An Overview of Phytochemical and Biological Activities: Ficus deltoidea Jack and Other Ficus spp.

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Ficus deltoidea Jack (Moraceae) is a well-known medicinal plant used in customary medication among the Malay people to reduce and mend sicknesses such as ulcers, psoriasis, cytotoxicity, cardioprotective, inflammation, jaundice, vitiligo, hemorrhage, diabetes, convulsion, hepatitis, dysentery injuries, wounds, and stiffness. Ficus deltoidea contains a wide variety of bioactive compounds from different phytochemical groups such as alkaloids, phenols, flavonoids, saponins, sterols, terpenes, carbohydrates, and proteins. The genus Ficus has several hundreds of species, which shows excellent therapeutic effects and a wide variety of helpful properties for human welfare. Searching information was collected by using electronic databases including Web of Science, Science Direct, Springer, SciFinder, PubMed, Scopus, Medline, Embase, and Google Scholar. This review is, therefore, an effort to give a detailed survey of the literature on its pharmacognosy, phytochemistry, phytochemical, and pharmacological properties of Ficus and its important species. This summary could be beneficial for future research aiming to exploit the therapeutic potential of Ficus and its useful medicinal species.

Keywords: Ficus deltoidea, mas cotek, medicinal uses, pharmacological study, phytochemical study

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Introduction

Human interest has moved, in the past few years, to focus more on the natural plant product rather than synthetic medication in multiple preventive...
Ficus deltoidea, commonly referred as Mas Cotek, is one of the most popular plant used for medicinal purposes for various diseases. Ficus deltoidea is cultivated as an ornamental shrub or housing plant in different regions of the world. It belongs to family Moraceae (synonymously also known as F. diversifolia Blume and mistletoe fig, mistletoe rubber plant). The genus Ficus has over hundreds of species that occur all over the pantropics. Because of its habit of regularly growing on large tree, it is called as mistletoe fig, although scientifically known as deltoidea. Leaves of male and female Ficus show identification characteristic features such as morphology dimension that helps in identification of male and female plants. The male and female flowers have small and thick massive leaves, respectively. Spot coloration of F. deltoidea leaves also helps in differentiating two flowers as purple spot indicates for male and black spot for female flowers.

Approximately 1000 species of Ficus are found in subtropical and pantropical origins. Ficus deltoidea is an evergreen shrub or tiny tree that usually starts as an epiphyte in the form of a bush with aerial roots. It generally grows up to 22 feet, roughly 15–22 feet high and 3–10 feet wide in fashion of zigzagging branches. The bark and trunk is usually gray and slender, respectively. The leaves are extensively spoon-formed, which are 1.5–3 inches (4–8 cm) long and intense. The leaves are dark, leathery, and succulent. The plant generated spherical to round figs that are roughly 1.5 cm in length, whereby during maturation, the coloring of figs turns from dull yellow to orange and purple that can be manufactured freely in pairs. In Malaysia, people use this plant for many medicinal purposes such as antidiabetic, anti-inflammatory, anticancer anti-melanogenic, and antioxidant.

A study showed the presence of polyphenols and flavonoids such as genistin, alkaloids, and tannins. A recent published report by Kumari and Dhanalekshmi also confirmed the presence of phenols, flavonoids, tannins, and saponins in F. deltoidea leaf, stem, and fruit extract. Harun and Musapha reported the tannins, phlobatannins, flavonoids, saponins, steroids, terpenoids, cardiac glycosides, alkaloids, anthraquinones, and polyphenol in F. deltoidea var. kunstleri (King) leaves. Farsi et al. reported the presence of proteins, polysaccharides, glycosapponins, phenolics, flavonoids, and tannins in the leaf extracts of F. deltoidea. Solvent plays a very important role in extracting out the chemical constituents. Different solvents could extract different chemical constituents of the plant; each solvent gives different results. Choo et al. identified two bioactive components vitexin and isovitexin (flavonoids) in the leaves of F. deltoidea and also reported that these constituents are responsible for inhibition of α-glucosidase. Thus it can be used as antidiabetic.

In this review, the literature search was performed through specific databases (Web of Science, Science Direct, Springer, SciFinder, PubMed, Scopus, Medline, Embase, and Google Scholar) using different keywords: Ficus deltoidea, phytochemical, phytochemistry, pharmacological activity, pharmacological evaluation of extracts, fractions, or isolated compounds from F. deltoidea and species. Study selection was based on articles published in English only. All selected manuscripts were analyzed for year of publication, reported plant species, part of the plant, isolated chemical compounds, and evaluated biological activities.

**PHYTOCHEMICAL ANALYSIS OF Ficus deltoidea**

Ficus deltoidea is herbaceous plant that contains a large amount of chemical constituents. It contains various ranges of phytochemicals, including terpenoids, polyphenols, alkaloids, organic acids, saponins, and their derivatives. Literature showed that different plant parts of F. deltoidea contain different types of phytochemical constituents. Leaves are one of the main part used in various purposes and contain mainly polyphenols, triterpenoids, saponins, and tannins but it contains very less amount of alkaloids. Flavonoids, saponins, and alkaloids are found mainly in stem part, whereas fruits predominantly contain triterpenoids, alkaloids, and flavonoids.

