



Phytochemistry, traditional uses, and pharmacological activities of *Ficus elastica* Roxb. ex Hornem: A review

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ARTICLE INFO

Article Type:
Review**Article History:**

Received: 1 August 2022

Accepted: 5 November 2022

Keywords:

Rubber tree

Herbal medicine

Secondary metabolites

Biological activities

Phytoconstituent

ABSTRACT

Ficus elastica Roxb. ex Hornem is usually found in tropical and subtropical areas, used in traditional medicine for various health problems, including pain, rheumatism, diarrhea, hypertension, infection, skin allergies, anemia, wound, hernia, and hemorrhoids. This review aims to present the phytoconstituents and pharmacological activities of *F. elastica*. A literature search employing PubMed, Google Scholar, Semantic Scholar, and Library was done to retrieve the relevant articles. *F. elastica* is a good source of traditional medicine for the treatment of various types of diseases, especially for microbial infections and preeclampsia. Quercitrin and myricitrin, having strong antioxidant activity, as well as ficusamide, ficusoside B, elastiquinone, elasticoside, and elasticamide are compounds, which have potential to be developed as new drugs for these conditions. In sum, the data regarding the pharmacological and safety aspects of this plant and its components are still limited. However, *F. elastica* is a natural product that has beneficial to human health and might be a good source for the preparation of new drugs.

Implication for health policy/practice/research/medical education:

This review provides a detailed insight into the *F. elastica* plant, which can be considered as a potential source of candidate drug compounds, representing a new, safe, and effective agent to manage antimicrobial, anti-preeclampsia, antioxidant, and several other pharmacological activities.

Please cite this paper as: Arsyad AS, Fakhruddin N, Nurrochmad A. Phytochemistry, traditional uses, and pharmacological activities of *Ficus elastica* Roxb. ex Hornem: A review. J Herbmed Pharmacol. 2023;12(1):41-53. doi: 10.34172/jhp.2023.04.

Introduction

Traditionally, many people use plants for medication. Besides being affordable, these medicinal plants are usually easy to find as they grow in the surrounding area (1-3). Many plant species in the world significantly contribute to human health, especially in disease prevention and medicinal practices; however, they experience intense competition with chemical and combinatorial compounds (4). There are some obstacles to documenting the data of plant species, especially the lack of research data that is inadequate for evaluating traditional medicine. The process for collecting plant inventory that has been studied is important for those that have not been achieved to determine the research needed for the future. Plants are an important source of pharmacologically active compounds, and several natural product-derived compounds in the

clinical development stage are suitable as sources of new drug candidates (4-6). Natural resources as a good starting point to produce native isolates as candidates for semi-synthetic molecular development to overcome any limitations inherent in native molecules (7).

Ficus has more than 850 species and is the largest species in the *Moraceae* family (8,9). Similar to other members of *Moraceae* family such as *Artocarpus*, *Ficus* has a lot of milky white latex (10-12) on the bark, branches, and leaves (13). *Ficus* growth can be in the form of shrubs, vines, woody trees, epiphytes, or hemiepiphytes (14,15). Its distribution is found worldwide (16), especially in tropical and sub-tropical areas (17,18). About 500 species of *Ficus* are found in the Asia-Australasia region, 130 in Africa, and 110 in the neotropics (19). Apart from medication, several species of *Ficus* are also cultivated as ornamental

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plants (20,21). *Ficus elastica* is one of the *Ficus* species that has been developed as the most popular ornamental plant in the world (22) and was introduced more than 100 years ago (23). On the streets of Egypt, it is used as an ornamental plant, which is also found growing outside the banks of the canal (23), as well as in the main gardens of Cairo and Alexandria, such as in the Orman gardens and Antoniades gardens (24). In India, *F. elastica* is one of the most important plant species (25). It is a rubber-producing tree, often called *Rubber tree* or *Indian Rubber tree* (26).

Many species of *Ficus* such as *F. septica*, *F. racemose*, and *F. carica* have been used widely in traditional medicine practices (27-30), including in Jamu, Ayurveda, and traditional Chinese medicine (31). Thus, plants have attracted major attention worldwide because of their high therapeutic potential (32). *F. elastica* has been used in several countries as traditional medicine and has proven beneficial for many people (33). In this review, we present the traditional usage of *F. elastica* in medication, the chemical constituents present in the leaves, roots, bark, and latex, as well as pharmacological activities. This article provides scientific data on *F. elastica* for further development as bioactive agents for drugs.

Although several studies have been carried out on *F. elastica*, the biological and pharmacological aspects have not been reviewed. This review aims to analyze and summarize *F. elastica*-related information to identify gaps for further activities. To the best of our knowledge, there are no published literature reviews on these aspects of *F. elastica*. Therefore, this review needs to be continued to inventory research on this plant to help researchers design future studies of this plant species.

