Flavonoids of Morus, Ficus, and Artocarpus (Moraceae): A review on their antioxidant activity and the influence of climate on their biosynthesis

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ABSTRACT
Moraceae plants are widely distributed in various regions of the world in various climatic conditions. Morus, Ficus, and Artocarpus are the genera of the family Moraceae that have been widely studied for their health benefits such as anti-inflammatory, anticancer, antiplasmodial, antidiabetic, immunomodulator, anti spasmodic, and neurodegenerative diseases treatment. These activities are mostly related to the flavonoids that act as natural antioxidants. The flavonoids in plants vary and are influenced by environmental conditions. The objectives of this review were to provide the flavonoids of Morus, Ficus, and Artocarpus (family Moraceae) and their antioxidant activity and to study the influence of the climate on flavonoid biosynthesis. This review includes several studies published in the PubMed database obtained using the keywords (“Morus” OR “Ficus” OR “Artocarpus”) AND “flavonoids” NOT “opuntia” with “full-text” and “10 year” filter. Various classes of flavonoids found in these plants are mostly flavonols and flavones. These three genera of plants also exhibit a strong antioxidant activity through various mechanisms. The flavonoids in Morus, Ficus, and Artocarpus plants are influenced by climatic conditions including temperature and solar radiation by upregulating and downregulating the gene expression involved in flavonoid biosynthesis.

INTRODUCTION
The family Moraceae, often called the mulberry family or the fig family, grows in a wide range of climatic conditions. Thus, it is widely distributed in various types of regions (Tomczyk et al., 2019). The genera that have been widely studied for their health benefits are Morus, Ficus, and Artocarpus (Afzan et al., 2019). These plants are widely utilized traditionally in cosmetics, agriculture, food, and additives in the pharmaceutical industry (Ghavami et al., 2020). These benefits are due to the secondary metabolites contained in them (Afzan et al., 2019).

Recently, a group of compounds that have increased attention because of their bioactive properties, is flavonoids (Li et al., 2020a). Flavonoids are widely present in every part of the Moraceae plants (Zhu et al., 2019). Flavonoids in Morus, Ficus, and Artocarpus have shown antidiabetic (Junior et al., 2017), anti-inflammatory (Ribeiro et al., 2019), anticancer (Boonyaketgoson et al., 2020), antiplasmodial (Boonyaketgoson et al., 2020), immunomodulator (Septama et al., 2018), and anti spasmodic (Zoofishan et al., 2019) activity. Some studies also proved their ability to improve several diseases including neurodegenerative diseases such as Alzheimer’s and Parkinson’s disease (Paudel et al., 2019; Suttisansanee et al., 2020) and osteoporosis (Yuan et al., 2017) and to help lower blood pressure (Alamgeer et al., 2017).

The hydroxyl group in flavonoids plays a role in providing antioxidant properties that can fight oxidative stress (Zhao et al., 2018). However, the flavonoids in plants vary and are influenced by environmental conditions such as climate, solar radiation, temperature, and precipitation rate (Dalmagro et al., 2018; Krishna et al., 2018). The total flavonoid is an important

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parameter in determining the quality of a plant (Afzán et al., 2019).

Therefore, the objectives of this review were to provide the flavonoids of Morus, Ficus, and Artocarpus (family Moraceae) and their antioxidant activity and to study the influence of the climate on flavonoid biosynthesis. To the best of authors’ knowledge, this review is the first one that compiles all the pieces of information mentioned.

**METHODS**

This review included studies published in the PubMed database obtained using the keywords (“Morus” OR “Ficus” OR “Artocarpus”) AND “flavonoids” NOT “opuntia” with “full-text” and “10 year” publication date filtered from February 2021 to June 2021. The inclusion criteria were articles about Morus, Ficus, and Artocarpus genera which contain flavonoids and biosynthesis mechanism, contain the list of flavonoids present in the plant, contain the antioxidant activity of the plant, and contain the environmental influence on the flavonoid biosynthesis. The articles obtained from the initial search were 548 studies. Articles published before 2011, reviews, non-English studies, and unrelated studies such as studies on processed foods and studies that do not contain information about flavonoid content were excluded. The information obtained from articles was then supplemented with information about climate obtained through the network sites https://climatecharts.net/ (Zepner et al., 2020) and https://gml.noaa.gov/grad/solcalc/ (Global Monitoring Laboratory). The flowchart of literature searching is shown in Figure 1.

**BIOSYNTHESIS PATHWAY OF FLAVONOIDS**

Flavonoids are a substantial secondary metabolites group present in plants which can be classified according to their basic skeleton into certain groups such as flavonols, flavones, flavanols, isoflavonols, flavanones, anthocyanins, and proanthocyanidin (Li et al., 2020a). Other sources stated that flavanol, aurone, furan chromone, isoflavanone, biflavones, xanthones, chalcones, and dihydrochalcone are also included in the flavonoid classification (Wang et al., 2018). Generally, a schematic presentation of the biosynthesis pathway of flavonoids is shown in Figure 2.

Biosynthesis of flavonoids begins with phenylalanine which is catalyzed by phenylalanine ammonia lyase (PAL) to form cinnamic acid. The cinnamic acid is further oxidized and then catalyzed with the help of cinnamic acid 4-hydroxylase (C4H) and 4-coumaroyl CoA ligase (4CL) to form p-coumaric acid and 4-coumaroyl CoA. These stages are included in the phenylpropanoid pathway. Then, the resulting product will interact with three malonyl-CoA molecules from the shikimic pathway and produce naringenin. The stages from naringenin to various other types of flavonoids are the entry stages of the flavonoid biosynthesis pathway (Li et al., 2020a).

The formation of flavonols from dihydroflavonol is catalyzed by flavonol synthase (FLS), which converts dihydrokaempferol, dihydroquercetin, and dihidromyricetin into kaempferol, quercetin, and myricetin, respectively (Huang et al., 2020). In mulberry fruit, flavonoid biosynthesis is influenced by the level of maturity, where the ripe fruit has higher levels of flavonoids (Huang et al., 2020). The same thing also happened to fig fruit (Ficus carica) which showed that the anthocyanin levels in fruits that had changed color to red could contain 28 times more anthocyanins compared to fruits that were still yellow (Li et al., 2020c).
Compounds contained in each part of the plant are different. This happens because there are differences in proteins expressed in each plant organ. These proteins or enzymes affect the synthesis process in the flavonoid biosynthetic pathway. Organ-specific metabolic analysis in _M. alba_ showed that more flavonoids were accumulated in roots than leaves and twigs. Notably, the two root-specific proteins named flavonoid 3,5-hydroxylase and chalcone flavanone isomerase were accumulated in the flavonoid pathway (Zhu et al., 2019). The difference in the concentration of flavonoids in _Morus atropurpurea_ showed the highest flavonoid content in root bark, followed by stem bark, twigs, and old leaves (Wang et al., 2017)

**FLAVONOID COMPOUNDS IN MORUS, FICUS, AND ARTOCARPUS**

Moraceae plants, especially genus _Morus_, can be widely cultivated in tropical, subtropical, and temperate climates in Asia, Europe, and South and West America (Paudel et al., 2019). In China, _Morus alba_ and _Morus nigra_ have been used as traditional medicines since ancient times (Hao et al., 2018; Zhao et al., 2018) Guangxi and Chongqing are emerging sericulture areas in China where the production of mulberry leaves is huge. In order to identify high quality mulberry leaves that are suitable for healthy products to expand planting, 24 samples from three regions (Guangdong, Guangxi, Chongqing). They are also important in the economic sector, especially in sericulture (Zou et al., 2012). _Morus_ plants are known to be abundant with flavonoids. Hence, various studies of metabolic profiles to transcriptome analysis have been carried out on several _Morus_ species, both to understand the biosynthesis of flavonoids in _Morus_ and to determine the response of flavonoids as a defense against environmental conditions (Li et al., 2020a; Li et al., 2020b).

The biggest population of the family Moraceae is from _Ficus_ (Farag et al., 2014). This genus consists of around 800 species and is widely spread from Asia to the Mediterranean region (Alamgeer et al., 2017; Farag et al., 2014). _Ficus deltoidea_ is an indigenous plant in Indonesia, Thailand, and Malaysia and can be found easily in other Southeast Asian countries. The plant wildly grows near beaches, hilly forests, and peat soil (Afzan et al., 2019). It is complicated to find the distinction of the varieties based on the plant morphology, especially the leaves, because they tend to have a diverse leaf shape on both the same stem or a different stem of the same plant (Afzan et al., 2019; Shahinuzzaman et al., 2020). Therefore, the identification of secondary metabolite and chemical markers is needed to distinguish and choose the right plant to be used as a medicinal herb (Afzan et al., 2019). A previous study on _F. deltoidea_ Jack leaves from Kalimantan, Indonesia, harvested more than 6 months after being planted, revealed the highest flavonoids and total phenolic content (TPC) compared to the younger leaves, unripe fruits, and stems. This plant was seeded in a conditioned soil with pH = 6.12, N = 0.688%, using NPK Mutiara (16:16:16) as a basic fertilizer (Manurung et al., 2017). Another study on _F. carica_ collected in Lakhdaria, Algeria, also reported that the leaves of this plant contained a high flavonoid and TPC and antioxidant activity (Mahmoudi et al., 2016).

The genus _Artocarpus_ consists of a tropical plant that is mainly cultivated in Asia, especially in South and Southeast Asia (Boonyaketgoson et al., 2020). This genus is a rich source of prenylated flavonoid (PF) and more than 300 PFs have been isolated (Ye et al., 2019).

From Table 1, we could see that the _Morus_ species are mostly grown in a subtropical climate and humid climate. Despite their diverse growing place, every part of the _Morus_ plants shows a similar type of flavonoid. The leaves mostly consist of flavonol derivatives, when anthocyanins are mostly found in the fruits, and the root and stem barks contain various flavone derivatives, 2-arylbenzofuran flavonoid, and PFs. Many types of kuwanon (flavone derivatives), mulberrofuran (2-arylbenzofuran flavonoid), and morusin (prenylated flavone) exist in the root and stem bark of any species in the genus _Morus_ (Abdel Bar et al., 2019; Guo et al., 2019; Zheng et al., 2012). Surprisingly, morusin is also found in _Artocarpus heterophyllus_ and _Artocarpus xanthocarpus_ roots (Jin et al., 2015; Ye et al., 2019). This shows that morusin might be a typical compound of the family Moraceae.