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Phytoconstituents reported in other *Ficus* species are also shown in Table 1.

Chua\cite{15} reported isovitexin (apigenin) at 17.5 min retention time using negative ion mass spectrometry mode. Nontargeted mass screening shows the presence of isoflavones (genistein), flavonol (kaempferol), flavanol (catechin), flavanone (naringenin), and several phenolic organic and acidic acids in *F. deltoidea*. LC-PDA-MS/MS profiling identifies the natural acids, alkaloids, terpenoids, polyphenols, and their derivatives. Abdullah *et al.*\cite{16} have carried out LCMS/MS experiment and reported the vitexin biosynthesis in *F. deltoidea*. Mohd *et al.*\cite{17} examined the compositional differences among aqueous and methanol extract of *F. deltoidea* leaves var. *bilobata*, var. *angustifolia*, var. *kunstleri*, var. *mottleiana*, and var. *trengganuensis*. Two marker compounds, vitexin and isovitexin, were used. During experiment, all the samples show a dark band of glycoside flavones at 254 nm due to the quenching of double bonds within the compound. Azemin *et al.*\cite{18} studied the high-performance thin-layer chromatography (HPTLC) profiling of methanolic and aqueous extract of *F. deltoidea* of six different samples using vitexin and isovitexin as a marker. Result showed that methanol extract gave good results than water extract. Similarly, high-performance liquid chromatography (HPLC) is also used for the evaluation of non volatile compounds such as phenolics, terpenoids, alkaloids, lipids, and sugars, which are soluble in natural solvents.\cite{19} It may also be used for fingerprinting of biologically energetic extracts, or tracking chemical reactions of some metabolites in natural synthesis of strong compounds. Approximately 96% aqueous ethanol extract of *F. deltoidea* was found to contain methyl 10-epi-pheophorbide.\cite{20} 10-epi-pheophorbide was also tested on breast cancer cell line cell after purification using HPLC. Farsi *et al.*\cite{6} used HPLC method and analyzed *F. deltoidea*
### Table 1: Phytochemicals of different species of *Ficus* and their uses

