

## Review: Phytochemical activities of *Ficus* (Moraceae) in Java Island, Indonesia

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Manuscript received: 31 August 2020. Revision accepted: 27 November 2020.

**Abstract.** Putra KWE, Pitoyo A, Nugroho GD, Rai M, Setyawan AD. 2020. Review: Phytochemical activities of *Ficus* (Moraceae) in Java Island, Indonesia. *Bonorowo Wetlands* 10: 98-125. *Ficus* is a genus of about 850-900 species. Some mention more than 1000 species, making it the largest species in the family of Moraceae. There are approximately 91 species of *Ficus* found in Java, Indonesia. Some of them have been studied about their traditional uses and phytochemistry. This study aims to know the phytochemical activities of *Ficus* species in Java. We found at least 40 species of *Ficus* studied in phytochemistry and biological activities (majority in vitro). Alkaloids, phenols, flavonoids, saponins, tannins, terpenoids, steroids, glycosides, and anthocyanins are found in almost every *Ficus*. The biological activities include antioxidant activity, antibacterial activity, cytotoxic activity, anti-inflammatory and analgesic activities, anti-diabetic activities, hepatoprotective, anti-ulcer activities, wound healing, and other functions. Many species are still unexplored, especially in phytochemistry or pharmaceutical-based folklore. This could be an opportunity to study more deeply in the future.

**Keywords:** Biological activities, ethnobotany, *Ficus* species, Java Island, phytochemistry

### INTRODUCTION

*Ficus* is a genus of about 850-900 species; some mention more than 1000 species, making it the largest species in the family of Moraceae (Zhekun and Gilbert 2003; Britannica 2019). This genus is commonly spread throughout the tropical regions of the world and subtropics regions, living on low land to high land (Fongang et al., 2015). Indonesia has an extraordinary plant diversity, including *Ficus*, more than 250 species are distributed across the Indonesian Archipelago, and approximately 91 species of *Ficus* are found in Java (Berg 2003; Yusuf 2011).

*Ficus* spp. (Fig) are often found and scattered in various regions in Indonesia. Some species prefer riparian habitats near water bodies for growth and reproduction. *Ficus* can store water reserves because plants have wide and tall stems and have a deep root system up to underground streams that make the surrounding trees a source of water (Baskara and Wicaksono 2013). Lush *Ficus* tree canopy helps hold rainwater, reducing soil erosion; strong and branched taproots function to bind the soil to keep the soil from erosion and absorb water (Ulfah et al., 2015). *Ficus* is a plant that can live and good adaptation to various environmental conditions (Naharuddin 2017).

*Ficus* shows some growth forms of shrubs, wood trees, creepers, epiphytes, and hemiepiphytes (Wagner and Zotz

2020). *Ficus* consists of vast amounts of sap in bark, branching, and leaves (Gotsch et al., 2015). Fig species are characterized by their unique inflorescence and distinctive pollination syndrome, which uses wasp species belonging to the family Agaonidae for pollination.

Specific identification of many species can be difficult, but members of the genus *Ficus* are relatively easy to spot. Many have aerial roots and a distinctive shape or habit, and the fruit sets them apart from other plants. *Ficus* fruit is an inflorescence enclosed in an urn-like structure called a syconium, which is lined on the inside with tiny fig flowers that develop into multiple ovaries on the inner surface. In essence, figs are fleshy stems with many small, fruiting, fused flowers (Pothasin et al., 2014).

The unique fig pollination system, which involves very specific tiny wasps, known as fig wasps that enter through this closed inflorescence ostium to pollinate and lay their eggs, has been a source of inspiration and wonder for biologists (Rønsted et al. 2005). In particular, the three vegetative properties together are unique to figs. All figs present white to yellowish latex, some in excess; twigs showing paired stipules or circular scars if the stipules have fallen off; the lateral veins at the base of the leaf are steep, forming a closer angle to the midrib than the other lateral veins, a feature referred to as "triveined" (Rønsted et al. 2005).

Several *Ficus* species are very familiar with indigenous Indonesian culture, including the Javanese. *Ficus benjamina* is a sacred tree, a gathering place for magical powers; it is planted and used to mark important places such as royal palace squares and is planted in water sources such as springs and ponds. *Ficus racemosa* is very famous because it grows a lot in riverbanks to prevent erosion, with many fruits clustered on the trunk (Rasyid et al., 2017). Recently, *Ficus carica* is also widely grown as an ornamental plant and fruit crop. This alien plant was introduced from the Middle East and the Mediterranean to harvest the fruit and become one of the fruits mentioned in the Qur'an (at-Tin [95]:1). The fruits of many other *Ficus* species are also edible, although usually of only local economic importance or eaten as bush food. Wild figs fruit is a critical food source for wildlife. *Ficus* are also of great cultural importance throughout the tropics, both as objects of worship and for their many practical uses.

Several species of *Ficus* have been used in Java for drinks, food, and medicinal ingredients. In West Java, *Ficus deltoidea* is commonly used as an aphrodisiac and stamina enhancer (Rahayu et al., 2012); the leaves are boiled and then drunk (Fahrurrozi, 2014). The sap is used for warts, and the leaves are drunk as a tonic (Susiarti et al., 2018). In Banten, the fruits of *Ficus ribes* are consumed for uterine fertilizer. The fruits are dried, boiled, and drink (Sulistiarini 2011). In West Java, a stem of *F. ribes* is finished for cavities, malaria, diarrhea, and breast milk production (Fahrurrozi 2014). *F. ribes* have a similar function but are added for nausea medicine from latex and stem bark (Susilo 2016). In Banten, the fruit of *Ficus variegata* is used as fresh vegetables (Sulistiarini 2011). In West Java, the leaves and fruit can be eaten raw; the fruit and young leaves are used for stomachache (Fahrurrozi 2014). The fruit can cure dysentery in Ciremai (Herlina et al. 2018). Another species can be said to have similar functions. There are many new species in phytochemistry, although there are many benefits. Several species like *Ficus ampelas*, *Ficus copiosa*, *Ficus glabella*, *Ficus montana*, *Ficus vasculosa*, and *Ficus villosa* (Table 1) have many potencies in pharmaceutical and have not been researched yet. This could be an opportunity to study more deeply in the future.

This review aims to know about the medicinal use of *Ficus* in Java Island, especially their phytochemical activities.

### Phytochemistry of *Ficus* in Java

For all *Ficus* recorded in the Java Island (91 species), only about 40 species have been studied for their phytochemistry (Table 1). Phytochemical content obtained from various parts of *Ficus*, mainly obtained from leaves and fruits. The phytochemical contents varied in each part of the plants. But, generally, at least, there is still one secondary metabolite common in every plant. They are alkaloids, phenols, flavonoids, saponins, tannins, terpenoids, steroids, glycosides, and anthocyanins found in every *Ficus* in this review.

Those chemicals and other specific chemicals played a different role in biological activities (Table 1). Most of

them were studied in vitro to determine and screen their phytochemical content's initial potential. Some others have been applied in vivo and used as pharmaceutical or other ingredients.

The biological activities of *Ficus* are abundant. Still, the main activities of *Ficus* can be divided into some categories: antioxidant activity, antibacterial activity, cytotoxic activity, anti-inflammatory and analgesic activities, anti-diabetic activities, hepatoprotective, anti-ulcer actions, wound healing, and other functional activities (Salehi et al. 2020).

### ANTIOXIDANT ACTIVITY

This biological activity is the most studied in *Ficus* species. Approximately 25 species of *Ficus* have been studied in this activity. Not all of them had a vigorous antioxidant activity. Antioxidants play a significant role in the human body (Pramita et al., 2008; Setyawan, 2010; Ilonga et al., 2018). These compounds may protect cells against free radicals and reduce the risk of many diseases. The antioxidant is also essential to characterize plants' biological activities and their ingredient of secondary metabolites. This can be used as a preliminary screening of phytochemical constituents in plants (Rahmawati et al. 2018; Wutsqa et al. 2020).

Based on the review from Li et al. (2021), *F. carica* leaves were found to possess more vigorous antioxidant activity rather than fruits, wood, and his bark. In addition, ethanol, methanol, and aqueous extracts of leaves exhibited vigorous antioxidant activity. But, the leaves were reported to be dependent on harvest season. Each season has a variety of antioxidant content.

*Ficus deltoidea* fruits extract an excellent antioxidant activity. The hexane extract from fruits of *F. deltoidea* displayed the highest antioxidant (TPC value 259.2mg/gGAE) activity, followed by methanol (245.2 mg/g GAE) and chloroform extract (159.2 mg/gGAE) (Ramamurthy et al. 2014). Antioxidant activity from *F. deltoidea* is also found in leaves and callus for alternative sources (Mustapha and Harun 2014).

The fruits of *Ficus grossularioides* extract showed the highest antioxidant activity than *Ficus fistulosa*, *Ficus auriculata*, *Ficus elastica*, *F. racemosa*, and *Ficus microcarpa* in both of DPPH and ABTS assay also on free radical scavenging (Akhtar et al. 2019).

*Ficus padana* fruit extract also had a vigorous antioxidant activity, giving IC50 values of 55.7 mg/mL in DPPH assay (Syukri et al., 2014). Meanwhile, the ethanolic extract of *Ficus obscura* bark also had a vigorous antioxidant activity, IC50 values of 4.14 ppm (Zarta et al. 2020).

The methanol extract of aerial parts of *Ficus hispida* produces a substantial amount of antioxidant activity. In addition, the plant exhibits in vitro free radical scavenging activity, having numerous physiological effects and being used in various pathological conditions. The IC50 value of DPPH, H<sub>2</sub>O<sub>2</sub>, and nitric oxide radical (NO<sup>-</sup>) scavenging activity is 160.80µg/ml, 218.75µg/ml 350.83µg/ml,

indicating that methanol extract has significant antioxidant activity (Chatterjee et al. 2015).

Based on a review from Chaware et al. (2020), *F. racemosa* had antioxidant activity almost in all parts of this plant; root, stem bark, stem, and fruit. The stem bark of *F. racemosa* possesses high antioxidant activity with IC50 values of many, which is even better than the standard BHT., The extract from the fruit also showed 60% DPPH scavenging activity, and its 1-BuOH soluble part showed an 80% inhibition activity. In another study, the fruit extract with toluene had a higher antioxidant activity with IC50 0.75µg/ml and showed maximum percentage inhibition of 96.5% (Bagyalakshmi et al., 2019).

*Ficus auriculata*, according to Bertolotti et al. (2018;2020), has antioxidant activity on its branches, fruits, and leaves. The branches and fruits extracted with ethanol/water and ultrasound are the most significant in DPPH radical elimination assay, 190.57µg/mL. But the best antioxidant activity from this species was found in young leaves with the same extraction, 182.87µg/mL in DPPH scavenging assay.

Based on several studies (Ningsih et al. 2016; Raza et al. 2016; Lee 2020), *F. variegata* leaves, fruits, and stem bark has a vigorous antioxidant activity because they have IC50 below 200µg. While on stem bark extracts, the antioxidant activity showed extreme activity. This means stem bark needs further studies before being applied in pharmaceuticals, while other parts can be a potential source for antioxidants.

Several studies from Qi's review (2021) have reported the antioxidant effects of bioactive compounds or extracts from the root, stem, leaf, and fruit of *Ficus pumila*. Flavonoid glycosides isolated from the leaves showed strong antioxidant activities in superoxide radical inhibition and DPPH radical scavenging assays. In addition, Noronha et al. (2014) determined the antioxidant activities of hydroethanolic extracts from dried and fresh parts of *F. pumila*. Found that new stem exhibited the most potent antioxidant capacity by DPPH assay.

*Ficus benjamina* also showed high antioxidant activity with the IC50 values 59.07µg/ml in the DPPH assay. It was obtained from methanolic extracts of *F. benjamina* leaves, making it a potential source of antioxidants (Jain et al., 2013).

*Ficus elastica* leaves show good antioxidant activity and thus can be used as a safe and natural antioxidant compound source. *Ficus elastica* leaves extract was found to exhibit significant ( $p < 0.05$ ) dose-dependent DPPH radical scavenging activity with an IC50 value of 20.17µg/ml (Preeti et al., 2015). In another study, *F. elastica* ethanolic extract from the leaves has potential as an antioxidant agent with an IC50 value of 11.17µg/ml, which means it has moderate antioxidant activity in DPPH assay (Ginting et al. 2020).

Based on Chan et al. (2017), methanol extracts of bark, fruits, and leaves of *F. microcarpa* exhibited potent antioxidant activities of DPPH, ABTS, and superoxide radical scavenging. The strongest activities were observed in the bark with IC50 values of 7.8, 4, and 98µg/ml. In addition, flavonoids isolated from leaves of *F.*

*microcarpa* were reported to possess solid antioxidant activities of 6.6-9.5µM.

The antioxidant properties from the extract of *Ficus religiosa* bark and fruit have been proved by using different solvents. Diabetic rats treated with an aqueous extract of *F. religiosa* showed that oxidative stress was reduced and increased the bodyweight of diabetic rats (Devanesan et al., 2018).

