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Ketapang (*Terminalia catappa* L.): Potential utilization as foodstuffs and traditional medicine

Marina Silalahi *

Biology Education Department, Faculty of Teacher Training and Education, Universitas Kristen Indonesia. Jl. Mayjen Sutoyo No 2. Cawang, Jakarta Timur, Indonesia.

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Abstract

Indonesian local people use *Terminalia catappa* L. (TC) as a shade, traditional medicine and vegetables. This study aims to examine the utilization and bioactivity of TC. The research method uses online library research, especially from Google Scholar, using the keywords TC, uses TC and bioactivity of TC. The information obtained was synthesized so as to explain the botany and the use of TC in a comprehensive manner. The TC leaves and seeds can be used as food because they are rich in nutrients and mineral salts. TC seeds are carbohydrates, fats, saturated fatty acids, unsaturated fatty acids and mineral salts in the form of Calcium, Iron and Zinc. In traditional medicine, TC has been used to treat hypertension, hepatitis, colitis, depression and anti-aging. The bioactivity of TC such as anti-diabetes mellitus, anti-microbial, antioxidant, anti-neurodegenerative, anti-aging, hepatoprotective, anti-cancer, anti-depressant, anti-hypertensive, anti-ulcer and immunomodulatory activities. The potential of TC as an anti-neurodegenerative and anti-stress needs to be studied further as a new alternative in the treatment of nervous system disorders as well as a source of unsaturated fatty acids.

Keywords: *Terminalia Catappa*; Anti-Neurodegenerative; Fatty Acids

1. Introduction

Ketapang or *Terminalia catappa* (TC) is a multifunctional plant that is easily found in the surrounding environment, especially in Indonesia. Indonesian local people use TC as a shade because it has a shady canopy (Figure 1A) while young leaves are used as vegetables. Janporn et al [1] stated that TC is an ornamental tree which is widely planted in many countries. Ecologically, TC fruit is widely used as a food source for small mammals such as squirrels and bats.

The leaf of TC is a functional food to relieve symptoms of oxidative stress and neurodegenerative diseases [2]. In addition to leaves, TC seeds are rich in nutritional value and fiber, so they are also known as tropical almonds (Figure 1B) with high fat content and energy value [3]. In Nigeria, TC seeds are used to overcome nutritional deficiencies because they are rich in macro and micronutrient content of seeds [4]. TC seed kernel contains 43.89% saturated fatty acids and 56.1% unsaturated fatty acids [5]. TC seeds contain mineral salts in the form of Calcium, Iron, Zinc and tannins depending on the location [4].

Besides being used as food, TC is also used as traditional medicine. In Nigerian folklore, the leaves and bark of TC are used to treat hypertension [6], while in Taiwan it is used to prevent hepatoma and treat hepatitis [7]. The TC is also useful for treating inflammatory bowel disease, oxidative stress, immune dysfunction [8], overcoming depression [9] and anti-aging [10]. The hydrophilic extract of TC increases the production of type I procollagen by inhibiting the activity

* Corresponding author: Marina Silalahi
Biology Education Department, Faculty of Teacher Training and Education, Universitas Kristen Indonesia. Jl. Mayjen Sutoyo No 2. Cawang, Jakarta Timur.

of matrix metalloproteinase (MMP)-1, -3 and -9, so it has the potential to be used in anti-aging cosmetics [10]. The leaves and bark of TC can be a potential natural source for the development of a new compound antihypertensive agent [6].

The use of plants as traditional medicines is relatively safer than synthetic drugs, although understanding of their bioactivity needs to be increased so that side effects can be minimized. Minnel et al. [11] stated that the hydroalcoholic leaf extract of TC has mutagenic activity so that its use for medicinal purposes should be used with caution. This study aims to explain botany and the use of TC as a food ingredient and traditional medicine and its bioactivity.

2. Data collection

The research method uses online library research, especially from Google Scholar, using the keywords TC, uses TC and bioactivity of TC. The information obtained is synthesized so as to explain the botanical and comprehensive use of TC.

