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Traditional uses, phytochemistry, pharmacology activity and plant tissue culture of *ficus carica I.* (a mini review)

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Abstrak

Latar Belakang: Tanaman *Ficus carica* L. atau tin adalah tanaman yang berasal dari kawasan Timur Tengah dan Mediterania, yang kemudian menyebar ke berbagai belahan dunia. Tanaman tin dapat tumbuh di berbagai habitat, antara lain tanah berbatu yang tidak subur, hutan, semak belukar, bahkan tanah kering yang panas. Tanaman tin memiliki beberapa varietas yang dapat dibedakan dari bentuk batang, bentuk daun, dan warna buahnya. Tujuan dari kajian literatur ini memberikan dasar terbaru untuk pengembangan tanaman tin sebagai bahan baku obat tradisional.

Metode: Data aktivitas farmakologi, kandungan fitokimia dan perbanyakan tanaman tin secara *in vitro* diperoleh dari jurnal atau publikasi yang berasal dari berbagai situs jurnal online seperti PubMed, ResearchGate dan sciencedirect.

Hasil: Tanaman tin banyak digunakan sebagai obat tradisional baik daun maupun buahnya. Tercatat di beberapa negara telah menggunakan tanaman tin sebagai salah satu tanaman yang digunakan untuk pengobatan tradisional. Tanaman tin banyak digunakan sebagai antioksidan, antikanker, hepatoprotektif, antidiabetes, antibakteri, antipiretik, anti tuberkulosis, antispasmodik, antiplatelet di beberapa negara. Tanaman tin mengandung metabolit sekunder berupa alkaloid, lateksonin, fenol, dan flavonoid. Ada salah satu metode perbanyakan tanaman tin yang mulai banyak digunakan, yaitu kultur jaringan tanaman. Kultur jaringan tanaman adalah metode perbanyakan dengan menggunakan bagian jaringan atau tanaman yang berukuran kecil dan dalam kondisi aseptik.

Kesimpulan: Tanaman tin mempunyai aktivitas farmakologi yang baik sehingga potensial dikembangkan menjadi bahan baku obat tradisional. Untuk menjamin ketersedian bahan baku tanaman tin maka perlu dilakukan perbanyakan tanaman ini, salah satunya dengan teknik kultur *in vitro*.

Kata kunci: Ficus carica L, pemanfaatan tradisional, fitokimia, aktivitas farmakologi, kultur jaringan tanaman

Abstract

Background: Ficus carica L. or Figs plants are plants originating from the Middle East and the Mediterranean region, which then spread to various parts of the world through explorers who try to plant in various countries. Figs plants can grow in various habitats, including infertile rocky soils, forests, shrubs, and even hot dry soils. Figs plants have several varieties that can be distinguished from the shape of the stem, the shape of the leaves, and the fruit's color.

Methods: Data on pharmacological activity, phytochemical content and in vitro propagation of fig plants were obtained from journals or publications from various online journal sites such as PubMed, ResearchGate and ScienceDirect.

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Result: Figs plants are widely used as traditional medicine for both leaves and fruit. Noted in several countries have used the Figs plant as one of the plants used for traditional medicine. Figs plants are widely used for antioxidants, anticancer, hepatoprotective, antidiabetic, antibacterial, antipyretic, antituberculosis, antispasmodic antiplatelet in several countries. Figs plants contain secondary metabolites of alkaloids, latex onions, phenols, and flavonoids. There is one method of multiplication of Figs plants that began to be widely used, namely plant tissue culture.Plant tissue culture is a method of propagation using tissue slices or parts of plants that are small and in aseptic conditions. **Conclusion:** The fig plant has good pharmacological activity, so that it has the potential to be developed as a raw material for traditional medicine. To ensure the availability of raw materials for figs is necessary to propagate this plant using in vitro culture techniques.

Keywords: Ficus carica L, traditional uses, phytochemistry, pharmacology activities, plant tissue culture

Introduction

The Figs plant then grew widely in the Middle East and on the shores of the Mediterranean sea. Over the years, the cultivation of these Figs plants began a lot because of its easy rooting. This Figs plant is extended to the coast of Atlantica and North Africa. The Figs Plant was later introduced to England around 1525 and 1548. In 1550, it was noted that there was a Figs Plant garden in China (1).

