A review of the phytochemical compounds and pharmacological activities from selected Ficus plants

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**Article History:**
Received on: 21 May 2020
Revised on: 10 Aug 2020
Accepted on: 17 Sep 2020

**Keywords:**
Ficus, Moraceae, Traditional, Phytochemical

**ABSTRACT**

The Ficus genus belongs to the Moraceae family were used for medicinal purposes. Distributed in America, Asia, Africa, and Australia, there were sixteen species accepted in Indonesia. They were *Ficus callosa*, *Ficus melinocarpa*, *Ficus elastica*, *Ficus drupacea*, *Ficus geocarpa*, *Ficus Superba*, *Ficus heteropoda*, *Ficus fistulosa*, *Ficus hirta*, *Ficus ampalas*, *Ficus adenosperma*, *Ficus ardisioideis*, *Ficus consociate*, *Ficus ribes*, *Ficus lyrata*, *Ficus virens* Aiton. This article reviewed the scientific work of the Ficus genus. Their traditional usage, phytochemical compounds, and pharmacological activity were summarized. This study aims at providing a collection of publications on selected species of Ficus genus. A critical review of the literature data revealed secondary metabolite like triterpenoid, steroid, saponin, flavonoid, phenolic compound and alkaloid were found in some species of Ficus. Some pure compounds such as quercetin, quercetin 3-O-α-L-arabinopyranoside, epilupeol acetate, oleanolic acid, friedelin, elastiquinone, pinocembrin-7-O-D-glucoside, and ficusoxide B were isolated. A wide range of pharmacological activities was observed. Antimicrobial, antioxidant, antiviral, antiparasitic, cytotoxic, and antimalarial were found in previous researches. Ficus genus was potential to be developed as a medicinal plant.

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ISSN: 0975-7538
DOI: [https://doi.org/10.26452/ijrps.v11iSPL4.4225](https://doi.org/10.26452/ijrps.v11iSPL4.4225)

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**INTRODUCTION**

Family Moraceae consists of over 50 genera and nearly 1400 species distributed in the tropical and subtropical region as American, Asia, Afrika, and Australia (Zerega et al., 2005). Ficus is one large family plant comprises of over 800 species (Herre et al., 2008) and one of about 40 genera of mulberry family Moraceae (Hamed, 2011). Twenty-two species were recorded in Indonesian, among which 16 are accepted name and six synonyms, which are all deciduous plants, and most are essentially hemiepiphytic. Ficus plant species can be edible food and traditional medicine to improve the human health of about ten thousand years. Several species used were recorded in Ayurvedic and traditional Chinese medicine (Lansky et al., 2008). People who live at Xishuangbanna in Southwest China consumed Ficus leaves as wild vegetables by the ethnic group. Ficus have many edible species such as *Ficus virens* Ait var. sub lanceolata (Miq.) Corner, *Ficus auriculata* Lour., *Ficus vasculosa* Wall ex Miq., *Ficus callosa* Willd, *Ficus virens* Ait var. verins, *Ficus racemosa* L. and *Ficus oligodon* Miq (Shi et al., 2011).

**Traditional uses**

Several of Ficus plants have been applied in tradi-
Table 1: Traditional uses of Ficus genus in Pakistan

| Ficus species | Local name | Plant Part | Traditional uses                                                                 |
|---------------|------------|------------|----------------------------------------------------------------------------------|
| *F. elastica* | rubber plant | bark, fruits and leaves | Enlargement of liver and spleen, dysentery, diarrhea, diabetes, leprosy, lung complaints, leucorrhoea, heart diseases, cough, asthma, piles, ulcers, gonorrhea, rheumatism and for different skin diseases (Nisar *et al.*, 2014; Teinkela *et al.*, 2018) |
| *F. lyrata*   | beeri patta | whole plant | Gastrointestinal problems, anthelmintic, diabetes, anti-tumor activity, asthma, cough, sexual disorders, diarrhea, ear-ache and toothache, migraine, eye troubles, scabies, gonorrhea, bleeding, paralysis, bone fracture, antiseptic and astringent (Nisar *et al.*, 2014). |
| *F. virens*   | jangli pipit | leaves, fruit and bark | Diabetes, ulcer, menstrual disorder, leucorrhoea (Khan *et al.*, 2011) |