*Ficus virens* bark methanolic extract with its compound (F18) treatment to cigarette smoke-exposed showed a significant increase in liver and lung activity, further strengthening the potent free radical scavenging property. Histopathological observations well support this result. It indicates that *F. virens* extract a highly promising natural antioxidant and can be used as an antioxidant and antiatherogenic agent (Iqbal et al., 2016). In another study, *F. virens* leaf extract also has a protective role in oxidative stress. It may have great relevance in the prevention and therapies of disease in which oxidant or free radicals play a significant role (Pattar et al., 2018).

*Ficus benghalensis* possesses antioxidant activity, which is primarily due to phenolic compounds. DPPH free radical scavenging activity (%) of acetone and methanol extracts on aerial parts was about 50% (Khaliq 2017). In another study, *F. benghalensis* stem bark extracts with various chemicals also have antioxidant activity. The highest radical scavenging activity was methanolic extract ranging from 71.7-82.6 mg/ml. This is a good source of biologically active compounds with antioxidant and anti-cancer potentials (Raheel et al., 2017).

## CYTOTOXIC ACTIVITY

Cytotoxic is a substance or process that results in cell damage or cell death. This term is often used to describe chemotherapy drugs that kill cancer cells, but it may also describe toxins. Plants and their phytoconstituents have been indispensable in creating diverse diseases, including cancer. There are at least 13 species of *Ficus* with known cytotoxic activity in this review.

*Ficus carica* leaves, based on Li et al. (2021), possess anti-cancer activity on liver, cervical, breast, prostate, and colon cancers. In vitro methanolic leaves, extract showed inhibition activity against Huh7it cells on the liver with an IC50 value of more than 653µg/mL. Ethanolic, ethyl acetate, and dichloromethane extract also displayed cytotoxic activity against HeLa cells on the cervix with IC50 value 10,19 and 12µg/mL, respectively. As well as aqueous extract inhibits MDA-MB-231 cells in the breast, rutin extract against LNCaP cells in the prostate, and HCT-116 cells & DLD-1 cells in colorectal. In another study (Damayanti et al., 2021), the fruit of *F. carica* has a campesterol compound, which has the potential as an anti-HIV drug.

The leaves extract of *F. deltoidea* leaves has cytotoxic activity against ovarian cancer, breast cancer, and prostate cancer. In addition, leaf extract can inhibit cell growth with apoptosis pathway, inhibit cell migration and invasion, and inhibit angiogenesis (Silalahi 2019).

A pair of undescribed enantiomers with five known flavonoids was isolated from the roots of *Ficus hirta*. All the compounds were evaluated by MTT assay on HeLa, MCF-7, HepG2, and H460 cancer cells. Among the compounds, compound no 4 exhibited the most potent inhibitory effect against the proliferation of HeLa cells with the IC<sub>50</sub> value of 28.88  $\mu$ M. Furthermore, the apoptotic effect of 4 on HeLa cells and the level of several crucial proteins in AKT/MAPKs signaling pathways were analyzed by flow cytometer and western blot assay. As a result, 4 induced HeLa cell apoptosis in a dose-dependent manner. This compound could be considered a promising candidate for the prevention and treatment of cancer (Ye et al., 2021).

The anti-proliferative activity of *F. coronata* is being reported for the first time. Anti-proliferative activity was concentration-dependent, attaining a maximum at 5 mg/ml on the radicle length of guinea corn. The chloroform fraction of *F. coronata* could serve as promising anti-proliferative agents in developing cytotoxic drugs with 96.3% inhibition. In the tadpole test, *F. coronata* leaves at a 1-2 mg/ml concentration displayed a mortality profile. The chloroform fraction with LC<sub>50</sub> values 6.5 mg/ml is the most active cytotoxic on the tadpole test (Gbolade et al., 2019).

*Ficus fistulosa* leaves extract with its subfractions were tested against Huh7it cells and HCV JFH1a to find out the cytotoxic activity of HCV. The result showed that FFL inhibited HCV JFH1a with an IC<sub>50</sub> value of 20.43  $\mu$ g/ml. In addition, *F. fistulosa* leaves were fractioned by using chloroform and butanol. The result showed that chloroform fraction possessed anti-HCV activity with an IC<sub>50</sub> value of 5.67  $\mu$ g/ml and a CC<sub>50</sub> value of >100  $\mu$ g/ml. These results would become a good target for further purification to determine the constituents responsible for cytotoxic activity against HCV (Hafid et al., 2016). In another study (Al-Khdhairawi et al. 2017), *F. fistulosa* var. *tengerensis*, which has a tengerensine compound in their leaves, has cytotoxic activity against breast cancer cell MDA-MB-468 with an IC<sub>50</sub> value of 7.4  $\mu$ M in vitro. Then the other compound, pair of chlorinating phenanthroindolizidine enantiomers, showed pronounced in vitro cytotoxic activity against three breast cancer lines (MDA-MB-468, MDA-MB-231, and MCF7) with IC<sub>50</sub> values of 0.038-0.91  $\mu$ M. In the latest study, *F. fistulosa* leaves showed cytotoxic activity against HIV. The n-hexane fraction showed an active inhibition to HIV replication and was not toxic for healthy cells with an IC<sub>50</sub> value of 27.2  $\mu$ g/ml, CC<sub>50</sub> value of 377.9  $\mu$ g/ml, and SI value of 13.89 (Indriati et al. 2020).

The several compounds of *F. hispida* fruit were isolated with MeOH extract. Those compounds were evaluated for their inhibitory activities against the Epstein-Barr virus early antigen (EBV-EA) and cytotoxic activities against HL60, A549, SKBR3, KB, HeLa, HT29, HepG2 human cancer cell lines using the MTT method. The results showed potent inhibitory effects on EBV-EA from five compounds with IC<sub>50</sub> values in the range of 271-34 M. In addition, five phenolic compounds exhibited cytotoxic activity against two or more cell lines with an IC<sub>50</sub> capacity of 2.5-95.8  $\mu$ M (Zhan et al. 2017).

Extracts of *F. racemosa* leaves using ethanol and hexane solvent were evaluated against human lung cancer cell lines (A549) and human metastatic breast cancer cell lines (MDA-MB-435S) to estimate anti-cancer properties. All extracts showed their varying inhibition activities in a dose-dependent manner. The hexane extracts exhibited nearly 47.83% cell line inhibition against the A549 cell line at 200  $\mu$ g/mL dose (Gorla and Shankar 2016).

Alkaloids fractions from *F. septica* leaves extract by ethanol solvents showed cytotoxic activity against T47D breast cancer cells. These fractions, namely fraction A and B, exhibited high cytotoxic effects with IC<sub>50</sub> values of 2.57 and 2.73  $\mu$ g/mL, respectively. In addition, fraction A could decrease the cell viability in a concentration-dependent manner. For example, the highest concentration of fraction A (50  $\mu$ g/mL) could inhibit cell growth resulting in 2.059% cell viability. In contrast, fraction B at the same concentration had the lower inhibition with 0.381% viable cells (Nugroho et al., 2015).

Based on Larbie et al. (2015), *F. pumila* leaves and stem extract by hydroethanolic solvent exhibited an anti-proliferative effect toward three human leukemic cell lines (Jurkat, CEM, HL-60). The leaves extract gave the most potent inhibition concentration at 50% values of 130.97  $\mu$ g/ml against Jurkat and 56.31  $\mu$ g/ml against HL-60. In the other studies reviewed by Qi et al. (2021), *F. pumila* chloroform and butanol fractions showed cytotoxicity against human leukemia cell line (MT-4) with IC<sub>50</sub> values of 23  $\mu$ g/ml and 26  $\mu$ g/ml. Ethanol aqueous extract *F. pumila* showed cytotoxicity against HeLa, MCF-7, and A549.

Different concentrations of *F. drupacea* stem bark n-hexane extract and isolated compounds were screened for their anti-cancer activities against HeLa, MCF-7, Jurkat, HT-29, and T24 cancer cells using the MTT assay. The compound of 5-O-methylatifolin exhibited moderate anti-proliferative activity against all examined cancer cells. At the same time, other compounds such as oleanolic acid, epifriedelanol, friedelin, and epilupeol acetate showed high anti-proliferative against examined cancer cells. This anti-cancer data demonstrated that stem barks extract and its biochemicals contain essential compounds that are bioactive against important cancer diseases (Yessoufou et al., 2015).

Ficusamide was isolated from the bark of aerial roots of *F. elastica* displayed moderate in vitro growth inhibitory activity against the human A549 lung cancer cell line (Mbosso et al., 2012). In another study, other compounds from *F. elastica* aerial roots extract exhibited cytotoxic activity against B16F10 melanoma cells and U373n glioma cell lines. The compound, namely plastoquinone, showed cytotoxic activity with an IC<sub>50</sub> value of 14  $\mu$ M against melanoma cells, while Ficoside B displayed an IC<sub>50</sub> value of 11  $\mu$ M against glioma cells (Tienkala et al. 2016). Furthermore, aerial roots extract by methanolic solvent showed cytotoxic activity against HeLa cells with IC<sub>50</sub> value at 20  $\mu$ g/mL (Tienkala et al., 2017).

The cytotoxic activity of aqueous and ethanolic extract of *F. religiosa* bark was evaluated in cervical cancer cell lines, SiHa and HeLa. Both of them showed significant

cytotoxicity in SiHa and HeLa. In HeLa, aqueous induced apoptosis by increasing intracellular  $Ca^{2+}$  reduced the migration and invasion capability. Different fractions of *F. religiosa* also exhibited cytotoxic activity against MCF 7 (Al-Snafi 2017). Concentrations of direct killing effect and disruption of cellular processes of MDA-MB-231 were successfully established in the experiment for the extract of *F. religiosa* leaves. Extract demonstrated 25% cytotoxicity at the concentration of 1000  $\mu\text{g/ml}$  in Trypan Blue exclusion assay. The extract also showed biologically significant disruptions of cellular functions in human breast cancer cell lines at concentrations of 100 and 200  $\mu\text{g/ml}$  (Shaikh et al., 2020).

The first report of two phenolic compounds isolated from the leaves of *Ficus rumphii*, 1-isopentyl-3,4-dioxomethylene-2-phenol and 3-(2-hydroxyphenyl)-1-piperidine-1-yl propane-1-one, showed significant activity. Therefore, in vitro evaluation of the anti-cancer activity of the isolated compounds was carried out using an MTT assay. These two compounds exhibited cytotoxicity against HL-60 with IC50 values of 3.3 and 2.3  $\mu\text{M}$ , respectively (Parveen et al., 2014).

The study showed that the leaves, fruits, and stem barks proanthocyanidins isolated from *F. virens* were complex mixtures of homo- and heteropolymers of propelargonidins, procyanidins, and prodelphinidins. In addition, the stem bark proanthocyanidins exhibited potent free radical scavenging and cytotoxic activity against MDA-MB-231 and MCF-7 breast cancer cells (Chen et al., 2017).

The hydroalcoholic extract of *F. benghalensis* coarse powder from bark showed higher cytotoxicity in A549 cell lines than the Chinese hamster ovary (CHO). IC50 values of *F. benghalensis* is 193.78 against A549 cell lines more toxic than 257.47 against CHO (Khanal and Patil 2020).

### ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY

Anti-inflammatory is a drug or substance that reduces inflammation (redness, swelling, and pain) in the body. Anti-inflammatory agents block certain substances in the body that cause inflammation. Inflammation is the essential nonspecific defense mechanism of the body against the aggression produced by inflammatory agents such as pathogens, chemicals, or physical injury. Anti-inflammatory is used to treat many different conditions, and some are being studied to prevent and treat cancer.

The ethanolic extract of the leaves of *F. carica* had shown anti-inflammatory activity in carrageenan-induced rat paw edema and cotton pellet granuloma models. The rat paw volume and cotton pellet weight were reduced by 75.90% and 71.66%, respectively (Li et al. 2021).

The leaves extract of *F. deltoidea* exhibited anti-inflammatory properties on lipoxygenase, hyaluronidase, and TPA-induced edema. In addition, the leaves of *F. deltoidea* also possess anti-inflammatory activity against acute and chronic inflammatory responses and pain-associated inflammatory response in rat paw edema test,

cotton pellet-induced granuloma test, and formalin test (Ramamurthy et al. 2014; Silalahi 2019).

Twenty-nine phenolic derivatives, including four new compounds, were isolated and identified from the roots of *F. hirta*. Several compounds exhibited potent anti-inflammatory inhibitory effect with IC50 values of 12.96-46.08  $\mu\text{mol/L}$  compared with indomethacin on the lipopolysaccharides (LPS)-induced nitric oxide production in murine macrophage RAW267.7 (Cheng et al. 2017)

The ethanolic extract of *F. hispida* bark (200 and 400 mg/kg, orally) inhibited the inflammation to the extent of 44.94% and 54.49%, respectively. Furthermore, it effectively reduced the edema response between 3 and 5 hours after carrageenan injection, suggesting that the bark extract could inhibit one or more intracellular inflammatory signaling pathways (Howlader et al., 2017; Cheng et al., 2019).

