


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, antispasmodic, 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 (Boonyaketguson *et al.*, 2020), antiplasmodial (Boonyaketguson *et al.*, 2020), immunomodulator (Septama *et al.*, 2018), and antispasmodic (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 (Afzan *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, isoflavones, flavanones, anthocyanins, and proanthocyanidin (Li *et al.*, 2020a). Other sources stated that flavanolol, aurone, furan chromone, isoflavanone, biflavones, xanthenes, 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.

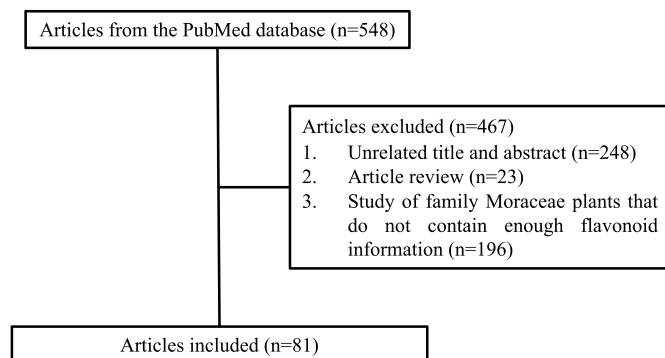


Figure 1. Flow chart of literature searching.

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 dihydromyricetin 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).

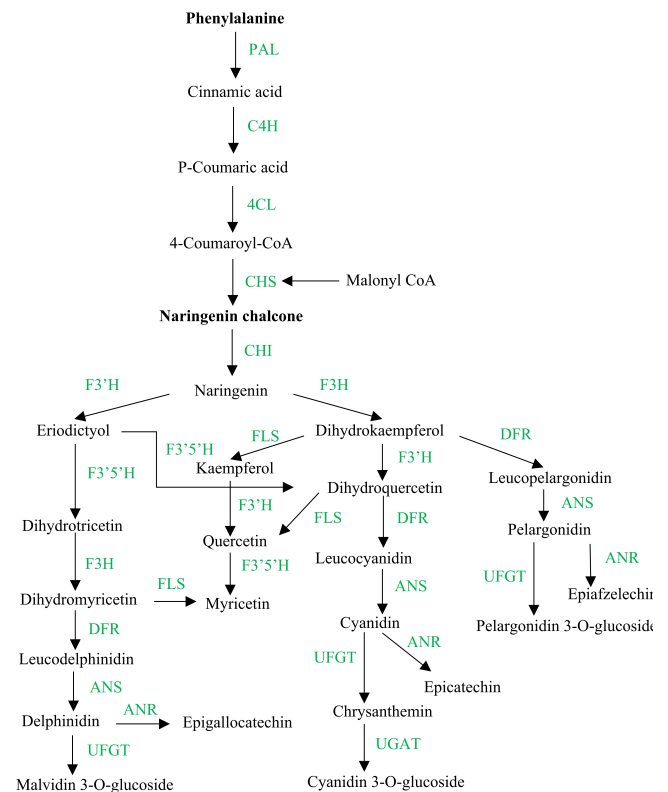


Figure 2. A schematic presentation of the flavonoid biosynthesis pathway (adapted from Huang *et al.*, 2020). PAL: phenylalanine ammonia-lyase, C4H: cinnamic acid 4-hydroxylase, 4CL: 4-coumarate-CoA ligase, CHS: chalcone synthase, CHI: chalcone isomerase, F3H: flavonoid 3-hydroxylase, F3'H: flavonoid 3'-hydroxylase, F3'5'H: flavonoid 3'5'-hydroxylase, FLS: flavonol synthase, DFR: dihydroflavonol 4-reductase, ANR: anthocyanin reductase, ANS: anthocyanidin synthase, UFGT: flavonoid 3-O-glucosyl transferase, UGAT: cyanidin-3-O-glucoside 2-O-glucuronosyltransferase.

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 (Boonyaketguson *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 flavonols 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 (astragalol), quercetin 3-O-glucoside (isoquercitrin), and kaempferol/quercetin 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 astragalol and isoquercitrin 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, isoquercitrin, and astragalol 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 flavones 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–C and/or C–O. 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 artocarmin 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*.

Genus <i>Morus</i>							
Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
<i>M. alba</i> L.	Fruit	Seoul, South Korea	37.57	Dfa	UHPLC-QTOF-HRMS	Astragaln; quercetin; kaempferol; kaempferol 3-O- β -rutinoside; luteolin; rutin; taxifolin; quercetin 3-O- β -glucoside Cyanidin hexoside; cyanidin pentoside; cyanidin hexosylhexoside; cyanidin rhamnosylhexoside; delphinidin acetylhexoside; delphinidin hexoside; delphinidin rhamnosylhexoside; epigallocatechin; galocatechin; isorhamnetin glucuronide; isorhamnetin hexoside; isorhamnetin hexosylhexoside; kaempferol glucuronide; kaempferol hexoside; kaempferol hexosylhexoside; kaempferol rhamnosylhexoside; morin; naringin; pelargonidin hexoside; petunidin rhamnosylhexoside; quercetin; quercetin glucuronide; quercetin hexoside; quercetin hexosylhexoside; rutin	Yu <i>et al.</i> , 2021
<i>M. alba</i> 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-galactoside dimer; cyanidin 3-glucoside; cyanidin 3-glucoside dimer; cyanidin 3-laminaribioside; 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; galloylcyanidin-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	Natic <i>et al.</i> , 2015
<i>M. alba</i> L.	Fruit	Guangzhou, China	23.13	Cfa	UHPLC-HR-ESI-TOF-MS/MS	Cyanidin 3-O-glucoside; cyanidin 3-O-rutinoside; quercetin 3-O-[(6"-O-malonyl)-glucosyl]-glucoside; kaempferol 3-O-glucosyl-glycoside-7-O-glucoside; quercetin 3-O-glucosyl-glycoside; kaempferol 3-O-rutinoside-7-O-glucoside; quercetin 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rhamnosyl-glycoside; kaempferol 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rutinoside; quercetin 3-O-[(6"-O-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	Li <i>et al.</i> , 2017
<i>M. alba</i> L.	Fruit	Rzeszow, Poland	50.00	Cfb	UPLC-PDA-ESI-MS	Cyanidin 3-O-glucoside; cyanidin 3-O-rutinoside; quercetin 3-O-[(6"-O-malonyl)-glucosyl]-glucoside; kaempferol 3-O-glucosyl-glycoside-7-O-glucoside; quercetin 3-O-glucosyl-glycoside; kaempferol 3-O-rutinoside-7-O-glucoside; quercetin 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rhamnosyl-glycoside; kaempferol 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rutinoside; quercetin 3-O-[(6"-O-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	Tomeczyk <i>et al.</i> , 2019