Methods

All scientific findings of *F. elastica* were collected from electronic databases such as PubMed, Google Scholar, Science Direct, Semantic Scholar, and Library Search. The keywords or terms used to search for publications and information included *F. elastica*, traditional uses of *F. elastica*, phytoconstituents of *F. elastica*, in vitro study of *F. elastica*, in vivo study of *F. elastica*, and pharmacological activity of *F. elastica*. In this study, we only used articles published from the last ten years (2012 to 2022). From the 103 journals, 82 were selected and included in the criteria. The data presented in this review is the original article only. Unpublished data, including thesis and conference articles, were excluded from this review.

Results

Botanical aspect

Taxonomy: Division: *Magnoliophyta*, Class: *Magnoliopsida*, Subclass: *Hammamelidie*, Ordo: *Urticales*, Family: *Moraceae*, Genus: *Ficus*, Species: *Ficus elastica* Roxb. ex Hornem (34). *F. elastica* is presented in [Figure 1](#).

In Indonesia, *F. elastica* has regional names *Kajai*, *Karet*



Figure 1. Leaves of *Ficus elastica* (a). *F. elastica* tree (b).

batang, *Rambung*, *Ki Karet*, and *Kolelet*. Meanwhile, the common foreign names found are *Karet boom*, *Caoutchouc d' Assam*, and *Gummifeigenbaum*. In China, *F. elastica* is known as *Yin du xiang jiao shu* and *Indian rubber tree* in India (35,36). *F. elastica* grows naturally in the foothills of the Himalayas, India, Nepal, Buthan, Myanmar, Malaysia, and Indonesia and is found in natural habitats of dry pine forests at an altitude of 800-1150 m (37). It is also widespread in the Mediterranean and is commonly found in the Middle East (31) in countries with a dry-warm climate (38). In addition, it can thrive into a large and sturdy tree without agronomic management with a diameter of up to 2 m (39) and can survive under extreme environments such as high temperatures and limited water stock (10). This plant is morphologically famous for having milky white sap, with leathery, glossy, and green leaves; it seems that it has a thick epicuticular wax layer on the leaf surface (40).

Although its exact origin is unknown (41), in 1814, William Roxburgh wrote the name of *F. elastica*, which was found in Garrow hills (Now called Garo Hills in Meghalaya), India for the first time in Hortus Bengalensis and described by Hornemann five years later (37). This species was an important latex-producing plant in the 18th and early 19th centuries (41). Besides for medicine, *F. elastica* is a potential source of natural rubber as a source of intermediate energy (10).

Ficus elastica grows widely and has a sturdy trunk with a tree height of up to 30 m (42) The stem is woody with a smooth surface, cylindrical, and dark brown. The branches of large trees are irregular, making the tree shady with hanging roots (43). *F. elastica* has dark green leaves that are oval, thick, and shiny, the edges of the leaves are smooth, and the tip is tapered. The length of the leaves is about 10-35 cm, with a width of 5-15 cm (42). The leaves of *F. elastica* grow with a single stalk and are arranged alternately, where the young leaves are red in color and green when they mature. The young leaf buds are covered with a sharp pinkish-colored ocrea (43).

Traditional uses

The *Ficus* genus usually includes edible fruits and vegetables and are used traditionally to treat many

diseases, including digestive, reproductive, endocrine, respiratory systems, gastrointestinal, and metabolic disorders, as well as cardiovascular diseases, diabetes and cancer (44-47). In using plants for treatment, we can consider the consistency of the use of certain plants for certain diseases. With the effect of improving symptoms or diseases after the use of these plants, it can be considered that they are related to each other (31). In West Africa, for example, herbal medicine practitioners use *F. elastica* as medicine for joint and muscle pain (24). In Indonesia, the root of the plant is used to treat several diseases such as improving blood circulation and overcoming stomach ulcers and rheumatism (36).

Several properties of *F. elastica* are often used traditionally to treat rheumatic diseases, diarrhea, bloating, diabetes, hypertension, ulcers, and so on. The plant parts used are leaves, stems, seeds, and sap (48). Besides its use as a diuretic agent, the leaf extract is used to treat infectious and allergic skin diseases (49), anemia, neurodegenerative disorders, and liver problems (50). Meanwhile, the bark is used as a styptic or wound because it has astringent properties. In addition, a decoction of its aerial roots is used for wound and cut healing (39). The latex from *F. elastica* has been reported to treat back pain, hernia, swelling, tuberculosis, and hemorrhoids (39). Currently, the standardized extract can be tested in traditional medicine as a cancer treatment (51).

Phytochemical constituents

Due to its pharmacological activity, *F. elastica* has a high diversity of compounds to be used as drug candidates. The list of plant compounds of *F. elastica* and their structures are presented in Table 1. Several studies have reported various compounds that have been isolated and proven their biological activity; of course, this is an opportunity to explore these compounds further. For instance, ficus elastic acid and (1'S,6'R)-8-O-β-D-glucopyranosyl abscisate sodium have been tested in vitro as antioxidants from *F. elastica* leaves. Ficusamide, ficoside B, elastiquinone, elasticoside, and elasticamide are compounds that can be developed as drug candidates in the future because they have significant antibacterial, antifungal, and antiproliferative properties. N-dotriacontanol and tetracosanoic acid are the two major compounds with promising bioactivity isolated from this plant.