| S. no. | *Ficus* species | Part used | Chemical constituents                                                                 | References |
|--------|----------------|-----------|--------------------------------------------------------------------------------------|------------|
| 1      | *carica*       | Leaves    | Rutin, chlorogenic acid, psoralen                                                      | [72]       |
| 2      | *carica*       | Leaves    | Proteolytic enzymes                                                                  | [73]       |
| 3      | *carica*       | Leaves    | Triterpenoids: calotropenyl acetate, methyl maslinate, lupeol acetate                  | [74]       |
| 4      | *carica*       | Leaves    | Bergapten, psoralen                                                                  | [75]       |
| 5      | *carica*       | Leaves    | Proteins                                                                              | [76]       |
| 6      | *carica*       | Latex     | Ficins C and D                                                                       | [77]       |
| 7      | *carica*       | Latex     | Mixture of 6-O-acyl-β-d glucosyl-β sitosterols                                        | [78]       |
| 8      | *carica*       | Latex     | Proteolytic components                                                                | [79]       |
| 9      | *carica*       | Latex     | Ficin                                                                                 | [80]       |
| 10     | *carica* var. *horaishi* | Latex | Ficins A, B, C, and D                                                                | [81]       |
| 11     | *carica*       | Root      | α-amyrin, β-sitosterol, coumarins: psoralen, bergapten                                | [82]       |
| 12     | *microcarpa*   | Leaves    | Triterpenes: 29(20→19) abelupane-3,20-dione and 19,20-secoursane-3,19, 20-trione; (3β)-3-hydroxy-29(20→19) abelupan-20-one, α-amyrone and lupenone | [83]       |
| 13     | *microcarpa*   | Root      | 3β-acetoxy-12,19-dioxo-13(18)-oleanene, 3β-acetoxy-19(29)-taraxasten-20α-ol, 3β-acetoxy-21α,22α-epoxytaraxastan-20α-ol, 3,22-dioxo-20-taraxastene | [84]       |
| 14     | *microcarpa*   | Root      | α-amyrin acetyl, β-sitosterol, β daucosterol, hexacosanoic acid, heneicosanoic acid   | [85]       |
| 15     | *semicorda*    | Leaves    | Flavonoids: quercetin, quercitrin, catechin                                           | [86]       |
| 16     | *platyphylla*  | Leaves    | α and β-amyrin, ceryl alcohol, β-sitosterol                                           | [87]       |
| 17     | *platyphylla* del | Bark    | β-amyrin, ceryl alc., β-sitosterol, ursolic acid                                      | [88]       |
| 18     | *platyphylla*  | Bark      | Saponins                                                                              | [89]       |
| 19     | *septica*      | Leaves    | Tyllophorine, α-amyrin acetate and β-amyrin acetate; β-sitosterol, stigmasterol, palmitic acid, myristic acid 4-hydroxy-3-methoxyacetophenone and 3,4,5 trimethoxyacetophenone | [90]       |
| 20     | *thunbergii*   | Leaves    | β-amyrin acetate, α-amyrin acetate, lupenyl acetate, lupeol, β-amyrin, α-amyrin, taraxerol, glutinol, ursolic acid, and betulinic acid | [91]       |
| 21     | *infectoria*   | Leaves    | Scutellarein 6-O-α-l-rhamnopyranosyl (1→2)-β d-galactopyranoside                      | [92]       |
| 22     | *infectoria*   | Leaves    | Flavone glycoside: infectorin                                                         | [93]       |
| 23     | *infectoria* roxb | Bark    | Methyl-ricinolate, β-sitosterol, lanosterol, caffeic acid, bergenin                     | [94]       |
| 24     | *yrata*        | Leaves    | 5-hydroxy-7,3,3′,4′ tetramethoxyflavone, 5,4′-dihydroxy-6,7,8- trimethoxyflavone, 5,4′-dihydroxy-7,8- dimethoxyflavone, 4-methoxychalcone | [95]       |
| 25     | *benghalensis* | Latex     | Rubber (17%)                                                                          | [96]       |
| 26     | *benghalensis* | Latex     | 12% Rubber; steroids; α-amyrin acetate; traces of wax containing stearic acid         | [97]       |
| 27     | *benjamina*    | Leaves    | Coumarins: α-amyrin, bergapten                                                        | [98]       |
| 28     | *benghalensis* | Bark      | β-sitosterol-α-d-glucose, meso-inositol                                                | [99]       |
| 29     | *benghalensis* | Bark      | Delphinidin-3-O-α-l-rhamnoside, pelargonidin-3-O-α-l-rhamnoside                        | [100]      |
| 30     | *benghalensis* | Bark      | 5,3′-dimethyl ether of leucocyanidin 3-O-α-d-galactosyl celllobioside                  | [101]      |
| 31     | *benghalensis* | Bark      | Leucopelargonidin quercetin                                                           | [102]      |
| 32     | *benghalensis* | Bark      | Leucopelargonidin glycoside                                                          | [103]      |
| 33     | *benghalensis* | Bark      | Bengalenoside                                                                        | [104]      |
| 34     | *benghalensis* | Bark      | β-sitosterol-α-d-glucose, meso-inositol                                                | [105]      |
| 35     | *alba*         | Latex     | β-amyрин, steaеic acid, lupeol                                                          | [106]      |
| 36     | *elastica*     | Latex     | Coumarins: α-amyрин; bergapten                                                         | [107]      |
| 37     | *elastica*     | Latex     | α-amyрине: β-amyрине; lupeol                                                           | [108]      |
| 38     | *elastica*     | Latex     | Ficin E (α serine centered protease)                                                   | [109]      |
| 39     | *glabrata*     | Latex     | Ficin : nine proteolytic components                                                    | [110]      |
| 40     | *glabrata*     | Latex     | Five sulfhydril endopeptidases                                                          | [111]      |
| 41     | *glabrata*     | Latex     | N-acetyl-β-dhexosaminidase                                                             | [112]      |
| 42     | *glabrata*     | Latex     | Ficin; nine proteolytic components                                                     | [113]      |
| 43     | *glabrata*     | Latex     | 7-hydroxycoumarin, bergapten, psoralen, (+)-catechin, apigenin, sucrose, vanillic acid, daucosterol, stigmasterol | [114]      |
methanolic leaf extracts and found enrichment with C-glycosylflavones especially, vitexin and isovitexin. Choo et al.\cite{12} also separated and quantified vitexin and isovitexin by HPLC method. This study confirmed that the content material of vitexin is pretty better than isovitexin. Suryati et al.\cite{21} used the proton nuclear magnetic resonance (\(1^H\) NMR) to describe the phenolic compounds that characterize the targeted species by elucidating crude methanol and aqueous methanol sub extracts of eight Ficus species. The effects indicated that the methanol sub extracts had significant peaks in all the species. The results showed that out of six species of Ficus, F. sansibarica is chemically specific primarily owning fragrant compounds with glycosidic bonds.