Metabolic profiling of mulberry leaves shows a variety of flavonols and flavones (Li et al., 2020a). Kaempferol 3-O-glucoside (astragalin), quercetin 3-O-glucoside (isouqueritrin), and kaempferol/queretin di-O-hexoside were found to be abundant in all _Morus_ leaves samples (Li et al., 2020a). This is consistent with the data collected in Table 1, where astragalin and isouqueritrin were detected in all samples of _M. alba_ leaves from various countries under different climatic conditions. This result is also in line with Kim et al. (2014) study where rutin, isouqueritrin, and astragalin were found to be the main flavonoid compounds in _M. alba_ leaves with concentrations of 3.10, 5.68, and 2.41 mg/g, respectively (Kim et al., 2014). Based on the flavonoid compound information collected in this review, the flavonoid compounds of _M. nigra_ leaves were identified by targeted screening so that only a few flavonoid compounds were detected. However, the flavonoids in _M. nigra_ leaves showed the same characteristics as _M. alba_ which was dominated by flavonols. Unlike flavonols which are abundant in O-glycosyl modification, flavones such as luteolin, apigenin, and chrysoeriol and their derivatives were also detected in _Morus_ leaves with O-hexosylated and O-pentosylated modifications (Li et al., 2020a).

Luteolin and apigenin and their glycosides were identified in almost all _Ficus_ plants. Luteolin was detected in two species of _Ficus_ from Egypt and one species each from Cameroon, China, and the Ivory Coast. Besides that, based on Table 1, other flavonoids also can be found in most _Ficus_ species.

Various PFs were identified in the roots of _A. heterophyllus_. PFs are chromone class derivatives that are structurally different and characterized by multiple prenyl units linked to the flavone core by C-3 and/or C-5. Various prenyl substitution patterns in the flavone skeleton give PF a high structural diversity (Ye et al., 2019). Many PFs were also identified in _Artocarpus nigrifolius_ twigs such as artocarin which can also be found in other _Artocarpus_ twigs and root barks and gemichalcone which also can be found in some _Morus laevigata_ twigs and _A. heterophyllus_ twigs (Di et al., 2013; Liu et al., 2018; Wang et al., 2015).

**TOTAL FLAVONOID CONTENT (TFC) AND TPC**

Various studies have estimated the flavonoid composition in some Moraceae plants. TFC and TPC have been determined from each part of Moraceae plants and summarized in Table 2. Most of the data originate from South Korea (Ju et al., 2018; Kim et al., 2014; 2020; Yu et al., 2021), Bangladesh (Khan et al., 2013; Sumi et al., 2016), China (Chen et al., 2020; Krishna et al., 2018), Brazil (Souza et al., 2018; Zeni et al., 2017), Malaysia (Abraham...
Table 1. Flavonoid compounds in *Morus*, *Ficus*, and *Artocarpus*.