Continued

Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
Genus <i>Morus</i>							
<i>M. alba</i> L.	Leaf	Chongqing, China	29.81	Cfa	LC-ESI-MS/MS	Apigenin; apigenin 7-O-glucoside; apigenin di-O-hexoside; apigenin O-hexosyl-O-malonylhexoside; apigenin O-malonylhexoside; apigenin O-pentosyl-O-hexoside; chrysoeriol O-hexoside; astragaln; kaempferol di-O-rhamnonyl-O-hexoside; kaempferol O-hexosyl-O-malonylhexoside; kaempferol O-malonylhexoside; kaempferol O-rhamnonyl-O-hexoside; kaempferol O-rhamnonyl-O-hexosyl-O-hexoside; kaempferol O-rhamnonyl-O-malonylhexoside; kaempferol O-rhamnonyl-O-hexoside; luteolin; luteolin O-hexoside; luteolin O-malonylhexoside; luteolin O-pentosyl-O-hexoside; naringenin; quercetin; quercetin di-O-rhamnonyl-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-rhamnonyl-O-hexosyl-O-malonylhexoside; quercetin O-rhamnonyl-O-malonylhexoside; quercetin O-hexosyl-O-hexoside; quercetin O-rhamnonyl-O-malonylhexoside; quercetin O-rhamnonyl-O-hexoside; quercetin O-rhamnonyl-O-hexosyl-O-hexoside; quercetin O-rhamnonyl-O-hexosyl-O-malonylhexoside; quercetin O-rhamnonyl-O-hexoside	Li <i>et al.</i> , 2020b
<i>M. alba</i> L.	Leaf	Beijing, China	39.96	Cfa	UPLC-QTOF-MS/MS	Rutin; isoquercitrin; astragaln	Cao <i>et al.</i> , 2020
<i>M. alba</i> L.	Leaf	Daejeon, South Korea	36.35	Cfa	HPLC/DAD	Rutin; isoquercitrin; astragaln	Kim <i>et al.</i> , 2014
<i>M. alba</i> L.	Leaf	Jeollabuk-do, South Korea	35.89	Dfa	UPLC-PDA-QTOF/MS	Kaempferol 3-O-(6"-O-malonyl)glucoside; kaempferol 3-O-rhamnonyl-7-O-glucoside; kaempferol 3-O-rutinonyl-7-O-glucoside; quercetin 3-O-(6"-O-malonyl)glucoside; astragaln; isoquercitrin; moragrol A; moragrol B; moragrol C; moragrol D; morkotin A; morkotin B; quercetin 3-gentiobioside; rutin	Kim <i>et al.</i> , 2020
<i>M. alba</i> L.	Leaf	Jeonju, South Korea	35.82	Cfa	UPLC-DAD-QTOF/MS	Kaempferol 3-O-(2"-O-malonyl)glucoside (moragrol D); kaempferol 3-O-(6"-O-malonyl)glucoside; kaempferol 3-O-rhamnonyl-7-O-glucoside; kaempferol 3-O-rutinonyl-7-O-glucoside; quercetin 3-O-(6"-O-malonyl)glucoside; quercetin 3-O-rhamnonyl-7-O-glucoside; quercetin 3-O-rutinonyl-7-O-glucoside; astragaln; isoquercitrin; moragrol A; moragrol B; moragrol C; morkotin A; morkotin B; rutin	Ju <i>et al.</i> , 2018
<i>M. alba</i> and <i>M. nigra</i>	Leaf	Alicante, Spain	38.09	BSk	UHPLC-ESI-MS	Astragaln; kaempferol rutinonylhexoside; kaempferol-acetylhexoside; kaempferol-hexoside-hexoside; kaempferol-hexoside-rhamnonylhexoside; kaempferol-malonyl-dihexoside; kaempferol-malonyl-rutinonylhexoside; kaempferol-rutinonylhexoside; quercetin malonyl-dihexoside; quercetin-acetylhexoside; quercetin-dihexoside; quercetin-hexoside (isoquercitrin); quercetin-malonyl-hexoside; quercetin-malonyl-rutinonylhexoside; quercetin-rhamnonyl-hexoside; quercetin-hexose-rhamnonylhexoside; quercetin-hexoside-hexoside; quercetin-hexoside-hexoside isomer; quercetin-hexoside-hexoside	Sanchez-Salcedo <i>et al.</i> , 2016