Table 1: Continued

| S. no. | Ficus species | Part used | Chemical constituents | References |
|-------|---------------|-----------|-----------------------|-----------|
| 46    | hirta         | Root      | 5-hydroxy-4', 6, 7, 8-tetramethoxy flavone, 4', 5, 6, 7, 8-pentamethoxy flavone, 4', 5, 7-trihydroxy-flavone, 3-β-acetoxy-β-amyrin, 3-β-acetoxy-α-amyrin, hesperidin | [111] |
| 47    | hirta         | Root      | Psoralex, umbelliferon, 5,3',4'-trihydroxy-3,7- dimethoxyflavone, kaempferol, astragalin, acacetin | [112] |
| 48    | hispida       | Bark      | β-amyrin acetate, gluconol acetate | [113] |
| 49    | glomerata     | Bark      | Lupeol, β-sitosterol, stigmasterol | [114] |
| 50    | racemosa      | Bark      | β-sitosterol | [115] |
| 51    | racemosa      | Bark      | Leucoyanidin 3-O-β- d-glucopyranoside, Leucopelargonidin 3-O-α-rhamnopyranoside | [116] |
| 52    | racemosa      | Bark      | Gluconol acetate, β-sitosterol | [117] |
| 53    | religiosa     | Bark      | β-sitosterol, stigmasterol, lupon-3-one | [118] |
| 54    | fulva         | Latex     | Wax containing stearic acid | [119] |
| 55    | sur           | Latex     | Two pentacyclic triterpenoids of oleanane and ursine structures | [120] |
| 56    | sycomorus     | Latex     | Sycomorus coumarins: α-amyrin, bergapten; imperatorin | [87] |
| 57    | anthelmintica | Latex     | Ficin: tryptophan | [121] |
| 58    | domestica     | Latex     | Anticoagulant substance | [122] |

**Pharmacological Properties of Ficus deltoidea**

**Anticancer effect**

Ficus deltoidea showed mild-to-good antiproliferative effect as reported in previous studies. A study showed the inhibition of cytotoxicity on prostate cancerous cell line.\cite{24} However, aqueous leaf extract of F. deltoidea has shown less cytotoxicity effect. Khan et al.\cite{9} also investigated cytotoxicity effect of water extract of F. deltoidea leaves on prostate cancer cells and found poor activity. Soib\cite{23} reported the antiproliferative activity at different concentrations of extract of F. deltoidea after 48h against prostate cancer cell line (DU145). Isovitexin and vitexin present in F. deltoidea could show this effect. Akhir et al.\cite{24} reported that 1 mg/mL of F. deltoidea extract can cause apoptosis of human ovarian cell carcinoma cellular. Cell detachment is performed by aqueous extract, whereas ethanolic extract strained just to avoid proliferation of cells. In another study, Ficus deltoidea leaf extract showed less toxicity to other human cancer cell lines, such as HL-60 (leukemia), DU145 (prostate cancer), HCT116 (colorectal carcinoma), and MDA-MB-231 (hormone-resistant breast cancer).\cite{23,25} However, report also showed the nonpoisonous nature of F. deltoidea leaf extract to ordinary cell lines, primarily human endothelial vein (HUVEC), and neuroblastoma (SH-SY5Y) cells.\cite{25} Ficus deltoidea is also found to show antiangiogenic effect as it prevents the development of the latest blood vessels. Strangely, the extract shows vigorous cytotoxicity toward hormone-resistant breast most cancers (MDA-MB-231) and colon most cancers cells (HCT 116).\cite{24,25}

**Antibacterial activity**

Literature showed that presence of flavonoid in the extract of F. deltoidea can cause the antimicrobial effect.\cite{26} Abdullah et al.\cite{10} reported antimicrobial effect of F. deltoidea extract in a membrane ultrafiltration method. They compared their results of protein hydrolysates with unhydrolyzed protein, and found that the protein hydrosyalted has greater radical scavenging activity. They also reported that the lower protein hydrolysate has the maximum inhibitory activity. Tkachenko et al.\cite{27} reported the antibacterial effects of ethanolic extract of F. deltoidea. Lee et al.\cite{28} showed the prospective of F. deltoidea leaf extract to make up to 30% of all bacterial isolates. It confirmed that methanol extract of F. deltoidea covertly inhibited the growth of S. aureus at lowest minimum inhibitory concentration (MIC) value (3.125 mg/mL), whereas the other extracts act as good antibacterial and antifungal against fungi, gram-positive and gram-negative bacteria strains. Another antimicrobial disk-diffusion study unveiled the inhibitory activity of chloroform, methanol, and
aqueous extracts of *F. deltoidea* on the fungus, gram-positive, gram-negative bacteria strains. But, it does not show the effect for the chloroform and aqueous extracts on *Bacillus subtilis*, *E. coli*, and *P. aeruginosa*.\[29\]

*Ficus deltoidea* was also assessed for their antibacterial activity against invasive oral pathogens, namely *Enterococcus faecalis*, *Streptococcus mutans*, *S. mitis*, *S. salivarius*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Fusobacterium nucleatum*, using the broth microdilution method (minimal inhibitory concentration [MIC] and minimal bactericidal concentration [MBC]). Results showed mild-to-powerful inhibition with MIC and MBC values ranging from 0.63 to 2.5 mg/mL, although none on monospecies biofilms displayed any inhibition.\[29,30\] Suryati *et al.*\[31\] recorded an antibacterial compound lupeol from *F. deltoidea* leaves that check the growth of *E. coli*, *B. subtilis*, and *S. aureus* at minimum inhibition concentration.