| Species | Part | Location          | Latitude | Climate | Identification method          | Identified compounds                                                                 | Reference       |
|---------|------|-------------------|----------|---------|-------------------------------|--------------------------------------------------------------------------------------|-----------------|
| *M. alba* L. | Fruit | Seoul, South Korea | 37.57    | Dfa     | UHPLC-QTOF-HRMS               | Astragalin; quercetin; kaempferol; kaempferol 3-O-β-rutinoside; luteolin; rutin; taxifolin; quercetin 3-O-β-glucoside | Yu et al., 2021 |
|          |      |                   |          |         |                               | Cyanidin hexoside; cyanidin pentoside; cyanidin hexosyhexoside; delphinidin acetylhexoside; delphinidin rhamnosylhexoside; epigallocatechin; gallocaechitin; isorhamnetin glucuronide; isorhamnetin hexoside; isorhamnetin hexosyhexoside; kaempferol glucuronide; kaempferol hexosylhexoside; kaempferol rhamnosylhexoside; morin; naringin; pelargonidin hexoside; petunidin rhamnosylhexoside; quercetin; quercetin glucuronide; quercetin hexoside; quercetin hexosylhexoside; quercetin rhamnoside; rutin Catechin; cyanidin 3-(glucosyl)rhhamnoside; cyanidin 3,5-diglucoside; cyanidin 3-galactoside; cyanidin 3-glucoside dimer; cyanidin 3-laminariobioside; cyanidin 3-O-(diglucoside)glucosylrutinoside; cyanidin 3-rutinoside; cyanidin 3-rutinoside dimer; cyanidin 3-sophoroside; delphinidin 3,5-diglucoside; delphinidin 3-galactoside; delphinidin 3-rutinoside; delphinidin 3-rutinoside-5-glucoside; dihydroquercetin; dihydroquercetin-3-glucoside; dihydroquercetin-7-rutinoside; galloylcyadin-glycoside; kaempferol; kaempferol-3-glucoside; kaempferol-3-rutinoside; myricetin-pentoside; pelargonidin 3-glucoside; pelargonidin 3-rutinoside; peonidin 3-rutinoside; petunidin 3-arabinoside; procyanidin dimer A; quercetin; quercetin-methylpentoside-dihexoside; rutin Cyanidin 3-O-glucoside; cyanidin 3-O-rutinoside; quercetin 3-O-[6"-O-(6"-malonyl)glucosyl]-glucoside; kaempferol 3-O-glucosyl-glucoside-7-O-glucoside; quercetin 3-O-glucosyl-glucoside; kaempferol 3-O-rutinoside-7-O-glucoside; quercetin 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rhamnosyl-glucoside; kaempferol 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-[6"-O-(6"-malonyl)glucosyl]-rhamnoside; quercetin 3-O-glucoside; quercetin 3-O-[6"-acetyl]glucoside; kaempferol 3-O-rutinoside; kaempferol 3-O-[6"-malonyl]glucosyl-rhamnoside; quercetin 3-O-rhamnoside; quercetin 3-O-[6"-malonyl]-glucoside; quercetin 3-O-[6"-malonyl]-glucoside; quercetin | Natic et al., 2015 |
| *M. alba* L. | Fruit | Vojvodina, North Serbia | 45.30    | Cfa     | UHPLC-DAD MS/MS               | Catechin; cyanidin 3-glucosyl]rhamnoside; cyanidin 3,5-diglucoside; cyanidin 3-galactoside; cyanidin 3-glucoside dimer; cyanidin 3-laminariobioside; cyanidin 3-O-(diglucoside)glucosylrutinoside; cyanidin 3-rutinoside; cyanidin 3-rutinoside dimer; cyanidin 3-sophoroside; delphinidin 3,5-diglucoside; delphinidin 3-galactoside; delphinidin 3-rutinoside; delphinidin 3-rutinoside-5-glucoside; dihydroquercetin; dihydroquercetin-3-glucoside; dihydroquercetin-7-rutinoside; galloylcyadin-glycoside; kaempferol; kaempferol-3-glucoside; kaempferol-3-rutinoside; myricetin-pentoside; pelargonidin 3-glucoside; pelargonidin 3-rutinoside; peonidin 3-rutinoside; petunidin 3-arabinoside; procyanidin dimer A | Li et al., 2017 |
| *M. alba* L. | Fruit | Guangzhou, China  | 23.13    | Cfa     | UHPLC-HR-ESI-TOF-MS/MS        | Catechin; cyanidin 3-glucosyl]rhamnoside; cyanidin 3,5-diglucoside; cyanidin 3-galactoside; cyanidin 3-glucoside dimer; cyanidin 3-laminariobioside; cyanidin 3-O-(diglucoside)glucosylrutinoside; cyanidin 3-rutinoside; cyanidin 3-rutinoside dimer; cyanidin 3-sophoroside; delphinidin 3,5-diglucoside; delphinidin 3-galactoside; delphinidin 3-rutinoside; delphinidin 3-rutinoside-5-glucoside; dihydroquercetin; dihydroquercetin-3-glucoside; dihydroquercetin-7-rutinoside; galloylcyadin-glycoside; kaempferol; kaempferol-3-glucoside; kaempferol-3-rutinoside; myricetin-pentoside; pelargonidin 3-glucoside; pelargonidin 3-rutinoside; peonidin 3-rutinoside; petunidin 3-arabinoside; procyanidin dimer A; quercetin; quercetin-methylpentoside-dihexoside; rutin Cyanidin 3-O-glucoside; cyanidin 3-O-rutinoside; quercetin 3-O-[6"-O-(6"-malonyl)glucosyl]-glucoside; kaempferol 3-O-glucosyl-glucoside-7-O-glucoside; quercetin 3-O-glucosyl-glucoside; kaempferol 3-O-rutinoside-7-O-glucoside; quercetin 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rhamnosyl-glucoside; kaempferol 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-[6"-O-(6"-malonyl)glucosyl]-rhamnoside; quercetin 3-O-glucoside; quercetin 3-O-[6"-acetyl]glucoside; kaempferol 3-O-rutinoside; kaempferol 3-O-[6"-malonyl]glucosyl-rhamnoside; quercetin 3-O-rhamnoside; quercetin 3-O-[6"-malonyl]-glucoside; quercetin 3-O-[6"-malonyl]-glucoside; quercetin | Tomczyk et al., 2019 |
| *M. alba* L. | Fruit | Rzeszow, Poland | 50.00    | Cfb     | UPLC-PDA-ESI-MS               | Catechin; cyanidin 3-glucosyl]rhamnoside; cyanidin 3,5-diglucoside; cyanidin 3-galactoside; cyanidin 3-glucoside dimer; cyanidin 3-laminariobioside; cyanidin 3-O-(diglucoside)glucosylrutinoside; cyanidin 3-rutinoside; cyanidin 3-rutinoside dimer; cyanidin 3-sophoroside; delphinidin 3,5-diglucoside; delphinidin 3-galactoside; delphinidin 3-rutinoside; delphinidin 3-rutinoside-5-glucoside; dihydroquercetin; dihydroquercetin-3-glucoside; dihydroquercetin-7-rutinoside; galloylcyadin-glycoside; kaempferol; kaempferol-3-glucoside; kaempferol-3-rutinoside; myricetin-pentoside; pelargonidin 3-glucoside; pelargonidin 3-rutinoside; peonidin 3-rutinoside; petunidin 3-arabinoside; procyanidin dimer A; quercetin; quercetin-methylpentoside-dihexoside; rutin Cyanidin 3-O-glucoside; cyanidin 3-O-rutinoside; quercetin 3-O-[6"-O-(6"-malonyl)glucosyl]-glucoside; kaempferol 3-O-glucosyl-glucoside-7-O-glucoside; quercetin 3-O-glucosyl-glucoside; kaempferol 3-O-rutinoside-7-O-glucoside; quercetin 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rhamnosyl-glucoside; kaempferol 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-[6"-O-(6"-malonyl)glucosyl]-rhamnoside; quercetin 3-O-glucoside; quercetin 3-O-[6"-acetyl]glucoside; kaempferol 3-O-rutinoside; kaempferol 3-O-[6"-malonyl]glucosyl-rhamnoside; quercetin 3-O-rhamnoside; quercetin 3-O-[6"-malonyl]-glucoside; quercetin 3-O-[6"-malonyl]-glucoside; quercetin | Tomczyk et al., 2019 |
| Species | Part   | Location          | Latitude | Climate | Identification method | Identified compounds                                                                                                                                                                                                 | Reference       |
|---------|--------|-------------------|----------|---------|-----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|
| *M. alba* L. | Leaf   | Chongqing, China  | 29.81    | Cfa     | LC-ESI-MS/MS          | Apigenin; apigenin 7-O-glucoside; apigenin O-hexosyl-O-malonylhexoside; apigenin O-malonylhexoside; apigenin O-pentosyl-O-hexoside; chrysoeriol O-hexoside; astragalin; kaempferol di O-rhamnosyl-O-hexoside; kaempferol di O-hexoside; kaempferol O-hexosyl-O-hexosyl-O-malonylhexoside; kaempferol O-hexosyl-O-malonylhexoside; kaempferol O-malonylhexoside; kaempferol O-hexosyl-O-malonylhexoside; kaempferol O-hexosyl-O-hexoside; kaempferol O-hexosyl-O-malonylhexoside; kaempferol O-hexosyl-O-hexoside; luteolin; luteolin O-hexoside; luteolin O-malonylhexoside; luteolin O-pentosyl-O-hexoside; naringenin; quercetin di O-rhamnosyl-O-hexoside; quercetin di O-hexoside; quercetin O-hexoside; quercetin O-hexosyl-O-hexosyl-O-hexoside; quercetin O-hexosyl-O-malonylhexoside; quercetin O-malonylhexoside; quercetin O-hexosyl-O-hexoside; quercetin O-rhamnosyl-O-malonylhexoside; quercetin O-rhamnosyl-O-hexoside; quercetin O-rhamnosyl-O-hexoside | Li et al., 2020b |
| *M. alba* L. | Leaf   | Beijing, China    | 39.96    | Cfa     | UPLC-QTOF-MS/MS       | Rutin; isoquercitrin; astragalin                                                                                                                                                                                   | Cao et al., 2020 |
| *M. alba* L. | Leaf   | Daejeon, South Korea | 36.35  | Cfa     | HPLC/ DAD             | Rutin; isoquercitrin; astragalin                                                                                                                                                                                   | Kim et al., 2014 |
| *M. alba* L. | Leaf   | Jeollabuk-do, South Korea | 35.89  | Dfa     | UPLC-PDA-QTOF/MS      | Kaempferol 3-O-(6"-O-malonyl)glucoside; kaempferol 3-O-rhamnoside-7-O-glucoside; kaempferol 3-O-rutinoside; quercetin 3,7-di-O-glucoside; quercetin 3-O-(6-O-malonyl)glucoside; astragalin; isoquercitrin; moragrol A; moragrol B; moragrol C; moragrol D; morkotin A; morkotin B; quercetin 3-gentiobioside; rutin Kaempferol 3-O-(2"-O-malonyl)glucoside; kaempferol 3-O-(6"-O-malonyl)glucoside; kaempferol 3-O-rhamnoside-7-O-glucoside; kaempferol 3-O-rutinoside; quercetin 3,7-di-O-glucoside; quercetin 3-O-(6-O-malonyl)glucoside; astragalin; isoquercitrin; moragrol A; moragrol B; morkotin C; morkotin B; morkotin D; morkotin A; morkotin B; morkotin C; rutin | Kim et al., 2020 |
| *M. alba* L. | Leaf   | Jeonju, South Korea | 35.82  | Cfa     | UPLC-DAD-QTOF/MS      | Rudin; isoquercitrin; astragalin; moragrol A; moragrol B; moragrol C; moragrol D; morkotin A; morkotin B; morkotin C; rutin; Astragalin; kaempferol rutinoside hexoside; kaempferol-acetylhexoside; kaempferol-hexoside-hexoside; kaempferol-hexoside-rhamnoside; kaempferol-malonyl-dihexoside; kaempferol-malonyl-rutinoside; quercetin malonyl-dihexoside; quercetin-acetylhexoside; quercetin-dihexoside; quercetin-hexoside (isoquercitrin); quercetin-malonyl-hexoside; quercetin-malonyl-rutinoside; quercetin-rhamnose-hexose-rhamnose; rutin; quercetin-rutinoside isomer; quercetin-hexoside-hexoside | Ju et al., 2018 |
| *M. alba* and *M. nigra* | Leaf   | Alicante, Spain   | 38.09    | BSk     | UHPLC-ESI-MS          | Astagalin; kaempferol rutinoside hexoside; kaempferol-acetylhexoside; kaempferol-hexoside-hexoside; kaempferol-hexoside-rhamnoside; kaempferol-malonyl-dihexoside; kaempferol-malonyl-rutinoside; quercetin malonyl-dihexoside; quercetin-acetylhexoside; quercetin-dihexoside; quercetin-hexoside (isoquercitrin); quercetin-malonyl-hexoside; quercetin-malonyl-rutinoside; quercetin-rhamnose-hexose-rhamnose; rutin; quercetin-rutinoside isomer; quercetin-hexoside-hexoside | Sanchez-Salcedo et al., 2016 |
| Species   | Part         | Location            | Latitude | Climate | Identification method      | Identified compounds                                                                                                                                                                                                 | Reference               |
|-----------|--------------|---------------------|----------|---------|----------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| M. alba L | Leaf         | Rzeszow, Poland     | 50.00    | Cfb     | UPLC-PDA-ESI-MS            | Quercetin 3-O-[(6″-O-malonyl)-glucosyl]-glucoside; kaempferol 3-O-rutinoside-7-O-glucoside; quercetin 3-O-glucosyl-glucoside; kaempferol 3-O-glucosyl-glucoside-7-O-glucoside; kaempferol 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-(6″-acetyl)-glucoside; kaempferol 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-(6″-malonyl)-glucosyl-7-O-rhamnoside; quercetin 3-O-(6″-malonyl)-glucoside; quercetin 3-O-(6″-acetyl)-glucoside | Tomczyk et al., 2019    |
| M. alba L | Root bark    | Yunnan, China       | 24.48    | Cfa     | HPLC-PDA                 | (R)-Cyclomorusin; (S)-cyclomorusin; 14-methoxy-dihydroxymorusin; cyclocarminol; cycromulberryin; astracone A; kuwanon F; morunigrol A; licoflavone C; sanggenone J; morusin; sanggenol; kuwanon C; kuwanon E; sanggenol P; sanggenol Q; cudraflavone C; 5′-(1″,1″-dimethylallyl)-5,7,2′,4′-tetrahydroxyflavone | Guo et al., 2018        |
| M. alba L | Root bark    | Shandong, China     | 35.89    | Cfb     | HR-ESI-MS and 1\H and 13\C-NMR | Dioxycudraflavone A; 5-hydroxethyl moracin M; sanggenon V; morusin; monsigin L; licoflavone C; moracin C; alfafuran; mulberrofuran G | Li et al., 2018          |
| M. alba L | Root bark    | Yunnan, China       | 22.01    | Cfa     | HPLC & 1\H and 13\C-NMR  | Albasm A–D; mulberrofuran C; mulberrofurans E–G; mulberrofuran J-K; chalcomoracin; kuwanon J; kuwanon R; kuwanol A; morulin C; mulberrofuran B; mulberrofuran Y; moracin M; kuwanon C; albamin A | Huang et al., 2017      |
| M. alba L | Root bark    | Seoul, South Korea  | 37.57    | Dfa     | Chromatography, 1\H and 13\C-NMR | Mulberrofuran G; kuwanon G; albanol B | Paudel et al., 2019 |
| M. alba L | Root bark    | Sungnam, South Korea| 37.44    | Dfa     | NMR, MS, CD, and IR       | Sanggenon J; sanggenon U; sanggenon V; sanggenon W; eucharinone A; kuwanon E; kuwanon S | Jung et al., 2016       |
| M. alba L | Root bark    | Ulsan, South Korea  | 35.50    | Cfa     | HPLC                      | Morusalin A–D; albanon T; albanin B; maccorulin G; yunanensin A; 5′-4′,1″-dimethylallyl)-5,7,2′,4′-tetrahydroxyflavone; morusinol C; albanol B; mulberrofuran G; mulberrofuran H; mulberrofuran K; mulberrofuran L; (E)-4-isopenteny1-1,3,5,2′,4′-tetrahydroxystilbene; moracin S; 5′-geranyl-5-7,2′,4′-tetrahydroxy-flavone; morusinol; albanin A | Ha et al., 2018          |
| M. alba L | Root bark    | Sichuan, China      | 30.26    | Cfb     | HPLC-HRMS-SPE-NMR         | Kuwanon C; kuwanon L-M; kuwanon T; mulberrofuran G; moracenin B (kuwanon G); moracenin A (kuwanon H); morusinol, morusin, cycromorusin; mulberrofuran B; sanggenofuran A; sanggenon G | Zhao et al., 2018        |
| M. nigra L | Fruit        | Chiang Mai, Thailand| 18.79    | A       | HPLC                      | Cyanidin; cyanidin-3-O-rutinoside; cyanidin-3-O-glucoside | Suttisansnee et al., 2020 |