Continued

Genus <i>Morus</i>							
Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
<i>M. alba</i> 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; quercetin 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rhamnosyl-glucoside; kaempferol 3-O-glucosyl-glucoside-7-O-glucoside; kaempferol 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-rutinoside-7-O-rhamnoside; quercetin 3-O-(6"-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	Tomczyk <i>et al.</i> , 2019
<i>M. alba</i> L.	Root bark	Yunnan, China	24.48	Cfa	HPLC-PDA	(R)-Cyclomorusin, (S)-cyclomorusin; 14-methoxy-dihydromorusin; cyclocommunol; cyclomulberrin; austraione 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 <i>et al.</i> , 2018
<i>M. alba</i> L.	Root bark	Shandong, China	35.89	Cfb	HR-ESI-MS and ¹ H and ¹³ C-NMR	Dioxyacudraflavone A; 5-hydroxyethyl moracin M; sanggenon V; morusin; morusignin L; licoflavone C; moracin C; alfafuran; mulberrofurran G	Li <i>et al.</i> , 2018
<i>M. alba</i> L.	Root bark	Yunnan, China	22.01	Cfa	HPLC & ¹ H and ¹³ C-NMR	Albasins A-D; mulberrofurran C, mulberrofurans E-G; mulberrofurans J-K; chalcocomoracin; kuwanon J; kuwanon R; kuwanol A; mongolicin C; mulberrofurran B; mulberrofurran Y; moracin M; kuwanon C; albanin A	Huang <i>et al.</i> , 2017
<i>M. alba</i> L.	Root bark	Seoul, South Korea	37.57	Dfa	Chromatography, ¹ H and ¹³ C-NMR	Mulberrofurran G; kuwanon G; albanol B	Paudel <i>et al.</i> , 2019
<i>M. alba</i> L.	Root bark	Sungnam, Korea	37.44	Dfa	NMR, MS, CD, and IR	Sanggenon J; sanggenon U; sanggenon V; sanggenon W; euchrenone a7; kuwanon E; kuwanon S	Jung <i>et al.</i> , 2016
<i>M. alba</i> L.	Root bark	Ulsan, South Korea	35.50	Cfa	HPLC	Morusalbins A-D; albanin T; albasin B; macrourin G; yunanensin A; 5'-(1',1'-dimethylallyl)-5,7,2',4'-tetrahydroxyflavone; mongolicin C; albanol B; mulberrofurran G; mulberrofurran H; mulberrofurran K; mulberrofurran L; (E)-4-isopentenyl 1-3,5,2',4'-tetrahydroxystilbene; moracin S; 5'-geranyl-5-7-2',4'-tetrahydroxy-flavone; morusinol; albanin A	Ha <i>et al.</i> , 2018
<i>M. alba</i> L.	Root bark	Sichuan, China	30.26	Cfb	HPLC-HRMS-SPE-NMR	Kuwanon C; kuwanons L-M; kuwanon T; mulberrofurran G; moracenin B (kuwanon G); moracenin A (kuwanon H); morusinol, morusin, cyclomorusin; mulberrofurran B; sanggenofuran A; sanggenon G	Zhao <i>et al.</i> , 2018
<i>M. nigra</i> L.	Fruit	Chiang Mai, Thailand	18.79	A	HPLC	Cyanidin; cyanidin-3-O-rutinoside; cyanidin-3-O-glucoside	Suttisansanee <i>et al.</i> , 2020