**Anti-inflammatory and antinociceptive properties**

Inflammation is a process in which white blood releases a chemical (basophilic, dendritic cell, macrophage, and natural killer cell) into the impacted region of the blood to safeguard our body, followed by release of inflammatory material into the joint, resulting in irritation, inflammation of the joint lining, and ultimately cartilage destruction. This involves additives, leukotrienes, prostaglandin, and kinin. Inflammation’s cardinal sign involves pain, heat, redness, swelling, and function loss. The other signs of inflammation are fever, leukocytosis, fibrinogen, serum amyloid-A protein, sepsis, and presence of acute-phase protein. *In vitro* experiment of three assays, lipoygenase, hyaluronidase, and 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced edema of leaf extract of *F. deltoidea*, also confirms the anti-inflammatory effect.\[31\] Che Ahmad Tantowi *et al.*\[32\] have reported the anti-inflammatory activity of *F. deltoidea* leaf extract and downregulation of the raised interleukin-1β, prostaglandin E, and C-telopeptide type II collagen level similar to diclofenac. The constituents, vitexin and isovitexin, present in *F. deltoidea* showed greater influence on lessening postmenstrual osteoarthritis joint demolition. Zakaria *et al.*\[33\] have reported the anti-inflammatory activity of *F. deltoidea* extracts in both acute and chronic inflammation models. The acute and choric inflammation models were measured by the Carrageenan-induced paw edema test and cotton pellet-induced granuloma test, respectively. Formalin test is generally used for antinociceptive activity and interestingly *F. deltoidea* extracts showed antinociceptive activity inflammatory-mediated pain.

A study showed the anti-inflammatory effects of aqueous leaf extract of *F. deltoidea* at doses 1, 50, and 100 mg/kg in three kinds of nociception acetic acid-induced abdominal writhing, formalin, and hot plate testing. In formalin and hot plate test antagonist naloxone, the nonselective opioid receptor antagonist naloxone could be used to reverse the antinociceptive effect of the extract. Endogenous opioid system, therefore, plays a role in the mechanism of action for analgesics.\[34\]

**Antiulcerogenic effect**

Peptic ulcer is one of the most prevalent gastrointestinal disorders nowadays. A study showed the reduction in ulcer region after treatment with aqueous extract of *F. deltoidea* on gastric walls of rats. The impact of ethanol-induced ulcer at a dose of 500 mg/kg was considerably reduced by *F. deltoidea* extract, as the same impact was noted in omeprazole.\[34,35\]

The antiulcerogenic effect of *F. deltoidea* extract was also supported by other researcher.\[36\] *Ficus deltoidea* extract had significantly reduced ulcer area against absolute ethanol lesion induction. This mechanism may be due to stimulus of gastric mucous secretion and reticence of edema and leucocytes intrusion in submucosal gastric tissue.\[37\]

**Wound-healing activity**

*Ficus deltoidea* leaf extract’s wound-healing activity is well proven. This could be due to pretty wound enclosure and fibroblast proliferation, which essentially contributed to angiogenesis.\[38\] A study showed good wound-healing activity that may be caused by the regulation of collagen 1, and an increase in tensile strength of the wound.\[39,40\] Due to presence of flavonoid, it protects the tissues from oxidative damage and thus helps in healing.\[41\] Mustaffa *et al.*\[42\] examined *F. deltoidea* leaf extract for wound-healing activity on skin cell. Cell proliferative and migration assays on the human skin fibroblast cell (HSF 1184) at different concentrations of *F. deltoidea* leaf extract showed significance proliferative and wound cessation effect and it could be effective in wound-healing potential and may be useful for the development of effective wound-healing drug.

**Antioxidant properties**

Antioxidant is a component of our complex system of protection that protects our body from the oxidative damage of free radicals. Phenolic compounds and their derivatives are closely linked to their antioxidant activity.\[43,44\] This statement was parallel to Hakiman and Maziah’s\[45\] research. Another research showed that *F. deltoidea* fruit extract var. *angustifolia* is a useful
antioxidant source. They reported good antioxidant activity of hexane extract even better than vitamin E. Apart from hexane, other solvents tested were chloroform and methanol.\(^{47,48}\) Hakiman and Maziiah\(^{46}\) compared the polyphenol, phenolic acid, flavonoid, and compounds as nonenzymatic antioxidant, whereas ascorbate oxidase, peroxidase, catalase, and ascorbate peroxidase with enzymatic in \(F. \) deltoidea leaf extract. Maizatul et al.\(^{49}\) have reported that 85% of the aqueous \(F. \) deltoidea showed good antioxidant activity due to presence of flavan-3-ol monomers, proanthocyanidins, and C-linked flavone glycosides. Adam et al.\(^{50}\) reported water-soluble insulin-secreting constituents in aqueous extract of \(F. \) deltoidea, which gave better effects than glibenclamide.