The stem bark extract of *F. racemosa* showed anti-inflammatory activities. The ethanol extract in vitro ATP-based luminescence assay showed an inhibitory effect on the biosynthesis of PGE 2 and PGD 2 with an IC50 value of 83.1  $\mu\text{g/ml}$ . Stem bark ethanol extract also showed anti-inflammatory activity on the Wister rats and Swiss albino mice. In addition, the leaves of *F. racemosa* exhibited anti-inflammatory by suppressing the inflammatory activity produced by histamine and serotonin in male albino Wister rats (Chaware et al. 2020).

*Ficus pumila* exhibits quite evident anti-inflammatory properties in well-recognized animal inflammatory models of xylene-induced ear swelling, carrageenan-induced toe swelling, and glacial acetic acid-induced celiac capillary permeability. The water and ethyl acetate extracts were the practical parts that significantly inhibited the xylene-induced auricular inflammation in rats and carrageenan-induced footpad inflammation in mice. They increased the celiac capillary permeability of mice as well. In another study, the water, ethanol, ethyl acetate, and butanol of *F. pumila* in the ear swelling mouse model and acetic capillary permeability assay exhibited active anti-inflammatory effects. Then, the methanol extract of *F. pumila* had a similar inhibitory effect as indomethacin on carrageenan-induced paw edema in mice and had an analgesic effect demonstrated by recording the writhing response and licking time in mice models (Qi et al. 2021).

Petroleum ether extract from *Ficus binnendijkii* leaves in a dose of 50 and 100 mg/Kg body weight inhibited the edema on mice paw starting from the first hour by 26.78 and 24.85% of change respectively and during total fifth hour by 19.08 and 12.42% of the difference. This extraction also showed analgesic activity. Furthermore, petroleum ether considerably inhibited the number of writhing responses in a dose-dependent manner within 30min of acetic acid injection (El-Rafie et al. 2016).

The anti-inflammatory activity of the compounds found in *F. elastica* leaves was predicted based on their structural properties. All compounds found in *F. elastica* leaves had a high probability as an anti-inflammatory, except eleutheroside B Myricitrin had the highest probability as an anti-inflammatory (0.76 respectively). Therefore, these compounds may be beneficial for treating Preeclampsia

(PE) through its anti-inflammatory and inhibition of beta-adrenergic receptor 2, ADRB2 (Ginting et al. 2019).

The hydroalcoholic leaves extract of *F. microcarpa* was screened for analgesic and anti-inflammatory activities in experimental animals, Sprague Dawley rats, and Swiss mice. Hydroalcoholic of the test drug at doses of 250 mg and 500 mg per body weight showed significant analgesic activity through various models of nociception. That extract also showed important anti-inflammatory activity in carrageenan and formaldehyde-induced hind paw edema methods. At the same doses (500 mg/kg body weight) exhibited 29.28% (carrageenan) and 31.06% (formaldehyde) inhibition still below the standard drug group (Kumar et al. 2021).

The aqueous bark extract from *F. religiosa* exhibited an anti-inflammatory effect in acute and chronic models of inflammation. The extract also protects mast cells from degranulation induced by various degranulation. Furthermore, methanol extract of *F. religiosa* leaves inhibited LPS-induced NO and proinflammatory cytokines in a dose-dependent manner. Five different fractions isolated from *F. religiosa* dried leaves at the dose level of 20, and 40 mg/kg were tested for an anti-inflammatory test. Two fractions (FRI and FRIII) were found more effective in preventing carrageenan-induced rat paw edema, cotton pellet granuloma formation, acetic acid-induced writhing, and increasing latency period in the tail-flick method (Al-Snafi 2017).

*Ficus thonningii* has been reported to possess analgesic activity comparable to aspirin in both peripheral and central induced pain. In addition, the methanolic extracts of *F. thonningii* had a percentage inhibition, 79.7%, close to aspirin, 80%. Meanwhile, the anti-inflammatory activity of *F. thonningii* has been validated using egg albumin and carrageenan-induced edema in rats. Phytol, the aliphatic diterpene found in *F. thonningii*, has anti-inflammatory effects and has been reported as a potential therapeutic agent for treating rheumatoid arthritis and possibly asthma (Dangarembizi et al. 2013).

The inhibition of hypotonicity induced human red blood cells (HRBC) membrane lysis was taken to measure the anti-inflammatory activity. The methanolic extract of *F. virens* bark effectively inhibits the heat-induced hemolytic of HRBC at different concentrations. The maximum inhibition is 64% at 200 µg/ml (Ramadevi et al. 2014). Ethanol extract leaves of *F. virens* at 250mg/kg and 500 mg/kg body weight inhibited inflammation 63.3% and 76.7% with a carrageenan-induced method in Wistar rats (Fitriansyah et al. 2015).

Ethanol extract of *F. benghalensis* bark, a young and mature plant, possesses anti-inflammatory activity. The ethanol extract of the younger plant has relatively more anti-inflammatory activity than the mature plant. At the dose level of 300 and 600 mg/kg/day p.o. younger plants caused a 37.64% and 69.04% reduction in paw volume after 3 h in the induced paw edema model. While in the cotton pellet granuloma model, more immature plants exhibit a 19.27% and 39.03% reduction in paw volume after three hours (Khaliq 2017).

## ANTIDIABETIC ACTIVITY

Diabetes is a chronic metabolic disease characterized by elevated blood glucose levels, which leads over time to severe damage to the heart, blood vessels, eyes, kidneys, and nerves. There are 2 types of diabetes. The common ones, namely diabetes type 2, usually occur in adults when the body becomes resistant to insulin or doesn't make enough insulin. The other one, namely diabetes type 1, is a chronic condition in which the pancreas produces little or no insulin by itself.

Scientific research on plant products used as hypoglycemic agents in traditional medicine has revealed the active principles and the anti-hyperglycemic mechanisms of action of many plant products used traditionally for this purpose. Natural anti-hyperglycemic agents act by stimulating pancreatic beta cells to produce insulin, decreasing gluconeogenesis and increasing peripheral glucose utilization, delaying glucose absorption, and reducing glycated plasma protein concentration.

Many experimental studies have demonstrated the anti-hyperglycemic efficacy of *Ficus*. In this review, several species possess potential antidiabetic activity.

Ethanol extract of *F. carica* leaves reduced the increased blood glucose levels in diabetic rats to the average level. At the same time, the aqueous extract of leaves was reported to reduce the plasma glucose levels in diabetic rats via increased glucose uptake by skeletal muscle (Li et al., 2021).

Two fruit varieties of *F. deltoidea* (var. *angustifolia* and var. *kunstleri*) were extracted using water and partitioned using ethyl acetate. Antidiabetic activities were assessed based on the ability of the samples to inhibit yeast and mammalian alpha-glucosidase and alpha-amylase. All extracts of two variations of *F. deltoidea* showed antidiabetic activity. The water fraction of *F. deltoidea* var. *angustifolia* showed the highest percentage of alpha-glucosidase inhibition while having the highest amount of protein (Misbah et al., 2013). In another animal study, the ethanol, methanol, and hot aqueous extracts of *F. deltoidea* reduce postprandial hyperglycemia following sucrose administration at a dose of 1000mg/kg. However, scientific evidence to confirm its efficacy is still lacking (Ramamurthy et al., 2014).

The fruits of *F. palmata* were extracted using methanol and fractionated using n-butanol, ethyl acetate, methanol, and water. All four fractions were evaluated for alpha-amylase and alpha-glucosidase inhibitory activity at different concentrations (50-500 µg/ml). They all exhibited inhibitory action against alpha-amylase and alpha-glucosidase enzymes in a concentration-dependent manner. The highest inhibitory activity was MeOH fraction with 90.63% against alpha-amylase and 93.43% against alpha-glucosidase at 500 µg/ml (Anjum and Tripathi 2019b).

*Ficus hispida* leaves methanolic extract was designed to evaluate acute and chronic effects of antidiabetic potential against alloxan-induced diabetic rats. In the acute study, the hypoglycemic potency of methanol extract of *F. hispida* was assessed by an oral glucose tolerance test (OGTT). In addition, the extract in different doses was screened for its

antidiabetic activity in the chronic study. The results showed that the extract at a 400 mg/kg dose exhibited a significant reduction in blood glucose level. In the chronic model, the methanol extract effectively reduced blood glucose levels at 200 and 400mg/kg doses (Ravichandra and Paarakh 2014). In other studies, ethanolic extract of *F. hispida* bark reduced blood glucose levels and enhanced the peripheral uptake of glucose. Moreover, the methanolic extract of *F. hispida* leaves exhibited potent antidiabetic activity by decreasing blood glucose, serum glutamate oxaloacetate transaminase, triglyceride, and cholesterol levels in alloxan-induced diabetic rats (Cheng et al. 2019).

The stem's bark extract of *F. racemosa* was evaluated against alpha-amylase and alpha-glucosidase enzyme to know the antidiabetic activity in vitro. The stem bark was extracted at different concentrations using several solvents, hexane, chloroform, ethyl acetate, acetone, and methanol. The chloroform extract of *F. racemosa* showed the highest alpha-amylase inhibitory activity. Chloroform and acetone extracts exhibited the most increased alpha-glucosidase inhibitory activity (Vijayagiri and Mamidala 2013). In another study, the methanolic roots of *F. racemosa* showed hypoglycemic activity in Swiss-albino rats. That extract has statistically significant blood glucose lowering activity at a dose of 400mg/kg (Mohiuddin and Lia 2020).

The methanolic extraction and four fractionated (n-butanol, ethyl acetate, methanol, and water) of *F. auriculata* fruits were evaluated to alpha-amylase and alpha-glucosidase inhibitory activity. All fractions possess inhibitory activity. However, the methanolic fraction had the highest inhibitory action in alpha-amylase and alpha-glucosidase with above 90% and IC50 values of 161.73 and 103.43, respectively, compared with acarbose (Anjum and Tripathi 2019a).

The aqueous extract of *F. pumila* fresh and dried leaves were studied to known inhibitory activity against alpha-amylase. The test compared to acarbose (inhibitory value of 92%). Dried leaves of *F. pumila* showed the highest inhibitory activity with a value of 91.91% (Fresga et al., 2018). In another study, a review from Qi et al. (2021) revealed that the extracts from the rhizome of *F. pumila* have alpha-glucosidase activity inhibitory with an IC50 up to 0.018 g/L, which is better than the effect of acarbose. Then, the pectic polysaccharide obtained from fruits of *F. pumila* significantly ameliorated hyperglycemia and improved hepatic glycogen metabolism.

*Ficus drupacea* possesses an alpha-glucosidase inhibitory effect with 39% at a 100 µg/mL concentration. Further research, ten compounds isolated from *F. drupacea* leaves exhibited alpha-glucosidase inhibitory activity at concentration 100 µM compared with acarbose. Oleanolic acid showed the most potent inhibitory activity with 49.9% inhibitory activity, followed by friedelin and epilupeol acetate (Kiem et al., 2013).

The methanolic extract of *F. microcarpa* leaves possesses significant antidiabetic activity in an alloxan-induced diabetic animal model. Therefore, two model studies are used, acute and chronic effects, in induced diabetic rats. Hypoglycemic potency of methanolic extract was assessed by OGTT in the acute study, while extract at

different doses was screened for its antidiabetic potency in 21 days. The 400mg/kg extract has shown a significant reduction in blood glucose level in OGTT and more effective reducing blood glucose levels in the chronic model (Ravichandra and Paarakh 2011).

The aqueous root bark extract of *F. religiosa* in three doses (25,50, and 100 mg/kg) was administered orally in glucose-loaded and streptozotocin-diabetic rats. The reduction of blood glucose was highly evident in 50 and 100 mg/kg. In comparison, the bodyweight of streptozotocin-diabetic rats increases, and serum insulin and glycogen amount (Devanesan et al., 2018).

Anti-hyperglycemic activity of alpha-amyrin acetate isolated from aerial of *F. benghalensis* was testified in STZ-induced diabetic rats and db/db mice at a 50 mg/kg dose p.o, compared with metformin. The average anti-hyperglycemic effect of that compound on glucose tolerance in db/db mice was calculated to be around 35.6%, while in STZ-induced diabetic rats, only 22.3%. The stem bark extract showed relatively hypoglycemic activity in alloxan-induced diabetic rats rather than aerial roots at the same dose level of 100mg/kg (Khaliq 2017).

## HEPATOPROTECTIVE

Hepatoprotection or antihepatotoxicity is the ability of a chemical substance to prevent damage to the liver. Hepatoprotective effects are attributed to its antioxidant activity, which restores the activity of superoxide dismutase, catalase, and glutathione peroxidase to normal levels, and increases glutathione content and levels of lipid peroxidation and hydroperoxides in the liver.

The extracts and constituents of *F. carica* leaves could reverse the liver injury. In vivo hepatoprotective study showed that ethanol extract of leaves reduces the fibrosis and inflammation in carbon tetrachloride-induced liver injury in mice. In addition, the methanol and petroleum ethyl extracts from leaves normalized the dysregulated serum levels in a rat liver (Li et al., 2021).

Treatment with *F. palmata* leaves extract showed dose-dependent reduction levels such as AST, ALT, GGT, ALP, and total bilirubin in CCl4 hepatic toxicity in Wistar rats. Rat treated with 400 mg/kg body weight showed a significant reduction indicating good protection against liver damage induced by CCl4. While fractions were tested for hepatoprotective effect showed the best protective effect was obtained with petroleum ether and chloroform fractions (Alqasoumi et al. 2014).