In the middle of 1560, the Figs tree was first introduced to America by Spanish explorers in Mexico In 1769, the cultivation of Figs plants had begun to become popular in the West Coast part of the State of California (2).

The Figs Plant was initially adapted to semi-arid subtropical regions. However, it can diet on natural flora in temperate and tropical regions as a green plant.

Figs are widely planted in regular plantations between latitudes 200 and 400 in both North and South Hemispheres. In most Figs-producing countries, commercial gardens are located at lower altitudes, but they can be found at an altitude of 3000 meters above sea level in the tropics. Low temperatures also increase the risk of insects.

Figs plants can grow in various habitats, including infertile rocky soils, forests, shrubs, and even hot dry soils. Figs can be planted on all soil types but prefer sandy loam and clay in a pH range of 6.0 - 8.0.

Morphology

Ficus carica L. can grow openly until dense and droop to spread, depending on the particular cultivation. Tree size and tree density also depend on crop cultivation, although maintenance factors and soil quality can significantly impact tree size in the end. Specimens recorded that Figs plants can grow 9 to 12 m high and 10 m wide, although commercially planted trees may only grow on average 5-8 m high and 6-7 m wide. Some cultivations produce round and dense trees with many branches. Other cultures have more apical branches, producing more open or long-stemmed trees (3).

Root

The root of the Figs plant is usually a shallow root that is on the surface, fibrous-rooted. However, depending on soil conditions, roots can spread horizontally or vertically.

Wood and Bark

Figs wood is bright, soft, and not too hard. The bark feels smooth, but some cultivation allows for a gap in the bark. More massive trunks and branches may have wood tubers, which are swellings formed from dormant shoots whose apices have died but have vascular connections with wood.

Latex Cell

Latex cells are single cells that grow in plant tissue similar to parasitic fungal hyphae. Latex cells are found in most Figs plants. Latex cells produce exudate latex-like milk, which causes skin irritation because it contains the proteolytic enzyme.

Branches

Young twigs are generally bare and brown to green. However, it quickly turns gray as branches grow. Lenticels then become cork tissue, coarser, and darker with age. The length of the internodes increases towards the middle of the shoot.

Leaf

The shape of the leaves of the Figs plant is like a finger of 3 or 5 segments. On the surface of the Figs, plant leaves have fine hairs. The presence of fine hairs or spicules is an additional criterion used for identification.

Fruit

Figs appear in lateral buds on the leaves. Flowers appear on lateral leaf buds (4). The initial period of growth is characterized by growth in diameter and weight. At this stage, there is almost no difference in sugar accumulation. The next stage is to start the level of maturity by increasing the fruit's weight and size, but there is no increase in sugar accumulation. The last step is characterized by the acceleration of fruit diameter, maturity, and water and sugar content (5).

Traditional Uses

Figs (*Ficus carica L.*) can be used traditionally to treat the body's metabolism, help improve blood circulation, help expedite breathing, and are anti-inflammatory. Leaves, fruits, and roots of the fig can be used traditionally in various disorders such as gastrointestinal Traditional uses, phytochemistry, pharmacology activity and plant tissue culture of *ficus carica I.* (a mini review)

such as colic, digestive disorders, loss of appetite, and diarrhea. They can treat respiratory problems such as sore throat, cough, inflammation of the digestive tract, and cardiovascular (6). Figs plants can be consumed fresh or processed into jam. The fruits of the Figs plant are good sources of minerals, vitamins. carbohydrates, and dietary fiber because they are free of fat and cholesterol and contain high amounts of amino acids (7). If the fruit is made into drinks and mixed with honey, it can be used to treat bleeding.

In Indian medicine, the fig is used as a laxative, expectorant, and diuretic [8]. In other treatments, it can be used as an aid in liver and spleen diseases. Dried figs can be consumed by people with diabetes who are then commercialized into candied figs (7). The latex from figs can be applied to the area of swelling and inflammation to relieve pain (6).