3. Botany of *Terminalia catappa* L.

The *Terminalia* is the second largest genera in the Combretaceae. The scientific name comes from the Latin (Terminalis = end) which indicates the position of the leaves, i.e. clustered at the tip of the shoot [12] (Figure 1A). The genus *Terminalia* is estimated to have about 200 species [13]. The *Terminalia catappa* is one of the many species in Indonesia as a shade and also as a food ingredient. The wide canopy with a unique branch arrangement makes this plant often used as shade in various city parks or other parks.

Description: it has the stature of a deciduous tree, 35 m tall (Figure 1A). Trunk with buttress at the base. Rough bark surface. The branching pattern is known as the Terminalia pattern. Leaves: Leaves without a support, grow in clusters at the ends of the branches. The leaf blade is relatively large with a length of 8 – 38 cm and a width of 5 – 19 cm, the secondary bones are clear, each side of the mother and child leaves as many as 6 – 9. Flowers: Fruit white or whitish, inflorescence grain in the leaf axils. The inflorescence length is between 8 – 16 cm. Male flowers and sissy flowers, with only a few sissy flowers at the base of the rakis. Fruit and Seeds: Fruit at the edges form stiff and hard wings, oblong-shaped with a length of 3.5 – 7 cm and a width of 2 – 5.5 cm. Single seed [14, 15].

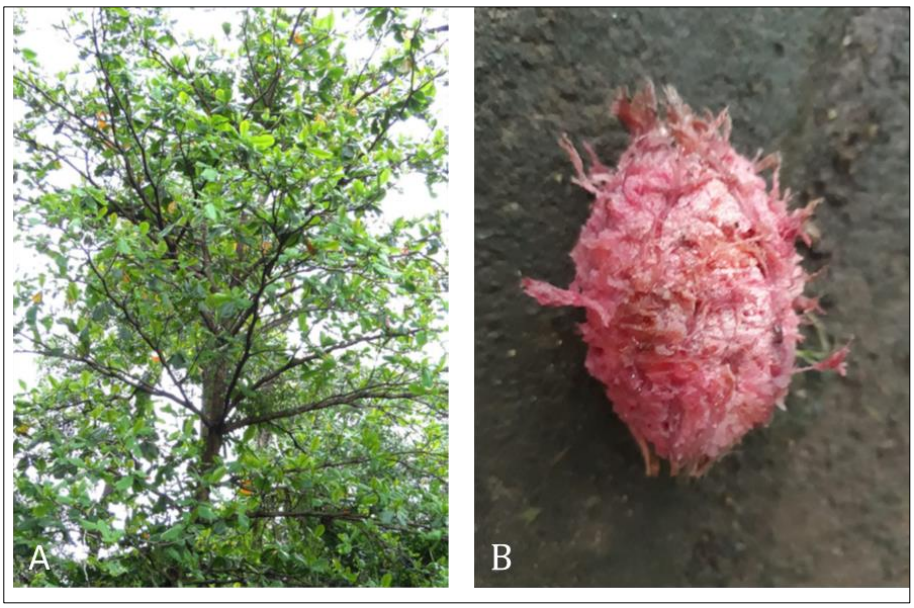

Figure 1 Ketapang or *Terminalia catappa* L. A. Habitus and canopy; B. Old fruit with peeled fruit skin

4. Uses and Bioactivity

4.1. Foodstuff

Various types of wild plants have long been used as food, including TC. Empirically in Indonesia, the young leaves of TC are used as vegetables and have been traded in traditional markets. Oyeniran et al [2] stated that TC leaf is a functional food to relieve symptoms of oxidative stress and neurodegenerative diseases. In addition to leaves, it turns out that TC

fruit is rich in nutritional value and fiber, so it is also called tropical almond (Figure 1B) with its fat content and high energy value [3]. TC seeds contain mineral salts in the form of Calcium, Iron, Zinc and tannins depending on the location [4]. Analysis of the chemical composition of TC kernel oil showed that it was composed of 43.89% and 56.1% saturated and unsaturated fatty acids [5]. Edible TC seeds contain high oil content (600 g/kg) making them suitable for use on vegetable oil diets [1].

