

Pharmacology of *Ficus*: A review

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ABSTRACT

Ficus is a medicinal plant that is commonly used in Malaysia, China, India, Thailand, South Africa, and other countries due to its pharmacological properties such as antimicrobial, anticancer, anti-inflammatory, antioxidant, analgesic, and antihypertensive activities. Based on the ethnological reports, this genus has been used to treat fever, skin diseases, hypertension, diabetes, cardiovascular diseases, and diarrhea. Women also have used the decoction of the whole plant as an herbal drink to recover after childbirth. It also improves blood circulation and regains body strength, as well as treats disorders related to the menstrual cycle. Recently, there were a lot of researches about the isolation of the chemical constituents in the *Ficus* genus to understand the functions and the mechanisms of these constituents that attributed to the pharmacological properties of the plant. These chemical constituents, such as flavonoids, triterpenoids, steroids, and furocoumarins, have shown diverse applications in the pharmacotherapeutic field. Therefore, this comprehensive review summarises the background and pharmacological properties of the *Ficus* genus.

Keywords: *Ficus*; pharmacology; phytochemicals; extract

INTRODUCTION

The genus *Ficus* of the Moraceae family includes a large number of species, which is more than 800 species (Berg, 2003), mostly found in tropical areas of East Asia. The leaves are usually simple and waxy, and most exude white or yellow latex when

broken. Many species have aerial roots, and a number are epiphytic. The unusual fruit structure, known as a syconium, is hollow, enclosing an inflorescence with tiny male and female flowers lining the inside. The growth forms of *Ficus* are varied, including shrubs, woody lianas, hemiepiphytes, epiphytes, and trees. Some indoor varieties of *Ficus*, such as fiddle-leaf fig and Audrey fig can be grown as outdoor ornamental plants as well (Al-Boudi and Afifi, 2011). *Ficus* species are rich in nutritional components and used as a source of food in Egypt, India, south China, Turkey, and Malaysia. Not all fruits from this genus can be eaten. For example, mistletoe fig or *F. deltoidea*, a tropical shrub that has rounded leaves and readily bears small fruits, unfortunately inedible. Only a handful with fruits considered edible such as *Ficus carica* L. or common fig, which is the only *Ficus* species that is cultivated for its fruit (Figure 1). This species is native to southwest Asia and the Mediterranean region. Other species like *F. erecta* often cultivated as pot plants in Taiwan, Indonesia and Japan (Aghel et al., 2009).



Fig. 1: Fruit of the common fig (*Ficus carica*) (Peter Firus, 2021)

ECOLOGY

Ficus trees are ecologically significant keystone species because they provide food and shelter to many seed-dispersing animals in tropical forest ecosystems. A large number of vertebrates feed on their fruits more than other plants. Shanahan et al. (2001) stated that figs are the most widely eaten fruit because approximately >10% of

the world's birds and >6% of the world's mammals consume figs. The fruits are an important food resource to some frugivores, including fruit bats, capuchin monkeys, gibbons, and orangutans. Other than that, bird species like hornbill, Asian barbets, pigeons, and fig-parrot rely on fig fruits as their source of food. High levels of carbohydrate and calcium in figs make them attractive to frugivorous birds and mammals (Kinnaird and O'Brien, 2005). Fig wasp plays an important role in the pollination system in tropical forest ecology. The fruit ripens quickly after the pollen-bearing wasp leaves a *Ficus* plant, providing a rich feast that attracts a host of mammals and birds. If the plants were to be cut out of a forest or the fig wasps were removed, there would certainly be a dramatic change in the animal population, as reported by the reduction of population densities of fruit-eating mammals on small islands that lack *Ficus* species (Shanahan et al., 2001). The taxonomy of *Ficus* is described in Table 1.

Table 1: Taxonomy of *Ficus* (Gupta and Singh, 2012)

Domain	Eukaryota
Kingdom	Plantae
Subkingdom	Viridaeplantae
Phylum	Tracheophyta
Subphylum	Euphyllophytina
Division	Magnoliophyte
Class	Magnoliopsida
Subclass	Dilleniidae
Order	Urticales
Family	Moraceae
Tribe	Ficeae
Genus	<i>Ficus</i>