Continued

Genus <i>Morus</i>							
Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
<i>M. nigra</i> L.	Fruit	Xinjiang, China	42.52	BSk	UPLC-TUV/Qda	Cyanidin-3-O-glucoside; cyanidin-3-O-rutinoside; pelargonidin-3-O-glucoside; rutin; isoquercetin; morin hydrate; quercetin; kaempferol	Chen <i>et al.</i> , 2017
<i>M. nigra</i> L.	Fruit	Minas Gerais, Brazil	-20.39	Cfa	RP-UPLC-DAD-MS	Delphinidin 3-O-rutinoside; delphinidin 7-O-rutinoside; delphinidin 3-O-glucoside; delphinidin 7-O-glucoside; cyanidin 3-O-glucoside; cyanidin 3-O-glucosyl-rhamnoside; quercetin 3-O-glucoside; quercetin 7-O-glucoside; rutin	de Padua Lucio <i>et al.</i> , 2018
<i>M. nigra</i> L.	Fruit	North-west of Italy	45.12	Cfa	HPLC-DAD-ESI HRMS	Apigenin-dihexoside; apigenin-hexoside; cyanidin-hexoside; cyanidin-pentosyl-hexoside; cyanidin-rhamnosyl-hexoside; cyanidin-sambubiosyl-glucoside; cyanidin-sambubiosyl-rhamnoside; delphinidin-dihamosyl-hexoside; delphinidin-pentoside; kaempferol-rhamnosyl-hexoside; kaempferol-dihexoside; kaempferol-hexoside; kaempferol-malonyl-hexoside; kaempferol-rhamnoside; myricetin-hexoside; peonidin-hexoside; petunidin-pentoside; quercetin; quercetin-hexoside; quercetin-rhamnoside; quercetin-dihamosyl-hexoside; quercetin-malonyl-hexoside; quercetin-rhamnosyl-dihexoside; quercetin-rhamnosyl-hexoside; rutin; kaempferol; procyanidin trimer I	Zorzi <i>et al.</i> , 2020
<i>M. nigra</i> L.	Leaf	Minas Gerais, Brazil	-20.39	Cfa	RP-UPLC-DAD-MS	6-Hydroxy-luteolin-7-O-rutinoside; quercetin-3-O-furanosyl-2-ramosil; rutin; quercetin 3-O-glycoside	de Padua Lucio <i>et al.</i> , 2018
<i>M. nigra</i> L.	Leaf	Bahia, Brazil	-9.17	BSh	HPLC	Rutin; isoquercetin; kaempferitrin	Junior <i>et al.</i> , 2017
<i>M. nigra</i> L.	Leaf	Santa Catarina, Brazil	-26.90	Cfa	RP-HPLC	Quercetin; rutin; catechin	Zeni <i>et al.</i> , 2017
<i>M. nigra</i> L.	Root bark	Rome, Italy	42.01	Cfa	HPLC and ¹ H and ¹³ C-NMR	Kuwanon E; kuwanons G-H; kuwanon L; cudraflavone A; morusin; chalconoracrin; norartocarpetin	Mascarello <i>et al.</i> , 2018
<i>M. nigra</i> L.	Root bark	Asothalom Hungary	46.20	Cfa	RP-HPLC and ¹ H and ¹³ C-NMR	Morusin; kuwanon E; kuwanon U; moracin O-P; albanols A-B	Zoofishan <i>et al.</i> , 2019
<i>M. nigra</i> L.	Stem bark	Dakahlia, Egypt	31.17	BW'h	MPLC, TLC, IR, UV, and ¹ H and ¹³ C-NMR	2',3,4',5',5'-Pentahydroxy- <i>cis</i> -stilbene; norartocarpetin; kuwanon C; kuwanon G; morusin; cudraflavone; albufurane; mulberrofuran G; 2',3,4',5',5'-pentamethoxy- <i>cis</i> -stilbene; 2',3,4'-trimethoxy-5-hydroxy- <i>trans</i> -stilbene	Abdel Bar <i>et al.</i> , 2019
<i>M. nigra</i> L.	Twigs	Xinjiang, China	37.17	BWk	HPLC-ESI-MS	Nigragenons A-E; sanggenon A; sanggenol F; sanggenol H; nigrasin K; nigrasin I; cyclomulberrin	Xu <i>et al.</i> , 2018
<i>Morus australis</i>	Stem bark	Jiangxi, China	29.03	Cfa	UV, IR, MS, ¹ H and ¹³ C-NMR, and CD data	Benzokuwanon E; hydroxymorusin; dicyclokuwanon EA; dicyclokuwanon EB	Zheng <i>et al.</i> , 2012

Continued

Genus <i>Morus</i>							
Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
<i>M. australis</i>	Root	Shaanxi, China	34.34	Cfa	HPLC and ¹ H and ¹³ C-NMR	Cudraflavones B-C; morusin L; kuwanon C; kuwanon H; austroaone A; morusin; mulberrofuran F-G; moracenin B; morcin M; cathafuran B	Guo <i>et al.</i> , 2019
<i>M. laevigata</i>	Twigs	Yunnan, China	24.28	Cfb	HPLC, IR, UV, NMR, and HR-ESI-MS	Laevigasins A-C; notabilisin A; notabilisin D; notabilisin E; 3',4',5,7-tetrahydroxy-3-methoxy-6-geranylflavone; gemichalcone A; sanggenol F; taxifolin; hultenin	Wang <i>et al.</i> , 2015
<i>Morus mongolica</i>	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 <i>et al.</i> , 2017
<i>M. atropurpurea</i> (Roxb)	Fruit	Sichuan, China	30.26	Cfb	LC-ESI-MS/MS	Naringenin; dihydrokaempferol; eriodictyol; dihydroquercetin; dihydromyricetin; quercetin; cyanidin 3-O-glycoside; cyanidin 3-O-rutinoside; cyanidin; pelargonidin 3-O-glucoside	Huang <i>et al.</i> , 2020
Genus <i>Ficus</i>							
Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
<i>Ficus auriculata</i>	Root	Hainan, China	18.75	Cfa	HPLC, HR-ESI-MS, and ¹ H and ¹³ C-NMR	5,7,4'-Trihydroxy-3'-hydroxymethylisoflavone; ficuisoflavone; methoxyisoflavone; alpinumisoflavone	Qi <i>et al.</i> , 2018
<i>F. carica</i>	Fruit	Shandong, China	37.51	Cfa	HPLC-DAD-QTOF	Ficucaricenes A-D and 12 other PF analog compounds	Liu <i>et al.</i> , 2019
<i>F. carica</i>	Fruit	Bragança, Portugal	41.81	Cfa	LC-DAD-ESI/MSn	Taxifolin-O-hexoside; quercetin-O-hexoside-O-acetylhexoside; apigenin-C-hexoside-C-pentoside; kaempferol-O-deoxyhexosyl-hexoside; quercetin-3-O-rutinoside; quercetin-O-acetylhexoside; apigenin-2''-O-rhamnose-C-acetylhexoside	Palmeira <i>et al.</i> , 2019
<i>F. cordata</i>	Aerial part	Abha, Saudi Arabia	18.22	BSk	HPLC-ESI-MS	Acanthophorbins A-B; myricitrin; infectorin; quercetin-3,4'-dirhamnoside; 2''-O-methylarctonin V	Al-Musayeb <i>et al.</i> , 2017
<i>F. deltoidea</i>	Leaf	Terengganu, Malaysia	5.33	Am	LC-MS	Isovitexin 2''-O-rhamnoside; rhoifolin; vitexin; flavone with three sugar moieties (hexose, rhamnose, and arabinose); orientin 2''-O-rhamnoside; isovitexin; vicenin-2; schaftoside; vicenin-3; 6-C-β-D-xylopyranosyl-8-C-α-L-arabinopyranosylapigenin; isoschaftoside; 6,8-di-C-α-L-arabinosylapigenin; 8-C-glucopyranosyl-6-C-xylopyranosylapigenin; 6-C-L-arabinopyranosyl-8-C-D-xylopyranosylapigenin	Afzan <i>et al.</i> , 2019
<i>Ficus exasperata</i> 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-(6-rhamnoside)hexoside; luteolin-6,8-di-C-hexoside; apigenin-6-C-pentoside-8-C-hexoside; apigenin-6-C-hexoside-8-C-pentoside; 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 <i>et al.</i> , 2018