Leaf

Leaves of *F. elastica* contain emodin, morin, sucrose, and rutin compounds (52), saponins, glycosides (53), carbohydrates, proteins, phenolics, flavonoids, and tannins (50). Two antioxidant compounds from *F. elastica* leaves, ficus elastic acid and (1'S,6'R)-8-O-β-D-glucopyranosyl abscisate sodium, were isolated along with 12 other compounds, namely kaempferin, feroxidin, myricitrin, quercitrin, syringin, corchoionoside C, citroside B, ursolic

Table 1. Compounds of *Ficus elastica*

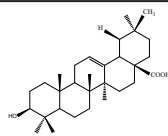
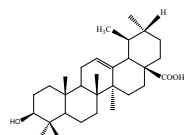
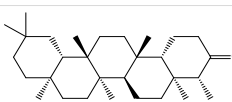
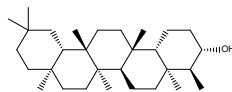
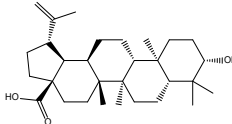
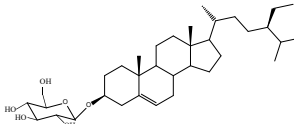
Class	Compound	Part of Plant	Structure	References
	Oleanolic acid	Leaves		(49,56,59)
	Ursolic acid	The leaves and bark of aerial roots		
Triterpenes	Friedelin	The bark of aerial roots		
	Friedelinol	The bark of aerial roots		(56,59,60)
	Betulinic acid	The bark of aerial roots		
Steroids	Sitosterol 3-O-β-D-glucopyranoside	The bark of aerial roots		(56,61,62)

Table 1. Continued

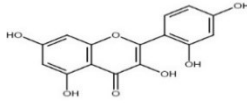
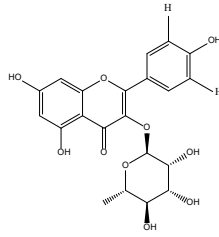
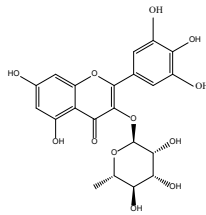
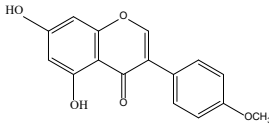
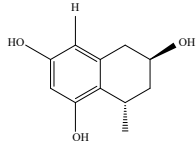
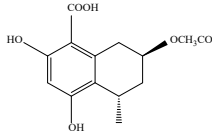
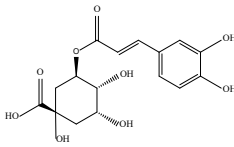
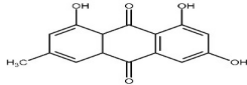
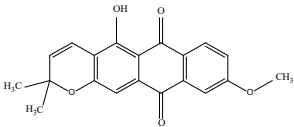
Class	Compound	Part of Plant	Structure	References
	Morin	Leaves		(52,63,64)
Flavonoids	Quercitrin	Leaves		(49,65,66)
	Myricitrin	Leaves		
	Biochanin A	Aerial roots		(51,67,68)
	Feroxidin	Leaves		(49,69)
Phenolics	Ficus elastic acid	Leaves		
	Chlorogenic acid	Leaves		(70,71)
	Emodin	Leaves		(52,72)
Anthraquinone	Elastiquinone	Aerial roots		(51,62)