*Ficus lyrata* leaves extract in ethanol was fractionated by butanol showed higher hepatoprotective in vivo. In addition, treatment with *F. lyrata* butanol fraction decreased AST, ALT, GGT, and total protein levels compared to the CCl4 (Awad et al. 2018).

The hepatoprotective effect of four extracts (petroleum ether 60-80, ethyl acetate, ethanol, and aqueous) of *F. microcarpa* bark was studied in chronic ethanol-induced liver damage. The protective potential is measured by monitoring biochemical parameters and histopathological alterations. Results showed the ethyl acetate extract of *F.*

*microcarpa* bark extract produces significant hepatoprotection by stabilizing the biochemical parameters in a dose-dependent manner, comparable to that of standard drug silymarin (Surana et al. 2017).

The hepatoprotective effect of methanolic extract of *F. religiosa* (100, 200 and 300 mg/kg bw, po) was studied in isoniazid-rifampicin and paracetamol-induced hepatotoxicity in rats. Administration of methanolic extract significantly prevented isoniazid-rifampicin and paracetamol-induced elevation in serum liver marker enzymes and TBARS level of rats. Furthermore, the latex of *F. religiosa* in cisplatin-induced liver injury in Wistar rats showed hepatoprotective. It's marked by increasing multiple serum tests (Al-Snafi 2017).

The fruit of *F. benghalensis* was extracted with different solvents such as petrolechemical ether, chloroform, ethyl acetate, ethanol, and water. The ethanol extract of *F. benghalensis* fruit at doses 100, 250, and 500 mg/kg were used to observe its hepatoprotective effect against standard molecule, Silymarin. The ethanol extract showed promising activity in restoring reduced enzyme levels compared to the standard drug, which also fixed the altered status of catalase very nearby in CCl<sub>4</sub> induced liver damage. While in acetaminophen-induced liver damage, the ethanol extract showed moderate activity as well as erythromycin-induced liver damage (Karmakar et al. 2020).

## ANTIBACTERIAL ACTIVITY

*Ficus carica* showed that the extracts and constituents of leaves possess antibacterial activity in many studies. Based on Li et al. (2021), the leaves displayed excellent activity against gram-negative bacteria: *Chromobacterium violaceum* and *Pseudomonas aeruginosa*. Vanillic acid showed activity against *Enterobacter cloacae* via destroying the cell membrane. Ethanol extract of leaves showed inhibitory activity against gram-positive bacteria, *Enterococcus faecalis*. Meanwhile, the methanolic extract showed antibacterial activity against *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus pyogenes*. Dichloromethane extract of leaves was also reported to inhibit the activity of quorum sensing between bacteria and thus prevent the adaptation of bacteria to the environment.

*Ficus deltoidea* showed a wide range of antibacterial activity. The leaf extracts displayed growth inhibition against diverse gram-positive and negative species: *Escherichia coli*, *Bacillus subtilis*, *S. aureus*, *E. faecalis*, *Streptococcus mutans*, *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, and *Fusobacterium nucleatum* (Silalahi 2019). That also inhibits *S. epidermidis*, *P. aeruginosa* (Krisyanella et al. 2009), and against fish pathogen *Citrobacter freundii* (Tkachenko et al. 2016b).

The in vitro antibacterial activity of petroleum ether, chloroform, ethyl acetate, acetone, methanolic, ethanolic, and water extracts from *Ficus palmata* was tested against ten bacterial strains by disc diffusion method. The

ethanolic bark extracts of *F. palmata* showed significant activity (18mm) against *S. aureus* (Joshi et al., 2014). The magnitude of antibacterial activity of pure latex and its methanolic and ethanolic extracts were found to be more against *E. coli*, a gram-negative bacterium, rather than *S. aureus* (Kumar et al., 2013).

The bark and leaves extract of *Ficus coronata* have been shown to possess antibacterial properties against methicillin-resistant *S. aureus* (MRSA). Five fractions separated by column chromatography from ethyl acetate bark and leaf displayed bactericidal activity against MRSA. Twenty-eight compounds from the thin layer chromatography (TLC) band had molecular masses and fragmentation patterns which precluded their identification, so their structures are likely to be novel. The isolated pure compounds could be tested to determine whether they are responsible for the antibacterial activity against MRSA, possibly leading to discovering potentially new drug molecules active against multidrug-resistant microorganisms (Smyth et al., 2012).

*Ficus obscura* bark extract showed a potent growth inhibition against *E. coli* and *S. mutans* in higher concentrations. But it is not significant against *Propionibacterium acne* in many extract concentrations (Zarta et al. 2020).

The leaves extract of *F. fistulosa* possesses inhibitory activity against gram-positive and harmful bacteria, *E. coli*, *S. mutans*, *S. aureus*, *B. subtilis*, *Klebsiella pneumoniae*, and *P. aeruginosa*. In addition, the aqueous extract and methanolic extract of *F. fistulosa* leaves possess inhibitory activity at 0.4 mg/well against all bacterial strains (Raka et al., 2019).

Antibacterial activity from methanol, acetone and aqueous extract of all parts of *F. hispida* was tested against four bacterial strains, *Enterobacter aerogenes*, *P. aeruginosa*, *E. coli*, and *S. aureus*. Methanol extract showed better antibacterial activity than others (Dhawale and Ghyare 2016). In another study, the water, methanolic, and ethyl acetate extracts of *F. hispida* leaves possessed moderate inhibitory effects against gram-positive *S. aureus* and gram-negative *E. coli* with zones of inhibition above 13 mm. Ethyl acetate extract appeared to be more sensitive than the standard antibiotics streptomycin (Cheng et al. 2019).

The antibacterial activity is also found in *F. racemosa* in the stem, leaves, and fruit extracts. In stem extract with dichloromethane and hexane, antibacterial was carried out against *Staphylococcus* and *Bacillus* species. Leaves extract using petroleum ether, toluene, and ethanol showed antibacterial activities against several species of bacteria, *E. coli*, *B. pumilus*, *B. subtilis*, *P. aeruginosa*, *S. aureus*, *K. pneumoniae*, *S. mutans*, and *Actinomyces viscosus*. The ethanol extract showed 10µg/ml and hydroalcoholic extract were suitable for antimicrobial activity. The methanolic extract from the fruit also displayed antibacterial activity against gram-negative and gram-positive bacteria (Chaware et al. 2020).

Ethanolic extract of fruit from *Ficus septica* has vigorous antibacterial activity against *S. aureus*. The

highest antibacterial activity was 175mg concentration using the good method (Bawondes et al., 2021).

The antibacterial activity of methanol and chloroform leaf extracts of *F. auriculata* was tested in vitro against two bacterial pathogens, *E. coli*, and *Salmonella typhimurium*. The methanolic extracts showed the highest zone of inhibition against *E. coli* at 18.33 mm. In comparison, leaf chloroform extract showed the highest zone of inhibition against *S. typhimurium* at 17.67 mm (Kumari et al. 2018). In another study, the antibacterial activity of methanolic fruit extract of *F. auriculata* was active against seven different bacteria by the disc diffusion method. The methanolic fruit extract showed a wide range of activity against all bacteria, *Phaseolus vulgaris*, *S. epidermidis*, *E. coli*, *K. pneumoniae*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, and *P. aeruginosa*. The methanolic extracts were more active against *M. genitalium* and *S. epidermidis* at 28 mm (Raja et al., 2021).

Subfraction of methanol and n-hexane fruit extract from *F. variegata* showed antibacterial activity against *S. aureus* (Ningsih et al. 2016). Methanolic and n-butanol bark extract also showed antibacterial activity against *E. coli* and *S. aureus* diffusion method. The effective concentration of methanol extract was 10% for an antibacterial agent (Saleh et al. 2016).

The extraction of fresh and dried leaf, stem, root, and fruit of *F. pumila* showed antibacterial activities against *B. subtilis*, *Bacillus cereus*, *Micrococcus luteus*, *E. faecalis*, *S. aureus*, and *Proteus mirabilis*. The best antibacterial activity was exhibited on dried root extract (Noronha et al., 2014). In another study reviewed by Qi et al. (2021), the stem and leaf acetate extract showed a 95.83% inhibition rate against *S. aureus* but had a weak inhibitory activity against *Staphylococcus albus*, *B. cereus*, and *B. subtilis*. In addition, the ethanol extract of *F. pumila*'s stems and leaves had antibacterial effects on *S. aureus*, *E. coli*, and *Candida albicans*, with the best antibacterial effect being on *S. aureus*. Moreover, the ethanolic leaves extracts of *F. pumila* showed antibacterial against fish pathogen *Aeromonas hydrophila*.

The antibacterial assay of *Ficus sagittata* leaves with methanol extract indicated this plant exhibited antibacterial activity against seven bacteria, *B. subtilis*, *S. aureus*, *E. coli*, *P. aeruginosa*, *Salmonella typhi*, *B. cereus*, and *Salmonella paratyphi*. The extract showed no zone of inhibition against *S. paratyphi* but showed potent activity against *E. coli* with a zone of inhibition of 23 mm at a concentration of 1000µg/disk (Zaman et al. 2016). *Ficus sagittata* leaves extract at two different concentrations, 1000µg/disc and 700µg/disc, showed significant zone of inhibitions against several bacteria *S. aureus*, *B. subtilis*, *B. cereus*, *S. typhi*, *S. paratyphi*, *E. coli*, and *P. aeruginosa*. The highest inhibition against *P. aeruginosa* at concentration 1000µg/disc (Hasan et al. 2015).

The ethanol extract, chloroform, ethyl acetate, and acetone of the fruits of *F. benjamina* have shown a remarkable inhibition zone against *Streptococcus pyogenes*, *S. aureus*, *E. coli*, and *P. aeruginosa*. The potency was comparable to the control antibiotic, chloramphenicol, possessing inhibitions against *E. coli* of 25 mm, *S.*

*pyogenes* of 27 mm, *S. aureus* of 24 mm, and *P. aeruginosa* of 19 mm, respectively 30mg/ml (Rahama and Mashi 2015). In another study review by Mahomoodally et al. (2019), the concentrates and divisions of stem, root, and leaves displayed vast antibacterial action against four bacterial. Methanol concentrate showed movement against 22.63 mm against *P. aeruginosa*, and the n-butanolic part showed motion in opposition to 22.83 in opposition to *B. subtilis* of stem indicated generous gesture. The n-hexane, chloroform, and ethyl acetate derivation grew mild estimation of DIZ with most intense well worth revealed by way of ethyl acetate derivation (16.88 mm)

*Ficus drupacea* stem bark with n-hexane extraction and its isolated compounds exhibited antibacterial activities against several gram-positive and gram-negative bacteria, *B. cereus*, *S. aureus*, *Listeria monocytogenes*, *Mariniluteicoccus flavus*, *E. coli*, *S. typhimurium*, *P. aeruginosa*, and *E. cloacae*. But the antibacterial potential of isolated compounds was much higher than the crude extract in general. The most sensitive bacterium to isolated compounds was *B. cereus*, while the most resistant one was *E. cloacae* (Yessoufou et al., 2015).

*Ficus elastica* showed high antimicrobial activity in the methanolic leaves extract against several bacteria such as *B. cereus*, *P. aeruginosa*, *E. coli*, and *K. pneumonia*, whereas showed no antibacterial activity against *S. aureus* (Preeti et al. 2015). The CHCl<sub>3</sub>/MeOH 1:1 crude extract and pure compounds of the aerial root barks of *F. elastica* were screened for their antibacterial activity using the micro broth dilution method against several bacteria, *E. faecalis*, *S. aureus*, *Staphylococcus saprophyticus*, *S. epidermidis*, *E. coli*, *K. pneumoniae*, and *S. typhi*. The extracts showed rather good bactericidal and bacteriostatic activities. In particular, the activities of crude extract were better against *S. saprophyticus* and *K. pneumonia*. In comparison, the compounds showed excellent antimicrobial activities against all the tested bacterial strains (Mbosso et al., 2012). Antibacterial activity of wild fig fruits latex was tested using an agar well diffusion method. The results revealed that all bacteria species: *S. aureus*, *S. pyogenes*, *E. coli*, *P. aeruginosa*, *P. mirabilis*, *K. pneumonia*, *Salmonella* spp., and *Serratia* spp., are susceptible to fig latex. It was examined by the presence of inhibition zone diameter (Faisal 2017).

The ethanolic extract of *Ficus lyrata* leaves exhibited moderate activity against the gram-positive bacteria (11 mm of inhibition zone diameter for *S. aureus*) and the gram-negative bacteria (10.3 mm for *E. coli*). *Klebsiella pneumonia*, *P. aeruginosa*, *S. aureus*, and *S. pneumonia* appeared to be less sensitive to extracts (Tkachenko et al. 2016a). The fruit extract from *F. lyrata* also has antibacterial activity against *P. aeruginosa*, *E. coli*, and *B. subtilis* but not as high as the leaves extract (Wira et al. 2018).