Table 2: IC_{50} from various extracts of Ficus species

| Ficus species | Plant Part | Extract | IC_{50}   | Ref. |
|---------------|------------|---------|-----------|------|
| *F. carica*   | Leaves     | Water   | 76.38 mg/ml | (Wahyuni and Hertiani, 2016). |
|               |            | Methanol| 275.23 µg/ml| (Ayoub *et al.*, 2019). |
| *F. pareintalis* | Fruits   | Water   | 33.38 mg/ml | (Wahyuni and Hertiani, 2016). |
| *F. deltoidea* | Leaves     | Water   | 44.01 mg/ml | (Wahyuni and Hertiani, 2016). |
|               | Fruits     | Water   | 35.69 mg/ml | |
| *F. maclellandii* | Fruits  | Methanol| 111.2 µg/ml | (Misbah *et al.*, 2013). |
|               |            | Ethanol | 16.5 µg/ml  | (Aslam *et al.*, 2017). |
| *F. racemosa* | Fruits     | Ethanol | 210.3 µg/ml | (Tamuly *et al.*, 2015). |
|               |            | Ethanol | 228.4 µg/ml | |
| Ficus species       | Plant Part | Extract       | Bacterial/Fungi                                                                 |
|---------------------|------------|---------------|--------------------------------------------------------------------------------|
| F. callosa          | Leaves     | Methanol      | *Escherichia coli, Staphylococcus aureus, Bacillus subtilis*                     |
|                     |            |               | (Wibowo et al., 2018b)                                                         |
| F. drupacea         | Leaves     | Methanol      | *E. coli, S. aureus, B. subtilis*                                               |
|                     | Stem/      | n-Hexane      | *Aspergillus flavus, A. versicolor, A. niger, A. ochraceus, Candida albicans,* |
|                     | bark       |               | *Penicillium funiculosum, P. ochrochloron*                                      |
|                     |            |               | *B. cereus, Listeria monocytogenes, Micrococcus flavus, S. aureus, E. coli,*    |
|                     |            |               | *Salmonella typhimurium, Pseudomonas aeruginosa, Enterobacter cloaceae*         |
|                     |            |               | (Yessoufou et al., 2015)                                                       |
| F. melinocarpa      | Leaves     | Methanol      | *S. aureus, B. subtilis*                                                        |
|                     | Leaves     | Methanol      | *E. coli, S. aureus, B. subtilis*                                               |
| F. geocarpa         | Leaves     | Methanol      | *E. coli, S. aureus, B. subtilis*                                               |
|                     | Leaves     | Methanol      | *E. coli, S. aureus, B. subtilis*                                               |
| F. consociata       | Leaves     | Methanol      | *E. coli, S. aureus, B. subtilis*                                               |
| F. ribes            | Leaves     | Methanol      | *E. coli, S. aureus, B. subtilis*                                               |
| F. ardisioides      | Leaves     | Methanol      | *E. coli, S. aureus, B. subtilis*                                               |
|                     | Root       | MeOH/CHCl3    | *Enterococcus faecalis, S. aureus, S. saprophyticus,*                            |
|                     | barks      |               | *S. epidermidis, Trichophyton rubrum,*                                           |
|                     |            |               | *C. albican, E. coli, Klebsiella pneumoniae,*                                   |
|                     |            |               | *and S. typhi*                                                                   |
|                     |            |               | (Teinkela et al., 2018)                                                        |
| F. heteropoda       | Leaves     | Methanol      | *S. aureus, B. subtilis*                                                        |
| F. hirta            | Leaves     | Methanol      | *S. aureus*                                                                     |
| F. elastica         | Roots      | Methanol      | *S. aureus, E. coli, Proteus vulgaris,*                                          |
|                     |            |               | *Providencia stuartii, P. aeruginosa,*                                           |
|                     |            |               | *C. albicans*                                                                   |
|                     | Root       | MeOH/CHCl3    | *Enterococcus faecalis, S. aureus,*                                             |
|                     | barks      |               | *S. saprophyticus,*                                                             |
|                     |            |               | *S. epidermidis,*                                                               |
|                     |            |               | *Trichophyton rubrum,*                                                          |
|                     |            |               | *C. albican,*                                                                   |
|                     |            |               | *E. coli,*                                                                      |
|                     |            |               | *Klebsiella pneumoniae,*                                                        |
|                     |            |               | *and S. typhi*                                                                  |
|                     |            |               | (Mbosso et al., 2012)                                                           |
| F. fistulosa        | Leaves     | Methanol,     | *E. coli, E. coli mutants,*                                                      |
|                     |            | Water         | *S. aureus, B. subtilis*                                                        |
|                     |            |               | *K. pneumoniae,*                                                                |
|                     |            |               | *P. aeruginosae*                                                                |
|                     |            |               | (Raka et al., 2019)                                                            |
| F. hirta            | Fruits     | Ethanol       | *Penicillium italicum*                                                          |
| F. lyrata           | Latex      | Ethyl acetate | *C. albicans*                                                                   |
|                     | Leaves     | Ethanol       | *S. aureus, E. coli,*                                                           |
|                     |            |               | *K. pneumoniae,*                                                                |
|                     |            |               | *P. aeruginosae,*                                                               |
|                     |            |               | *mecillin-resistant*                                                            |
|                     |            |               | *Staphylococcus aureus,*                                                        |
|                     |            |               | *S. pneumoniae*                                                                 |
|                     |            |               | (Tkachenko et al., 2016)                                                       |
| F. carica           | Leaves     | Ethanol       | *E. coli, P. aeruginosa,*                                                       |
|                     |            |               | *MRSA, S. aureus*                                                               |
|                     |            |               | (Tkachenko et al., 2017)                                                       |
tional medicine for many countries. Thailand people used fresh young leaves of leab (F. Superba) and phak hueda Daeng (F. virens) as a vegetable as a curry or used in a salad (Chantarasuwan and Welzen, 2012). The Ayurveda book recorded that traditional people use bark, latex, leaves and fruit of F. virens Aiton for vertigo, blood diseases, diabetes, rheumatism and antioxidant (Rajani et al., 2008). People in Vanuatu used latex from leaves of F. adenosperma for menorrhagia; this plant is added to the coconut water (Bourdy and Walter, 1992). Different from people in Papua New Guinea, used for sores and scabies, but fresh roots of F. adenosperma is chewed to treat malaria (Mahyar et al., 1991). In Vietnam, leaves of F. drupacea is taken to treat malaria, paragonimiasis, nasosinusitis, sinusitis, and anasarca (Phan et al., 2013). Still, the leaves, roots and bark from F. microcarpa were applied to reduce fever and anti-inflammatory. The usage of Ficus species in Pakistan for traditional medicine can be seen in Table 1.