Phytochemistry Qualitative Secondary Metabolite

Most species of Figs or *Ficus carica L.* contain organic acids, volatile compounds and phenolic compounds. Phenolic acids, such as quercetin-3-O-glucoside, quercetin-3-Orutinosid, ferulic acid, 3-O- and 5-O-caffeoylquinic acid, bergapten, psoralen and organic acids have been isolated from water extracts of Figs leaves (9). The other secondary metabolite such as coumarin has been isolated from methanol extracts. Four triterpenoids like lupeol acetate, oleanolic acid, bauerenol and methyl maslinat, have been isolated from Figs leaves (Figure 1).

Total and individual phenolic acids, chlorogenic acids, phenolic compounds, flavonols, and flavones, have been isolated from dried and fresh fruit peels. Dry figs contain a higher total phenolic amount than fresh fruit due to the contribution of dry skin. Rutinoside quercetin is the main individual phenolic compound, while microbial β -D-glucan has

been isolated from the Libyan Figs fruit (6).

Phenolic acids, such as, ferulic acid, quercetin-3-O-rutinoside, quercetin-3-O-glucoside, 3-O- and 5-Ocaffeoylquinic acid, psoralen, bergapten, and organic acids isolated from the flesh and skin of figs. Phenolic compounds, sucrose glucose, fructose and anthocyanins can be identified from figs (20).

Various volatile constituents of the five Portuguese varieties of flesh and skin of isolated Figs fruit including aldehydes such as 2-methylbutanal; ketones: 6-methyl-5-hepten-2-one, esters: ethyl salicylate, methyl salicylate, and methyl hexanoate, monoterpenes: menthol, linalool, α -pinene, β - pinene, limonene, eucalyptol, sesquiterpenes: germacrene D, copaene, α -cubenene, τ -cadinene, τ -muurolene, and β -caryophyllene (23).

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organic acids (9). In the flesh of the fruit and the skin of the fruit, there is no quinic acid. The quantity of quinic acid is higher than other organic acids that are 10.502 mg/kg of leaf extract and followed by malic acid with 8.704 mg/kg of the extract, citric acid with 2.280 mg/kg of the extract, oxalic acid with 155 mg / kg of the extract, cyclic acid with 142 mg/kg of extract and fumaric acid with 23 mg/kg of extract (24).

The profile of fatty acid in the latex of Figs (Ficus carica L.) plant was determined by ion mass chromatography gas chromatography (GC-ITMS). From the results of the determination using these tools, there were 14 main fatty acids detected. These acids are identified as cis-10-heptadecenoic, margaric, myristic, palmitic, pentadecylic, arachidic, elaidic, oleic, linoleic, stearic. lignoceric. heneicosylic, tricosylic, and behenic. Their quantities are reported as 0.10, 0.66, 0.56, 28.94, 1.35, 91.29, 0.35, 5.54, 14.59, 8.62, 1.90, 0.77, 1.25 and 13.1 mg/kg of latex tissue, respectively (23).

Use	Part	Locality	Reference
Cough Leaf		Malaysia	(10)
Anemia	Fruit	Iran	(11)
Indigestion	Fruit	India	(12)
Diabetes	Leaf	Pakistan	(12)
Hemorrhoids	Leaf	Turkey	(13)
Hepatitis	Fruit	Turkey	(13)
Anthelmintic	Latex	Pakistan	(14)
Anorexia	Leaves and latex	Pakistan	(15)
Heart disease Fruit		Pakistan	(16)
Anti-inflammation Figs		not specified	(17)
Antiplatelet Figs		Pakistan	(17)
Earache Leaf		Nepal	(18)
Fever Fruit		Bangladesh	(19)
Kidney stones Fruit and leaf		Pakistan	(15)
Nutritious diet Fruit		The Mediterranean	(20)
Tuberculosis Leaf		Malaysia	(21)
Digestive Cancer Latex		Iran	(22)
Diuretic Fruit		India	(21)