The antibacterial activity showed in *F. religiosa* leaves extracted by petroleum ether, water, ethyl acetate, and ethanol. Those extracts exhibited antibacterial against gram-positive and harmful bacteria, *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa* at a concentration of 100µg/ml. The antibacterial activity of ethanol extract is better than

another (Chavan et al., 2019). In other studies, reviewed by Devanesan et al. (2018), the ethanolic and aqueous extracts of *F. religiosa* leaves showed antibacterial activity against many bacteria, *S. paratyphi*, *S. aureus*, *Shigella dysenteriae*, *P. aeruginosa*, *B. subtilis*, *E. coli*. Meanwhile, chloroform extract of fruits showed antibacterial against *Azotobacter chroococcum*, *Bacillus megaterium*, *B. cereus*, *Lactococcus lactis*, *E. faecalis*, and *K. pneumonia*.

Synthesis of silver nanoparticles (AgNPs) using *Ficus retusa* aqueous leaf extract was checked against a few gram-negative and positive bacteria, *Aeromonas* sp., *E. coli*, *K. pneumonia*, *B. subtilis*, and *S. epidermidis*. The concentration of AgNPs determined using ICP-MS analysis was 588 ppm. *Staphylococcus epidermidis* was most sensitive to the synthesized AgNPs as inferred by the size of the inhibition zone, 10.5 mm (Singhal et al., 2017).

The extracts and fractions of *Ficus thonningii* showed broad-spectrum antibacterial activity on susceptible and multi antibiotic-resistant isolates. The ethyl acetate leaves extract showed potent bactericidal activity in a concentration-dependent manner on the microorganisms, with 100% bactericidal activity at 25 mg/mL within six hours for *S. aureus* rather than against *E. coli* for 24 hours. Leaf extracts of *F. thonningii* possess potent antibacterial activity and may help develop chemotherapeutic agents (Coker and Oiakhenah 2019).

The crude extract of *Ficus natalensis* with n-hexane, ethyl acetate, and methanol extraction showed antibacterial activity against *E. coli*, *S. pyogenes*, and *Helicobacter pylori*. The ethyl acetate extract showed a higher zone of inhibition. The most increased activity was recorded on *E. coli*, with a zone of inhibition at 28 and the lowest at 25 mm on *S. aureus* (Sheyin et al. 2018). In another study, crude extraction with ethanolic extract of *F. natalensis* leaves showed intermediate antibacterial activity against *Pseudomonas fluorescens* (fish pathogens), causing a zone of inhibition at least 10-12 mm for 200 µL bacterium strain. That extracts also showed intermediate antibacterial against *Y. ruckeri* with a lower inhibition zone (Tkachenko et al. 2018).

The methanolic extracts of the leaves of *F. benghalensis* were testified for their antimicrobial activity by using the diffusion method at a dose level of 100 µg/ml. That extracts and their compounds exhibited antibacterial activity against *B. cereus* and *P. aeruginosa*. Aqueous extract stem bark showed maximum antibacterial activity against *B. subtilis*, *P. aeruginosa*, *K. pneumonia*, *S. aureus*, and *E. coli*. Hydroalcoholic extract of stem bark also showed antibacterial activity against *A. viscosus* (Khaliq 2017).

## ANTIFUNGAL ACTIVITY

The antifungal activity of *F. hirta* ethanolic extracts of fruit and isolates against *Penicillium italicum* was evaluated by the Oxford Cup method. The antifungal activities of all of the isolates were tested at two concentrations (2.0 and 4.0 mg/mL). The results showed that the pinocebrin-7-O-beta-D-glucoside (compound 8)

possesses antifungal activity with the DIZs of 19 mm and 24 mm at both concentrations, respectively. Compound 8 exhibited more than 90% inhibitory effect against *P. italicum* at 400 µg/mL, while a 100% inhibition rate was achieved at 800 µg/mL (Wan et al., 2017). In another study, nine monosubstituted benzene derivatives isolated from the *F. hirta* fruits were evaluated for antifungal activity against *P. italicum*. Compound 1 exhibited more potent antifungal activity than ethanol extract of *F. hirta* fruits at an equivalent concentration (Wan et al., 2016). The fruit extract of *F. hirta* also showed antifungal activity against *P. italicum*, *Penicillium digitatum*, *Aspergillus niger*, *Aspergillus oryzae*, *Saccharomyces cerevisiae*, and *Candida Utilis*. The results showed that *F. hirta* extract (10 mg/mL) had to vary in vitro antifungal activity (diameters ranged from 12.25 to 41.75 mm). The acetone extract of *F. hirta* had excellent activity against all fungal strains and was pretty strong against *A. niger* and *C. utilis* (Chen et al. 2020).

Dichloromethane and hexanes of *F. racemosa* stem possess antifungal activity against *Saccharomyces* spp. and *C. albicans*. Stem bark extracts were evaluated using Kirby Bauer disc diffusion assay (Chaware et al. 2020).

The leaves extract of *F. septica* was evaluated for antifungal activity against *Colletotrichum acutatum*, the cause of anthracnose disease on the chili pepper. The in vitro experiment was conducted on potato dextrose medium (PDA) and potato dextrose broth (PDB) medium in fifteen extracts concentrations, ranging from 0.1 to 5%. The antifungal activity was determined based on the effects of plant extract on fungal growth, spore formation, germination, and total biomass. The result with leaves extracts significantly inhibited the fungal growth, spore's formation spore's germination, and fungal biomass of *Colletotrichum* spp. (Sudirga et al. 2014). Furthermore, the SEM and TEM analyses and mode of action leaves extract confirmed that the growth of fungus *C. acutatum* was inhibited and controlled through the diffusion process into the fungal cells and then interfered with the structure of the cell organelles. Consequently, the cells suffer from lysis and become empty (Sudirga and Suprapta 2021).

Antifungal activity of aqueous extract of *F. benghalensis* stem bark, leaves, and root was evaluated by agar diffusion at a dose level of 30 mg/ml using nystatin as a reference standard. The stem bark extract showed antifungal activity against *Trichophyton rubrum* and *C. albicans* (Khaliq 2017).

## ANTIMALARIA ACTIVITY

*Plasmodium* parasites cause malaria. The parasites are spread to people through the bites of infected female *Anopheles* mosquitos. Five parasite species cause malaria in humans. *Plasmodium falciparum* remains the most dangerous species and causes the most lethal form of malaria. The best available treatment is artemisinin. However, the natural products remain essential potential sources of new and selective substances for treating malaria, including *Ficus*.

The MeOH extract of *F. septica* twigs exhibited potent anti-malarial activity. The isolation of chemical compounds, known as phenanthroindolizidine alkaloid, is evaluated as anti-malarial potential drugs. The compound from phenanthroindolizidine showed a vigorous growth-inhibiting activity on malaria *Plasmodium*, including *P. falciparum*. These results suggest that the alkaloid compound from *F. septica* twigs may be a therapeutic lead of the new pharmacophore of anti-malarial (Kubo et al. 2016).

The crude petroleum ether and hydroalcoholic extract of *F. benjamina* leaves were evaluated for anti-plasmodial activity by schizont maturation inhibition assay using 3D7 *Plasmodium* strains. The petroleum ether extract of *F. benjamina* leaves showed the most promising inhibitory effect on the growth of schizont with IC<sub>50</sub> 14.5 µg/ml. The hexane and chloroform fraction also possess high antiplasmodial activity (IC<sub>50</sub> 4.0 µg/ml and 7.8 µg/ml, respectively) (Mukhtar et al., 2018). In another study, an unsaponified fraction of petroleum ether extract of *F. benjamina* leaves was subjected to silica gel column chromatography, which isolated two triterpenoids. These compounds were evaluated for antiplasmodial activity by schizont maturation inhibition assay using 3D7 *Plasmodium* strains. Ursolic acid and lupeol were found to exhibit a significant anti-plasmodial effect with an IC<sub>50</sub> of 18 µg/ml and 3.8 µg/ml, respectively (Singh et al. 2018).

The investigation of in vivo anti-plasmodial activity of the bark of *F. elastica* was conducted to examine its impact on mice infected with the malaria parasite. In vivo, cell-growth inhibition assessment of the graded doses (100, 200 and 400 mg/kg) of *F. elastica* tree bark methanol extract against *Plasmodium berghei* strain revealed a significant rise in the inhibitory activity (68%, 70%, and 71%) (Ifijen et al. 2020).

The zinc oxide nanoparticles (ZnO NPs) and titanium dioxide nanoparticles (TiO<sub>2</sub>NPs) were synthesized using the aqueous leaf extract of *F. religiosa*. The synthesized nanoparticles were tested as larvicidal against the larvae of *Anopheles stephensi*. Probit analysis observed the larvicidal mortality after 24 h and 48 h. The larvae of *A. stephensi* were found highly susceptible against the ZnO NPs than the TiO<sub>2</sub>NPs, and aqueous leaves extract. The highest mortality was observed in ZnO NPs against first to third instars (LC<sub>50</sub> 50.75 and 5 ppm) and 100% in fourth instars (Soni and Dhiman 2020).

## ANTI-ULCERS ACTIVITY

Peptic ulcers are open sores that develop on the inside lining of the stomach and the upper portion of the small intestine. Peptic ulcers include gastric ulcers and duodenal ulcers. The leading cause of ulcers is infection with *H. pylori*, a gram-negative *Bacillus*. This microorganism secretes cytotoxins that act directly on the gastroduodenal mucosa, causing local inflammation that is subsequently chronic. Another cause is from long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs).

The objectives of anti-ulcer treatment are a rapid improvement of the symptoms, healing of the ulcer, prevention of recurrences and complications, also eradication of *H. pylori*. Herbal remedies support the alleviation of ulcer symptoms and support the fight against *H. pylori* infection; *Ficus* is one of the natural alternatives.

*Ficus palmata* whole leaves extract was tested at 200 and 400mg/kg body weight for possible anti-ulcer effect against 80% ethanol-induced lesions. Protection against ulcers by *F. palmata* extract was dose-dependent and highly statistically significant. The best defense was observed with the higher dose of the total extract, where the ulcer index is 2.00. Good protection also resulted from treatment with petroleum ether and chloroform fraction with ulcer indexes of 3.33 and 4.00, respectively (Alqasoumi et al., 2014).

The effect of chloroform, ethyl acetate, and ethanolic extract of *Ficus nervosa* bark was investigated in rats to evaluate the anti-ulcer activity by using aspirin, alcohol, and pyloric ligation models induced gastric ulcer. All the extracts in different doses reduced the ulcer index, gastric volume, free acidity, total acidity, and raised gastric pH significantly. The 200mg/kg of the ethanolic extract showed almost similar effects to ranitidine, a standard drug, in reducing the gastric volume, acidity of the gastric juice, gastric free edge, and the mean ulcer score. The maximum effect of ulcer protection in aspirin-induced ulcers was produced at 200 mg/kg from ethanolic extract (70.46%). While in the alcohol-induced ulcer, the ethanolic extract also reduced the severity of the ulcer and caused a reduction of ulcer index with maximum ulcer protection of 67.42% (Devi et al., 2012).

The ethanolic extract *F. racemosa* latex is evaluated using in-vitro H<sup>+</sup>K<sup>+</sup>ATPase inhibitory activity spectrophotometrically. Ethanolic latex extract at 50 µg/ml showed a comparable proton pump inhibitory effect with standard Omeprazole on goatskin gastric mucosal homogenate (Sathish et al. 2018).

The ethanolic extract of *F. religiosa* leaves has anti-ulcer activity and is proved by arresting the production of ulcers encouraged by stress. The 250mg/kg and 500mg/kg ethanolic extract showed a preventive effect against ulceration, and it is not toxic even at moderate-high concentrations (Devanesan et al., 2018). The anti-ulcer potential of the ethanol extract *F. religiosa* leaves was investigated against in vivo aspirin-induced ulcer and pylorus ligation assays in Swiss albino rats by oral administration. The results indicated that the extract significantly decreased gastric acid secretions, free acidity, total acidity, and ulcer index. The ethanol extract of stem bark also showed anti-ulcer activity. Aqueous-ethanol extracts of stem bark completely inhibited the growth of *H. pylori* at 500 µg/ml (Al-Snafi 2017).

Aqueous extracts of *F. thoningii* bark were evaluated on Wistar rats to know its anti-ulcer activity. The experimental model used to induce gastric ulcers was absolute ethanol 100%. As a result, in the preventive anti-ulcer study, the percentage protection of the mucous membrane was 81.18% at 500 mg/kg dose, which means it had a promising gastro-protective activity both

preventively and curatively (Fokunang et al. 2019). In another study, the aqueous fruits extract of *F. thonningii* was evaluated against ethanol and hydrochloric acid solution. The result showed the aqueous extract exhibited a dose-dependent increase in ulcer-preventive activity with the three treatment aqueous extracts doses, 125, 250, and 500 mg/kg (Uku et al. 2020).

### WOUND HEALING

Various substances of plant origin have been used in the folk medicine of different cultures as wound healers, some of which have been identified pharmacologically to exert their effects on the epithelial tissues. The research from Singh et al. (2014), *F. hispida* methanolic extract from leaves enhances rats' wound healing. The healing proceeds with an increase in the number of collagen tissues. New tissues are formed in the wound area, and the wound starts healing with a significant increase at doses 75 and 150 mg/kg body weight. In another study, reviewed by Cheng et al. (2019), oral administration of the ethanolic extract of *F. hispida* showed marginal dryness with the regeneration of the healing tissue, and the wound area also decreased. In addition, the extract of *F. hispida* increased the dry and wet granulation tissue weight and granulation tissue breaking strength.