Phytochemical constituents

Ficus genus is reported to be responsible for the treatment of various disease conditions because it contains a number of biologically active compounds, which are also known as phytochemicals. These bioactive compounds are naturally expressed by the plant in response to biotic and abiotic stresses (Chawla et al., 2012). The major phytochemicals such as flavonoids and phenolic compounds are reported to be concentrated in the leaves, fruit pulp, roots, stem bark or wood, peel and seeds of different species of *Ficus* plant along with polyphenol, polysterols and triterpenoids (Mandal et al., 1999). Fig fruit, especially the skin or exocarp and seeds, consist of monosaccharide sugars and a mix of phytochemicals such as gallic acid, flavonoids, rutin, chlorogenic acid and epicatechin. Various pigments like polyphenols, flavonoids, and anthocyanins are responsible for the various colors shown in different species of *Ficus* (Ahmed and Urooj, 2010).

Table 2. List of *Ficus* species

Species name	Locality	Phytochemical compound	Part used	Pharmacological properties
<i>F. abutilifolia</i>	Nigeria	Tannins, saponins and flavanoids	Leaves	Antimicrobial activity (Taiwo et al., 2016)
<i>F. afzelii</i>	Egypt	Tannins, flavonoids and phenolics	Pulp and leaves	Antioxidant activity (Abdel-Hameed, 2009)
<i>F. amplissima</i>	India	Sterols, phenolic acids and triterpenoids	Bark and fruit	Antidiabetic and antioxidant activities (Arunachalam and Parimelazhagan, 2013)
<i>F. arnottiana</i>	India	Alkaloids, glycosides, saponins, flavonoids,	Leaves	Mucoprotective activity and gastric secretory (Babu et al., 2017)

		phenolics and carbohydrates.		
<i>F. asperifolia</i>	Africa	Flavonoids, alkaloids, tannins and phenolic acids	Roots and stem	Antioxidant, antiulcer, anticancer activities (Okwu, 2004)
<i>F. auriculata</i>	China	Phenolic acids, flavonols and sterols	Fruit and leaves	Hepatoprotective and antidiabetic activities (El-Fishawy et al., 2011)
<i>F. beecheyana</i>	Taiwan	Sterols and gallic acids	Rhizome and roots	Antidiabetic, antioxidant and anticancer properties (Yen et al., 2017)
<i>F. benghalensis</i>	India, Pakistan and Nepal	Amino acids, pigments, furocoumarins, steroids and triterpenes	Bark, fruit, root and whole	Antioxidant, hypolipidemic, antibacterial, anti-inflammatory, analgesic and anticancer activities (Aswar et al., 2008)
<i>F. benjamina</i>	Hawaii and Australia	Steroids, flavonoids and phenolic acids	Leaves	Antioxidant, antimicrobial and antidiarrheal activities (Jain et al., 2013)
<i>F. capensis</i>	Tropical Africa, Cape Island	Polyphenols	Stem bark and leaves	Antibacterial, antiulcer, antidiarrheal, immune-boosting properties (Oyeleke et al., 2008)

<i>F. caprefolia</i>	South Africa	Phenolics	Leaves and latex	Antidiabetic activity (Olaokun et al., 2013)
<i>F. carica</i>	Asia, South America and Europe	Furocoumarins, flavonoids, phenolic acids and coumarins	Leaves, latex, fruit and roots	Hepatoprotective, laxative, antidiarrheal activities (Jeong et al., 2009)
<i>F. chlamydocarpa</i>	Cameroon	Triterpenoids and flavonoids	Stem bark	Antimicrobial, hepatoprotective and antioxidant activities (Donfack et al., 2010)
<i>F. cordata</i>	Egypt, Saudi Arabia and Africa	Flavonoids, coumarins, phenolics and terpenoids	Leaves and stem bark	Antioxidant activity (Ahmed et al., 2017)
<i>F. craterostoma</i>	South Africa	Phenolics	Leaves	Antibacterial (Oyeleke et al., 2008)
<i>F. crocata</i>	Mexico	Triterpenoids and sterols	Leaves	Anticancer, antioxidant and analgesic activities (Sánchez-Valdeolívar et al., 2020)
<i>F. decora</i>	Egypt	Phenolics, flavonoids and tannins	Leave	Antioxidant activity (Abdel-Hameed, 2009)
<i>F. dekdekana</i>	Africa and Senegal	Phenolics	Roots and leaves	Antioxidant activity (Olaokun et al., 2013)
<i>F. deltoidea</i>	Malaysia and	Triterpenoids, terpenoids and	Roots and	Antidiabetic, anti-inflammatory,