A study showed the directly proportional relationship between 2, 2-diphenyl-1-picyrylhydrazyl radical activity and concentration of samples. Different solvent extracts showed different phenolic and flavonoid contents.\(^{51}\) Another study showed that quantity of flavonoid content varied in leaves and stem extract and leaf extract showed strong antioxidant activity as compared to stem extract. Interestingly, female leaves of \(F. \) deltoidea species gave higher antioxidant activity, higher flavonoid, and phenolic content as compared to male leaves.\(^{48,52}\) Misbah et al.\(^{53}\) examined free radical scavenging power in \(F. \) deltoidea fruits by DPPH method and reported good antioxidant results. Hakiman and Maziiah\(^{46}\) used male and female leaves of \(F. \) deltoidea using DPPH free radical scavenging and found female leaves of \(F. \) deltoidea have the highest antioxidant activity (1.30 mg/g) as compared to male leaf extract (0.49 mg/g).

The morphology of the leaves of plant also plays a significant role in the yield of phenolic content. The surface area of the leaves may produce important differences in the quantity of extracted phenolic compounds. A research showed that the difference in leaf size (tiny [FDS], medium [FDM], and large-type leaf [FDB]) of \(F. \) deltoidea contributed significant difference in amount of phenolic compounds being extracted. The outcome showed that the crude extract from FDM had the largest phenolic content, followed by FDB and FDS contents.\(^{53}\) Moreover, a recent study showed that the phenolic content of the male and female leaves was considerably different. The female plant showed significantly more phenolic compounds than male \(F. \) deltoidea.\(^{54}\) In addition, a previous study showed that the leaves of two accessions of \(F. \) deltoidea showed variations in total phenolic and flavonoid content.\(^{55}\)

A study stated that 80% ethanolic extracts had the highest total phenolic compounds compared to 80% methanolic and aqueous extracts.\(^{56}\) Furthermore, the yield of vitexin and isovitexin decreased with increasing the sample to water ratio.\(^{57}\) In addition, the total phenolic content (TPC) rises with the increasing of ethanol concentration, which 70% ethanol concentration showed to be the maximal TPC from 0.1 g of the extracts.\(^{58}\) The reported yield was found to be highest in methanol extract followed by chloroform extract and lastly hexane with low phenolic concentration.\(^{56}\)

Temperature during plant extraction of phenolic and flavonoid compounds plays a major role in optimizing phenolic and flavonoid yield.\(^{59}\) The latest research recorded the impact of temperatures on the output of vitexin and isovitexin. Increase in the temperature causes increase in the yield until it reaches the best temperature at 70°C and then decreases.\(^{57}\)

The other study also stated that the extraction temperature at 75°C could show the good phenolic yield.\(^{60}\) A recent study showed that the ripe fruits of \(F. \) deltoidea have highest flavonoid content as compared to unripe fruits, senescent leaves (SL), fresh leaves (FL), and stem (ST) extracts.\(^{55}\) Moreover, the aqueous leaf and fig extracts of four varieties of \(F. \) deltoidea, namely var. angustifolia (Fdva), var. deltoidea (Fdvd), var. intermedia (Fdvi), and var. kunstleri (Fdvk), showed that the fig extracts of each variety have higher total flavonoid content compared to the leaf extract.\(^{61}\) In a recent experiment of \(F. \) deltoidea, methanol extract showed the highest scavenging activity as compared to ethyl acetate, butanol, and chloroform extracts. Butanol extract showed poor scavenging activity.\(^{62}\)

**Antidiabetic activity**

In recent days, diabetes has become a major public concern. Nowadays, many institutions and researchers are trying hard to find a solution to develop a new antidiabetic agent so that it can be helpful in reducing the incident of diabetic.\(^{63,64}\) Recently, Nurdiana et al.\(^{65}\) showed the increment on the insulin secretion when rats treated with extract of \(F. \) deltoidea. Choo et al.\(^{12}\) also showed that the isovitexin and vitexin form \(F. \) deltoidea extract has the ability to reduce postprandial blood glucose. Abu Bakar et al.\(^{66}\) reported its inhibiting activity against α-amylase enzyme. The vitexin of \(F. \) deltoidea extract works well against α-amylase enzyme. Another study also confirmed the antidiabetic property of \(F. \) deltoidea fruits.\(^{67}\) Kalman et al.\(^{67}\) also found out the reducing ability of lipid and glucose level in human adults.
Table 2: Pharmacological actions of constituents of different species of *Ficus*