In Nigeria, TC seeds are used to overcome nutritional deficiencies because they are rich in macro and micronutrient content of seeds [4] (Mbah et al., 2013). This is thought to be related to the physicochemical properties of TC seed oil comparable to soybean oil [1]. Although TC seeds are rich in vegetable fats, their levels are greatly influenced by the processing process. Temperature, time, type of solvent, and particle size affect the extracted oil from TC kernel and solvent n-hexane gives the highest oil yield of 60.45% [5].

Besides being rich in fat or oil, it turns out that TC seeds are also rich in protein and carbohydrates, but the levels vary greatly depending on the origin and processing [4]. The roasting of TC beans reduces the carbohydrate content from 35.6 to 33% while roasting beans will increase the protein, fat and fiber content [4]. TC fruit mesocarp contains ash (8.10-12.65%), carbohydrates (84.93-89.25%), oil (0.37-0.95%), glucose (238-316 mg/g) and anti-nutrition (1.30 mg/g). The mesocarp of TC fruit is also rich in mineral salts mg/100 g, namely Ca, Mg, Fe, Cu and Zn so they are suitable for use as a food source [16].

4.2. Traditional Medicine

4.2.1. Anti-diabetes Mellitus

Diabetes mellitus (DM) is a lifelong chronic condition due to inadequate insulin production [17] which results in above normal blood glucose levels, which is also known as hyperglycemia. Various synthetic drugs have been commercialized as anti-diabetes mellitus with trademarks such as amlodipine and glimepiride. The way TC extract works to reduce blood sugar levels is very diverse. Plants used as anti-diabetes mellitus are plants that produce compounds that are able to inhibit the activity of enzymes that play a role in the breakdown of carbohydrates such as α-glucosidase and α-amylase through non-competitive way [18]. The activity of ethanol extract as anti-diabetic by changing blood glucose concentration and increasing insulin levels [17]. The inhibitory effect of TC on α-amylase and α-glucosidase from the synergistic action of terpenes [18].

Exploration of natural ingredients that have activity as anti-diabetes mellitus continues to be carried out, including TC. The bioactivity of TC as an anti-DM has been reported by Divya et al [17], Nagappa et al [19], and Iheagwam et al [18]. The ability of TC to overcome DM depends on various factors such as dose, solvent polarity, and the part used. The ethanol extract of TC leaves administered to diabetic rats with diabetes had similar activity to the standard drug glibenclamide [17]. Petroleum ether, methanol, and TC water extracts had significant antidiabetic activity at a dose level of 1/5 of the lethal dose [19]. The aqueous extract and ethanol of TC leaves have inhibition of α-glucosidase (IC50 = 3.28 ± 0.47 mg/mL) and α-amylase (IC50 = 0.24 ± 0.08 mg/mL) with non-competitive action [17].

4.2.2. Anti-microbial

Pathogenic microbes are the cause of infectious diseases in humans such as the digestive tract, respiratory tract and skin. Chanda et al [20] stated that the combination of plant extracts and antibiotics is an alternative to overcome multidrug-resistant microbes. Some facts show that some commercial antibiotics have proven ineffective in curing many infectious diseases, because the search for new compounds as antimicrobials continues [21]. Piperacillin and gentamicin are standard antibiotics as anti-bacterial, while nystatin and fluconazole are antifungal tests [22].