Continued

Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
<i>F. exasperata</i> Vahl.	Leaf	Ile Ife, Nigeria	7.49	Aw	UV shift reagent, ¹ H and ¹³ C-NMR	Apigenin C-8-glucoside; isoquercetin 6-O-4-hydroxybenzoate; quercetin-3-O-β-rhamnoside	Taiwo and Igbeneghu, 2014
<i>Ficus hirta</i> Vahl.	Fruit	Jiangxi, China	28.05	Cfa	HR-ESI-MS, ¹ H and ¹³ C-NMR, and 2D NMR	Naringenin-7-O-β-D-glucoside; eriodictyol-7-O-β-D-glucoside; pinocebrin-7-O-β-D-glucoside	Wan <i>et al.</i> , 2017
<i>Ficus hirta</i> Vahl.	Fruit	Jiangxi, China	28.06	Cfa	HPLC-QTOF-MS	Naringenin-7-O-β-D-glucoside; pinocebrin-7-O-β-D-glucoside; eriodictyol-7-O-β-D-glucoside; luteolin; apigenin 5,7,4'-Trihydroxy-3'-methoxy-3-(3-methylbut-2-en-1-yl) flavone; carpachromene; isoderrone; fucisoflavone; isowightone; 3'-(3-methylbut-2-en-1-yl)biochanin A; myrsininone A; fucisin A; 4,5,7-trihydroxy-6-[(1R*,6*)-3-methyl-6-(1-methylethyl)cyclohex-2-en-1-yl]isoflavone; lupiwightone; mallotus A	Chen <i>et al.</i> , 2020
<i>Ficus hispida</i>	Twigs	Yunnan, China	22.01	Cfa	TLC, UV, IR, HR-ESI-MS, and ¹ H and ¹³ C-NMR	(Epi)catechin digalloyl rhamnoside; (epi)afzelechin-(epi)gallo catechin; epicatechin; (epi)afzelechin-(epi)catechin; (epi)afzelechin(epi)afzelechin-epigallo catechin; benzyl rutinoides; luteolin-2; vicenin-2; rutin; orientin; 3-O-p-coumaroyl epigallo catechin; isoquercetin; luteolin; quercetin; apigenin; fucisoflavone	Shi <i>et al.</i> , 2016
<i>Ficus lyrata</i>	Leaf	Cairo, Egypt	30.04	BWh	UPLC-PDA-MS	(Epi)catechin digalloyl rhamnoside; (epi)afzelechin-(epi)gallo catechin; epicatechin; (epi)afzelechin-(epi)catechin; (epi)afzelechin(epi)afzelechin-epigallo catechin; benzyl rutinoides; luteolin-2; vicenin-2; rutin; orientin; 3-O-p-coumaroyl epigallo catechin; isoquercetin; luteolin; quercetin; apigenin; fucisoflavone	Farag <i>et al.</i> , 2014
<i>Ficus lyrata</i>	Fruit	Cairo, Egypt	30.04	BWh	UPLC-PDA-MS	(Epi)catechin digalloyl rhamnoside; epicatechin; o-p-coumaroyl epigallo catechin; luteolin; apigenin; dihydroxy trimethoxyflavone; fucisoflavone; dihydroxy dimethoxyflavone; parvisoflavone B	Farag <i>et al.</i> , 2014
<i>Ficus pandurata</i>	Aerial roots	Zhejiang, China	27.97	Cfa	HPLC/QTOF-MS/MS	Rutin; kaempferol-3-O-rutinoides; diosmetin-7-O-rutinoides; acacetin-7-O-rutinoides; quercetin-3-O-rutinoides-rhamnoside; acacetin 7-O-glucoside-rhamnoside-glucoside; acacetin 7-O-glucoside-rhamnoside-acetyl-glucoside	Zhang <i>et al.</i> , 2014
<i>Ficus thoningii</i> Blume.	Roots and stem bark	Bagangté, Cameroon	5.25	A	UV, FT-IR, and HR-EIMS NMR	Thoningii flavanols A-B; shuterin; naringenin; p-hydroxyflavanone; luteolin; aromadendrin; garbanzol; dihydroquercetin; 5,7,3'-trihydroxyflavanone	Ango <i>et al.</i> , 2016
<i>Ficus vasta</i> Forssk.	Leaf	Giza, Egypt	30.01	BWh	PC, UV, ¹ H-NMR, MS, and HPLC-PDA/ESI-MS	Luteolin; quercetin, vitexin, quercetin 3-O-β-galactoside; rutin; catechin, naringenin, isoquercitrin, naringin, quercetin-3-galactoside, kaempferol-3-glucoside	Taviano <i>et al.</i> , 2018)
<i>Artocarpus altilis</i>	Leaf	Ho Chi Minh, Vietnam	10.82	A	FT-ICR-MS	Artocauraone; cycloaltilislin 7; sopheraflavanone 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-acetoxycycloart-25-ene-24-one; 3β-acetoxycycloart-25-methoxy-23-ene; 3β-acetoxycycloart-25-ene-11-one	Huong <i>et al.</i> , 2012