Table 1. Continued

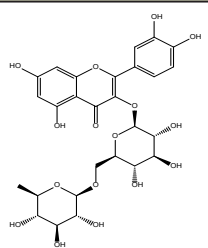
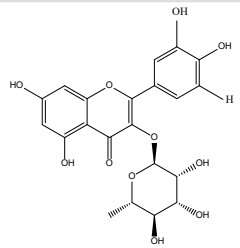
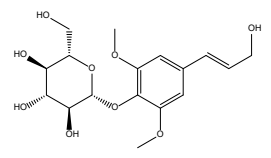
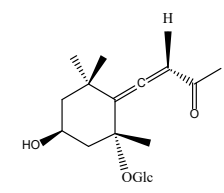
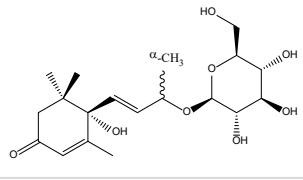
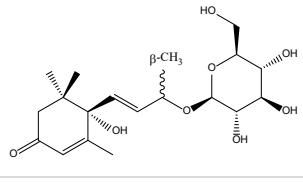
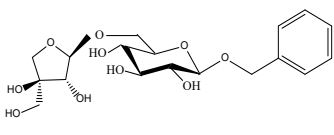
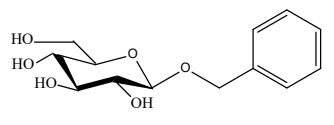
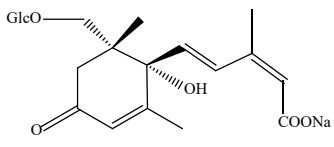
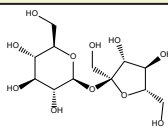
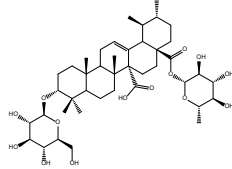
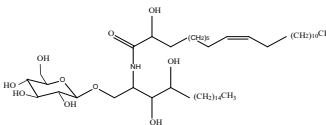
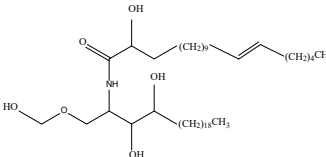
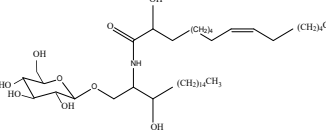
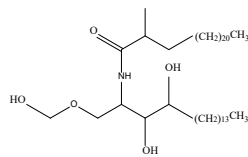
Class	Compound	Part of Plant	Structure	References
	Rutin	Leaves		(49,73)
	Kaempferin	Leaves		(49,74,75)
	Syringin	Leaves		
Glycosides	Citroside B	Leaves		
	Corchoionoside C	Leaves		(49,76,77)
	(6 <i>S</i> ,9 <i>R</i>)-roseoside	Leaves		
	Icariside F ₂	Leaves		
	Benzyl O-β-D-glucopyranoside	Leaves		(49,78,79)
(1' <i>S</i> ,6' <i>R</i>)-8-O-β-D-glucopyranosyl abscisate sodium	Leaves			

Table 1. Continued

Class	Compound	Part of Plant	Structure	References
Disaccharides	Sucrose	Leaves		(52)
Saponin	Elasticoside	The bark of aerial roots		(56)
	Ficososide	The bark of aerial roots		(56,80,81)
	Ficosamide	The bark of aerial roots		
Sphingolipids	Ficososide B	Aerial roots		(51,62)
	Elasticamide	Aerial roots		

acid, oleanolic acid, (6*S*,9*R*) roseoside, benzyl *O*- β -D-glucopyranoside, icaroside F₂, (49), and chlorogenic acid (38).

Leaf oil

Ficus elastica leaf oil contains 1,8-cineole (8.2%), heneicosene (8.4%), geranyl acetone (9.9%), and 6,10,14-trimethyl-2-pentadecanone (25.9%) (54). *F. elastica* leaf oil has been analyzed for its physicochemical properties to view the fatty acid profile using GC-FID (gas chromatography-flame ionization detector) containing caproic acid (27.34%), isovaleric acid (23.59%), capric acid (20.28%), valeric acid (6.76%), isobutyric acid (6.50%), caprylic acid (5.41%), butyric acid (3.38%), lauric acid (3.36%), and myristic acid (3.12%). Thus, it is suitable to be applied to the soap and cosmetic industry (23).

Aerial roots

In the aerial root of *F. elastica* extract from hydrodistillation followed by diethyl ether separation, there were 15 essential oils analyzed using gas chromatography and mass spectroscopy (GCMS), consisting of: Benzene,[1-

methyl-dodecyl] (15.72%); Benzene,[1-propylheptadecyl] (4.96%); 6-Monoacetylmorphine (0.83%); Benzene,[1-ethylundecyl] (14.14%); Propanamide, N, N-didecyl-3-phenyl (1.42%); 3,9 β , 14,15-di-epoxy-pregn-16-en-20-one,3,11 β ,18-triacetoxy (12.44%); Benzene,[1-propyldecyl] (9.96%); 9,12,15-octadecatrienoic acid,2,3-bis[trimethylsilyl-oxy propylester (7.13%); Octadec-9-enoic acid icosyl ester (7.07%); Octadecane, 3-ethyl-5-[2-ethylbutyl] (3.25%); Diethyl phthalate (5.24%); Propanoic acid, 2-[3-acetoxo-4,4,1,4-trimethylandrost-8-en-17-yl] (6.76%); Propanoic acid, 2-[3-acetoxy-4,4,4-trimethylandrost-8-en-17-yl] (4.42%); D-glucose, 6,*O*- α -D-galactopyranosyl, bis-*O*-[trimethylsilyl] (3.62%); and Cyclopropanebutanoic acid, 2-2-2-[2-pentylcyclopropyl]methylcyclopropylmethylcyclopropylmethyl-methyl ester (2.96%) (55).