	Indonesia	flavonoids	leaves	anticancer, antibacterial (Zakaria et al., 2012)
<i>F. drupacea</i>	Vietnam	Triterpenoids and steroids	Stem bark, leaves	Antimalaria, anticancer, antimicrobial activities (Yessoufou et al., 2016)
<i>F. elastica</i>	India	Phenolic, flavonoids and tannins	Leaves	Antioxidant and antimicrobial activities (Preeti et al., 2015)
<i>F. exasperata</i>	Asia and South Africa	Phenolics and tannins	Leaves	Antidiabetic, anticonvulsant, antiinflammatory, antimicrobial, hypolipidemic, antioxidant and antiulcer activities (Ahmed et al., 2012)
<i>F. foveolata</i>	Thailand and Pakistan	Coumarins, flavonoids and triterpenoids	Stem bark	Antimicrobial activity (Meerungrueang et al., 2014)
<i>F. glumosa</i>	Ivory Coast and Central African	Flavanoid, alkaloids and tannins	Roots and stem bark	Hypolipidemic, anti inflammatory and hyperglycemic activities (Abu et al., 2020)
<i>F. hirta</i>	China	Furocoumarins, steroids and triterpenoids	Roots	Anticancer and antifungal properties (Wan et al., 2017)

<i>F. hispida</i>	India, Malaysia	Flavonoids, sterols and phenols	Leaves, stem bark and roots	Antiulcerogenic, cardioprotective and antidiabetic activities (Ali and Chaudhary, 2012)
<i>F. ingens</i>	Zimbabwe, Nigeria and Southen Arabia	Tannins and phenols	Stem bark and leaves	Analgelsic and antimicrobial activities (Olayinka et al., 2017)
<i>F. insipida</i>	Bolivia, Amazon	Triterpenoids	Leaves and fruits	Antianaemic and antipyretic activities (Gonzales et al., 2019)
<i>F. lacor</i>	India	Steroids and triterpenoids	Roots	Antiarthritic activity (Sindhu and Arora, 2013)
<i>F. lutea</i>	South Africa	Phenolics	Leaves	Antioxidant activity (Olaokun et al., 2013)
<i>F. lyrata</i>	Egypt	Flavonoids, tannins and phenolics	Leaves	Antibacterial and antioxidant activities (Abdel-Hameed, 2009)
<i>F. mollis</i>	India	Triterpenoids and flavonoids	Leaves and stem bark	Hypoglicemic and hypolipidemic activities (Munna and Saleem, 2013)
<i>F. mysorensis</i>	Egypt	Sterols and triterpenoids	Leaves	Antiinflammatory and anticancer activities

(Abbass et al., 2015)

<i>F. natalensis</i>	Uganda and Nigeria	Flavonoids, alkaloids, saponins and steroids	Leaves	Antimicrobial activity (Sheyin et al., 2018)
<i>F. nitida</i>	Egypt	Flavonoids, tannins and phenolics	Leaves	Antioxidant activity (Abdel-Hameed, 2009)
<i>F. nymphaefolia</i>	Brazil	Isoflavones	Stem bark and latex	Wound healing (Darbour et al., 2007)
<i>F. oligodon</i>	China	Flavonoids and phenolics	Leaves	Antioxidant activity (Shi et al., 2011)
<i>F. palmata</i>	Mid-Himalayan region, Somalia and Sudan	Sterols, anthocyanins, flavonoids, furocoumarins and terpenoids	Stem bark, leave and roots	Antimicrobial, hepatoprotective and antiulcer activities (Joshi et al., 2014)
<i>F. pandurata</i>	Egypt	Steroids and triterpenes	Leaves	Analgelsic and antipyretic activities (Khedr et al., 2015)
<i>F. platyphylla</i>	Nigeria	Saponins and tannins	Stem bark	Antimicrobial and anticonvulsant properties (Kubmawara et al., 2009)
<i>F. polita</i>	Sourthen Africa	Phenolic acids and antocyanins	Leaves and roots	Antiviral, antimalaria and antimicrobial activities (Kuete et al., 2011)