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Genus <i>Ficus</i>							
Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
<i>Artocarpus communis</i>	Leaf	Manado, Indonesia	1.47	A	HPLC and ¹ H and ¹³ C-NMR	Sophoraflavanone A; (S,E)-2-(3,4-dihydroxyphenyl)-8-(3,7-dimethyl-2,6-dien-1-yl)-5,7-dihydroxychroman-4-one; (2S)-5,7-dihydroxy-8-(E)-6-hydroxy-3,7-dimethyl-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-dimethyl-2,5-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-methyl-3-pentenyl)-2H-1-benzopyran-1-yl]-1-propanone; 1-(2,4-dihydroxyphenyl)-3-[8-hydroxy-2-methyl-2-(4-hydroxy-4-methyl-2-pentenyl)-2H-1-benzopyran-5-yl]-1-propanone	Inoue <i>et al.</i> , 2018
<i>Artocarpus heterophyllus</i> Lam.	Roots	Guangxi Zhuang, China	22.82	Cfa	UPLC-QTOF-MS/MS	6-(3-Methylbutyl-2-enyl)apigenin; albanin A; 14-hydroxyartoinin E; artoindonesianin B; artoindonesianin G-I; artoindonesianin P-R; artoindonesianin T; artelastoxanthone; artobioxanthone; cyclocommunol; artolon E; cycloartobioxanthone; artocarpetin A-B; heteroflavone; artocarpesin; 6-(3-methylbut-2-enyl)apigenin; styrafolin D; cycloartocarpesin; norartocarpin; mulberochromene; dihydroisocycloartominin; morusin; heterophyllin; artelastofuran; 5'-hydroxycudraflavone A; isocycloheterophyllin; artocarpin; camflavin C; artonins A-B; artonins E-H; artonins J-K; artonin S; artonin U; cudraflavone A; cycloartocarpin; cycloheterophyllin; artelastochromene	Ye <i>et al.</i> , 2019
<i>A. heterophyllus</i> Lam.	Stem and leaf	Hainan, China	20.04	Cfa	HPLC	2-(4-Hydroxyphenyl)-8-(3-methylbut-2-enyl)-chroman-4-one; bracteolavone B; dinklagin C; 6-(3-methyl-(E)-1-butenyl) chrysin; 5,7,3',5'-tetramethoxy-6-C-prenylflavone	Liu <i>et al.</i> , 2020
<i>A. heterophyllus</i> Lam.	Twigs	Yunnan, China	22.01	Cfa	HPLC	Artocarpusins A-C; artocarsilbene A; artocarpitins A-B; 3'-[γ-hydroxymethyl-(Z)-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 <i>et al.</i> , 2013
<i>A. heterophyllus</i> Lam.	Roots	Guangxi, China	22.82	Cfa	¹ H and ¹³ C-NMR, UV, IR, CD, and HR-ESI-MS	Artobeteroids A-D; morin; artocarpin A; albanin A; euechrenon A; norartocarpinone; stepogenin	Yuan <i>et al.</i> , 2017
<i>A. heterophyllus</i> Lam.	Roots	Guangxi, China	22.82	Cfa	¹ H and ¹³ C-NMR, UV, IR, CD, and HR-ESI-MS	Artobeteroids A-B; 2,3-dihydro-5,7-dihydroxy-2-(2-hydroxy-4-methoxyphenyl)-4H-1-benzopyran-4-one; artocarpinone	Ren <i>et al.</i> , 2015
<i>A. heterophyllus</i> Lam.	Heartwood	Songkla, Thailand	7.01	Am	HPLC	Artocarpinone; artocarpin; cycloartocarpin; cyanomacclurin	Septama <i>et al.</i> , 2018

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Genus <i>Artocarpus</i>							
Species	Part	Location	Latitude	Climate	Identification method	Identified compounds	Reference
<i>Artocarpus hypargyreus</i>	Stem	Hainan, China	19.57	A	HPLC, HR-EI-MS, and ¹ H and ¹³ C-NMR	Hypargyflavones A–C; hypargystilbene A; mulberrofuran N; rubraflavone C; cudraflavones A and C; cycloartocarpin A; brosimone I; norartocarpin	Yu <i>et al.</i> , 2012
<i>Artocarpus lakoocha</i> Roxb	Twigs and bark	Chiang Mai, Thailand	18.93	A	HRLC-TOF-MS	Lakoochanone, (+)-afzelechin-3-O- α -L-rhamnopyranoside; (+)-catechin; moracin C; sanggenofuran B, integrin, cyclocommunin, oxyresveratrol; (E)-2-methoxy-4,3',5'-trihydroxystilbene; engeletin; isomigealcone B; morachalcone A	Boonyaketguson <i>et al.</i> , 2020
<i>Artocarpus nigrifolius</i>	Twigs	Yunnan, China	21.46	Cfa	HR-ESI-MS	Cycloheterophyllin; artocarpin A; artocarmins B-C; gemichalcons A–C; artocarpusin A; isogemichalcone B; eleocharin A; 5,4'-dihydroxy-3'-methoxy-(6:7)-2,2-dimethylpyrano flavone; carpachromenol; 2,4,2',4'-tetrahydroxy-3-(3-methyl-2-butenyl)-chalcone; carpachromenol; 6-prenyl-4',5,7-trihydroxyflavone; artocarpesin	Liu <i>et al.</i> , 2018
<i>Artocarpus rigida</i>	Stem	Đông Nai, Vietnam	11.94	A	¹ H and ¹³ C-NMR, UV, IR, and HR-ESI-MS, HR-FAB-MS	Artocarmins G–M; norartocarpetin; artocarpin; artogomezianone; artochamin A; pyranocycloartobiloxanthone A; cycloartobiloxanthone; artocarpone B; artonin J; artonol A; p-hydroxybenzoic acid	Nguyen <i>et al.</i> , 2017
<i>A. xanthocarpus</i>	Roots	Lanyu, Taiwan	22.04	Cfa	¹ H and ¹³ C-NMR, UV, IR, CD, and HR-ESI-MS	Artoxanthocarpunes A-B; hydroxylakoochin A; methoxylakoochin A; epoxylakoochin A; artoxanthol; artoxanthochromane; lakoochin A; alboatol; (-)-catechin; steppogenin; norartocarpentin; isoeitin-5'-methyl ether; morusin; cyclocommunol; albanin A; cudraflavone C; artonin A; chlorophorin	Jin <i>et al.</i> , 2015