Aerial roots from *F. elastica* are reported to contain elasticamide, elastiquinone, biochanin A, and ficososide B compounds (51). Meanwhile, the barks of aerial roots contain fatty acid compounds such as *n*-hexacosanol, tetracosanoic acid, a mixture of alcohol, and a mixture of alkanes. In addition, there are friedelin, friedelinol,

betulinic acid, phytosterols with stigmasterol and β -sitosterol compounds, sitosterol 3-O- β -D-glucopyranoside, ursolic acid, ficusamide, ficososide, and elasticoside (56).

Latex

Latex from *F. elastica* leaves is reported to contain phenolics, flavonoids, tannins, saponins, enzymes (57), and glycoprotein compounds (58).

Pharmacological activities

Table 2 presents study data on the pharmacological activities of *F. elastica*. Extracts from leaves, barks, root barks, woods, aerial roots, aerial root barks, and latex of *F. elastica* exhibit various biological effects. The leaf part is the most commonly studied well compared to the other parts. Although comprehensive bioprospective studies of *F. elastica* are still limited, the pharmacological effects of different plant parts will be discussed in this study. Several pharmacological activities discussed in this review include anticancer, antibacterial, antifungal, antioxidant, anti-inflammatory, anticoagulant, antitrypanosomal, anthelmintic, antiplasmodial, antischistosomiasis, anti-proliferative, and anti-preclampsia properties.

Anticancer activity

Ficusamide isolated from the bark of *F. elastica* aerial roots showed moderate anti-proliferative effect against the human A549 NSCLC lung cancer cell line with the IC₅₀ value of 79 μ M; whereas friedelin and ficusamide Ac showed weak activity. Although the methanol extract of *F. elastica* did not have anticancer activity, ursolic acid and betulinic acid isolated from the extract demonstrated anticancer activity in melanoma, glioma, and lung cancer cell lines (56). These findings indicate that *F. elastica* is a promising source of natural anticancer agents.

Antibacterial activity

Investigation of the antibacterial activity from chloroform extract of *F. elastica* leaves was done using the disc diffusion method (by measuring inhibition zone diameter). Morin and rutin demonstrated strong activity (15-19 mm) on *Bacillus cereus* and *Pseudomonas aeruginosa*, followed by emodin (10-14 mm) at the concentration of 100 μ g/mL (52). This finding was in line with a study conducted by Preeti et al (50) showing that methanol extract of *F. elastica* leaves had high antibacterial activity against *B. cereus*, followed by *P. aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae*.

In a research by Mbosso et al (56), the CHCl₃/methanol extract of the aerial root barks demonstrated relatively good bactericidal and bacteriostatic activities compared to standard gentamicin against *Staphylococcus saprophyticus*, *Enterococcus faecalis*, and *K. pneumoniae*. Ficusamide and elasticoside showed potent antimicrobial activities on seven gram-positive bacteria (*E. faecalis*, *S. epidermidis*,

S. aureus, and *S. saprophyticus*) and gram-negative bacteria (*E. coli*, *K. pneumoniae*, and *Salmonella typhi*). Minimum inhibitory concentration (MIC) and minimum microbicidal concentration (MMC) values were best shown by Ficusamide against *S. saprophyticus*, namely 3 and 6 μ g/mL, while elasticoside was 30 and 60 μ g/mL against *E. faecalis*. Gentamicin as standard had values of 980 and 1950 μ g/mL against these two bacteria.

Ficososide B isolated from the wood methanol extract displayed a MIC value of 4.9 μ g/mL in *E. coli*, *Proteus vulgaris*, and *S. aureus*, while the value of MMC was 19.5 μ g/mL. Likewise, elastiquinone had the same MIC and MMC value as ficososide B but in different bacteria, *Providencia stuartii* and *P. aeruginosa*. Gentamicin used as a comparison had 25 μ g/mL MIC and 50 μ g/mL MMC for all bacteria tested. From this study, it can be seen the potential of *F. elastica* as an antibacterial agent (62).

Antifungal activity

The antifungal activity *F. elastica* against *Candida albicans* was confirmed by the presence of two antifungal compounds, elasticoside dan ficusamide with the MIC of 0.50 mg/mL dan 1.00 mg/mL and MMC of 0.75 mg/mL dan 1.50 mg/mL, respectively. The chloroform and methanol extracts of *F. elastica* aerial root also demonstrated activity against *C. albicans* with MIC and MMC values of 3.13 mg/mL and 6.25 mg/mL, respectively; where nystatin had MIC and MMC of 3.91 mg/mL and 7.81 mg/mL, respectively. In *Trichophyton rubrum*, a filamentous fungi, only elasticoside showed MIC and MMC values close to clotrimazole (0.49 and 0.98 mg/mL, respectively) (56). Another study showed that ficososide B, elasticamide, and elastiquinone isolated from the wood of *F. elastica* demonstrated MIC values of 4.9, 19.5, and 19.5 μ g/mL and MMC values of 19.5, 39.1, and 39.1 μ g/mL, respectively, against *Candida albicans* (62).