Continued
| Species          | Part       | Location           | Latitude | Climate | Identification method | Identified compounds                                                                 | Reference                        |
|------------------|------------|--------------------|----------|---------|-----------------------|--------------------------------------------------------------------------------------|----------------------------------|
| *M. nigra* L.    | Fruit      | Xinjiang, China    | 42.52    | BSk     | UPLC-TUV/Qda          | Cyanidin-3-O-glucoside; cyanidin-3-O-rutinoside; delphinidin-3-O-glucoside; delphinidin 7-O-rutinoside; delphinidin 7-O-glucoside; cyanidin 3-O-glucosyl-rhamnoside; quercetin 3-O-glucoside; quercetin 7-O-glucoside; rutin | Chen et al., 2017                |
| *M. nigra* L.    | Fruit      | Minas Gerais, Brazil | -20.39   | Cfa     | RP-UPLC-DAD-MS        | Delphinidin 3-O-rutinoside; delphinidin 7-O-rutinoside; cyanidin 3-O-glucoside; delphinidin 3-O-glucoside; cyanidin 3-O-glucosyl-rhamnoside; quercetin 3-O-glucoside; quercetin 7-O-glucoside; rutin | de Padua Lucio et al., 2018      |
| *M. nigra* L.    | Fruit      | North-west of Italy | 45.12    | Cfa     | HPLC-DAD-ESI HRMS     | Apigenin-di-hexoside; apigenin-hexoside; cyanidin-hexoside; cyanidin-pentosyl-hexoside; cyanidin-rhamnosyl-hexoside; cyanidin-sambubiosyl-glucoside; cyanidin-sambubiosyl-rhamnoside; delphinidin-dirhamnosyl-hexoside; delphinidin-pentoside; kaempferol-rhamnosyl-hexoside; kaempferol-di-hexoside; kaempferol-hexoside; kaempferol-malonyl-hexoside; kaempferol-rhamnoside; myricetin-hexoside; peonidin-hexoside; petunidin-pentoside; quercetin; quercetin hexoside; quercetin rhamnoside; quercetin-dirhamnosyl-hexoside; quercetin-malonyl-hexoside; quercetin-rhamnosyl-hexoside; rutin; kaempferol; procyanidin trimer 1 | Zotzi et al., 2020               |
| *M. nigra* L.    | Leaf       | Minas Gerais, Brazil | 20.39    | BSh     | HPLC                 | 6-Hydroxy-luteolin-7-O-rutinoside; quercetin-3-O-furanosyl-2-ramosil; rutin; quercetin 3-O-glucoside | de Padua Lucio et al., 2018      |
| *M. nigra* L.    | Leaf       | Bahia, Brazil      | -20.39   | Cfa     | RP-HPLC              | Apigenin; apigenin-hexoside; cyanidin-hexoside; cyanidin-pentosyl-hexoside; cyanidin-rhamnosyl-hexoside; cyanidin-sambubiosyl-glucoside; cyanidin-sambubiosyl-rhamnoside; delphinidin-dirhamnosyl-hexoside; delphinidin-pentoside; kaempferol-rhamnosyl-hexoside; kaempferol-di-hexoside; kaempferol-hexoside; kaempferol-malonyl-hexoside; kaempferol-rhamnoside; myricetin-hexoside; peonidin-hexoside; petunidin-pentoside; quercetin; quercetin hexoside; quercetin rhamnoside; quercetin-dirhamnosyl-hexoside; quercetin-malonyl-hexoside; quercetin-rhamnosyl-hexoside; rutin; kaempferol; procyanidin trimer 1 | Junior et al., 2017              |
| *M. nigra* L.    | Leaf       | Santa Catarina, Brazil | -26.90  | Cfa     | RP-HPLC              | Quercetin; rutin; catechin                               | Zeni et al., 2017                |
| *M. nigra* L.    | Root bark  | Rome, Italy        | 42.01    | Cfa     | HPLC and 1H and 13C-NMR | Kuwanon E; kuwanons G-H; kuwanon L; cudraflavone A; morusin; chaleomoracin; norartocarpetin | Mascarello et al., 2018           |
| *M. nigra* L.    | Root bark  | Asotthalom, Hungary | 46.20    | Cfa     | RP-HPLC and 1H and 13C-NMR | Morusin; kuwanon E; kuwanon U; moracin O-P; albanols A-B | Zoofishan et al., 2019           |
| *M. nigra* L.    | Stem bark  | Dakahlia, Egypt    | 31.17    | BWh     | MPLC, TLC, IR, UV, and 1H and 13C-NMR | 2',3,4',5,5'-Pentahydroxy-cis-stilbene; norartocarpetin; kuwanon C; kuwanon G; morusin; cudraflavone; albufurane; mulberrofuran G; 2',3,4',5,5'-pentamethoxy-cis-stilbene; 2',3,4'-trimethoxy-5-hydroxy-trans-stilbene | Abdel Bar et al., 2019           |
| *M. nigra* L.    | Twigs      | Xinjiang, China    | 37.17    | BWk     | HPLC-ESI-MS          | Nigragenons A–E; sanggenon A; sanggenol F; sanggenol H; nigrasin K; nigrasin l; cyclomalberrin | Xu et al., 2018                  |
| *Morus* australis | Stem bark  | Jiangxi, China     | 29.03    | Cfa     | UV, IR, MS, 1H and 13C-NMR, and CD data | Benzokuwanon E; hydroxymorusin; dicyclokuwanon EA; dicyclokuwanon EB | Zheng et al., 2012               |