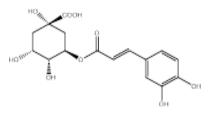
Quantitative Secondary

The organic acid profile of Figs (Ficus carica L.) leaves composed of six

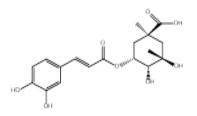
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No	Plant parts	Metabolite	Example	Reference
1	Leaves	Flavonoids	Luteolin, luteolin-6C-hexose-8Cpentose, Kaempferol routineoside, Quercetin, Quercetin routineoside, Quercetin acetilglucoside, Quercetin glucoside, apigenin rutinoside, biochanin-A.	(26) and (27)
2	Fruit	Anthocyanin	Cyanidin-3, cyanidin-3-glucoside, cyanidin-3-rutinoside, (epi) catechin- (4- 8)-cyanidin-3-rutinoside, cyanidin-3- rhamnoglucoside, , cyanidin 3-dimmer routine, pelargonidin-3-glucoside, (epi) catechin- (4-8) - pelargonidin 3- rutinoside, cyanidin 3-dimmer routine, (epi) catechin- (4-8) -cyanid 3-routine - glucoside, cyanidin 3,5-diglucoside, (epi) catechin- (4-8) -cyanidin 3-rutinoside, pelargonidin-3-glucoside, carboxypyrano-cyanidin 3-rutinoside, cyanidin 3-malonylglycosyl-5-glucoside, Pelargonidin 3-glucoside, (epi) catechin- (4-8) - cyanidin 3-rutinoside, pelargonid 3- rutinoside, cyanidin 5-diglucoside, (epi) catechin- (4-8) -pelargonidi 3- rutinoside, 3-malonylglucoside.	(8) (28)
3	Leaves	Organic acid		(9)
4	Latex	Fatty acid	pentadecylic acid, margaric acid, Myristic acid, stearic acid, oleic acid, elaidic acid, linoleic acid, arachidic acid, heneicosylic acid, behenic acid, trichosylic acid, palmitic acid, heptadecenoic acid cis-10, lignoseric acid	(23)
5	Latex	Amino acid	Leucine, glutamine, cysteine, phenylalanine, glycine, lysine, asparagine, alanine, serine, ornithine, tyrosine, tryptophan, histidine,	(23)
6	Leaves	Phenolic compounds	Q-3-Glu (quercetin 3-O-glucoside), 5- CQA (5-O-caffeoylquinic acid), 3-CQA (3- O-caffeoylquinic acid), Q-3-rut (quercetin 3-O-rutinoside), vanillin, cinnamic, ferulic acid, pirogalik, phenol, 3-5 dimethoxy, coumaric, psoralen, pinocembrin, protocetchol, quercetin, galangin, bergapten, phenolphthalein, pinostrobin, chrysin.	(9)
7	Leaves	Triterpenoid	Bauerenol, methyl maslinate, oleanolic acid lupeol acetate and calotropenyl acetate.	(29)

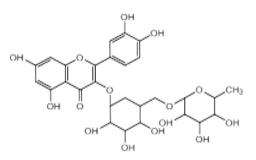
Table 2 Secondary	y Metabolites of Ficus carica L.
	y Melaboliles of Ticus carica L.



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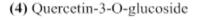


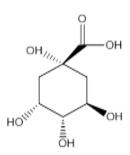
(1) 3-O-caffeoyquinic acids



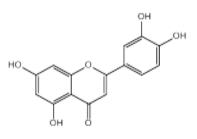
(2) 5-0-caffeoylquinic acids

(3) Quercetin-3-O-rutinoside





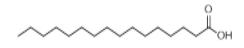
(5) Quinin acid



(6) Luteolin



(7) Lenolenic acid



(8) Palmitic acid

Figure 1. Structure of the active compound of fig plant (continue)

Arachidic, palmitic, and behenic acids are the primary fatty acids (respectively 44.1, 21.4, and 13.1% of total fatty acids). Some of them are also counted from dried figs with the help of gas chromatography. The most dominant fatty acid was linolenic acid with 53.1% in dried figs, followed by linoleic acid with 21.1%, palmitic acid with 13.8%, and oleic acid with 9.8% (25).