Many kinds of Ficus have been used in Indonesian culture like leaves of uyah-uyah (F. quercifolia) to treat skin disease in Balinese people. Gayo ethnic used leaves of leng (F. deltoidea) for aphrodisiac like Sundanese people. Another kind of Ficus, fruits of amis Mata (Ficus Montana) is used by Sundanese ethnic to treat urinary stones. Ficus fistulosa leaves also are used to treat wounds by sharp objects and for anthelmintic in Sumba people. The bark of Ficus septic is used for sprue, but the leaves can use for mothers who have just given birth.

**Phytochemical compound**

Phytochemical screening found that many secondary metabolites such as flavonoid and phenolic compound, p-coumaric acid, caffeic acid, kaemferol, quercetin and leucoanthocyanins frequently occurred in leaves. Triterpenoid (Chiang et al., 2001, 2005), steroid, flavonoid (Kiem et al., 2011), lignin (Li and Kuo, 2000), saponin, and alkaloid were known from some species of Ficus (Berg et al., 2006). The structure of some phytochemical compound is shown in Figure 1.

Flavonoid was discovered in all Ficus genus, and several isolates were found from methanol extract of F. callosa leaves as megastigmene glycoside, ficalloside (Van et al., 2011). Quercetin, quercetin-3-O-α-D-arabinopyranoside, quercetin-3-O-β-D-galactopyranoside, kaempferol-3-O-α-D-arabinopyranoside, kaempferol-3-O-β-D-galactopyranoside, and vogelin J. were obtained from methanol extract of F. virens Aiton (Orabi and Orabi, 2016). Other biochemical compounds from stem bark extracts of F. drupacea included β-amyrin, β-sitosterol-3-O-β-D-glucopyranoside, 5-O-methylatilifolin, oleanolic acid, epifriedelanol, friedelin and epilupeol acetate were isolated and identified (Yessoufou et al., 2015).