The effects of *F. septica* leaves extract has been performed on topical curing of cow skin to determine the epithelial capability in cattle. Three treatment groups of cows given the extract with concentration levels of 50%, 75%, and 100% were topically 2 times daily. The results showed that *F. septica* leaves extract has better wound disposal ability with a mean percentage of decreasing wound value of 24.99% (Supriyanto 2017).

The fruit of *F. variegata* with various concentrations (1%, 2.5%, and 5%) formulated with Na-CMC gel and HPMC was evaluated by organoleptic, homogeneity, pH, spread-ability, and viscosity assays to determine gel formulation to be wound healer. The result displayed that 5% of *F. variegata* extract has the best concentration with a pH value of 4.5, spreadability of 5.3 cm, and viscosity value of 5.01 Pa.s (Zakaria et al. 2017).

Plant latex proteases (PLPs) are considered an integral part of herbal wound care as it interferes at different phases of the wound healing process. *Ficus drupacea* exhibited potent fibrinolytic activity. Drupin, a cysteine protease responsible for fibrinolysis, was purified from *F. drupacea* latex. It was accelerated wound healing by downregulation of matrix metalloprotease without altering MMP-8 expressions. Drupin also increased the expression of arginase 1 in macrophages and was involved in cell proliferation also migration via MAP kinase and PI3 K/Akt pathways (Manjuprasanna et al. 2020).

### ALLELOPATHY ACTIVITY

Allelopathy is defined as direct or indirect interaction, whereby allelochemicals released by one organism influence the physiological processes of other neighbouring organisms. The allelochemicals can have beneficial or detrimental effects on the target organisms and the community. Allelopathy is characteristic of certain plants. For weed management purposes, allelopathy is considered a strategy of control.

A study described the allelopathic potential of two *Ficus* species, *F. deltoidea* varieties and *F. microcarpa*, by testing the leaf-litter through the sandwich method and the leaf extracts through the methanolic extraction method against lettuce radicle. The sandwich method was carried out using the donor plant's leaf's 5, 10, and 50 mg dry weight. *Ficus deltoidea* var. *kunstleri* had the highest growth inhibition on lettuce radicle elongation (57.51%), followed by *F. deltoidea* var. *trengganuensis* (45.50%) and *F. microcarpa* (39.95%). Meanwhile, the methanolic extraction with different concentrations (0.1, 1, 10, and 100 mg/mL) showed *F. deltoidea* var. *kunstleri*, and var. *trengganuensis* had the highest inhibition on lettuce radicle elongation at 66.63% and 64.95% at a concentration of 100 mg/mL (Asis et al. 2018).

The field study indicated that the cover of selected understorey species and species richness was reduced under the canopy of *F. retusa* trees. The greenhouse experiments showed that litter-affected soil suppressed selected species' germination and growth parameters (*Melilotus indicus*, *Trifolium resupinatum*, and *Amaranthus viridis*). The biochemical analysis of the litter-affected soils confirmed the presence of elevated levels of many phenolic and flavonoid compounds. The compounds are phytotoxins that negatively affect the germination and growth of some understorey species (Hassan et al., 2021). In another study, *F. retusa* leaf residue (250, 500, and 1,000 g/m<sup>2</sup>) was applied to the soil at two locations to control weeds in the green beans (*P. vulgaris*) crop. At both sites, the treatments significantly reduced the density and the biomass of several weed species in a dose-dependent and weed species-dependent manner. The total weed density and weed biomass were also substantially reduced, but there were no effects on the yield growth of *P. vulgaris* plots. It means *F. retusa* leaf residue can be used as part of the weed management strategy to control weeds in *P. vulgaris* crops (Mohamed et al., 2021).

Aqueous extract of *F. virens* leaves was studied for its effect on growth (radicle and plumule length) and seed germination of *Brassica campestris*. The leaves were collected in 5, 10, and 15 g weight, powdered, and soaked separately in 100 ml of distilled water. Then, the exudates were applied to *B. campestris* seeds in 24-72 hours. The results showed that a gradual decrease in *B. campestris* occurred with increased extract concentrations. Furthermore, dry leaves have a more inhibitory effect on germination percentage (82%) at 72 h. Then, the inhibitory effect of *Ficus* was more influential in plumule rather than radicle length (Khalid et al., 2021).

**Table 1.** Phytochemistry and biological activity of *Ficus* spp. in Java Island, Indonesia

Species name	Part of plant	Phytochemistry (secondary metabolites)	Other chemicals	Biological activity
<i>Ficus carica</i> L.	Leaves	Hydroxybenzoic acids, hydroxycinnamic acids, flavonoids, coumarins, furanocoumarins, volatile constituents, triterpenoids, and miscellaneous		Antioxidant, anticancer, antidiabetic, hepatoprotective activity, anticholinesterase, anti-HSV-1, antibacterial activity, anti-inflammatory activity (Li et al. 2021)
	Fruit	Phenols, flavonoids, anthocyanins (Teruel-Andreu et al. 2021)		
	Leaves			Antibacterial against <i>Escherichia coli</i> , <i>Staphylococcus</i> , and antifungal against <i>Aspergillus niger</i> (Shafique et al. 2021)
	Leaves	Alkaloids, phenols, flavonoids, lipophilic	Anthocyanins, flavon, biflavonol (Anisa et al. 2018)	
	Fruit		Kampesterol	Antiviral potential against HIV (Damayanti et al. 2021)
	Fruit		Vit C (Ngginak et al. 2019)	
<i>Ficus deltoidea</i> Jack	Leaves	Alkaloids, flavonoids, coumarins, saponins, polyphenols, tannins		Antibacterial against <i>Staphylococcus aureus</i> (Arbi et al. 2021)
	Leaves	Anthraquinones, tannins, phlobatannins, saponins, flavonoids, steroids, terpenoids, and polyphenols		Allelopathy against lettuce (Asis et al. 2018)
	Leaves		Pro-inflammatory, NF- $\kappa$ B, TNF- $\alpha$ , and IL-6 mRNA expressions	Prevented bone loss in preclinical osteoporosis/osteoarthritis (Tantowi et al. 2018)
	Leaves			Antibacterial against <i>Citrobacter freundii</i> (Tkachenko et al. 2016b)
	Leaves	Alkaloids, saponins, phenols, flavonoids, and tannins		Increases antioxidant in wounds and restore inflamed tissue by increasing blood supply, therapy of chronic congestive heart failure, scavenging the free radical activity, treatments of many ailments (Mustapha and Harun 2014)
	Leaves	Phenolics and flavonoids	Ursolid acid	Angiogenesis in mice (Shafaei et al. 2014)
	Leaves and fruit	Flavonoid, tannins, triterpenoids, and phenols		Antidiabetic, anti-ulcerogenic, antioxidant, anti-melanogenic, anti-inflammatory, analgesic, antihypertensive properties (Ramamurthy et al. 2014)
	Fruit	Phenols		Antidiabetic and antioxidant (Misbah et al. 2013)
	Leaves	Polyphenols, saponins		Anti-diabetic potential (Cahyanto and Supriyatna 2013)
	Leaves	Flavonoids, phenols, terpenoids, steroids		Antibacterial against <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Pseudomonas aeruginosa</i> , and <i>Escherichia coli</i> (Krisyanella et al. 2009)
	Whole part	Ursolic acid, phenols, flavonoids, isovitexin, moretenol, betulin, lupenone, lupeol		Anti-diabetic, anti-cancer, antimicrobial, aphrodisiac, anti-inflammatory, antioxidant, anti-obesity (Silalahi 2019)

<i>Ficus glandulifera</i> Jack	Leaves	Alkaloids, flavonoids, saponins, tannins (Zulfa et al. 2021)		
<i>Ficus padana</i> Burm. f.	Leaves	Alkaloids, flavonoids, saponins, tannins (Zulfa et al. 2021)		
<i>Ficus villosa</i> Blume	Leaves	Alkaloids, flavonoids, saponins, tannins (Zulfa et al. 2021)		
<i>Ficus grossularioides</i> Burm. f.	Fruit	Phenols		Antioxidant drugs potential (Akhtar et al. 2019)
<i>Ficus hirta</i> Vahl	Fruit	Alkaloids, sesquiterpenoids/norsesquiterpenoids, flavonoids, phenylpropane-1,2-diol		Antifungal against <i>Penicillium italicum</i> (Wan et al. 2017)
	Root	Phenols		Anti-inflammatory (Cheng et al. 2017)
	Fruit		Monosubstituted benzene	Antifungal against <i>Penicillium Italicum</i> (Wan et al. 2016)
	Fruit	Flavonoids, carboline alkaloids, monosubstituted benzene derivatives, sesquiterpenoids		Antifungal against <i>Penicillium Italicum</i> , <i>Aspergillus oryzae</i> , <i>Saccharomyces cerevisiae</i> (Chen et al. 2020)
	Root		Undescribed enantiomers, Ficusflavonoid A, five known analogues	Apoptotic effect of 4 HeLa Cell, anti-cancer drugs potential (Ye et al. 2021)
<i>Ficus padana</i> Burm. f.	Fruit	Anthocyanins		Antioxidants (Syukri et al. 2014)
<i>Ficus palmata</i> Forssk.	Leaves		Trans-psoralenoside, germanicol acetate, psoralene, bergapten, vanillic acid, flavone glycoside rutin	Hepatoprotective, nephroprotective, anti-ulcer, anticoagulant, and antioxidant (Alqasoumi et al. 2014)
	Whole part	Alkaloids, tannins, flavonoids, terpenoids, and cardiac glycosides		Antibacterial and antifungal, anti-proliferative, anti-carcinogenic, hepatoprotective, nephroprotective, anti-ulcer and anticoagulant (Joshi et al. 2014)
	Fruit	Aliphatic, aromatic carboxylic acids, flavonoids		Analgesic peripheral (Tewari et al. 2021)
	Fruit	Phenolics, tannins, flavonoids, terpenoids, steroids, alkaloids, glycosides, saponins, coumarins, anthocyanins		Antidiabetic, inhibitor $\alpha$ -amylase and $\alpha$ -glucosidase (Anjum and Tripathi 2019b)
	Latex			Antibacterial against <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> (Kumar et al. 2013)
	Latex			Coagulation effect in yogurt production (Godifey et al. 2015)
	Fruit			Raw material for jam (Kumari et al. 2018)
<i>Ficus erecta</i> Thunb.	Stem		P-hydroxybenzoic acid, methyl p-hydroxybenzoate, vanillic acid, methyl vanillate, syringic acid, beta-sitosterol, alpha amyirin acetate, and ethyl linoleate	Tyrosinase inhibitor (Park et al. 2012)

<i>Ficus nervosa</i> Roth	Bark	Alkaloids, flavonoids, terpenoids, steroids, tannins, and carbohydrates		Anti-ulcer (Devi et al. 2012)
	Leaves		Beta-friedelinol, squalene, beta-sitosterol, cycloeucalenol, lupeol, alpha amyirin, beta amyirin (Ragasa et al. 2013)	
<i>Ficus vasculosa</i> Wall. ex Miq.	Young leaves		Naringenin, vanillic acid; 9,16 dioxo 10,12,14 octadeca-trienoic acid; 2,6-dimethoxy-1,4-benzoquinone; apigenin; norartocarpetin	Antioxidant, reducing oxidative stress (Li et al. 2019)
	Root	Methyl p-hydroxycinnamic (Bahri et al. 2020)		
<i>Ficus coronata</i> Spin	Stem and leaves		Suberenol; dihydrocoumarin; chalepin; rutamarin; bergapten; skimmianine; 7-(1,1-dimethylallyloxy) coumarin; 7-hydroxycoumarin	Antibacterial against MRSA, possibly leading to the discovery of potentially new drug molecules active against multidrug-resistant microorganisms (Smyth et al. 2011)
	Leaves	Flavonoids, phenols		Antiproliferative and antioxidant, potential to the development of antitumor drugs (Gbolade et al. 2019)
<i>Ficus obscura</i> Blume	Bark	Flavonoids, saponins, alkaloids, triterpenoids, steroid		Antioxidant, growth inhibitor against <i>Escherichia coli</i> , <i>Streptococcus mutans</i> , and <i>Propionibacterium acne</i> (Zarta et al. 2020)
<i>Ficus parietalis</i> Blume	Leaves	Polyphenol, flavonoid, glycoside, alkaloid, prosalen, tannin, steroid, vitamin		Antioxidant, scavenging radical (Wahyuni and Hertiani 2016)
<i>Ficus sinuata</i> Thunb.	Leaves	Phenol, flavonoid, tannin, terpenoid, steroid (Afifudin et al. 2015)		
<i>Ficus fistulosa</i> Reinw. ex Blume	Leaves			Antiviral against Hepatitis C virus (Hafid et al. 2016)
	Leaves	Tannins, alkaloids, reducing sugar		Antioxidant and antibacterial against positive/negative gram bacteria (Raka et al. 2019)
	Leaves	Tengerensine, tengechlorenine, alkaloids		In vitro cytotoxic against breast cancer cell lines (Al-Khdhairawi et al. 2017)
	Leaves	Flavonoids, terpenoids, chlorophyll		Anti-HIV potential (Indriati et al. 2020)
<i>Ficus hispida</i> L.f.	Leaves	Alkaloids, flavonoids, saponins (Zulfa et al. 2021)		
	Whole part	Sesquiterpenoids, triterpenoids, flavonoids, coumarins, phenyl propionic acids, benzoic acid derivatives, alkaloids, steroids, glycosides, alkanes		Wound healing, anti-inflammatory, antinociceptive, sedative, antidiarrheal, anti-ulcer, antimicrobial, antioxidant, hepatoprotective, antineoplastic, antidiabetic (cheng et al. 2019)
	Leaves	Carbohydrates, flavonoids, tannins, glycosides, triterpenoids, fat, and fixed oils		Anti-diarrheal (Rahman et al. 2018a)
	Fruit	Isoflavones, coumarins, caffeoylquinic, phenolics and steroid glucoside		Chemo-preventive and anti-cancer agents (Zhan et al. 2017)