<i>F. pomifera</i>	India	Phenols, tannins and triterpenoids	Leaves	Anticancer property (Wangkheirakpam et al., 2015)
<i>F. pumila</i>	South china and Malaysia	Steroids and flavonoids	Stem and leaves	Analgesic and anti-inflammatory activities (Liao et al., 2012)
<i>F. racemosa</i>	India, Pakistan, Sri Lanka	Steroids and triterpenoids	Whole plant	Hypoglycemic, anti-cancer, hepatoprotective activities (Ahmed and Urooj, 2010)
<i>F. religiosa</i>	Nepal, Pakistan and India	Alkaloids, polyphenols, furocoumarin, steroids and triterpenoids	Leave, fruit and bark	Cardioprotective, antidiabetic, antitumor, antioxidant, antihelminthic, antimicrobial and antiparasitic activities (Damanpreet and Rajesh, 2009)
<i>F. retusa</i>	Peninsular Malaysia and India	Polyphenols	Leaves and stem barks	Hepatoprotective properties (Jaya Raju and Sreekanth, 2011)
<i>F. semicordata</i>	Iraq, India, Bangladesh and Myanmar	Tannins, alkaloids and steroids	Leaves, fruit and latex	Antidiarrheal and antioxidant activities (Gupta and Acharya, 2019)
<i>F. septica</i>	Papua new guinea	Alkaloids and tannins	Leaves	Antimicrobial activity (Damu et al., 2005)

<i>F. sur</i>	Somalia, Yemen and Nigeria	Saponins, tannins and phenols	Stem bark	Anticonvulsant activity (Ishola et al., 2013)
<i>F. sycomorus</i>	Israel and Zimbabwe	Flavonoids, phenolic acids and sterols	Whole plant	Antibacterial activity (Mohamed et al., 2010)
<i>F. thonningii</i>	Nigeria, Senegal, Angola and Mali	Alkaloids, terpenoids, flavonoids and tannins	Leaves, stem bark and roots	Antimicrobial and antidiarrheal activities (Dangarembizi et al., 2012)
<i>F. tikoua</i>	China	Phenolics and isoflavonoids	Stem bark	Anti-diarrheal, antioxidant and antifungal activities (Jiang et al., 2013)
<i>F. tinctoria</i>	India	Flavonoids, alkaloids, glycosides, tannins and saponins	Whole plant	Antioxidant, antiulcer and antidiabetic properties (Gini <i>et al.</i> , 2017)
<i>F. tsiela</i>	India	Alkaloids flavanoids coumarins saponins and terpenoids	Leaves	Antipneumonia and antimicrobial activities (Vaya and Mahmood, 2006).
<i>F. ulmifolia</i>	Philippine	Steroids, terpenoids and sterols	Leaves	Antioxidant activity (Ragasa et al., 2009)
<i>F. umbelatte</i>	Africa	Coumarins	Stem bark	Menapousal problem (Zingue et al., 2016)

<i>F. vallis-choudae</i>	Ivory Coast and Cameroon	Triterpenoids and sterols	Leaves, stem	Anticonvulsant, antifungal and anti-inflammatory properties (Bnakeu et al., 2017)
<i>F. virens</i>	Pakistan and Egypt	Phenolics and flavonoids	Bark, latex and leaves	Antioxidant, anti-diabetic properties (Orabi and Orabi, 2016)

Pharmacological properties

Due to their great pharmacological benefits, *Ficus* species have been described by many authors in both traditional and modern medicines.

Antioxidant activity

The presence of flavonoids in *F. carica* leaves could be responsible for the antioxidant activity, as reported by Ali et al. (2012). In another report by Konyaloğlu et al. (2015), antioxidant capacity based on the TAC method revealed tocopherol equivalents/g dry mass ranged from 14.04±1.42 to 23.51±1.15 mM in *F. carica* leaves extract of methyl alcohol, ethyl alcohol, *n*-hexane, ethyl acetate, and water. The highest antioxidant activity was evident from the water extract of *F. carica* leaves. Using well-established modified DPPH (2,2-diphenyl-1-picrylhydrazyl) method, the highest polarity of crude extract of *F. carica* and *F. sycomorous* detected a high content of flavonoids and phenol compounds which contributed to the antioxidant activity in *Ficus* (Al-Matani et al., 2015; Weli et al., 2015). In the research conducted by Kaur et al. (2010), the DPPH test revealed antioxidant activity ranging from 6.34 to 13.35% for *F. religiosa* in different concentrations of ethanolic extract of the leaf (200-1000g/ml). In a comparison of methanolic stem bark and root extracts of *F. glomerata*, the investigation revealed high antioxidant activity in the stem bark extract (Channabasavaraj et al., 2008).

