keyword occurrence in publication with "tannic acid application" keywords

5. CONCLUSIONS

Tannic acid having various types of pharmacological activities including anti-viral, anti-cancer, anti-oxidant, anti-microbial, anti-helminthic, anti- haemorrhoids, and anti-diarrhea. Tannic acid can be isolalated from various parts of herbaceous and woody plants via different methods such as maceratio, soxhletation, microchanneling and solvent distillation. Tannic acid also found other prospective use in numerous fields such as in textile, leather, corrosion prevention and in rubber based epoxy resin. Bibliometric analysis shows research on tannic acid application trend is move towards the application of tannic in hydrogel formulations and incorporation.

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