Antioxidant activity

A study by Kiem et al (49) found that methanol extract of *F. elastica* leaves and its fractions showed strong antioxidant activity in oxygen radical absorbance capacity (ORAC) assay. The extract at 5.0 μ g/mL demonstrated 4.2 μ M Trolox equivalent (TE), whereas the water fraction demonstrated the strongest antioxidant activity, followed by the ethyl acetate, and n-hexane fractions with the TE of 23.4 μ M, 17.9 μ M, and 5.8 μ M, respectively. Further separation of the aqueous fraction and the ethyl acetate fraction yielded 14 compounds. All isolates obtained were tested by ORAC and measured the concentration of ionic Cu (I) reduced from Cu (II). Quercitrin, myricitrin, and kaempferin showed strong antioxidants at ORAC, while the reduction of Cu, myricitrin, and kaempferin ions showed significant reduction capacities of 21.4 and 19.2 μ M TE. These three compounds can be attributed to their potential to donate hydrogen atoms and single electrons in the antioxidant activity.

Table 2. Summarized pharmacological activities of *Ficus elastica*

Plant part	Tested sample	Pharmacological activity	Study design	Study method	Study results	Ref.
Leaf	Methanol extract	Antioxidant	<i>In vitro</i>	1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity, phosphomolybdate method, iron chelating assay, and reducing power potential	The extract demonstrated dose-dependent antioxidant activity in various methods.	(49,50)
				Oxygen radical absorbance capacity (ORAC).	The extract (at 5.0 µg/mL) showed radical scavenging activity equivalent to Trolox 4.2 µM.	
	Ethanol and methanol extract	Anthelmintic	<i>In vitro</i>	Paralysis and death time against the Indian earthworm <i>Pheretima posthuma</i>	Both ethanol and methanol extracts caused paralysis. Ethanol extract is slightly more potent than methanol extracts	(42)
	Ethanol extract	Anti-preeclampsia	<i>In vitro</i>	3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay	The extract suppressed tumor necrosis factor-alpha and increased interleukin-10 levels in hypoxia-induced EA.hy926 cells without causing cytotoxic effects.	(82)
	Water fraction Ethyl acetate fraction	Antioxidant	<i>In vitro</i>	ORAC.	The water and ethyl acetate fractions (at 5.0 µg/mL) showed 23.4 and 17.9 µM Trolox equivalent values, respectively.	(49)
	Methanol extract	Antibacterial	<i>In vitro</i>	The disc diffusion by measuring the diameter of the inhibition zone	The methanol extract showed potent antibacterial activity against <i>Bacillus cereus</i> , followed by <i>P. aeruginosa</i> , <i>E. coli</i> , and <i>K. pneumoniae</i> .	(50,52)
	Methanol extract	Anticoagulant	<i>In vitro</i>	Evaluated in healthy human plasma, using Prothrombin time and also activated partial thromboplastin time methods.	The crude methanol extract had a prothrombin Time (PT) value of 18.3 ± 0.9 and an Activated Partial Thromboplastin Time (APTT) of 58.7 ± 4.5.	(83)
Bark	Methanol extract isolated compound	Anticancer	<i>In vitro</i>	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) calorimetry assay	Methanol extract was not active. The compound isolated from the bark methanol extract showed moderate activity against human NSCLC A549 lung cancer cells (IC ₅₀ : 79 µM).	(56)
	Methanol extract	Anti-malarial	<i>In vivo</i>	Acute toxicity test in mice	Curative treatment with doses of 100, 200, and 400 mg/kg showed 47%, 45%, and 33% inhibition, respectively. The extract is not toxic in the acute toxicity test at doses of 100-1000 mg/kg extracts.	(39)
Root bark	Crude aqueous extract	Anti-inflammatory	<i>In vivo</i>	Carrageenin-induced edema using rats	The extract at a dose of 2-10 mg/kg inhibited inflammation in rats.	(84)
Wood	Methanol extract	Antitrypanosomal	<i>In vitro</i>	Cell-growth inhibition in <i>Trypanosoma brucei</i>	The extract showed IC ₅₀ of 0.9 µg/mL.	(85)
	Methanol extract Isolated compounds	Antibacterial and Antifungal	<i>In vitro</i>	Minimum Inhibitory Concentration (MIC) and Minimum Microbicidal Concentration (MMC) values	The isolated compounds had MIC values of 4.9 µg/mL and MMC 19.5 µg/mL in <i>P. vulgaris</i> , <i>E. coli</i> , <i>S. aureus</i> , <i>P. aeruginosa</i> , and <i>P. stuartii</i> . Those compounds were also active against <i>Candida albicans</i> .	(62)
Aerial root	Methanol extract	Anti-proliferative	<i>In vitro</i>	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) calorimetry assay	The compounds isolated from the methanol extract showed cytotoxic activity with IC ₅₀ range of 11-100 µM in Glioma (U373n and Hs683), Carcinoma (A549 and MCF7), and Melanoma (SK-MEL28 and B16F10) cell lines.	(51)
				Cell-growth inhibition against <i>Plasmodium falciparum</i> (strain 3D7)	The extract showed antiplasmodial activity (IC ₅₀ : 9.5 µg/mL).	
Aerial root	CHCl ₃ /Methanol crude extract	Antibacterial and Antifungal	<i>In vitro</i>	MIC and MMC values	The extract showed good bactericidal and bacteriostatic activities against <i>S. saprophyticus</i> , <i>Enterococcus faecalis</i> , and <i>K. pneumoniae</i> , and antifungal property against <i>Candida albicans</i>	(56)
Latex	<i>F. elastica</i> latex	Anthelmintic	<i>In vitro</i>	Paralysis and death time against the Indian earthworm <i>Pheretima posthuma</i>	The latex was able to immobilize worms in 7.4 minutes and kill worms in 18.4 minutes.	(86)
				Acute oral toxicity in mice	A combination of latex extract with Ranitidine 30 mg/kg reduced <i>Schistosoma mansoni</i> rash in mice at a dose of 500 mg/kg orally	