Antimicrobial compounds are compounds that can inhibit the growth of microorganisms. The leaf extract of TC showed better antibacterial activity than the commercially used antibiotics [22]. The extract of TC inhibited the growth of microbes *Staphylococcus aureus* [23-25], *Escherichia coli* [21,24-26], *Pseudomonas aeruginosa* [23], *Klebsiella pneumonia, Candida albicans* [24], *Salmonella typhi* [26], *Bacillus subtilis, Enterobacter aerogenes* [25], and *Helicobacter pylori* [27]. The antibacterial activity of TC was more pronounced against bacteria than fungal strains and activity against Gram-positive bacteria was more susceptible than that of Gram-negative bacteria [22]. The bioactivity of TC as an antimicrobial is thought to be related to the endophytic fungi that are symbiotic with its [28].

The bioactivity of TC inhibits microbial growth is influenced by leaf age, concentration, type of microbe and solvent polarity. The leaf aqueous extract of TC against various pathogenic microorganisms, namely: *K. pneumonia* > *S. aureus* > *E. coli* > *C. albicans*, but its potency is smaller when compared to standard antibiotics, Ampicillin, Nystatin, Penicillin under standard conditions [24]. The size of the diameter of the ethanolic inhibition zone of the TC leaf extract was directly proportional to the concentration of the extract [23]. The ethanolic extract of the leaves of TC (dark brown) inhibited the growth of *S. aureus* and *P. aeruginosa* [23]. The bioactivity of TC as an antimicrobial is related to the content

of its secondary metabolites. Dried ethanol extract from brown TC leaves contains flavonoids, quinones, phenolics, triterpenoids, and tannins [23]. The chloroform fraction showed activity against *E. coli* and *S. typhi* at a concentration of 500 g/disc, while the ethanol and methanol fractions were active against Salmonella typhi at a concentration of 300 – 500 g/disc [26].

The ethanol and water extracts of the leaves and bark of TC inhibited the growth of pathogenic bacteria, namely *E. coli, B. subtilis, S. aureus* and *E. aerogenes* [25]. The TC methanol extract inhibited the growth of *B. subtilis* and *S. aureus* but had no inhibitory effect on *P. aeruginosa, S. typhi* and *E. coli* [29]. The age of TC leaves affects its anti-microbial activity. The young leaf extract had a higher inhibitory affinity (10.2-20.6 mm) compared to mature (10.6mm-18.5mm) and old (5mm-10mm) leaves [21].

4.2.3. Antioxidant

Free radicals are one of the main causes of health that are directly or indirectly related to diabetes mellitus, stroke and cancer. Compounds that inhibit the activity of free radicals are known as antioxidants. The main component of TC leaf aqueous extract (TCE) is a tannin in the form of punicalagin [7]. TCE or punicalagin treatment prevented bleomycin-induced mutation of the hgprt gene (genotoxic compound) and DNA strand breaking. This bioactivity is related to the ability of TCE and punicalagin to suppress intracellular free radical formation [7]. TC leaves contain flavone glycosides, namely apigenin 6-C- (2^2-O-galloyl) -b-D-glucopyranoside and apigenin 8-C- (2^2-O-galloyl)-b-D-glucopyranoside showed a significant antioxidant effect with IC50 value. 2.1 and 4.5 mM, respectively [30].

4.2.4. Anti Neurodegeretive

The TC is a medicinal plant that is traditionally used as food and medicine to prevent or treat various metabolic and neurodegenerative diseases. The TC leaves contain polyphenols which are associated with antioxidant properties. TC leaves are effective in treating diseases related to oxidative stress and neurodegeneration [2].

4.2.5. Anti-aging

Hydrophilic leaf extract of TC (TCLW) prevents photoaging of human skin fibroblasts after exposure to UVB radiation. The inhibition rate of collagenase by methanol extract and hydrophilic TC leaf and its hydrolysate was greater than 100% at a concentration of 1mg/mL. The inhibition was related to TCLW inhibiting the expression of MMP-1 and MMP-9 proteins at a concentration of 25 g/mL. and inhibited the expression of MMP-3 protein at a concentration of 50 g/mL and increased the expression of type I procollagen protein [10].