Another research done by Jahan et al. (2009), antioxidant efficacy of *F. racemosa* fruits extract was proven using in vitro assay of DPPH free radical scavenging capacities. Five ethanolic extracts of *Ficus* species, namely *F. auriculata*, *F. virens*, *F. callosa* and *F. vasculosa* were tested for antioxidant efficacy via in vitro assay. Both *F. auriculata* and *F. virens* have shown IC₅₀ values of 0.3 mg/ml, which were higher than other *Ficus* extracts, making them the most promising species for antioxidant activity (Shi et al., 2011). Meanwhile, Omar et al. (2011) investigated the flavonoids and phenolic compounds extracted from the leaf of *F. deltoidea*. The chromatographic method on a reversed-phase C₁₂ column revealed a high total of flavonoid content. The result of the HPLC method exhibited that 85% of total antioxidant activity was produced by the leaf extract.

Antimicrobial activity

F. religiosa has shown antimicrobial activity against a various type of pathogenic microorganisms (Salehi et al., 2020). In other works, a minimum inhibitory concentration (MIC) was tested in several bacteria namely, *Shigella flexneri*, *Enterococcus faecalis*, *Shigella dysenteriae*, *Proteus vulgaris*, *Shigella sonnie* and *Staphylococcus saprophyticus* using ethanolic extract of *F. religiosa*. The result showed that the extract can inhibit these bacterial with the MIC value ranged from 250 to 500µg/ml (Rahman et al., 2014). Antibacterial activity of the ethanolic fruit extract from *F. religiosa* also has been done in India. The researchers reported that this extract had shown an inhibition against *S. aureus* and *S. epidermidis* with MIC of 15 mg/ml. This extract also showed inhibition against *K. pneumoniae* and *P. vulgaris* with an effective MIC of 30 mg/ml (Kumar Goyal et al., 2014).

The methanolic extract and a compound, namely ficusoside isolated from the root of *F. elastica*. Ficusoside showed a MIC of 4.9 µg/mL, which lower than gentamicin and fluconazole (25 µg/mL) against *S. aureus*, *E. coli*, *P. vulgaris* and *C. albicans*. In comparison, the methanolic extract showed a MIC of 39.1 µg/mL (Mbosso et al., 2017). Acetone leaf and stem bark extract of *F. sycomorous* showed a good antibacterial activity by inhibiting resistant *A. baumannii*. The leaf extract

recorded a MIC of 2.5 mg/ml, whereas stem bark showed 4.9 mg/ml of MIC (Saleh et al., 2015). Manimozhi et al. (2012) reported the antibacterial activity of the flavonoids extracted from the bark of *F. bengalensis*. The evaluation showed that the flavonoids are excellent in inhibiting the growth of *P. vulgaris*, *S. aureus* and *P. aeruginosa* with MIC ranging from 25 to 100 mg/ml. Evaluation of antibacterial activities of methanol bark extract of *F. microcarpa* showed that the extract was effective against the tested gram-negative and gram-positive bacteria. The result of inhibition zones against *B. brevis*, *B. cereus*, *B. subtilis*, *E. coli* and *A. polymorph* were 18.0, 15.5, 16.5, 16.0 and 8.0 mm, respectively (Ao et al., 2008).

Wound healing activity

The healing property of the root extract of *F. racemosa* in albino rats was evaluated. In aqueous and ethanolic root extract of treated groups, the application of extract increased the breaking strength of the incision wounds which may be due to the presence of an individual or combined action of phytochemicals such as saponins, flavonoids, alkaloids and tannins (Murthi and Kumar, 2012). In other studies, 5% and 10% of hydroalcoholic leaf extract of *F. religiosa* has exhibited a healing process in the incision wound, excision wound and burn wound induced to the rats (Naira et al., 2009). Aqueous extract of *F. racemosa* was found to possess a wound healing property. When a 10% dose of the extract was applied to the wound, the healing process was accelerated (Mehta et al., 2012).

The wound-healing efficacy of ethanolic and aqueous extracts of *F. benghalensis* was evaluated in albino rats (Garg and Paliwal, 2011). It was evident that the 200 mg/kg b.w. dose of the extract showed a healing activity by the improvement in the wound region. In the wound healing experiment, the aqueous extract of *F. deltoidea* was used in induced wounds of rats. The evaluation has shown that the wounds applied with 5% and 10% of *F. deltoidea* extract significantly promoted the rate of wound healing compared to wounds treated with sterile deionized water or dressed with blank placebo (Abdulla et al., 2010). Murthi et al. (2011) also investigated the healing activity of *F. bengalensis* in albino rats. The healing process in the excision, incision and dead space wound was accelerated with

the treatment of the aqueous and ethanolic root extract. The extracts showed that the period of epithelialization reduced, the breaking strength increased, the rate of wound contraction increased and the hydroxyproline content elevated.