	Leaves			Potential source of depressant as well as anti-depressant agent (Rahman et al. 2018b)
	Leaves			Inhibitor of steel corrosion (Muthukrishnan and Prakash 2020)
	Leaves		1,3-benzenedicaroylic acid, n-hexadecanoic acid, methyl ester, linolenate, 9,12,15-octadecatrienoic acid, phthalic acid, butyl undecyl ester, 9-octadecenamide, di-n-octyl phthalate	Preserving goatskin (Hashem et al. 2020)
	Leaves	Saponins, sterols, tannins		Wound healing in folk medicines (Singh et al. 2014)
	Aerial parts	Alkaloids, phenols, flavonoids, glycosides, protein		Antioxidant and antimicrobial against <i>Salmonella typhi</i> and <i>Staphylococcus aureus</i> (Chatterjee et al. 2015)
	Bark	Beta amyryn acetate, lupeol acetate, phenols, flavonoids		Antinociceptive, anti-inflammatory, sedative (Howlader et al. 2017)
	Leaves			Potential antidiabetic agents (Ravichandra and Paarakh 2014)
	Stem, leaves, fruit, and root			Antimicrobial against <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Enterobacter aerogenes</i> , <i>Pseudomonas aeruginosa</i> , and antifungal <i>Fusarium proliferatum</i> and <i>Fusarium oxysporum</i> (Dhawale and Ghyare 2016)
<i>Ficus lepicarpa</i> Blume	Leaves	Flavonoids, saponins, sterols, phytosterols		Antioxidants are used to treat or prevent degenerative diseases where oxidative stress is implicated (Vun-Sang et al., 2017)
<i>Ficus racemosa</i> Willd.	Fruit		Ascorbic acid, gallic acid, catechin, tannins acid, chlorogenic acid, ferulic acid (Sharma et al. 2020)	
	Whole part	Flavonoid, alkaloids, phenolic acids, sterols, saponins, coumarins, tannins, triterpenoids, ursolic acid, protocatechuic acid, maslinic acid		Medicinal treatment of diarrhea, astringent treatment of hematuria, menorrhagia, hemoptysis, powerful tonic, remedy for tonsillitis (Mohiuddin and Lia 2020)
	Whole part	Alkaloids, tannins, saponins, beta sitosterol, lupeol		Anti-analgesic, antidiuretic, anti-hydrophobic, antimicrobial, antioxidant, wound healing, anti-inflammatory, hypoglycemic, antidiarrheal, anti-ulcer, anti-asthma, antipyretic, antifungal, anticarcinogenic, antileucohorric effect (Chaware et al. 2020)
	Bark	Alkaloids, glycosides, saponins, tannins, phenols, flavonoids, quinones, sterols, amino acids, terpenoids		Antidiabetic (Vijayagiri and Mamidala, 2013)
	Fruits	Phenols		Antioxidant and antiarthritic (Lakshmi et al. 2020)
	Bark	Steroids, glycosides, tannins, terpenoids, alkaloids, flavonoids, beta-sitosterol		Potentially used to anti-asthmatic (Suvarna et al. 2019)
	Leaves and fruit	Alkaloids, flavonoids, phenols		Antioxidant, antibacterial against <i>Staphylococcus</i> , <i>Pseudomonas</i> , <i>Klebsiella</i> , and <i>Escherichia coli</i> (Bagyalakshmi et al. 2019)
	Latex			Treatment of gastric ulcer (Sathish et al. 2018)

	Leaves		Crude protein, lipids, ascorbic acid, phenols, anthocyanin, lycopene, carotenoids, reducing sugars, crude fat, and crude fiber (Bhogaonkar et al. 2014)	
<i>Ficus septica</i> Burm.f.	Root bark	Flavonoids: quercetin		Antioxidant potential (Sudarmanto and Suhartati 2015)
	Leaves			Antifungal against <i>Colletotrichum acutatum</i> (Sudirga et al. 2014)
	Leaves	Alkaloids (Ragasa et al. 2016)	B-sitosterol-3 $\beta$ -glucopyranoside-6'-O-fatty acid esters, $\alpha$ -amyirin fatty acid ester, $\beta$ -sitosterol, stigmasterol, $\beta$ -amyirin, and long-chain saturated fatty alcohols	
	Leaves	Alkaloids		Potential anti-cancer of breast cancer cells (Nugroho et al. 2015)
	Stem	Alkaloids; dehydrotylophorine, dehydroantofine and tylophoridicine		Antimalarial (Kubo et al. 2016)
	Root bark, leaf	Alkaloids		Anti DENV (Dengue Virus DBD) (Huang et al. 2017)
	Leaves	Alkaloids, phenols		Fungicide against <i>Colletotrichum acutatum</i> , anti-anthraxose disease (Sudirga and Suprpta 2021)
	Leaves	Tylophorine and Ficuseptine (alkaloids group)		Antiangiogenic agent (Nurhidayati et al. 2021)
	Leaves	Alkaloids, flavonoids, saponins, tannins (Dewi 2020)		
	Leaves	Flavonoids, saponins, triterpenoids, and sterols		Larvicidal against <i>Artemia salina</i> (Aritan et al. 2019) Wound healing on cow legs (Supriyanto 2017)
	Fruit	Alkaloids, tannins, flavonoids, saponins, phenols		Antibacterial against <i>S. Aureus</i> (Bawondes et al. 2021)
<i>Ficus auriculata</i> Lour.	Leaves	Flavonoids		Antipiretik potential (Tawi et al. 2019)
	Leaves	Phenols, tannins, terpenoids, flavonoids, alkaloids		Antibacterial against <i>Escherichia coli</i> and <i>Salmonella typhimurium</i> , antioxidant (Kumari et al. 2018)
	Fruit	Alkaloids, terpenoids, steroids, flavonoids, phenolics, tannins, anthocyanins, coumarins, glycosides, saponins		Potent alpha-amylase and alpha-glucosidase inhibitor (Anjum and Tripathi 2019a)
	Young leaves	Phenols, flavonoids, isoflavonoids, benzoic and cinnamic acid derivatives, tannins, coumarins, terpenoids, polyacetylenes		Potential herbicide, antioxidant, and antimicrobial (Bertoletti et al. 2018)
	Fruit	Glycosides, phenols, tannins, alkaloids, flavonoids, saponins, terpenoids, phytosterols		Antibacterial against <i>Proteus vulgaris</i> , <i>Staphylococcus epidermidis</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumonia</i> , <i>Neisseria gonorrhoeae</i> , <i>Mycoplasma genitalium</i> , <i>Pseudomonas aeruginosa</i> (Raja et al. 2021)
	Branch, fruit	Phenolics compound		Antioxidant, antimicrobial, bioherbicide (Bertoletti et al. 2020)

<i>Ficus variegata</i> Blume	Aerial parts	Phenolics and flavonoids	Antioxidant and anti-acetylcholine esterase (Raza et al. 2016) Potential source of antioxidant, cytotoxic, antibacterial, larvicidal on <i>Aedes aegypti</i> larvae (Lee 2020)
	Fruit	Alkaloids and saponins	
	Leaves	Phenol, flavonoid, alkaloid (Febrina et al. 2015)	
	Fruit	Alkaloids, phenols, flavonoids, steroid	
	Stem bark	Alkaloids, phenols, tannins	
<i>Ficus pumila</i> L.	Stem bark	Alkaloids, phenols, tannins	Antibacterial and antioxidant (Ningsih et al. 2016) Antioxidant (Utami et al. 2016) Antibacterial against <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> (Saleh et al. 2016) Gel potential to wound healing (Zakaria et al. 2017)
	Fruit		
	Leaves	Alkaloids, tannins, flavonoids, saponins, glycosides, steroids/triterpenoids (Kaur 2012)	
	Leaves, fruits, stem barks	Phenolics, tannins, and flavonoids	
	Stem, leaves, flower, and fruit	Phenolic acids, flavonoids, terpenoids, alcohols, and steroids	
<i>Ficus sagittata</i> Vahl	Leaves and bark	Tannins, glycosides, saponins, terpenoids, alkaloids, flavonoids, sterols	Antibacterial against <i>Bacillus subtilis</i> , <i>Bacillus cereus</i> , <i>Micrococcus luteus</i> , <i>Enterococcus faecalis</i> , <i>Staphylococcus aureus</i> and <i>Proteus mirabilis</i> , cytotoxicity potential (Noronha et al. 2014) Antioxidant, anti-inflammatory, antibacterial, antitumor, hypoglycemic, cardiovascular protective (Qi et al. 2021) Anti-proliferative against leukemia cells, antioxidant (Larbie et al. 2015) Potential of essential oils (Sorkhabadi et al. 2017) Inhibitor $\alpha$ -amylase (Fresga et al. 2018)
	Leaves	Alkaloids, flavonoids, phenols, saponins, steroids	
	Leaves	Phenols, tannins, flavonoids, alkaloids, saponins, glycosides, steroids, carbohydrates	
	Leaves		
	Leaves		
<i>Ficus benjamina</i> L.	Leaves	Carbohydrates, phenolic compounds, oil, fats, saponins, flavonoids, alkaloids, proteins, and tannins	Potentially as an antimicrobial against <i>Escherichia coli</i> , cytotoxic agent (Zaman et al. 2015) Antibacterial against gram-positive and gram-negative bacteria, the potential of antithrombotic, cytotoxic (Hasan et al. 2015) Antioxidant, cytotoxic towards brine shrimp nauplii (Jain et al. 2013) Antibacterial against <i>Clostridium perfringens</i> and <i>Staphylococcus aureus</i> (Jassal and Sharma 2019) Possible source of natural antimicrobial, antioxidants, hemolysis, and antiviral agent (Ashraf et al. 2020) Antibacterial against <i>Streptococcus pyogenes</i> and <i>Pseudomonas aeruginosa</i> (Rahama and Mashi 2015) Skin ailments, infection, intestinal illness, retching, antimicrobial, antipyretic, and anti-nociceptive (Mahomoodally et al. 2019) Anti-plasmodial against malaria (Mukhtar et al. 2018) Antiviral against Herpes Simplex Virus 1 and 2 (Yarmolinsky et al. 2011)
	Leaves and stem	Amino acid, saponins, carbohydrates, phenols, terpenoids, alkaloids	
	Leaves	Phenolic and flavonoid	
	Fruit	Saponins, flavonoids, alkaloids, tannins	
	Leaves and bark	Cinnamic acids, lactose, naringenin, quercetin, caffeic acid, and stigma sterols	
Leaves	Steroids, terpenoids, phytosterols	Quercetin 3-O-rutinoside, kaempferol 3-O-rutinoside, kaempferol 3-O-robinobioside	
Leaves	Flavonoids		