Chemical investigation of the ethyl acetate extract of F. consociata leaves led to the isolation and structural elucidation of seven compounds. They were luteolin, cirsiliol, isouquerctin, quercetin 3-O-α-L-arabinopyranoside, nikotoflin, hesperidin, and (2E,4E,1’S,2’R,4’S,6’R)- dihydrophaseic acid (Dat et al., 2019). Ursolic acid and oleanic acid were isolated from the dichloromethane extract F. ampelas. Butyrospermol cinnamate and isolation of lutein from leaves of F. ampelas were also exposed (Ragasa et al., 2014).

Methanol extract roots of Ficus elastic contained steroidal glucosides called as sitosteroyl 3-O-β-D-glucopyranoside, elasticamide, and the highest antimicrobial are elastiquinone, ficusoside B (Teinkela et al., 2018), ficusamide, and elasticoside (Mbossou et al., 2012). Pinocembrin-7-O-β-D-glucoside, in the ethanol extract of F. hirta fruits, had antifungal activity (Wan et al., 2017).

**Pharmacological activities**

Pharmacological activities of some Ficus species were shown in the explanation below:

**Antioxidant Activity**

Ethanol extract of young leaves of F. virens Aiton and Ficus callosa had antioxidant activity with DPPH and ABTS assays, which IC<sub>50</sub> of DPPH F. virens Aiton was 0.34 mg/ml, and IC<sub>50</sub> of ABTS 0.23 mg/ml. It was different with F. callosa, IC<sub>50</sub> of DPPH 0.95 mg/ml, and ABTS 0.35 mg/ml. F. virens Aiton had higher

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**Table 4: Cytotoxic activity of isolated compound**

| Compounds         | HeLa    | MCP-7   | Jurkat | HT-29   | T24    |
|-------------------|---------|---------|--------|---------|--------|
| Oleanolic acid    | 20.38 ± 2.6 | 16.28 ± 1.3 | 21.17 ± 2.2 | 25.58 ± 1.3 | 27.61 ± 1.3 |
| Friedelin         | 20.42 ± 2.3 | 22.81 ± 2.1 | 29.15 ± 2.3 | 37.21 ± 3.61 | 12.81 ± 1.4 |
| Epilupeol acetate | 15.16 ± 1.6 | 20.03 ± 3.2 | 19.64 ± 2.6 | 26.21 ± 1.7 | 58.26 ± 2.3 |
flavonoid and phenolic compounds, which correlated with its antioxidant activity (Shi et al., 2011).

Quercetin from methanol leaves extract of *F. virens Aiton* was the most active DPPH radical scavenging activity with IC_{50} 14 ± 1.12 μg/ml (Orabi and Orabi, 2016). (Hilfi, 2019), reported that ethanol extract of *F. elastic* gave antioxidant activity with EC_{50} DPPH 6.4166 mg/ml and 0.0768 mg/ml with ABTS. Ficuselastic acid and (1'S,6'R)-8-O-D-glucopyranosyl abscisate sodium showed antioxidant activity (Kiem et al., 2012). The methanol extract of leaves of *Ficus ϔistulosa* presented IC_{50} DPPH 16.66 μg/ml (Raka et al., 2019).

Some Ficus from other country had antioxidant compounds, such as C-glycosylϐlavone from ethanolic leaves extract of *F. microcarpa* (Kiem et al., 2011), and aqueous roots extracts of *F. beecheyana* (Yen et al., 2018). Philippines peoples used antioxidants from the ethanol extract of leaves and fruits of *F. nota* (Santiago et al., 2017). *F. sur* is a traditional medicine from Togo, had antioxidant activity for the whole plant, the highest activity was given by ethanolic bark extract (56.50 ± 0.29 μg QE/mg), and the ripe fruit had lowest activity (7.3 ± 0.30 μg QE/mg) (Saloufou et al., 2018). The old leaves of *F. deltoidea* had more potent antioxidant activity than the fresh leaves (Manurung et al., 2017). The value of IC_{50} from other extracts of Ficus species are reported in Table 2.

**Antiparasitic Activity**

Methanol roots extract of *Ficus elastica* exhibited antiparasitic activity against *Trypanosoma brucei*, with IC_{50} 0.9 μg/mL (Teinkela et al., 2018). The antischistosomal activity was shown by ether latex extract of *F. elastica* (after washing off toxic rubber materials) (el Din et al., 2014).