¹H and ¹³C-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, 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, TUV/Qda: tunable ultraviolet/mass single-quadrupole detection, UHPLC: ultrahigh-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 semiarid (steppe) climate, BSk: cold semiarid (steppe) climate, BWk: 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
Genus <i>Morus</i>										
<i>Morus alba</i> 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 <i>et al.</i> , 2021
<i>Morus alba</i> L.	Fruit	Vojvodina, North Serbia	45.29	Cfa	45.3	21.9	15.7	—	326.29 ± 8.21 mg GAE/100 g FW	Natic <i>et al.</i> , 2015
<i>Morus alba</i> 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 <i>et al.</i> , 2013
<i>Morus alba</i> L.	Fruit	Jiangsu, China	32.18	Cfa	53.5	11.4	11.98	—	147.69 ± 0.02 mg GAE/g DW	Krishna <i>et al.</i> , 2018
<i>Morus alba</i> L.	Fruit	Rzeszow, Poland	50.00	Cfb	110.4	19.9	16	—	1,041.1 ± 56.7 mg GAE/100 g DW	Tomczyk <i>et al.</i> , 2019
<i>Morus alba</i> L.	Leaf	Jeollabuk-do, South Korea	35.89	Dfa	1,417.1/year	10.7/year	—	37.87 ± 0.59 mg OE/g FDW	38.49 ± 2.06 mg GAE/g FDW	M. Kim <i>et al.</i> , 2020
<i>Morus alba</i> 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 <i>et al.</i> , 2014
<i>Morus alba</i> 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 <i>et al.</i> , 2018
<i>Morus alba</i> 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 <i>et al.</i> , 2013
<i>Morus alba</i> L.	Leaf	Rzeszow, Poland	50.00	Cfb	110.4	19.9	16	—	761.4 ± 56.2 mg GAE/100 g DW	Tomczyk <i>et al.</i> , 2019
<i>Morus alba</i> 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 <i>et al.</i> , 2013
<i>Morus alba</i> L.	Stem bark	Rajshahi, Bangladesh	24.37	A	117.1	30.2	13.3	102.469 ± 6.19 mg CAE/g DE	285.62 ± 2.54 mg GAE/g DE	Khan <i>et al.</i> , 2013
<i>M. bombycis</i> var. <i>Kenmochi</i>	Leaf	Rzeszow, Poland	50.00	Cfb	110.4	19.9	16	—	665.5 ± 63.3 mg GAE/100 g DW	Tomczyk <i>et al.</i> , 2019
<i>M. bombycis</i> var. <i>Kenmochi</i>	Fruit	Rzeszow, Poland	50.00	Cfb	110.4	19.9	16	—	1,114.8 ± 86.6 mg GAE/100 g DW	Tomczyk <i>et al.</i> , 2019
<i>Morus nigra</i> L.	Fruit	Chiang Mai, Thailand	18.78	A	1,050/year	25.1/year	—	—	6.93 ± 0.58 mg GAE/g DW	Suttisansanee <i>et al.</i> , 2020

Continued

Species	Part	Location	Latitude	Climate	Precipitation rate (mm)	Temperature (°C)	Day-time (hour)	TFC	TPC	Reference
<i>Morus nigra</i> L.	Leaf	Santa Catarina, Brazil	-26.90	Cfa	134.8	26.5	11.9	79.96 QE µg/g,	83.85 GAE mg/g	Zeni <i>et al.</i> , 2017
<i>Morus nigra</i> 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 <i>et al.</i> , 2018
Genus <i>Ficus</i>										
<i>Ficus hirta</i> 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 <i>et al.</i> , 2020
<i>F. deltoidea</i>	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 GAE/g of DW	Abraham <i>et al.</i> , 2018
<i>F. carica</i>	Fruit	Bragança, Portugal	41.80	Cfa	531.7/year	20.3 to 22.3	16	0.747 ± 0.005 mg/g extract	0.542 ± 0.001 mg/g	Palmeira <i>et al.</i> , 2019
<i>F. carica</i>	Fruit	Faisalabad, Pakistan	31.45	BSh	120.1	33	14	538.20 ± 1.17% w/w	31.88 ± 1.48 mg GAE/100 g DW	Alamgeer <i>et al.</i> , 2017
<i>F. carica</i>	Fruit	Cosenza, Italy	39.29	Cfa	48.6	21.8	12.47	2.6 ± 0.1–3.0 ± 0.1 mg QE/g DW	10.1 ± 0.2–14.8 ± 0.1 mg ChAE/g DW	Loizzo <i>et al.</i> , 2014
<i>Ficus racemosa</i>	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 <i>et al.</i> , 2016
<i>F. racemosa</i>	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 <i>et al.</i> , 2016
Genus <i>Artocarpus</i>										
<i>A. lakoocha</i> 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 <i>et al.</i> , 2020
<i>A. heterophyllus</i>	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 <i>et al.</i> , 2020
<i>Artocarpus altilis</i>	Fruit	Kuantan, Malaysia	3.76	Af	174.7	27	12.32	913.33 ± 24.44 to 6,213.33 ± 142.22 mg QE/g DW	203.17 ± 7.65 to 781 ± 52.97 mg GAE/g DE	Jalal <i>et al.</i> , 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.