	Leaves	Triterpenoids	Lupeol and ursolic acid	Anti-plasmodial of malaria (Singh et al. 2018)
	Leaves		Alpha pinene, abietadiene, cis alpha bisabolene, germacrone D-4-ol	Essential oil potential (Ogunwande et al. 2012)
	Aerial roots	Alkaloids, glycosides, carbohydrates, sterols, saponins, phenolic compounds, tannins, flavonoids		Antihypertensive, antimicrobial, antipyretic, antidiarrheal properties (Sharma et al. 2019)
	Leaves	Polyphenols, flavonoids,		Antidiabetic, an inhibitor of alpha-glucosidase and alpha-amylase (Mumtaz et al. 2018)
	Leaves	Glycosides, phytosterols, steroids, phenols, tannins, flavonoid		Anti-plasmodial, treatment of malaria (Mukhtar et al. 2018)
<i>Ficus binnendijkii</i> Miq.	Leaves	Carbohydrates, steroids, flavonoids, tannins, proteins, alkaloids		Potential to analgesic, antipyretic, and anti-inflammatory (El Rafie and Sleem et al. 2016)
<i>Ficus drupacea</i> Thunb.	Bark		Beta amyryn, beta-sitosterol, 5-O methylatifolin, oleanolic acid, epifriedelanol, friedelin, and epilupeol acetate	Antifungal against <i>Aspergillus versicolor</i> , <i>Aspergillus ochraceus</i> , antibacterial against <i>Bacillus cereus</i> , antiproliferative potential for HeLa, MCF-7, Jurkat, HT-29, and T24 (Yessoufou et al. 2015)
	Latex		Drupin (cysteine protease)	Wound healing by increased arginase, collagen synthesis, and cell proliferation (Manjuprasanna et al. 2020)
<i>Ficus elastica</i> Roxb. ex Hornem.	Leaves		Oleanolic acid	Potential treatment of diabetes mellitus (Kiem et al. 2013)
	Leaves	Carbohydrates, phenolics, flavonoids, proteins, tannins		Potential source of natural antioxidants, antimicrobial against <i>Bacillus cereus</i> , <i>Klebsiella pneumoniae</i> , <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , and cytotoxic compounds (Preeti et al. 2015)
	Leaves	Flavonoids, morin		Antioxidant, anti-inflammatory, treatment to Preeclampsia, antihypertensive agent (Ginting et al. 2019)
	Root bark	Ficusamide, Ficososide, elasticoside, triterpens, steroids, alkaloids		Potential inhibitor against human A549 lung cancer cell line, antibacterial against <i>Staphylococcus saprophyticus</i> and <i>Enterococcus faecalis</i> (Mbosso et al. 2012)
	Bark and leaves	Glycosides, terpenoids, alkaloids, saponins, flavonoids, phenolics, tannins, eugenols		Potential anti-plasmodial, treating malaria parasites (Ifijen et al. 2020)
	Aerial roots	Elasticamide, elastiquinone, Ficososide		Potential anti-proliferative agent against melanoma cells and glioma cells (Tienkala et al. 2016)
	Aerial roots			Anti-plasmodial and antitrypanosomal but it's low, cytotoxic on HeLa but it's low (Tienkala et al. 2017)
	Leaves	Quercitrin, myricitrin, morin, eleutheroside B		Potential antioxidant agent (Ginting et al. 2020)
	Latex	Phenolic compounds, flavonoids, tannins, saponins, and enzymes		Antimicrobial against pathogenic bacteria and fungi (Faisal 2017)
	Exudate gum		Rich in sodium, calcium, magnesium, iron, potassium, manganese, and cobalt	Potential utilized in gum-based industries, as an emulsifier in food processing, effective binder in drug formulations (Adeyanju et al. 2014)
	Endophytic bacteria from leaves	Isocoumarin		Antimicrobial against <i>Escherichia coli</i> (Ding et al. 2020)

<i>Ficus lyrata</i> Warb.	Leaves	Tannins, saponins, flavonoids, glycoside, phenols		Antibacterial against <i>Staphylococcus aureus</i> (Zukhri and Nurhaini 2019)
	Leaves	Triterpenoids, flavonoids, glycosides		Antibacterial especially on gram-positive bacteria rather than gram-negative (Tkachenko et al. 2016a)
	Leaves and fruit	Flavonoids, benzoic acids, caffeoylquinic acids, fatty acid, and sphingolipids		Potential antioxidant agent (Farag et al. 2014)
	Leaves and fruit	Phenolics, flavonoids, triterpenoids, tannins		Antimicrobia against <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Bacillus subtilis</i> (Wira et al. 2018)
	Leaves	Phenols, flavonoids, triterpenoids, tannins		Mild antibacterial against <i>Aeromonas</i> (Pękala-Safińska et al. 2019)
<i>Ficus microcarpa</i> L.f.	Leaves	Phenolic compounds, flavonoids, tannins		Antimicrobial, to save chicken carcass (Djali et al. 2019)
	Leaves	Phenolic compounds, flavonoids, tannins		Antibacterial, antiseptic composition for hand-sanitizer (Wira et al. 2019)
	Leaves	Flavonoids and phenolics compound		Potential antioxidant, hepato-protective, and hypo-cholesterolemic in rat liver (Awad et al. 2018)
	Leaves	Alkaloids, steroids, terpenoids, tannins		Potential anti-diarrheal (Bairagi et al. 2014)
	Leaves	Phenolic compounds, flavonoids, volatile oils, carotenoids, vitamins		Potential source of natural antioxidant (Kumari and Rani 2020)
<i>Ficus religiosa</i> L.	Leaves	Proteins, carbohydrates, saponins, tannins, and flavonoids		Potential antinociceptive, anti-inflammatory agent (Kumar et al. 2021)
	Bark	Phenolics, triterpenoid compound		Antioxidant potential to Hepatoprotective (Surana et al. 2017)
	Leaves	Flavonoids, tannins, polyphenols, steroids, and carbohydrates		Potential antidiabetic activity (Ravichandra and Padmaa 2011)
	Bark	Carbohydrate, glycoside, alkaloids, protein, amino acids, phytosterol, tannins, and flavonoids (Tiwari and Gupta 2020)		
	Leaves	Alkaloids, tannins, saponins, carbohydrates, glycosides, flavonoids, phytosterols, and triterpenoids		Antimicrobial against <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Pseudomonas aeruginosa</i> and <i>Staphylococcus aureus</i> (Chavan et al. 2019)
	Whole part	Flavonoids, tannins, phenolics, alkaloids, saponins, and terpenoids	Beta sitosteryl-D-glucoside, vit. K, n-octacosanol, kaempferol, quercetin and myricetin	Antioxidant, antibacterial, hypoglycemic, hypo-lipidemic, wound healing, antihelmintic, immune-modulatory, anticonvulsant, and anti-ulcer in Humans (Devanesan et al. 2018)
	Leaves	Alkaloids, flavonoids, carbohydrates, steroids, saponins, glycosides, tannins, terpenoids		Have sedative properties, anxiolytic actions, treatment of different psychiatric disorders, including insomnia (Hasan et al. 2019)
	Root bark	Alkaloids, flavonoids, phenols, saponins, tannins, glycosides, carbohydrates (Jyoyhisree and Umadevi 2021)		
	Leaves and stem	Alkaloids, terpenoids, tannins, anthraquinone, cardiac glycosides, and flavonoids		Antioxidants (Shahid et al. 2019)
	Whole part	Tannins, phenols, saponins, sugars, alkaloids, methionine, terpenoids, flavonoids, glycosides, proteins, amino acids, essential and volatile oils, steroids		Antimicrobial, antiparasitic, anti-Parkinsons, anticonvulsant, anti-amnesia, anticholinergic, antidiabetic, anti-inflammatory, analgesic, cytotoxic, anti-ulcer, wound healing, antioxidant, anti-asthmatic, reproductive, hepatoprotective, nephroprotective dermato-protective (Al Snafi 2017)

	Leaves		Convallatoxin, umbelliferone, embelin, dihydrocoumarin, fendiline, hydroxyibuprofen	Anti-cancer potential against human breast cancer (Shaikh et al. 2020)
	Leaves			Larvicidal against <i>Anopheles stephensi</i> and antimicrobial (Soni and Dhiman 2020)
<i>Ficus retusa</i> L.	Leaf	Phenols and flavonoids		Allelopathic potential (Hassan et al. 2021)
	Leaf residue	Phenols and flavonoids		Weed controlling agents (Mohamed et al. 2021)
	Leaves	Flavonoids, carotenoids, triterpenoids, fatty alcohol, steroids, flavone-4-hydroxybenzoate, and isoflavones		Antibacterial activity (Singhal et al. 2017)
<i>Ficus rumphii</i> Blume	Leaves and bark	Flavonoids, tannins, phenols compound, beta-sitosterol, and flavonol glycoside		Anti-proliferative activity (Parveen et al. 2014)
<i>Ficus thonningii</i> Blume	Whole part	Alkaloids, terpenoids, flavonoids, tannins, and active proteins		Antimicrobial, anti-diarrhoeal, anti-helminthic, antioxidant, anti-inflammatory, and analgesic properties (Dangarembizi et al. 2013)
	Leaves	Carbohydrate, saponin, tannins, flavonoid (Egharevba et al. 2015)		
	Bark	Saponins, quinones, coumarins, catechin tannins, phlobatanins, anthocyanin, polyphenols, flavonoids, and betacyanins		Gastro-protective activity, anti-ulcer potential (Fokunang et al. 2019)
	Stem bark	Flavonoids, saponins, quinones, alkaloids, coumarins, catechin tannins, polyphenols, flavonoids, phlebotanis, and antho cyanides		Pharmacologic and therapeutic activity for management of ulcers by a gastroprotective, anti-ulcer, and antioxidant action (Pougoue et al. 2020)
	Leaves	Terpenoids, saponins, tannins, and flavonoids		Potential antimicrobial against pathogens isolated from the human urinary tract (Coker and Oaikhena 2019)
	Fruit	Flavonoids, mucilages, saponins, gallic tannins, betacyanins, and polyphenols		Anti-ulcer potential (Uku et al. 2020)
	Leaves	Alkaloids, tannins, anthraquinones, terpenoids saponins (Bala et al. 2021)		
<i>Ficus natalensis</i> Hochst	Whole part	Alkaloids, flavonoids, glycosides, terpenes, tannins, saponins, and steroids		Antimicrobial activity against pathogens (Sheyin et al. 2018)
	Stem bark	Ceramide, anthraquinones, triterpenes, polyols, steroids (Mbougna et al. 2021)		
	Leaves			Antibacterial against fish pathogens <i>Aeromonas hydrophila</i> , <i>Citrobacter freundii</i> , <i>Pseudomonas fluorescens</i> , <i>Yersinia ruckeri</i> (Tkachenko et al. 2018)
	Leaf, stem bark, and fruit	Triterpenoids		Anti-adhesion potential against <i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Enterococcus faecalis</i> , <i>Pseudomonas aeruginosa</i> , and <i>Staphylococcus xylosus</i> (Awolola et al. 2017)
<i>Ficus maclellandii</i> King	Fruit			Biochar to remove lead and copper ions (Musumba et al. 2020)
<i>Ficus consociata</i> Blume	Aerial parts	Phenols and flavonoids		Antioxidant and anti-acetylcholine (Raza et al. 2016)
	Leaves	Luteolin, cirsiolol, isoquercetin, quercetin, nikotoflorin, hesperidin, dihydrophaseic acid (Dat et al. 2019)		

<i>Ficus benghalensis</i> L.	Bark	carbohydrates (Tripathi and Sikarwar 2015) Alkaloids, phenolics, flavonoids, and tannins		Anti-inflammatory potential (Ramadevi et al. 2014)
	Leaf	Carotenoids, flavonoids, phenols		Protective role in oxidative stress, potential prevention, and therapies of diseases in which oxidants or free radicals play a major role (Pattar et al. 2018)
	Leaves, fruits, stem barks	Proanthocyanidins		Potent free radical scavenging activities cytotoxic activities against breast cancer cells (Chen et al. 2017)
	Dry and fresh leaves			Potential allelopathic against mustard crop <i>Brassica campestris</i> (Khalid et al. 2021)
	Bark			Natural antioxidant and antiatherogenic agent (Iqbal et al. 2016)
	Leaves	Flavonoids, phenols, steroids		Anti-inflammatory (Fitriansyah et al. 2015)
	Bark	Alkaloids, flavonoids, terpenes, phenolics, and anthraquinones	Synephrine, asparagine, glucose, fructose, and fatty acids	Neuroprotective potential (Malik et al. 2020)
	Fruit	Flavonoids and phenolics, quercetin, myricetin, gallic acid, caffeic acid, chlorogenic acid, coumaric acid, ferulic acid, and ellagic acid		Antioxidant and radical scavenging activities prevent oxidative stress (Tharini et al. 2018)
	Aerial roots	Steroidal glycosides, cardiac glycosides, flavonoids, triterpenoids, phenols		Potential antioxidant and analgesic activity (Mazumder et al. 2018)
	Leaf, stem, bark, fruit	Flavonoids, tannins, carbohydrates, proteins, saponins, terpenoids, steroids, glycosides, phenols, starch (Tripathi et al. 2019)		
	Fruit	Alkaloids, steroids, flavonoids, carbohydrates, glycosides		Hepatoprotective agent potential (Karmakar et al. 2020)
	Whole part	Phytosterols, anthocyanidin, fatty acids, amino acids, polysaccharides, flavonoids, flavonols, leucoanthocyanidins, and triterpenoids		Anti-hyperglycemic, antidiabetic, antihyperlipidemic, hypocholesterolemic, anti-inflammatory, analgesic, antibacterial, antifungal, larvicidal, anti-diarrhoeal, antimutagenic, antioxidant, cytotoxic, hepatoprotective, anti-arthritic, antiallergic, and immunostimulatory (Khaliq 2017)
	Fruit	Flavonoids, tannins, and alkaloids		Antistress activity potential (Jahagirdar et al. 2020)
Bark	Flavonoids, polyphenols, triterpenoids, and steroids		Cytotoxic potential in normal and tumor cell lines, probable antioxidant mechanics, predictable biological activities (Khanal and Patil 2020)	
Stem bark	Glycosides, saponins, tannins, flavonoids, anthraquinones, triterpenes, coumarins, terpenoids, xanthoproteins, phenols, sterols		Source of biologically active compounds with antimitotic, antiproliferative, and antioxidant activities (Raheel et al. 2017)	

## ACKNOWLEDGEMENTS

The authors thank reviewers for the valuable and constructive comments.

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