**Antimalarial Activity**

The methanol extract of *F. elastica* roots demonstrated plasmocidal activity (IC_{50} 9.5 μg/ml) against *Plasmodium falciparum* strain 3D7 (Teinkela et al., 2018).

**Antimicrobial Activity**

The antimicrobial activity of Ficus species has been evaluated by the agar diffusion method. It can be proposed that flavonoids, triterpenoid, and steroid had antimicrobial activities (Wibowo et al., 2018a). Ficus species showed antimicrobial activity against at least one bacteria, which can be seen in Table 3.

**Antiviral Activity**

Antiviral activity *in vitro* of flavonoids, which was found from *F. virens Aiton* on Coxsackie B4 (CVB4), and hepatitis A virus (HAV) were also carried out. Antiviral activities were also given by quercetin and quercetin-3-O-β-D-glactopyranoside isolated from *F. virens Aiton*. It was tested by 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide (MTT) assay. Quercetin gave the highest inhibitory activity (20.3%) on CVB4; meanwhile, quercetin-3-O-β-D-glactopyranoside presented the highest inhibitory activity (12.3%) on HAV (Orabi and Orabi, 2016).

*F. ϔistulosa* leaves extract showed antiviral activity (IC_{50} 15.0 μg/ml) against HCV J6/JFH1-P47 strain
and HCV J6/IFH1-P1 strain with IC_{50} 5.7 µg/ml. The chloroform fraction had an anti-HCV activity with IC_{50} 5.67 ± 1.54 µg/ml, while butanol fraction gave lower activity (IC_{50} 74.10 ± 18.24 µg/ml) (Hafid et al., 2016). Methanol leaves extract of F. septica had antiviral activity against Dengue virus (DENV-1 and DENV-2) with IC_{50} 13.3±2.6 µg/ml and 10.6±1.1 µg/ml (Huang et al., 2017).

**Cytotoxic Activity**

Flavonoid compounds are the secondary metabolites responsible for pharmacological activity in Ficus species. The flavonoid from F. virens Aiton showed low cytotoxic activity in Vero cells by the MTT method (Orabi and Orabi, 2016). The ethanol leaves extract of F. fistulosa had cytotoxicity concentration (CC_{50}) >200 µg/ml, which was not toxic, while butanol and chloroform fractions gave CC_{50} >100 µg/ml (Hafid et al., 2016). The methanol extract of F. septica root inhibited nasopharyngeal carcinoma (HONE-1) and gastric adenocarcinoma (NUGC) cell (Damu et al., 2009) while the ethanolic extract of roots from F. beecheyana inhibited HL-60 cell (Yen et al., 2018).

Ficusamide is an isolated compound from F. elastica that had medium cytotoxic activity on A-549 lung cancer (Mbossou et al., 2012). Other compounds from F. elastica showed weak cytotoxic activity (IC_{50} values 20 µg/ml) on HeLa cell (Teinkela et al., 2018). Meanwhile, compounds from F. drupacea stem barks demonstrated the highest antiproliferative activities against most cancer cells, are reported in Table 4 (Yessoufou et al., 2015).

**Other Pharmacological Activities**

Methanol fruit extract of Ficus carica with a concentration of 924 µmol/l reduced 54% the formation of uric acid in mice, which injected with potassium oxonate (Mohamed and Al-Okbi, 2008). F. carica leaves showed oedema inhibitory activity (anti-inflammatory) in rats induced by carrageenan as much as 48.8% (Ali et al., 2012). Previous research demonstrated that ethanolic fruit extract of F. carica could inhibit α-glucosidase, α-amylase, and pancreatic lipase (Mopuri and Islam, 2016).

**CONCLUSIONS**

We summarized the traditional usage, phytochemical compounds, and pharmacological activity of selected Ficus plants. Based on the literature review was reported that most of the species were used as a traditional medicine in Asian countries such as Indonesia, Papua New Guinea, Vietnam, Pakistan, Thailand, and Vanuatu. Some species of the Ficus genus need further research on pharmacological activities, based on mechanisms and chemical contents.

**ACKNOWLEDGEMENT**

The authors are thankful to the Department of Pharmaceutical Biology, School of Pharmacy, Bandung Institute of Technology, Bandung, Indonesia, for providing the facilities.

**Conflict Of Interest**

The authors declare that they have no conflict of interest for this study.

**Funding Support**

The authors declare that they have no funding support for this study.

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