Non-glycoside flavonoids found in the plant Figs (*Ficus carica L.*), which is found most often is luteolin. Luteolin (5,7,30 40tetrahydroxy-flavone) turns out to be the main flavonoid in Ficus's leaves. From the data obtained, luteolin contains 680 mg/kg of the extract, while quercetin contains 630 mg/kg of extract. Another flavonoid identified in the Figs plant, although in smaller amounts, is biochanin A, which is 5,7-dihydroxy-40 - methoxy-isoflavone with a content of 17 mg/kg extract (26).

Pharmacology Activities Antioxidant Activity

The fig plant (*Ficus carica L.*) contains high polyphenol, flavonoid, and anthocyanin compounds. The content shows a capacity for the fruit to be used as an antioxidant (20). From the data obtained, there is a Sianidin profile that contains many of all the varieties tested. NMR spectroscopy shows cyanidin-3-O-rutinoside is the main anthocyanin in all fruits. Cyanidine 3-O-routineoside contributes to the total antioxidant capacity (8).

Anticancer Activity

Bioactive compounds such as 6-O-acyl- β -d-glucosyl- β -Sitosterol can be found in the isolation of the latex of the Figs plant (*Ficus carica L.*). The bioactive compound has several derivatives, namely palimtoil, linoleil, stearyl, and oleyl. Palmitoil derivative acts as a more effective inhibitor than other derivatives. 6-O-acyl- β -d-glucosil- β -Sitosterol is reported to carry out in vitro inhibition of Traditional uses, phytochemistry, pharmacology activity and plant tissue culture of *ficus carica I.* (a mini review)

DG-75, Jurkat, and DU-145 cancer cell lines (30).

Hepatoprotective Activity

The oral dose of L500 mg/kg *Ficus carica* L leaf methanol extract has a hepatoprotective effect because it can reduce serum aspartate aminotransferase levels, alanine aminotransferase, total serum bilirubin and malondialdehyde equivalent, and liver lipid peroxide index (31). Petroleum ether extract from the leaves of *Ficus carica* L has potential as a hepatoprotective (32).

Hypoglycemic Activity

The water extract of Figs leaf significantly induced the hypoglycemic effect in oral administration to rats conditioned in diabetes. The administration of Figs leaf extract can result in weight loss in diabetic rats and changes in plasma insulin levels, which alter the survival index of rats (33).

Antibacterial and Antifungal Activities

The methanol extract of *Ficus carica* L leaves has potential as a natural antibacterial agent (34). Extracts from the plant sap of *Ficus carica* L can be antimicrobial against five bacterial species and seven fungal strains. The methanol fraction showed excellent inhibitory activity on Candida albicans (100%), and the methanol extract inhibited the growth of Microsporum canis (35).

Antipyretic

The ethanolic extract of Figs (*Ficus carica L.*) leaves can be used as an antipyretic where this extract can be active at a dose of 100,200,300 mg/kg in reducing the dawn of the body. Then the effect is extended to five hours after compared with paracetamol, which is an antipyretic drug with a dose of 150 mg/kg) (36).

Antispasmodic and Antiplatelet

The ethanol extract of water from the fruit of *Ficus carica* L has a naturally relaxing effect. The extract also inhibits adenosine 50-diphosphate.. The study shows that Figs can be used together as an excellent antispasmodic agent in the treatment of intestinal motility and inflammatory disorders (17).

Anthelmintic

The anthelmintic activity of the sap of *Ficus carica* L was tested on mice infected with *Vampirolepis nana*, *Syphacia obvelata*, and *Aspiculuris tetraptera*. Latex is given in a dose of 3ml / kg/day for three consecutive days. From the results obtained, the latex Figs effectively removed 41.7% Syphacia obvelata, but it was not effective in removing Aspiculuris tetraptera and Vampirolepis nana (2.6% and 8.3%, respectively) (37).