Continued
| Genus | Species | Part | Location   | Latitude | Climate | Identification method | Identified compounds                                                                                     | Reference  |
|-------|---------|------|------------|----------|---------|----------------------|---------------------------------------------------------------------------------------------------------|------------|
| Morus | M. australis | Root | Shaanxi, China | 34.34 | Cfa | HPLC and ¹H and ¹³C-NMR | Cudraflavones B-C; morusin G; kuwanon C; kuwanon H; australone A; morusin; mu bertofurans F-G; moracenin B; morcin M; catharuran B | Guo et al., 2019 |
|       | M. laevigata | Twigs | Yunnan, China | 24.28 | Cfb | HPLC, IR, UV, NMR, and HR-ESI-MS | Laevigasin A–C; notabilisin A; notabilisin D; notabilisin E; 3',4',5,7-tetrahydroxy-3-methoxy-6-geranylflavone; gemichalcone A; sa gengol F; taxifolin; hultenin | Wang et al., 2015 |
| Morus | M. mongolica | Fruit | Chongqing, China | 29.83 | Cfa | UPLC-TUV/Qda | Cyanidin-3-O-glucoside; cyanidin-3-O-rutinoside; pelargonidin-3-O-glucoside; rutin; isoquercetin; morin hydrate; quercetin; kaempferol | Chen et al., 2017 |
|       | M. atropurpurea (Roxb) | Fruit | Sichuan, China | 30.26 | Cfb | LC-ESI-MS/MS | Naringenin; dihydromyricetin; eriodictyol; dihydroquercetin; quercetin; cyanidin 3-O-glucoside; cyanidin 3-O-rutinoside; cyanidin; pelargonidin 3-O-glucoside | Huang et al., 2020 |
| Ficus | Ficus auriculata | Root | Hainan, China | 18.75 | Cfa | HPLC, HR-ESI-MS, and ¹H and ¹³C-NMR | 5,7,4'-Trihydroxy-3'-hydroxymethylisoflavone; ficusino flavone; methoxyisoflavone; alpinutosisoflavone | Qi et al., 2018 |
|       | F. carica | Fruit | Shandong, China | 37.51 | Cfa | HPLC-DAD-QTOF | Ficucaricones A–D and 12 other PF analog compounds | Liu et al., 2019 |
|       | F. carica | Fruit | Bragança, Portugal | 41.81 | Cfa | LC-DAD-ESI/MSn | Taxifolin-O-hexoside; quercetin-O-hexoside-O-acetyethylhexoside; apigenin-C-hexoside-C-pentoside; kaempferol-O-deoxyhexosyl-hexoside; quercetin-3-O-rutinoside; quercetin-O-acetylhexoside; apigenin-2"-O-rhamnosose-C-acetylhexoside | Palmeira et al., 2019 |
|       | F. cordata | Aerial part | Abha, Saudi Arabia | 18.22 | BSk | HPLC-ESI-MS | Acanthophorbins A-B; myricitrin; infectorin; quercetin-3,4′-dirhamnoside; 2′-O-methylartorin V | Al-Musayeib et al., 2017 |
|       | F. deltoidea | Leaf | Terengganu, Malaysia | 5.33 | Am | LC-MS | Isovitisin 2"-O-rhamnoside; rhoifolin; vitexin; flavone with three sugar moieties (hexose, rhamnose, and arabinose); orientin 2"-O-rhamnoside; isovitisin; vicenin-2; schaftoside; vicenin-3; 6-C-β-D-xlyopyranosyl-8-C-α-L arabinopyranosylapigenin; isoschaftoside; 6,8-di-C-α-L-arabinosylapigenin; 8-C-glucopyranosyl-6-C-xlyopyranosylapigenin; 6-C-L-arabinopyranosylapigenin; 6,8-di-C-α-L-arabinosylapigenin; 6,8-di-C-β-D-xlyopyranosylapigenin; 6-C-L-arabinopyranosylapigenin | Afza et al., 2019 |
|       | Ficus exasperata Vahl. | Leaf | Bingerville, Ivory Coast | 5.35 | A | UPLC-TUV/Qda and UPLC-ESI-QTOF-MS | Quercetin-3,7-di-hexoside; quercetin-3-(6-rhamnoside) glucoside; quercetin-3-glucoside; kaempferol-3-92-rhamnoside)hexoside; quercetin-3-(6-malonyl)hexoside; quercetin-3-hexoside-7-ketorhamnoside; kaempferol-3-hexoside; apigenin-7-(4′-methyl-3,4′-ketorhamnoside)hexoside; luteolin-6,8-di-C-hexoside; apigenin-6-C-pentoside-8-C-hexoside; apigenin-6-C-rhamnoside-8-C-hexoside; apigenin-6-C-pentoside-8-C-(3/4-ketorhamnoside)hexoside; apigenin-8-C-glucoside; luteolin-8-C-(3/4-ketorhamnoside)hexoside; apigenin-7-O-ketorhamnoside-8-C-hexoside; apigenin-8-C-(3/4-ketorhamnoside)hexoside | Mouho et al., 2018 |
| Genus | Species | Part       | Location     | Latitude | Climate | Identification method | Identified compounds                                                                                                                                                                                                 | Reference               |
|-------|---------|------------|--------------|----------|---------|-----------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------|
| Ficus | F. exasperata Vahl. | Leaf | Ile Ife, Nigeria | 7.49     | Aw      | UV shift reagent, $^1$H and $^{13}$C-NMR | Apigenin C-8-glucoside; isoquercetin 6-O-$\beta$-D-glucoside; quercetin-3-O-$\beta$-rhamnoside                                                                 | Taiwo and Igbeneghu, 2014 |
|       | F. hirta Vahl. | Fruit | Jiangxi, China | 28.05    | Cfa     | HR-ESI-MS, $^1$H and $^{13}$C-NMR, and 2D NMR | Naringenin-7-O-$\beta$-D-glucoside; eriodictyol-7-O-$\beta$-D-glucoside; pinocembrin-7-O-$\beta$-D-glucoside                                                                 | Wan et al., 2017        |
|       | F. hirta Vahl. | Fruit | Jiangxi, China | 28.06    | Cfa     | HPLC-QTOF-MS | Naringenin-7-O-$\beta$-D-glucoside; pinocembrin-7-O-$\beta$-D-glucoside; luteolin; apigenin 5,7,4′-Trihydroxy-3-methoxy-3′-(3-methylbut-2-en-1-yl) flavone; carbapachrome; isoserodore; ficusflavone; isowighteone; 3′-(3-methylbut-2-en-1-yl)biochanin A; myrsininone A; ficusin A | Chen et al., 2020       |
|       | Ficus hispida | Twigs | Yunnan, China | 22.01    | Cfa     | TLC, UV, IR, HR-ESI-MS, and $^1$H and $^{13}$C-NMR | 5,7,4′-Trihydroxy-3-methoxy-3′-(3-methylbut-2-en-1-yl) flavone; carpa-chrome; isoserodore; ficusflavone; isowighteone; 3′-(3-methylbut-2-en-1-yl)biochanin A; myrsininone A; ficusin A | Shi et al., 2016        |
|       | Ficus lyrata | Leaf | Cairo, Egypt | 30.04    | BWh     | UPLC-PDA-MS | (Epi)catechin digalloyl rhamnoside; (epi)afzelechin-(epi)galloycathein; (epi)afzelechin-(epi)catechin; (epi)afzelechin-(epi)epigallocatechins; benzyl rutinoside; lucenin-2; vicenin-2; rutin; orientin; 3-O-p-coumaroyl epigallocatechin; isoquercetin; luteolin; quercetin; apigenin; ficusflavone | Farag et al., 2014      |
|       | Ficus lyrata | Fruit | Cairo, Egypt | 30.04    | BWh     | UPLC-PDA-MS | (Epi)catechin digalloyl rhamnoside; epicatechin; o-p-coumaroyl epigallocatechin; luteolin; apigenin; dihydroxy trimethoxyflavone; ficusflavone; dihydroxy dimethoxyflavone; parvisoflavone B | Farag et al., 2014      |
|       | Ficus pandurata | Aerial roots | Zhejiang, China | 27.97    | Cfa     | HPLC/QTOF-MS/MS | Rutin; kaempferol-3-O-rutinoside; diosmetin-7-O-rutinoside; acacetin-7-O-rutinoside; quercetin-3-O-rutinoside-rhamnoside; quercetin 7-O-glucoside-rhamnoside-glucoside; acacetin 7-O-glucoside-rhamnoside-acetyl-gluoside | Zhang et al., 2014      |
|       | Ficus thonningii Blume. | Roots and stem bark | Bagangté, Cameroon | 5.25     | A       | UV, FT-IR, and HR-ESI-MS NMR | Thonningiiiflavanonols A-B; shuterin; naringenin; $\beta$-hydroxyflavonanone; luteolin; aromadendrin; garbanzol; dihydroquercetin 5,7,3′-trihydroxyflavanone | Ango et al., 2016       |
|       | Ficus vasta Forsk. | Leaf | Giza, Egypt | 30.01    | BWh     | PC, UV, $^1$H-NMR, MS, and HPLC-PDA/ESI-MS | Luteolin; quercetin, vitexin, quercetin 3-O-$\beta$-galactoside; rutin; catechin, naringenin, isoorceitrin, naringin, quercetin-3-galactoside, kaempferol-3-gluco side | Taviano et al., 2018     |
|       | Artocarpus altilis | Leaf | Ho Chi Minh, Vietnam | 10.82    | A       | FT-ICR-MS | Artocarpaurone; cycloaltilisin 7; sophorflavanone A; 1-(2,4-dihydroxyphenyl)-3-[8-hydroxy-2-methyl-2-(4-methyl-3-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone; 2-geranyl-2′,3,4,4′-tetrahydroxydihydrochalcone; 2′-geranyl-3′,4,7-trihydroxyflavanone; 3β-acetoxycyclart-25-ene-24-one; 3β-acetoxycyclart-25-methoxy-23-ene; 3β-acetoxy-urs-12-ene-11-one | Huong et al., 2012      |

Continued
| Genus | Species | Part | Location | Latitude | Climate | Identification method | Identified compounds | Reference |
|-------|---------|------|----------|----------|---------|-----------------------|----------------------|-----------|
| Ficus | Artocarpus communis | Leaf | Manado, Indonesia | 1.47 | A | HPLC and 1H and 13C-NMR | Sophoraflavanone A; (S,E)-2-(3,4-dihydroxyphenyl)-8-(3,7-dimethylocta-2,6-dien-1-yl)-5,7-dihydroxychroman-4-one; (S)-5,7-dihydroxy-8-((E)-6-hydroxy-3,7-dimethylocta-2,7-dien-1-yl)-2(4-hydroxyphenyl)chroman-4-one; 1-(2,4-dihydroxyphenyl)-3-(8-hydroxy-2(3-hydroxy-4-methylpent-4-en-1-yl)-2-methyl-2H-chromen-5-yl)propan-1-one; (S)-5,7-dihydroxy-8-((2E,5E)-7-hydroxy-3,7-dimethylocta-2,7-dien-1-yl)-2(4-hydroxyphenyl)chroman-4-one; 2-geranyl-2′,3,4,4′-tetrahydroxydihydrochalcone; 1-(2,4-dihydroxyphenyl)-3-[8-hydroxy-2-methyl-2-(4-hydroxy-4-methyl-2-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone | Inoue et al., 2018 |
| Ficus | Artocarpus heterophyllus Lam. | Roots | Guangxi Zhuang, China | 22.82 | Cfa | UPLC-QTOF-MS/MS | 6-(3-Methylbutyl-2-enyl)apigenin; albanin A; 14-hydroxyartonin E; artoindonesianins G-I; artoindonesianins P-R; artoindonesianins T; artelastoxanthone; artoisofuran; artocarmin; artocarpesin; norartocarpin; artocarpin; cudraflavone A; cycloartocarpin; artonins A-B; artonin E-H; artonin J-K; artonin S; artonin U; artocarpenone | Ye et al., 2019 |
| Ficus | Artocarpus heterophyllus Lam. | Stem and leaf | Hainan, China | 20.04 | Cfa | HPLC | 2-(4-Hydroxyphenyl)-8-(3-methyl-but-2-enyl)chroman-4-one; bracteflavone B; dinklagin C; 6-(3-methyl(E)-1-butenyl) chrysins; 5,7,3′,5′-tetramethoxy-6-C-prenylflavone | Liu et al., 2020 |
| Ficus | Artocarpus heterophyllus Lam. | Twigs | Yunnan, China | 22.01 | Cfa | HPLC | Artocarpusins A–C; artocarstilbene A; artocarmitins A-B; 3′-7-hydroxymethyl-(2′-γ-methylallyl)-2′,4′,4-trihydroxychalcone; isobavachalcone; gemichalcones A-B; isogemichalcone B; 2′,4′,2,4-tetrahydroxy-3′-(3-methyl-2-butenyl)-chalcone; 6-(3-methylbut-2-enyl)apigenin; artocarpesin; norartocarpin; artocarpin; cudraflavone C; 5,7,4′-trihydroxyflavone; norartocarpesin | Di et al., 2013 |
| Ficus | Artocarpus heterophyllus Lam. | Roots | Guangxi, China | 22.82 | Cfa | 1H and 13C-NMR, UV, IR, CD, and HR-ESI-MS | Artotetraoids A-D; morin; artocarmin A; albanin A; euchrenon A; norartocarpesin; steppogenin | Yuan et al., 2017 |
| Ficus | Artocarpus heterophyllus Lam. | Roots | Guangxi, China | 22.82 | Cfa | 1H and 13C-NMR, UV, IR, CD, and HR-ESI-MS | Artotetraoids A-B; 2,3-dihydro-5,7-dihydroxy-2(2-hydroxy-4-methoxyphenyl)-4H-1-benzopyran-4-one; artocarpesin | Ren et al., 2015 |
| Ficus | Artocarpus heterophyllus Lam. | Heartwood | Songkla, Thailand | 7.01 | Am | HPLC | Artocarpone; artocarpin; cycloartocarpin; cyanomaclurin | Septama et al., 2018 |