The antioxidant properties of *F. elastica* leaves have also been tested using four methods by Preeti et al (50) namely DPPH radical scavenging activity, total antioxidant activity (the phosphomolybdate method), iron chelating assay, and reducing power potential. These results showed that methanol extract was a potential source of natural antioxidants.

Anti-inflammatory activity

A previous study showed that the aqueous extract of the root bark of *F. elastica* given orally at a dose of 2-10 mg/kg in rats significantly inhibited inflammation in carrageenin-induced edema, namely 5.41-68.92%. This inhibition was similar to Indomethacin, which had 27.03-69.26% at the doses of 1-5 mg/kg. Similarly, aqueous extracts of *F. elastica* and indomethacin inhibited secondary and primary lesions of adjuvant-induced arthritis in rats. This anti-inflammatory activity is thought to exist because *F. elastica* contains flavonoid compounds (84).

Anticoagulant activity

The anticoagulant activity of *F. elastica* leaves was tested through activated partial thromboplastin time (APTT) and prothrombin time (PT) methods. The results showed that the crude methanol extract had a PT value of 18.3 ± 0.9 and an APTT of 58.7 ± 4.5 . The highest anticoagulant properties were shown by the N-hexane fraction and followed by the chloroform and the ethyl acetate fractions, where the results were compared with normal control (plasma alone with vehicle only) and heparin (0.5 U/mL) as a positive control. This activity might be related to the phenolic and flavonoid contents in *F. elastica* leaves, especially in the N-hexane fraction of methanol extract (83).

Anti-trypanosomal activity

Ficus elastica has never been used in traditional medicine as an anti-trypanosomal drug, especially in Cameroon. A study conducted by Tienkela et al (85) showed a potent anti-trypanosomal activity of the methanol extract of *F. elastica* on *Trypanosoma brucei* (IC₅₀ value of 0.9 µg/mL). However, in the same experiment, Pentamidine (the reference drug) showed stronger activity with an IC₅₀ of 0.17 nM.

Anthelmintic activity

Latex and leaves of *F. elastica* as anthelmintic have been investigated by Hari et al (86) and Gupta et al (42) in vitro against the Indian earthworm *Pheretima posthuma* by testing the paralysis time and death time of the worm. *F. elastica* latex 500 µL was able to immobilize worms in 7.4 minutes and worm death in 18.4 minutes. Meanwhile, the amount of latex 250 µL paralysis and death of worms in 6.4 and 15.5 minutes, respectively. *F. elastica* leaves also showed similar activity, at concentrations of 25 and 50 mg/mL giving paralysis within 16.5 and 9.6 minutes,

respectively, with a dead time of 23.7 and 15.5 minutes in the ethanol extract. Meanwhile, methanol extract with 25 and 50 mg/mL concentrations gave paralysis times of 18.3 and 15.5 minutes and death in 29.4 and 22.3 minutes, respectively.

This is comparable to metronidazole as standard at a concentration of 10 mg/mL with paralysis and death of worms within 5 and 13.2 minutes, respectively. The anthelmintic activity in the sap and leaves of *F. elastica* is associated with the content of tannins that can bind free protein for larval nutrition to reduce the availability of these nutrients. This causes the larvae to starve and directly reduces gastrointestinal metabolism through the inhibition of oxidative phosphorylation, causing larval death.