Anti Constipation

Research was conducted to determine the anti-constipation effect of the latex of Figs (Ficus carica L.) in mice that have been induced by loperamide. Figs latex is given for four weeks to assess the effects of constipation. The amount, weight, and water content of rat droppings increased in mice given Figs resin. Symbiotes are reduced when Figs resin is given to mice (Lee, 2012). Clinical studies are carried out in the form of supplements to patients suffering from symptomatic functional symptoms. The study was randomly assigned to 20 female patients with functional constipation. Things that are obtained after the patient is given the supplement are increasing the number of bowel movements, reducing the time of bowel movements, and increasing the desire to defecate (38)

Hypolipidemic Activity

Leaf extract from the plant Figs (*Ficus* carica L.) is reported to reduce triglycerides in poultry livers, triglyceride

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secretions, and cholesterol in the liver. Then, the liver's triglyceride value decreases significantly with an increase in the dose of the Figs leaf extract used. This shows that Figs leaf extract can be used and is useful for modulating triglycerides and cholesterol secretion from the liver (39).

Anti Virus

Extracts of n-hexane from the plant Figs (*Ficus carica L.*) are reported to be used as a possible herbal drug for herpes virus, echovirus, and adenovirus infectious diseases. The extract was tested in in vitro testing by evaluating the inhibition of viral replication, including adsorption and penetration, intracellular inhibition, and virucidal activity (40).

Plant Tissue Culture

Plant tissue culture is based on cellular totipotency theory, which states that each plant cell can regenerate to form plants as a whole. Plants to be obtained by culture are identical to their parents and are called planets.

The number of new plants produced is not only one, but can be tens to hundreds (from one planting material or explants). so that tissue culture techniques are used to propagate plants. Plant propagation method carried out by tissue culture techniques classified as vegetative propagation, meaning that it does not involve the fertilization between eggs and male sex cells and the formation of seeds in plants; that is why the plantlet produced will be identical to its parent. Plant propagation by tissue culture technique is also called micropropagation or micropropagation. The word micro refers to the initial plant material used, a small explant, even reaching less than 1mm (41).

There have been several studies that developed the growth of Figs plants by using tissue culture techniques. In this research plant tissue culture Figs uses

several parts of the plant, both shoots and leaves of plants.

Figs plant shoots were planted on different culture media, namely on the media Murashige and Skoog, Gamborg media, and Schenk and Hildebrant media. Each media used has added growth regulators that function to accelerate the growth of planted shoots, namely 6benzylaminopurine (BAP), which functions as a cytokinin. Each media was given BAP with each concentration, i.e., 0, 0.5, 1, 2, 3, 4, 5 ppm concentrations, and was given. Each media was also given cytokinin growth regulators, namely indole-3- acetic acid (IAA), indole-3butyric acid (IBA), and naphthalene-acetic acid (NAA). Each media was given one cytokinin with each concentration: 0.2, 0.5, 1, 2, 3 ppm at each BAP concentration (42).

Subsequent studies used shoots as explants implanted in Murashige and Skoog (MS) media. Several treatments carried were out, namelv benzylaminopurine (BAP) with concentrations of 1 and 2 ppm and coconut water with concentrations of 100 and 150 ml / L. Coconut water can be used a natural growth regulator because cytokinin content is 5.8 ppm and 0.07 ppm auxin. The results obtained show that the Figs plant shoots can grow well on MS media by adding 100 ml / L coconut water growth regulator, seen after 30 days of planting (43).

Subsequent research used leaves to grow callus Figs plants on Murashige and Skoog (MS) media. This study aims to describe the effect of giving various combinations of Indole-3-butyric acid (IBA) growth regulators and 6-furfuryl amino purine (kinetin) to the induction and growth of figs leaf callus on MS media (Murashige and Skoog) in vitro and determine the combination the best concentration of IBA and kinetin for the induction and growth of callus tin. The results obtained show that a combination Traditional uses, phytochemistry, pharmacology activity and plant tissue culture of *ficus carica I.* (a mini review)

of growth regulators 0.5 mg / I IBA and 1, 5 mg / I kinetin has better results than the combination of other growth regulators. With an induction time of 20 days, a green compact callus was obtained, and a total of 0.712 grams of shirt biomass (44).

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