Continued
| Species             | Part          | Location          | Latitude | Climate | Identification method                                    | Identified compounds                                                                                                                                                                                                 | Reference            |
|---------------------|---------------|-------------------|----------|---------|--------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| *Artocarpus hypargyreus* | Stem          | Hainan, China     | 19.57    | A       | HPLC, HR-El-MS, and $^1$H and $^{13}$C-NMR            | Hypargylavones A–C; hypargystilbene A; mulberrofuran N; rubraflavone C; cudraflavones A and C; cycloartocarpin A; brosimone I; norartocarpin                                                                                       | Yu et al., 2012       |
| *Artocarpus lakoocha*   | Twigs and bark | Chiang Mai, Thailand | 18.93 | A       | HRLC-TOF-MS                                         | Lakoochanone, (+)-aelechin-3-O-α-l-rhamnopyranoside; (+)-catechin; moracin C; sanggenofuran B; integrin; cyclocommunin, oxymesoveratol; (E)-2-methoxy-4,3,5'-trihydroxystilbene; engelentin; isomigechalcone B; morachalcone A                   | Boonyakhetgoson et al., 2020 |
| *Artocarpus nigrifolius* | Twigs         | Yunnan, China     | 21.46    | Cfa     | HR-ESI-MS                                            | Cyclohexethylphenyll; artocarin A; artocarmins B-C; gemichalcones A–C; artocarpusin A; isogemichalcone B; eleocharin A; 5,4'-dihydroxy-3'-methoxy-(6,7)-2,2-dimethylpyranoflavone; carphchromenol; 2,4,2'-tetrahydroxy-3-(3-methyl-2-butenyl)-chalcone; carphchromenol; 6-prenyl-4,5,7-trihydroxy flavone; artocarpesin | Liu et al., 2018       |
| *Artocarpus rigida*     | Stem          | Đồng Nai, Vietnam | 11.94    | A       | $^1$H and $^{13}$C-NMR, UV, IR, and HR-ESI-MS, HR-FAB-MS | Artoxanthocarpus A-B; hydraxylakoochin A; methoxylakoochin A; epoxylakoochin A; artoxanthol; artoxanthochromane; lakoochin A; alboctalol; (+)-catechin; steppogenin; norartocarpentin; isoetin-5'-methyl ether; morusin; cyclocommunol; albanin A; cudraflavone C; artotinin A; chlorophorin | Nguyen et al., 2017    |
| *A. xanthocarpus*       | Roots         | Lanyu, Taiwan     | 22.04    | Cfa     | $^1$H and $^{13}$C-NMR, UV, IR, CD, and HR-ESI-MS    |                                                                                                                                                                                                _mgrmsystem: tandem mass spectrometry, MS: mass spectrometry, MSn: multistage mass spectrometry, PC: paper chromatography, PDA: photodiode array detector, QTOF: quadrupole time of flight, RP: reversed phase, SPE: solid-phase extraction, TLC: thin-layer chromatography, TOF: time of flight, UQV/Quad: tunable ultraviolet/mass single-quadrupole detection, UHPLC: ultra-high-performance liquid chromatography, UPLC: ultra-performance liquid chromatography, UV: ultraviolet. |

*H* and *$^{13}$C*-NMR: hydrogen-1 and carbon-13 nuclear magnetic resonance, CD: circular dichroism, DAD: diode array detector, EI: electron ionization, ESI: electrospray ionization, FT: Fourier transform, HPLC: high-performance liquid chromatography, HR: high resolution, HRLC: high-resolution liquid chromatography, HRMS: high-resolution mass spectrometry, ICP: inductively coupled plasma, ICR: ion cyclotron resonance, IR: infrared, LC: liquid chromatography, MPLC: medium-pressure liquid chromatography, MS/MS: tandem mass spectrometry, MS: mass spectrometry, PC: paper chromatography, PDA: photodiode array detector, TOF: time of flight, TOF-MS: time of flight, UQV/Quad: tunable ultraviolet/mass single-quadrupole detection, UHPLC: ultra-high-performance liquid chromatography, UPLC: ultra-performance liquid chromatography, UV: ultraviolet.

A: tropical, Af: tropical rainforest climate, Am: tropical monsoon climate, Aw: tropical savanna climate with dry winter characteristic, BSh: hot semi-arid (steppe) climate, BSk: cold semi-arid (steppe) climate, BWh: hot desert arid climate, BWk: cold desert arid climate, Cfa: humid subtropical climate, Cfb: oceanic climate, Dfa: hot summer humid continental climate.
Table 2. Total flavonoid and phenolic content in several Moraceae plants.

| Species          | Part          | Location       | Latitude | Climate | Precipitation rate (mm) | Temperature (°C) | Day-time (hour) | TFC               | TPC               | Reference         |
|------------------|---------------|----------------|----------|---------|-------------------------|------------------|-----------------|------------------|------------------|-------------------|
| *Morus alba* L.  | Fruit         | Seoul, South Korea | 37.56    | Dfa     | 8.7                     | -2.4             | 7.73            | 74.9 ± 8.6 mg CAE/g | 177.9 ± 4.7 mg GAE/g | Yu et al., 2021   |
| *Morus alba* L.  | Fruit         | Vojvodina, North Serbia | 45.29    | Cfa     | 45.3                    | 21.9             | 15.7            | —                | 326.29 ± 8.21 mg GAE/100 g FW | Natic et al., 2015 |
| *Morus alba* L.  | Fruit         | Rajshahi, Bangladesh | 24.37    | A       | 117.1                   | 30.2             | 13.3            | 4.198 ± 2.26 mg CAE/g DE | 52.71 ± 3.17 mg GAE/g DE | Khan et al., 2013 |
| *Morus alba* L.  | Fruit         | Jiangsu, China   | 32.18    | Cfa     | 53.5                    | 11.4             | 11.98           | —                | 147.69 ± 0.02 mg GAE/g DW | Krishna et al., 2018 |
| *Morus alba* L.  | Fruit         | Rzeszow, Poland  | 50.00    | Cfb     | 110.4                   | 19.9             | 16              | —                | 1,041.1 ± 56.7 mg GAE/100 g DW | Tomczyk et al., 2019 |
| *Morus alba* L.  | Leaf          | Jeollabuk-do, South Korea | 35.89    | Dfa     | 1,417.1/year             | 10.7/year        | —               | 37.87 ± 0.59 mg QE/g FDW | 38.49 ± 2.06 mg GAE/g FDW | M. Kim et al., 2020 |
| *Morus alba* L.  | Leaf          | Daejeon, South Korea | 36.35    | Cfa     | 1,353.1/year             | 11.8/year        | —               | —                | 28.2 to 55.4 mg GAE/g extract | Kim et al., 2014  |
| *Morus alba* L.  | Leaf          | Jeonju, South Korea | 35.82    | Cfa     | 1,366.6/year             | 11.3/year        | —               | 748.5 to 1,297.9 mg/100 g DW | —                | Ju et al., 2018   |
| *Morus alba* L.  | Leaf          | Rajshahi, Bangladesh | 24.37    | A       | 117.1                   | 30.2             | 13.3            | 6.667 ± 2.45 mg CAE/g DE | 103.68 ± 17.471 mg GAE/g DE | Khan et al., 2013 |
| *Morus alba* L.  | Leaf          | Rzeszow, Poland  | 50.00    | Cfb     | 110.4                   | 19.9             | 16              | —                | 761.4 ± 56.2 mg GAE/100 g DW | Tomczyk et al., 2019 |
| *Morus alba* L.  | Root bark     | Rajshahi, Bangladesh | 24.37    | A       | 117.1                   | 30.2             | 13.3            | 12.59 ± 2.96 mg CAE/g DE | 165.27 ± 3.28 mg GAE/g DE | Khan et al., 2013 |
| *Morus alba* L.  | Stem bark     | Rajshahi, Bangladesh | 24.37    | A       | 117.1                   | 30.2             | 13.3            | 102.4 ± 6.19 mg CAE/g DE | 285.62 ± 2.54 mg GAE/g DE | Khan et al., 2013 |
| M. bombycis var. Kenmochi | Leaf | Rzeszow, Poland  | 50.00    | Cfb     | 110.4                   | 19.9             | 16              | —                | 665.5 ± 63.3 mg GAE/100 g DW | Tomczyk et al., 2019 |
| M. bombycis var. Kenmochi | Fruit | Rzeszow, Poland  | 50.00    | Cfb     | 110.4                   | 19.9             | 16              | —                | 1,114.8 ± 86.6 mg GAE/100 g DW | Tomczyk et al., 2019 |
| *Morus nigra* L. | Fruit         | Chiang Mai, Thailand | 18.78    | A       | 1,050/year               | 25.1/year        | —               | —                | 6.93 ± 0.58 mg GAE/g DW | Suttisansanee et al., 2020 |

Continued
| Species                  | Part   | Location              | Latitude | Climate | Precipitation rate (mm) | Temperature (°C) | Day-time (hour) | TFC              | TPC              | Reference        |
|-------------------------|--------|-----------------------|----------|---------|-------------------------|------------------|-----------------|------------------|------------------|-----------------|
| *Morus nigra* L.        | Leaf   | Santa Catarina, Brazil | –26.90   | Cfa     | 134.8                   | 26.5             | 11.9            | 79.96 ± 0.44 QE µg/g | 83.85 GAE mg/g | Zeni et al., 2017 |
| *Morus nigra* L.        | Leaf   | Bahia, Brazil         | –9.17    | BSh     | 33.2                    | 28.1             | 12.46           | 35.48 ± 6.86 mg CAE/g | 58.05 ± 5.20 mg GAE/g | Souza et al., 2018 |

**Genus Ficus**

| Species                  | Part   | Location              | Latitude | Climate | Precipitation rate (mm) | Temperature (°C) | Day-time (hour) | TFC              | TPC              | Reference        |
|-------------------------|--------|-----------------------|----------|---------|-------------------------|------------------|-----------------|------------------|------------------|-----------------|
| *Ficus hirta* Vahl.     | Fruit  | Jiangxi, China        | 28.05    | Cfa     | 1,601.6/year Avg 18.9   | —                |                 | 144.22 ± 8.46 mg RE/g DW | 85.25 ± 1.72 mg GAE/g DW | Chen et al., 2020 |
| *Ficus deltoidea*       | Leaf   | Negeri Sembilan, Malaysia | 2.59    | Af      | 1,926.9/year             | 26.6             | 12.33           | 163.47 ± 0.01 mg QE/g of DW | 43.32 ± 0.45 mg GA/g of DW | Abraham et al., 2018 |
| *Ficus carica*          | Fruit  | Bragança, Portugal    | 41.80    | Cfa     | 53.1/7/year              | 20.3 to 22.3     | 16              | 0.747 ± 0.005 mg/g extract | 0.542 ± 0.001 mg/g | Palmeira et al., 2019 |
| *Ficus carica*          | Fruit  | Faisalabad, Pakistan | 31.45    | BSh     | 120.1                   | 33               | 14              | 538.20 ± 1.17% w/w | 31.88 ± 1.48 g GAE/100 g DW | Alamgeer et al., 2017 |
| *Ficus carica*          | Fruit  | Cosenza, Italy        | 39.29    | Cfa     | 48.6                    | 21.8             | 12.47           | 2.6 ± 0.1–3.0 mg QE/g DW | 10.1 ± 0.2–14.8 mg ChAE/g DW | Loizzo et al., 2014 |
| *Ficus racemosa*        | Leaf   | Khulna, Bangladesh    | 22.84    | Aw      | 1,777/year              | Avg 26.6         | 11 to 13        | 22.81 mg QE/g DE | 20.2 mg GAE/g DE | Sumi et al., 2016   |
| *Ficus racemosa*        | Fruit  | Khulna, Bangladesh    | 22.84    | Aw      | 1,777/year              | Avg 26.6         | 11 to 13        | 10.63 mg QE/g DE | 26.2 mg GAE/g DE | Sumi et al., 2016   |