| S. no. | *Ficus* species | Part used | Pharmacological actions | References |
|--------|-----------------|-----------|-------------------------|------------|
| 1      | *carica*        | Leaves    | Bergaptene and psoralen of aqueous extract showed strong antitumor activity | [123]      |
| 2      | *carica*        | Leaves    | Aqueous extract showed good anti-HSV-1 effect | [124]      |
| 3      | *carica*        | Leaves    | Controls postprandial glycaemia in insulin-dependent diabetes mellitus (IDDM). Decoction leaves lowered the glucose level | [125]      |
| 4      | *carica*        | Leaves    | Antidiabetic; aqueous decocted leaves decline the levels of total cholesterol level in streptozotocin-induced diabetes rat | [126]      |
| 5      | *carica*        | Leaves    | Hypotriglyceridemia | [127]      |
| 6      | *carica*        | Latex     | Milk coagulating; the milk-clotting enzyme from latex of *F. carica* can be replaced for animal rennet to produce Cheddar and achieved cheese | [128]      |
| 7      | *carica*        | Latex     | Hemostatic; It activates human coagulation factor X proteases; curbs the activated partial thromboplastin time and the prothrombin time of normal plasmas and plasmas deficient in coagulation factors | [129]      |
| 8      | *carica*        | Latex     | Anticancer; a mixture of 6-O-acyl-β-d-glucosyl-β-sitosterols, the acyl moiety act as a potent cytotoxic agent. It showed in vitro inhibitory properties on proliferation of many cancer cell lines | [130]      |
| 9      | *carica*        | Latex     | Antiangiogenic; confirmed by using human umbilical vein endothelial cell (HUVEC) tubule formation assay and MTT assay | [131]      |
| 10     | *carica*        | Latex     | Antimetastatic; antitumor | [132,133] |
| 11     | *carica*        | Latex     | Prevents the growth of subcutaneously transplanted benzopyrene sarcomas B, 616, and 2192; produces regression of some intraperitoneal and subcutaneous sarcoma transplants; necrotic action on the skin | [134]      |
| 12     | *carica*        | Latex     | Proteinase | [135,136] |
| 13     | *carica*        | Latex     | Proteolytic activity; latex from leaves and tender shoots of *F. carica* was measured the amount of tyrosine released from a casein substrate | [137,139] |
| 14     | *carica*        | Latex     | Antimetastatic; antitumor | [132,133] |
| 15     | *carica*        | Latex     | Antitumor | [140]      |
| 16     | *carica*        | Latex     | Proteolytic enzyme | [141]      |
| 17     | *carica*        | Latex     | Fibrinolytic | [142]      |
| 18     | *carica*        | Latex     | Hemostatic proteases; Ficin of *F. carica* shortened the activated partial thromboplastin time and the prothrombin time of normal plasmas and plasmas deficient in coagulation factors | [144-145] |
| 19     | *carica*        | Latex     | Anticancer; polyphenolic compounds present in *carica* can serve as a source of antioxidants thus resulted in decrease in proliferation, colony formation | [144]      |
| 20     | *carica*        | Latex     | Anthelmintic | [145]      |
| 21     | *carica*        | Latex     | Latex helps in hydrolysis of tributyrin and monobutyrin I | [146]      |
| 22     | *carica*        | Latex     | It helps in casein digestion, milk clotting | [147]      |
| 23     | *carica*        | Latex     | Bacteriolytic against *Micrococcus lysiselkticus* | [148]      |
| 24     | *carica*        | Latex     | Antifungal | [149]      |
| 25     | *carica*        | Latex     | It acts like inhibitory peptides of angiotensin I-converting enzyme (ACE) | [150]      |
| 26     | *carica*        | Latex     | Proteolytic activity | [151]      |
| 27     | *erecta*        | Leaves    | Proteasteoporotic; *F. erecta* leaves extract decreases the IL-6 and COX-2 mRNA expression level and also reduce the protein levels production of COX-2 and PGE2 as well | [152]      |
| 28     | *benjamina*     | Leaves    | Anti-inflammatory, antinoceceptive, and antipyretic activities | [153]      |
| 29     | *benjamina*     | Latex     | Allergen case of perennial rhino conjunctivitis caused by allergic reaction | [154]      |
| 30     | *benjamina*     | Latex     | Allergen non occupational, indoor-related rhino conjunctivitis | [155]      |
| 31     | *benjamina*     | Latex     | Allergen; latex-allergic patients are at higher risk of becoming sensitized to *Ficus* | [156]      |
### Table 2: Continued