Antiplasmodial activity

The methanol extract of *F. elastica* aerial roots showed antiplasmodial activity against *Plasmodium falciparum* strain 3D7 with an IC₅₀ value of 9.5 µg/mL, whereas the antimalaria drug, Chloroquine showed potent activity with the IC₅₀ of 0.0079 µM. However, the compound responsible for the antiplasmodial activity is currently under investigation (85). Ifijen (39) also investigated the in vivo antimalarial activity of methanol extract of *F. elastica* bark against *Plasmodium berghei* strains in mice. Acute toxicity of the methanol extract at doses of 100-1000 mg/kg showed that the extract was relatively harmless after 14 days of treatment. The curative treatment with 100, 200, and 400 mg/kg doses showed 47%, 45%, and 33% inhibition, respectively. Meanwhile, the prophylactic treatment resulted in stronger activity (68%, 70%, and 71% inhibition, respectively). However, Chloroquine (at 10 mg/kg) showed stronger activity (76% and 52%, respectively on curative and prophylactic treatment). These data suggested that *F. elastica* showed moderate antimalarial activity.

Anti-schistosomiasis activity

The latex extract of *F. elastica* combined with ranitidine 30 mg/kg could significantly reduce *Schistosoma mansoni* rash in mice at a dose of 500 mg/kg given orally for three consecutive days (24). Apparently, this effect might be due to the presence of bioactive compounds, including cysteine, sterols, tannins, terpenes, and flavonoids. However, further studies are needed to identify the active compounds and their mechanism of action.

Anti-proliferative activity

Anti-proliferative activity has been evaluated by Mbosso et al (51), who demonstrated that *F. elastica* aerial root extract was a potential source of anti-proliferative agents. The MTT calorimetry assay indicated that elastiquinone isolated from the methanol extract showed promising cytotoxic activity (IC₅₀: 14 µM) against B16F10 melanoma cells. Meanwhile, the acetylated ficusoside B (ficusoside B

hexaacetate)) demonstrated lower IC₅₀ (11 µM) for U373n Glioma cell lines. Other compounds such as elasticamide and ficoside B demonstrated weak cytotoxic activity (IC₅₀: 88 to 100 µM in Glioma (U373n and Hs683), Carcinoma (A549 and MCF7), Melanoma (SK-MEL28 and B16F10) cell lines. Interestingly, biochanin A showed moderate anti-proliferative activity in those cells with IC₅₀: 47-78 µM.

Anti-preeclampsia activity

The flavonoids contained in *F. elastica* leaves have been known for their anti-inflammatory and antioxidant activities. Antioxidants are important agents for preventing and treating oxidative stress by neutralizing reactive oxygen species (ROS). The presence of excessive ROS during the development of blood vessels in the placenta induces oxidative stress that might lead to preeclampsia. Thus, antioxidant compounds are promising agents for combating preeclampsia through their antioxidant as well as anti-inflammatory properties. Morin is one of the antioxidant flavonoids in *F. elastica* leaves. The docking study showed that morin forms hydrogen bonds to Asn312, an important amino acid residue in binding to adrenoceptor beta 2 (ADRB2) receptors. In addition, morin also formed a direct hydrophobic interaction with another amino acid residue in ADRB2 receptor, Phe192. Due to its affinity and intermolecular interactions, morin can occupy ADRB2 ligand binding pocket, which can reduce its activity. This indicated that morin can be further developed as an antihypertensive agent through ADRB2 receptor inhibition (87). In addition, the ethanol extract of *F. elastica* leaves can suppress tumor necrosis factor-alpha and increase interleukin-10 levels in EA.hy926 cells without causing cytotoxic effects. Both proteins represent inflammatory markers in preeclampsia (82). These results showed that *F. elastica* has the potency to be further explored as anti-preeclampsia agent.

Conclusion

This review provides the phytochemical contents, traditional uses, and pharmacological activities of *F. elastica*. Although the study on the phytochemical aspect of *F. elastica* is still limited, several compounds have been identified as having promising pharmacological activities. This plant demonstrated promising antioxidant, antibacterial, antifungal, antiproliferative antipreeclampsia, anthelmintic, anticancer, anticoagulant, antimalarial, antiparasitic, antiplasmodial, antitrypanosomal, and anti-inflammatory activities. The wide range of bioactivity and the high structural diversity of the compounds offer a big opportunity for further investigation, especially in drug discovery programs from this medicinal plant. Currently, studies on the mechanism of action of the bioactive compounds as well as toxicity studies of *F. elastica* extract and its compounds are required to ensure efficacy and safety.

Acknowledgment

The authors would like to express their gratitude to the Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia, for providing the Hibah Fakultas Farmasi Tahun 2022 Program.

Authors' contributions

ASA initiated and compiled the article review. NF and AN conducted revisions on the initial manuscript before submission to the journal website. All authors read, reviewed, and approved the manuscript and English language.

Conflict of interest

The authors declared no conflict of interest.

Ethical considerations

The authors have completely observed ethical issues (including plagiarism, data fabrication, double publication, etc).

Funding/Support

This study was supported by the Hibah Fakultas Farmasi Tahun 2022 Program, Universitas Gadjah Mada, Yogyakarta, Indonesia with Grant Number: 17.21.10/UN1/FFA.1/SETPIM/PT/2021.

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