**Genus Artocarpus**

| Species                  | Part   | Location              | Latitude | Climate | Precipitation rate (mm) | Temperature (°C) | Day-time (hour) | TFC              | TPC              | Reference        |
|-------------------------|--------|-----------------------|----------|---------|-------------------------|------------------|-----------------|------------------|------------------|-----------------|
| *A. lakoocha* Roxb.     | Flower | Assam, India          | 26.20    | Cfa     | 8.2                     | 23.9             | 10.88           | 168.26 ± 1.50 µg QE/g | 217.80 ± 1.25 µg GAE/g | Gupta et al., 2020 |
| *A. heterophyllus*      | Flower | Assam, India          | 26.20    | Cfa     | 8.2                     | 23.9             | 10.88           | 658.52 ± 5.60 µg QE/g | 883.20 ± 5.90 µg GAE/g | Gupta et al., 2020 |
| *Artocarpus altulis*    | Fruit  | Kuantan, Malaysia     | 3.76     | Af      | 174.7                   | 27               | 12.32           | 203.17 ± 7.65 to 781 ± 52.97 mg GAE/100 g DW | Jalal et al., 2015 |

CAE: catechin equivalent, ChAE: chlorogenic acid equivalent, DE: dry extract, DW: dry weight, FDW: freeze-dried weight, FW: frozen weight, GAE: gallic acid equivalent, QE: quercetin equivalent, RE: rutin equivalent, TFC: total flavonoid content, TPC: total phenolic content, w/w: weight/weight.
Studies have shown that the polyphenol content of mulberry leaves is influenced by the variety and the growing location (Krishna et al., 2018). Morus leaf TPC values ranged from 665.5 ± 63.3 mg gallic acid equivalent (GAE)/100 g dried matter (DW) or almost equivalent to 6.65 mg GAE/g DW to 103.68 ± 17.471 mg GAE/g DW. The lowest TPC is from the Morus bombycis species from Poland and the highest one is from M. alba from Bangladesh. The highest TFC of Morus leaves was achieved by M. nigra from Bahia, Brazil, with a 35.48 ± 6.86 mg catechin equivalent (CAE)/g extract. Both Brazil and Bangladesh are considered as low-latitude countries that are located between the equator (0°) and 30°N/S (Khan et al., 2013; Zeni et al., 2017). The low-latitude area receives more sunlight than the higher-latitude area which can be the reason for these TFC and TPC values.

The highest TFC value in the genus Morus was achieved by the stem bark of M. alba from Bangladesh with a value of 102.469 ± 6.19 mg CAE/g DE (Khan et al., 2013). Bangladesh is a tropical country with the highest temperature which might be related to the light intensity in that place. Solar ultraviolet-B (UVB) radiation can induce oxidative stress in the plant cells because of the overproduced reactive oxygen species (ROS) (Guan et al., 2018). Thus, the formation of flavonoids and phenolic compounds is induced to neutralize these free radicals (Li et al., 2020b; Mouho et al., 2018).

It is found that Morus fruits contain higher TFC and TPC in regions with lower temperature conditions. Compared to the M. alba fruit from Bangladesh which was collected when the average temperature was 30.2°C (Khan et al., 2013), the fruit from South Korea when the temperature was −2.4°C has almost 18 times higher TFC (Yu et al., 2021). The expression of the PAL enzyme could be induced in the lower temperature condition, which led to the enhancement of the flavonoid content (Hao et al., 2018).

Ficus hirta fruits, from Jiangxi, China, show the highest TFC among fruits and leaves in the same genus. Among F. carica fruits from Pakistan, Italy, and Portugal, figs from Pakistan had the highest flavonoid and phenolic contents with values of 538.20% ± 1.17% w/w or 5.832 g quercetin equivalent/g dry matter and 31.88 ± 1.48 g GAE/100 g dry matter, respectively (Alamgeer et al., 2017). The hot semiarid (steppe) climate of Pakistan is more favorable for fig cultivation than the wet and warm temperate (Cf) climate (Datiles, 2015). Pakistan’s higher average temperature at the time of fruit collection than the temperatures of the two countries may also contribute to the higher TFC values as F. carica fruits require higher heat and temperature to reach ripeness and good quality (Isa et al., 2020).

The highest levels of anthocyanins are at the fruit’s perfect maturity level, so if they were not ripe, the content would likely be less than in the fruit that was harvested at that time (Gupta et al., 2020). The Artocarpus altilis fruit shows a very high total flavonoid and phenolic content compared to the other species in Moraceae. The TFC of A. altilis varied from 913.33 ± 24.44 to 6,213.33 ± 142.22 mg quercetin equivalent (QE)/g DW. This species is known as breadfruit and grows best in a hot and humid climate. The fruits of A. altilis are commonly used as food, medicine, and also animal feed (Jalal et al., 2015).

As these plants are rich in flavonoids, they are relevant to their various activities such as antioxidants and anti-inflammatory properties. However, it cannot be avoided that the composition of flavonoids in plants in various studies is not constant because of several factors such as origin, fertilization, harvesting season, plant age, the process of drying, and storage conditions. In addition, the identification of these compounds is also influenced by the method of analysis (Ribeiro et al., 2019).

**ANTIOXIDANT ACTIVITY OF MORACEAE PLANTS**

Oxidative stress generally causes an increase in intracellular ROS levels which can cause fatal effects to oxygen toxicity and cellular function (Kim et al., 2020). Under normal circumstances, ROS participate against pathogens, which is considered the most efficient microbial mechanism. In addition to its defense purpose during infection, excessive ROS production can increase the inflammatory process (Septama et al., 2018).

The mechanism of action of antioxidants is based on the test method. Therefore, the antioxidant activity assay is carried out by various methods. The antioxidant activity of plants is notably affected by the concentration of phenolic compounds contained in them. Generally, flowers or fruits that have a darker color produce a stronger antioxidant potential (Gupta et al., 2020).

Among the various methods to determine antioxidant activity, the 1,1-diphenyl-2-picrylhydrazyl (DPPH) assay has been a preferred and widely used method to evaluate the free radical scavenging ability of various natural products (Krishna et al., 2018). This method is more rapid, simple, and inexpensive compared to other antioxidant activity assays, while the 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) or Trolox equivalent antioxidant capacity assay is suitable for lipophilic and hydrophilic samples (Shahinuzzaman et al., 2020). A strong positive correlation between TPC and DPPH radical scavenging ability was shown in the study of Tomczyk et al. (2019) with a correlation coefficient above 0.9 (Tomczyk et al., 2019).

Flavonoids also show a capability to act against hydroxyl and superoxide radicals, the two most powerful radicals generated during metabolism, through hydroxyl radical scavenging activity (HRSA) and superoxide radical anion scavenging activity (SAS) assay (Zeni et al., 2017). A good correlation of TPC with SAS assay was demonstrated at over 0.933 (Natic et al., 2015). Both the ferric-reducing ability power (FRAP) and reducing power (RP) methods measure the reduction of Fe³⁺ to Fe²⁺ in the presence of antioxidants (Loizzo et al., 2014). Another antioxidant activity against ROS products such as malondialdehyde (MDA) can be measured by the lipid peroxidation assay. MDA is formed by the reaction of ROS with the side chain of phospholipids containing polyunsaturated fatty acid on the cell membrane (Li et al., 2020b).

Various antioxidant activity tests that have been carried out in the Moraceae plants showed strong antioxidant activities, and the values are provided in Table 3. The DPPH test, which was expressed as IC₅₀, showed very strong to moderate activity in Morus, Ficus, and Artocarpus. The lowest IC₅₀ of Morus was achieved by the stem bark of M. alba from Rajshahi, Bangladesh, with 36.5 µg/ml (Khan et al., 2013). This is in line with the total flavonoid and phenolic contents contained in the plant which are higher compared to other plants. Other methods also showed a good value of antioxidant ability. This shows that Moraceae plants are promising antioxidant agents with various mechanisms.
Table 3. Antioxidant activity of *Morus*, *Ficus*, and *Artocarpus* plants using various methods.