Hypoglycemic activity

β -Sitosterol-D-glycoside was isolated from the root bark of *F. religiosa* and *F. glomerata*. This compound could be responsible for hypoglycemic activity in *Ficus*. The concentration of 25, 50 and 100 mg/kg of dose were administered orally in induced diabetic rats and normal rats. A significant decrease in blood glucose was observed using the dose of 50 and 10mg/kg compared to 25mg/kg (Chandrasekar et al., 2010). In combination with *F. racemosa* extract and hypoglycemic drug, hypoglycemic activity was studied in diabetic patients. The extract and the drug were taken orally for 15 days. The result showed that the blood glucose level was significantly reduced. The renal and liver functions were also tested to rule out the herb toxicity, which was observed to be in the normal range (Gul-e-Rana et al., 2012).

Isolated flavonoids from the stem bark of *F. racemosa* were evaluated for antidiabetic activity. At 100mg/kg dose, the flavonoids were administered to streptozotocin (STZ) rats. The level of blood glucose was measured on different days (1st, 3rd, 5th and 7th days). The finding showed that the flavonoids able to reduce the blood glucose level, which could be useful as a supplementary drug for future diabetic therapy (Keshari et al., 2016). The methanolic extract of the bark of *F. amplissima* was tested for hypoglycemic activity in streptozotocin-induced diabetic rats. At 50mg/kg and 100mg/kg of dose, the extract has exhibited a reduction in total cholesterol, blood glucose level and serum triglyceride and (Arunachalam et al., 2013). In other research conducted by Gayathri and Kannabiran, (2008), an aqueous extract from the bark of *F. benghalensis* was evaluated in diabetic rats. The result showed that the extract significantly reduces glucose levels. The level of hepatic cytochrome P450 dependent enzyme, blood electrolytes and systems glycolytic enzymes were also restored.

Hyperlipidemic activity

The hyperlipidemic activity of ethanolic extract of *F. racemosa* bark in alloxan-induced diabetic rats was investigated. The finding showed that 300 mg/kg dose able to restore the level of lipids and lipoproteins to near normal range (Sophia and Manoharan, (2007). This showed that this extract could be a potent supplementary drug in combination with the standard reference drug, glibenclamide. In the research of dexamethasone-induced hyperlipidemia in rats, ethyl acetate leaf extract of *F. mollis* was tested using two different doses, 200 and 400 mg/kg. The extract reverted the hyperlipidemia caused by dexamethasone in a dose-dependent manner. The extract showed a similar effect with the reference standard, glibenclamide (Munna and Saleem, 2013). In the experiment of Triton WR 1339-induced hyperlipidemia in swiss albino mice, leaf and twig extract of *F. carica* were evaluated. After administration of doses 150 and 300 mg/kg, the hyperlipidemic effect was examined by the various parameter of lipid profile. The result showed that the extracts cause a reduction in the level of serum total cholesterol, triglycerides and low-density lipoprotein (LDL) (Boukhalfa et al., 2018). In other research, isolated α -amyrin acetate from aerial roots of *F. bengalensis* was administered orally to db/db mice for ten days. At 50 mg/kg dose, the extract shows a reduction in triglycerides, cholesterol and LDL-C by 21.5%, 24.1% and 21.2%, respectively (Singh et al., 2009).

Anti-inflammatory effect

Ethanolic extract of *F. religiosa* leaf showed a significant anti-inflammatory property in the study conducted by Charde et al. (2010). The edema was induced in Wistar rat using carrageenan, and the extract was administered topically. At a concentration of 300 μ g/ml, the edema decreased as the extract could be inhibiting the release of serotonin, histamine, kinins and prostaglandins. The effect was similar with the application of ibuprofen as a control. An aqueous extract from the leaves of *F. racemosa* was tested for the anti-inflammatory property on serotonin, histamine, carrageenan and dextran-induced hind paw edema model in Wistar rats. The extract (400mg/kg) showed maximum inhibition of 32%, 34%, 30%, and 31% in serotonin, histamine, carrageenan, and dextran-induced rats, respectively. A similar effect was

also observed with the standard drug, phenylbutazone (Mandal et al., 2000).