4.2.6. Hepatoprotective

The hepatoprotective compounds are compounds that function to protect or restore liver function. TC leaf chloroform extract improved acute liver damage in rats induced with carbon tetrachloride (CCl_4) and D-galactosamine (D-GalN). Chloroform TC extract has hepatoprotective activity and its mechanism is related to liver mitochondrial protection and free radical scavenging action [31].

4.2.7. Anti-depressant

Chandrasekhar et al. [9] reported that the hydroalcoholic extract of TC had an antidepressant effect. Administration of TC significantly reversed chronic mild stress (CMS) induced by changes in hippocampal neurotransmitter concentrations and levels of acetyl cholinesterase (AchE), cortisol, monoamine oxidase and brain derived neurotrophic factor (BDNF). TC supplementation suppresses depression-induced stress by regulating monoamine neurotransmitters, BDNF, cortisol, AchE levels as well as by repairing oxidative stress [9].

4.2.8. Anti-cancer

The survival rate for malignant tumors, especially hepatocellular carcinoma (HCC) has not improved, mainly due to uncontrolled metastases. TC leaf extract exerts antimetastatic effect on HCC cells. Treatment of Huh7 cells with TC extract significantly reduced the activity, protein content and mRNA levels of urokinase-type plasminogen (u-PA). Chromatin immunoprecipitation (ChIP) assay showed that TC extract inhibited the transcription of core factor protein SP-1 and NF-κB. TCE also inhibits the effects of u-PA by reducing phosphorylation of the ERK1/2 pathway [32].

4.2.9. Anti-hypertension

Hypertension is a circulatory system disorder that results in above normal blood pressure. Compounds used as antihypertensives are compounds that cause the diameter of blood vessels to widen, resulting in a decrease in blood pressure. One of the ways antihypertensives work is to act as an acetylcholinesterase (ACE) inhibitor, which is a special

enzyme for producing the hormone angiotensin II, a hormone that can trigger constriction of blood vessels. Some of the trademarks of hypertension drugs are amlodipine and captopril. Phenol content and total flavonoid TC has antihypertensive potential through determination of acetylcholinesterase, arginase, phosphodiesterase-5 and inhibition of angiotensin-1 converting enzyme in vitro [6].

4.2.10. Anti-ulcer

Ulcers are sores found in the digestive tract, especially the stomach or also known as gastric ulcers. Oral administration of the aqueous fraction (FrAq) of TC (25 mg/kg) significantly reduced the number of ethanol-induced ulcerative lesions and ischemic injury. The leaf water fraction of TC contains many different phenolic compounds such as punicalagin, punicalin, and gallic acid. FrAq leaf TC has excellent preventive curative effect on chronic acute gastric ulcer and against Helicobacter pylori [27].

4.2.11. Immunomodulator

Immunomodulator compounds are compounds that can increase the body's immunity. The ethanolic extract of the bark of TC (ETCB) has immunomodulatory properties and anti-inflammatory effects on the gut in vitro (RAW macrophages 264.7) and in vivo rat colon inflammation induced by trinitrobenzenesulfonic acid (TNBS). ETCB was able to inhibit the production of yl-1β and nitrite in vitro in RAW264.7 macrophages. ETCB treatment decreased the expression of pro-inflammatory mediator genes (TNF-α, IL-23, IL-6 and CINC-1) and iNOS in incolitic mice. ETCB contains as many as 31 phenolic compounds including ellagic acid, catalamine and gallic acid [8].

5. Conclusion

The leaves and seeds of TC can be used as food because they are rich in nutrients and mineral salts. TC seeds are carbohydrates, fats, saturated fatty acids, unsaturated fatty acids and mineral in the form of Calcium, Iron and Zinc. In traditional medicine, TC has been used to treat hypertension, hepatitis, colitis, depression and anti-aging. TC's bioactivity includes anti-diabetes mellitus, anti-microbial, antioxidant, anti-neurodegenerative, anti-aging, hepatoprotective, anti-cancer, anti-depressant, anti-hypertensive, and anti-ulcer and immunomodulatory activities.

Compliance with ethical standards

Acknowledgments

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