| S. no. | Ficus species    | Part used | Pharmacological actions                                                                 | References |
|--------|------------------|-----------|----------------------------------------------------------------------------------------|------------|
| 32     | *benjamina*      | Latex     | Allergen                                                                               |            |
| 33     | *exasperata*     | Leaves    | Hypotensive; *F. exasperata* causes dose-dependent reduction in mean arterial blood pressure due to activation of muscarinic receptor in the heart | [137,138] |
| 34     | *exasperata*     | Leaves    | Antiulcerogenic; *F. exasperata* leaf extract causes substantial antiulcerogenic effects in a dose-dependent. It acts by protecting rats from aspirin-induced ulcerogenesis, adjourning intestinal transit, increasing pH, and reducing equally the volume and acidity of gastric secretion | [139] |
| 35     | *fistulosa*      | Leaves    | Inhibits the growth of *Plasmodium falciparum*: Macrocyclic trichothecene sesquiterpenoid inhibit the growth of *Plasmodium falciparum* | [140] |
| 36     | *hispidia*       | Leaves    | Antidiarrheal agent. It inhibits the activity against castor oil-induced diarrhea         | [141] |
| 37     | *hispidia*       | Latex     | Proteolytic                                                                           | [142] |
| 38     | *pumila*         | Leave     | Leaves extract showed antimicrobial activity against *Pseudomonas aeruginosa*, *Escherichia coli*, *Candida albicans* and *Bacillus subtilis* | [143] |
| 39     | *pumila*         | Latex     | Caseinolytic                                                                            | [144] |
| 40     | *racemosa*       | Leaves    | Crude ethyl acetate, hexane, petroleum ether, acetone, and methanol leaves extract of *F. racemose* showed mild larvicidal effects against *Culex quinquefasciatus* | [145] |
| 41     | *racemosa*       | Leaves    | Anti-inflammatory; confirmed by carrageenin, serotonin-, histamine, and dextran induced rat hind paw edema models | [146] |
| 42     | *racemosa*       | Leaves    | Antibacterial; the petroleum ether leaves extract of *racemosa* showed substantial antibacterial potential against *E. coli* ATCC 10536, *B. pumilus* ATCC 14884, *B. subtilis* ATCC 6633, *P. aeruginosa* ATCC 25619, and *Staphylococcus aureus* ATCC 29737 | [147] |
| 43     | *religiosa*      | Leaves    | Shelving of neurodegeneration in human brain diseases; anti-inflammatory; inhibition of microglial activation; therapeutic potential for various neurodegenerative diseases | [148] |
| 44     | *anthelminthica* | Latex     | Proteolytic                                                                           | [121,170] |
| 45     | *glabrata*       | Latex     | Anticoagulating; proteolytic action on fibrinogen and fibrin                           | [171] |
| 46     | *glabrata*       | Latex     | It acts and inhibits the coagulation of blood                                          | [172,173] |
| 47     | *glabrata*       | Latex     | Proteolytic                                                                           | [151,174] |
| 48     | *glabrata*       | Latex     | Peroxidases                                                                            | [175] |
| 49     | *glomerata*      | Latex     | Protease activity                                                                      | [176] |
| 50     | *glomerata*      | Latex     | Inhibits glucose-6- phosphatase from rat liver                                         | [177] |
| 51     | *glomerata* (syn. *racemosa*) | Root | Acts as antioxidant and protection against CCl₄-induced hepatic damage         | [178] |
| 52     | *laurifolia*     | Latex     | Proteolytic effect                                                                     | [174] |
| 53     | *microcarpa*     | Latex     | Antifungal                                                                             | [179] |
| 54     | *microcarpa*     | Root      | Cytotoxic                                                                              | [84,180] |
| 55     | *platyphylla*    | Latex     | It acts as an anthelmintic activity against *Ascardia galli* in chickens.               | [87,181] |
| 56     | *stenocarpa*     | Latex     | Proteolytic                                                                           | [151] |
| 57     | *virgata*        | Latex     | High toxicity and growth inhibition against lepidopteran larvae; cysteine protease activity | [182] |
| 58     | *ficus spp.*     | Latex     | Allergen                                                                               | [183] |
| 59     | *ficus spp.*     | Latex     | Anthelmintic                                                                            | [184,185] |
| 60     | *benghalensis*   | Root      | Improved diabetic condition in streptozotocin-induced diabetic rats                    | [186,187] |
| 61     | *benghalensis*   | Root      | Hypoglycemic effect. Decrease sugar level up to 40%–45% in normal rats and approximately 50%–55% in mildly diabetic rats | [188,189] |
Uterotonic agent

A uterotonic agent induces contraction of the uterus. Amiera et al. [69] have studied two main varieties of Ficus var. deltoidea and var. angustifolia and reported contraction in rats. In another research, F. deltoidea aqueous extracts cause uterine effects via muscarinic, oxytocin, and PGF2α receptors. Other Ficus species such as asperifolia also showed this effect. [70,71] Table 2 shows the different biological activities of other Ficus species.

CONCLUSION

The global use of natural product for the management of diseases has rapidly expanded over the past decade. Medicinal flowers have historically been a wealthy source for powerful pills, and still represent an important pool for the identification of new pharmacological leads nowadays. Ficus deltoidea is one of the medicinal plant that has been used as remedy for severe ailments. A range of species of Ficus has been cultivated in various parts of the world as a decorative shrub or residence plant. Ficus deltoidea is known to integrate several chemical components, which is likely for its many pharmacological activities. These activities are highlighting the chemical nature of F. deltoidea, its outcomes on numerous parameters, and mechanisms of the located biological moves. However, this record is not always sufficient to offer evidence for safety and efficacy of a natural product and requires similarly investigation.

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Conflicts of interest

There are no conflicts of interest.

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