In other studies, the anti-inflammatory effect of chloroform, petroleum ether and ethanol extracts from *F. carica* the leaves was studied on a carrageenan-induced rat paw edema model. The ethanol extract (600mg/kg) showed a maximum anti-inflammatory effect (76%) in acute inflammation and granuloma weight has exhibited a decrease of 72% (Patil and Patil, 2011). The anti-inflammatory effect of ethanolic bark extract of *F. bengalensis* was better than petroleum ether. Carrageenan was used to induce hind paw edema in rats and the oral administration was done with the dose of 300 and 600 mg/kg. Both ethanolic extracts for 300 and 600 mg/kg have shown an inhibitory effect against carrageenan-induced edema, which indicated that these extracts possess an anti-inflammatory effect for acute inflammation (Patil et al., 2009).

Hepatoprotective activity

The hepatoprotective activity of methanolic and petroleum ether of *F. racemosa* stem bark was tested in CCl₄-induced hepatic damage in rats. The administration of CCl₄ reduced the level of albumin, serum total protein and urea and increased the total bilirubin associated with an increment in alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) activities as compared to control rats. Both methanol and petroleum ether extracts restored albumin and total protein to near normal levels. Both extracts also reduced the level of ALT, AST and ALP. Total bilirubin content also reduced from 2.1 mg/dL to 0.3 mg/dL. These results showed that *F. racemosa* possesses potent hepatoprotective effects against CCl₄-induced hepatic damage in rats.

The hepatoprotective effect of *F. religiosa* latex on cisplatin-induced liver injury in Wistar rats was investigated. The increase of serum ALP, ALT, AST and hepatocytes cells degeneration inflammatory infiltrate and necrosis were due to the cisplatin-induced liver impairment. The methanolic extract of *F. religiosa* latex restored serum ALP, ALT, AST, lipid peroxidation, SOD and GSH of the liver to

near normal levels. Generally, *F. religiosa* latex is effective in protection and improvement against cisplatin-induced liver injury (Yadav, 2015). Leaf ethanolic extract of *F. carica* was tested in CCl₄-induced hepatic damage in albino rats. Liver markers and histopathological changes were examined. The result showed that the dose of the extract (200 mg/kg) had improved the hepatic damage by CCl₄- (Aghel et al., 2011). Joshi et al. (2014) also reported the hepatoprotective effect of total extract of *F. palmata* in animals with hepatic toxicity. The elevated AST, ALT, GGT, ALP and bilirubin have exhibited a significant reduction at a dose of 400 mg/kg body weight.

Antiulcer activity

The objectives of the antiulcer treatment are to accelerate the healing process, improve the symptoms, prevent ulcer recurrence, and eradicate the presence of *H. pylori*. In the study of antiulcer activity, stomach lesion was induced in the rats with the treatment of ethanol. The total extract of *F. palmata* was used at 200 and 400 mg/kg against 80% of ethanol-induced stomach lesion. The result showed that the best protection against ulcer was achieved by the highest dose (400 mg/kg), where the ulcer index was 2.00 ± 0.57 (Alqasoumi et al., 2014). In other works, hydroalcoholic and ethanolic of *F. religiosa* of leaves and stem bark extract were tested for antiulcer activity in Sprague–Dawley rats with gastric ulcer induced by aspirin, ethanol, and ligated pylorus (Saha and Goswami, 2010). A significant reduction in ulcer index can be seen when applying 250 and 500 mg/kg body weight of extract at the ulcer area. This effect was equivalent to the standard drug reference, antacid.

Antiulcer activity of *F. religiosa* ethanolic leaf extract was evaluated in albino mice. Treatment with the extract has shown a significantly reduced gastric lesion formation and submucosal edema similar to the ranitidine-treated mice. The result also showed that there was no sign of toxicity and mortality at the high dose of 2 000 mg/kg, which indicated that the extract was safe and non-toxic even at high concentrations (Gregory et al., 2013). According to Sivaraman and Muralidhara,

(2010), the application of *F. hispida* extract has reduced gastric ulceration in rats. An investigation of antiulcer efficacy has been done on methanolic extract of *F. hispida* with doses of 200 and 400 mg/kg. These doses were found to be effective in healing the ulcer by 64% (200mg/kg) and 69% (400mg/kg) and reducing free and total acidity as well.