| Species | Part     | Location                  | Extraction solvent       | Genus Morus | DPPH IC$_{50}$ | ABTS IC$_{50}$ | FRAP IC$_{50}$ | HRSA IC$_{50}$ | Lipid peroxidation | RP | Reference               |
|---------|----------|---------------------------|--------------------------|-------------|-----------------|----------------|----------------|-----------------|-------------------|----|------------------------|
| *M. alba* L. | Fruit | Jiangsu, China | 80% ethanol | *Morus* | 1.79 mg/ml | — | 1.016 mg/ml; 94.36% | — | — | — | Krishna et al., 2018 |
| *M. alba* L. | Fruit | Seoul, South Korea | Ethyl acetate fraction | *Morus* | 133.6 ± 4.7 µg/ml | 216.6 ± 28.8 µg/ml | 3.727 ± 0.055 mmol Fe$^{2+}$/g | — | — | — | Yu et al., 2021 |
| *M. alba* L. | Fruit | Rajshahi, Bangladesh | Methanol | *Morus* | 76 µg/ml | — | — | 177.05 µg/ml | 26.28 ± 0.75 µM | 62.83 ± 3.57 % | Khan et al., 2013 |
| *M. alba* L. | Fruit | Vojvodina, North Serbia | Methanol | *Morus* | 86.79 ± 0.19% | — | — | — | — | — | Natic et al., 2015 |
| *M. alba* L. | Fruit | Rzeszow, Poland | Deionized water (5% w/v) | *Morus* | 78.9 ± 1.5% | — | 5.43 ± 0.12 mmol TE/100 g | — | — | — | Tomczyk et al., 2019 |
| *M. alba* L. | Leaf | Rajshahi, Bangladesh | Methanol | *Morus* | 108.69 µg/ml | — | — | 211.72 µg/ml | — | — | Khan et al., 2013 |
| *M. alba* L. | Leaf | Jeollabuk-do, South Korea | Distilled water | *Morus* | 7.09 ± 0.91 mg/ml | — | — | — | — | — | Kim et al., 2020 |
| *M. alba* L. | Leaf | Daejeon, South Korea | Methanol | *Morus* | 139 ± 15 µg/ml | — | — | — | — | — | Kim et al., 2014 |
| *M. alba* L. | Leaf | Khorasan, Iran | 80% ethanol | *Morus* | 103.49 ± 0.75 µg/ml | — | — | — | — | — | Ghavami et al., 2020 |
| *M. alba* L. | Leaf | Rzeszow, Poland | Deionized water (5% w/v) | *Morus* | 63.5 ± 2.9% | — | 3.02 ± 0.22 mmol TE/100 g | — | — | — | Tomczyk et al., 2019 |
| *M. alba* L. | Root bark | Rajshahi, Bangladesh | Methanol | *Morus* | 41 µg/ml | — | — | 116 µg/ml | — | — | Khan et al., 2013 |
| *M. alba* L. | Stem bark | Rajshahi, Bangladesh | Methanol | *Morus* | 36.5 µg/ml | — | — | 83.25 µg/ml | — | — | Khan et al., 2013 |

*Morus bombycis* Fruit | Rzeszow, Poland | Deionized water (5% w/v) | *Morus* | 77.9 ± 1.6% | — | 5.20 ± 0.06 mmol TE/100 g | — | — | — | Tomczyk et al., 2019 |

*Morus bombycis* Leaf | Rzeszow, Poland | Deionized water (5% w/v) | *Morus* | 54.6 ± 2.8% | — | 2.15 ± 0.08 mmol TE/100 g | — | — | — | Tomczyk et al., 2019 |

*Morus nigra* L. Fruit | Chiang Mai, Thailand | Ultrapure water | — | *Morus* | 0.40 ± 0.033 µmol TE/100 g DW | — | 21.33 ± 0.35 µmol TE/100 g DW | — | — | — | Suttisansane et al., 2020 |
### Genus *Morus*

| Species       | Part    | Location              | Extraction solvent | DPPH          | ABTS | FRAP | HRSA | Lipid peroxidation | RP | SAS  | Reference       |
|---------------|---------|-----------------------|--------------------|---------------|------|------|------|-------------------|----|------|-----------------|
| *Morus nigra* L. | Leaf    | Santa Catarina, Brazil | Distilled water    | 83.85 ± 0.99% | —    | —    | —    | —                 | —  | —    | Zeni et al., 2017 |
| *Morus nigra* L. | Leaf    | Bahia, Brazil         | 95% ethanol        | IC<sub>50</sub> 69.10 ± 1.88 µg/ml | —    | —    | —    | —                 | —  | —    | Souza et al., 2018 |

### Genus *Ficus*

| Species       | Part    | Location   | Extraction solvent | Antioxidant assay          | Reference   |
|---------------|---------|------------|--------------------|----------------------------|-------------|
| *Ficus hirta* Vahl. | Fruit   | Jiangxi, China | Ethyl acetate     | IC<sub>50</sub> 2.52 mg/ml | Chen et al., 2020 |
| *F. exasperata* Vahl. | Leaf    | Bingerville, Ivory Coast | Distilled water   | IC<sub>50</sub> 222.5 ± 8 µg/ml | Mouho et al., 2018 |
| *F. deltoidea* | Leaf    | Negeri Sembilan, Malaysia | Double-distilled water, ethyl acetate fraction | IC<sub>50</sub> 182 µg/ml | Abraham et al., 2018 |
| *Ficus vasta* Forssk. | Leaf    | Giza, Egypt | 80% methanol       | IC<sub>50</sub> 67.2 ± 3.8 µg/ml | Taviano et al., 2018 |
| *F. carica* | Fruit   | Bragança, Portugal | 80% ethanol        | IC<sub>50</sub> 1.13 ± 0.05 mg/ml | Palmeira et al., 2019 |
| *F. carica* | Fruit   | Cosenza, Italy | 70% ethanol        | IC<sub>50</sub> 41.3 ± 1.7 µg/ml | Loizzo et al., 2014 |
| *F. racemosa* | Fruit   | Khulna, Bangladesh | Methanol           | IC<sub>50</sub> 8.59 µg/ml | Sumi et al., 2016 |
| *F. racemosa* | Leaf    | Khulna, Bangladesh | Methanol           | IC<sub>50</sub> 10.28 µg/ml | Sumi et al., 2016 |

### Genus *Artocarpus*

| Species       | Part    | Location | Extraction solvent | Antioxidant assay          | Reference   |
|---------------|---------|----------|--------------------|----------------------------|-------------|
| *Artocarpus altilis* | Fruit   | Kuantan, Malaysia | Methanol           | IC<sub>50</sub> 55 ± 5.89 µg/ml | Jalal et al., 2015 |

DPPH: 2,2-diphenyl-1-picrylhydrazyl, ABTS: 2,2'-azinobis-3-ethylbenzothiazoline-6-sulfonic acid, FRAP: ferric-reducing antioxidant power, HRSA: hydroxyl radical scavenging activity, RP: reducing power, SAS: superoxide anion radical scavenging activity, w/v: weight/volume, IC<sub>50</sub>: half maximal inhibitory concentration, TE: Trolox equivalent, DW: dried matter, ASE: ascorbic acid equivalent, SC<sub>50</sub>: half maximal scavenging concentration, RC<sub>50</sub>: half maximal reducing concentration.
PFs and Diels–Alder-type adduct flavonoids show remarkable ability to scavenge free radicals. This is also related to the abundance of free hydroxyl groups in these phenolic compounds which may contribute to the activity (Zhao et al., 2018). Rutin and quercetin which are present in the M. nigra leaves ethanolic extract have been reported to play a big role in the anti-inflammatory effect, feasibly by modulating bradykinin and serotonin pathways (Ribeiro et al., 2019). The anti-inflammatory effect was also shown by prenylated isoflavones which showed an inhibitory effect on nitric oxide (NO) production (Liu et al., 2019).

**CLIMATE INFLUENCES ON FLAVONOIDS**

In general, functional components in plants are influenced by differences in varieties and cultivation environments, including sunlight, amount of fertilizer, and temperature (Sugiyama et al., 2016). In observing the flavonoid content in plants, this is also influenced by season, temperature, and accumulation of rainfall. Observations made on M. nigra growing in Brazil by measuring quercetin levels regularly every season throughout the year showed that quercetin and flavonoids are routinely affected by climate (Dalmagro et al., 2018).

The continued depletion of the ozone layer in the last few years has led to increased damage to crops through ultraviolet (UV) radiation from the sun (Li et al., 2020b). The effects of UVB stress induction and dark treatment have been carried out to understand the genes that contribute to metabolic mechanisms in a plant under abiotic stress conditions. Transcriptomics of M. alba leaves which were treated with UVB and dark incubation showed an increase in flavonoid biosynthesis due to upregulation of gene expression involved in flavonoid biosynthesis pathways (Guan et al., 2018).

The effect of light deprivation was also observed on anthocyanin synthesis in F. carica cultivar Zibo, China. Lack of light greatly affects pigment synthesis in fruit. Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment showed significant changes in phenylpropanoid biosynthesis and flavonoid biosynthesis pathways in fruits where significant repression occurs in the transcripts of chalcone synthase, chalcone isomerase, flavonoid 3’-hydroxylases, dihydroflavonol 4-reductase, and flavonoid 3-O-glucosyl transferase (Wang et al., 2019).

One of the most abundant secondary metabolites in plants and the largest subclass of flavonoids is flavones. Flavonoids, including flavones, have various functions that are useful for plants to adapt to complex and constantly changing environments. Flavone plays a role in protecting plants from solar UV radiation, giving color to flowers, interactions between species, and plant self-defense. Several studies have shown higher flavone content in the leaves of plants grown at higher altitudes. This indicates a correlation between flavones and plant tolerance to UV stress (Li et al., 2020b).

Based on climate, the flavonoid content is more abundant in plants that grow around the equator. Nevertheless, other factors such as cultivation, soil conditions, and the processing of samples could not be ignored (Kim et al., 2014). Interestingly, a report on the effect of the season on the flavonoid content had confirmed that both young and mature leaves collected in the dry season gave higher flavonoid production compared to that of the rainy season (Luengas-Caicedo et al., 2007).

**CONCLUSION**

Various species of Morus, Ficus, and Artocarpus show many variations of the flavonoid content. Each plant part has a characteristic in the flavonoid content; for example, the fruit contains a lot of anthocyanins, especially cyanidin glycosides; the leaves are rich in flavonols and their glycosides such as quercetin and kaempferol, while the roots and stems contain lots of flavones and their glycosides such as apigenin and luteolin. Several PFs and Diels–Alder adduct flavonoids were also found in this family, especially in the genus Morus. The largest flavonoid content in Morus plants is in the stems and roots, while the leaves of the Ficus genus are rich in flavonoids and TPC. More interestingly, climatic conditions, particularly the altitude and UV radiation, as well as the dry and rainy seasons, play a significant role in the flavonoid biosynthesis pathways. Furthermore, as these plants are plentiful in flavonoids, they have been proven to exhibit a strong antioxidant activity through various mechanisms. This review provides more insight into the potential of Moraceae plants as herbs to help improve various disease conditions induced by free radicals. Further research on the use of Moraceae plant extract as a functional food as well as in vivo and clinical trials is needed to ascertain the beneficial effects of these plant extracts on human health.

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**AUTHORS’ CONTRIBUTIONS**

Jutti Levita (JL) was principally responsible for the conception and design of the study. Dina Hawari (DH) searched and collected the articles. DH, Mutakin (M), and Gofarana Wilar (GW) participated in the processing, selecting, and analyzing of the data. DH, GW, and M contributed to the writing of the manuscript. JL checked, finalized, and revised the manuscript. All authors read and approved the final manuscript to be published.

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