Anticancer activity

Some species of the *Ficus* genus show the anticancer property in cell lines of several cancer types. Hexane, dichloromethane and acetone extract of *F. crocata* have been evaluated for antiproliferative activity in cell line of breast cancer. Dichloromethane extract showed the strongest effect in reducing the proliferation of MDA-MB-231 cells (Sánchez-Valdeolívar et al., 2020). *F. carica* also showed anticancer activity when the methanolic extract of leaf and fruit were evaluated against Huh7it liver cancer cells using MTT assay (Purnamasari et al., 2019). The result showed that the extracts had IC₅₀ values >653 µg/mL for the leaf extract and >2000 µg/mL for the fruit extract. A higher percentage of Huh7it apoptosis and necrosis in the leaf compared with fruit extracts was also observed.

In another work by Bunawan et al. (2014), the anticancer activity of ethanolic and aqueous extracts of *F. deltoidea* was tested against human ovarian carcinoma cell line A2780 using MTT assay. The ethanolic and aqueous extracts gave IC₅₀ values of 143.03±20.21 µg/ml and 224.39±6.24 µg/ml, respectively. Both extracts also showed an apoptosis at 1000 µg/mL. It can be found that the ethanolic extract reduced cell proliferation, while aqueous extract induced cell detachment. Various phytochemical contents in the extracts could be attributed to this finding.

Antidiarrheal activity

Mandal and Kumar (2002) investigated the antidiarrheal activity in leaves extract of *F. hispida*. Diarrhea in rats was induced with castor oil and PEG₂. The result showed that the methanol leaves extract could be used as an antidiarrheal agent as it inhibited the activities of diarrhoea and enteropooling in rats. It was

assumed that tannins might be responsible for the antidiarrheal activity as it denatures the protein and forms protein tannate, which minimizes the intestinal mucosa permeability. Meanwhile, the leaf extract of *F. microcarpa* has been used in investigating the effect of antidiarrheal activity in rats. Castor oil was used to induce diarrhea in rats. The oral administration of the extract at doses of 300 and 600 mg/kg produced a significant antidiarrheal effect in rats. At 300 mg/kg, the percentage of inhibition based on the number and weight of faeces was 79% and 66%. While, at 600 mg/kg, the values for both number and weight were 32%. Based on the volume and weight of intestinal content, there was also a reduction in anti-enteropooling activity (Bairagi et al., 2014).

Cardioprotective effect

Leaf extract of *F. hispida* was prepared to investigate the cardioprotective effect on cyclophosphamide mediated myocardial injury due to oxidative stress in rat heart (Shanmugarajan et al., 2008). This finding revealed that lipid peroxidation was inhibited significantly. There was also an increased concentration of glutathione reductase, superoxide dismutase, glutathione peroxidase, catalase, and glutathione-S-transferase. Glutathione activity in heart tissue also decreased caused by cyclophosphamide. Its cardioprotective activity could be due to antioxidant constituents, which could be responsible for this finding such as hispidin, β -sitosterol, β -amyrin, and bergaptin.

The extract of *F. religiosa* showed an improvement in oxidative stress, diabetic markers, and inflammatory and cardiac markers in streptozotocin-induced diabetic cardiomyopathy rats. The control of cytokine, diabetes and modulation of oxidative marker could be attributed to the cardioprotective role of *F. religiosa* (Singh et al., 2011). The extract of *F. thonningii* was prepared to investigate the myocardial contractile performance on rat isolated atrial muscle strips. The result showed that there were negative inotropic and chronotropic effects on both spontaneously beating and electronically driven atrial muscle strips (Musabayane et al., 2007). According to

Baur and Sinclair, (2006). The resveratrol in *F. thonningii* could be attributed to the cardioprotective effects of *F. thonningii*. Other than cardiovascular diseases, resveratrol is also responsible for delaying the aging process and prevent the progression of various diseases, which include obesity, cancers and neurodegenerative disorders (Ramawat et al., 2009).

CONCLUSION

This review covers various pharmacological properties of *Ficus* spp., in vitro and in vivo trials including antiproliferative, antioxidant, antimicrobial and anti-inflammatory activities. The review also exposed the discovery and isolation of the plant metabolites such as sterols, flavonoids, terpenoids, saponins, coumarins and alkaloids, which could be contributed to the therapeutic potential of the plant. This plant also can be considered safe and non-toxic as no severe side effects were reported.

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