et al., 2018; Jalal *et al.*, 2015), Portugal (Palmeira *et al.*, 2019), Pakistan (Alamgeer *et al.*, 2017), Italy (Loizzo *et al.*, 2014), India (Gupta *et al.*, 2020), Serbia (Natic *et al.*, 2015), Poland (Tomczyk *et al.*, 2019), and Thailand (Suttisansanee *et al.*, 2020).

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 $538.20\% \pm 1.17\%$ 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 $6,213.33 \pm 142.22$ 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 microbicidal 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 Fe^{3+} to Fe^{2+} 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 IC_{50} , showed very strong to moderate activity in *Morus*, *Ficus*, and *Artocarpus*. The lowest IC_{50} of *Morus* was achieved by the stem bark of *M. alba* from Rajshahi, Bangladesh, with 36.5 $\mu\text{g/ml}$ (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 <i>Morus</i>							Reference	
				DPPH	ABTS	FRAP	HRSA	Lipid peroxidation	RP	SAS		
<i>M. alba</i> L.	Fruit	Jiangsu, China	80% ethanol	IC ₅₀ 1.79 mg/ml	—	IC ₅₀ 1.016 mg/ml; 94.36%	—	—	—	—	—	Krishna <i>et al.</i> , 2018
<i>M. alba</i> L.	Fruit	Seoul, South Korea	Ethyl acetate fraction	IC ₅₀ 133.6 ± 4.7 µg/ml	IC ₅₀ 216.6 ± 28.8 µg/ml	3.727 ± 0.055 mmol Fe ²⁺ /g	—	—	—	—	—	Yu <i>et al.</i> , 2021
<i>M. alba</i> L.	Fruit	Rajshahi, Bangladesh	Methanol	IC ₅₀ 76 µg/ml	—	—	IC ₅₀ 177.05 µg/ml	IC ₅₀ 200.08 µg/ml	—	—	—	Khan <i>et al.</i> , 2013
<i>M. alba</i> L.	Fruit	Vojvodina, North Serbia	Methanol	86.79 ± 0.19 %	—	—	—	—	26.28 ± 0.75 µM	—	—	Natic <i>et al.</i> , 2015
<i>M. alba</i> L.	Fruit	Rzeszow, Poland	Deionized water (5% w/v)	78.9 ± 1.5%	—	5.43 ± 0.12 mmol TE/100 g	—	—	—	—	—	Tomczyk <i>et al.</i> , 2019
<i>M. alba</i> L.	Leaf	Rajshahi, Bangladesh	Methanol	IC ₅₀ 108.69 µg/ml	—	—	IC ₅₀ 211.72 µg/ml	IC ₅₀ 165.72 µg/ml	—	—	—	Khan <i>et al.</i> , 2013
<i>M. alba</i> L.	Leaf	Jeollabuk-do, South Korea	Distilled water	IC ₅₀ 7.09 ± 0.91 mg/ml	IC ₅₀ 5.85 ± 0.03 mg/ml	—	—	—	—	—	—	Kim <i>et al.</i> , 2020
<i>M. alba</i> L.	Leaf	Daejeon, South Korean	Methanol	IC ₅₀ 139 ± 15 µg/ml	—	—	—	—	—	—	—	Kim <i>et al.</i> , 2014
<i>M. alba</i> L.	Leaf	Razavi Khorasan, Iran	80% ethanol	IC ₅₀ 103.49 ± 0.75 µg/ml	—	—	—	—	—	—	—	Ghavami <i>et al.</i> , 2020
<i>M. alba</i> L.	Leaf	Rzeszow, Poland	Deionized water (5% w/v)	63.5 ± 2.9%	—	3.02 ± 0.22 mmol TE/100 g	—	—	—	—	—	Tomczyk <i>et al.</i> , 2019
<i>M. alba</i> L.	Root bark	Rajshahi, Bangladesh	Methanol	IC ₅₀ 41 µg/ml	—	—	IC ₅₀ 116 µg/ml	IC ₅₀ 132.94 µg/ml	—	—	—	Khan <i>et al.</i> , 2013
<i>M. alba</i> L.	Stem bark	Rajshahi, Bangladesh	Methanol	IC ₅₀ 36.5 µg/ml	—	—	IC ₅₀ 57.25 µg/ml	IC ₅₀ 83.25 µg/ml	—	—	—	Khan <i>et al.</i> , 2013
<i>Morus bombycis</i>	Fruit	Rzeszow, Poland	Deionized water (5% w/v)	77.9 ± 1.6%	—	5.20 ± 0.06 mmol TE/100 g	—	—	—	—	—	Tomczyk <i>et al.</i> , 2019
<i>Morus bombycis</i>	Leaf	Rzeszow, Poland	Deionized water (5% w/v)	54.6 ± 2.8%	—	2.15 ± 0.08 mmol TE/100 g	—	—	—	—	—	Tomczyk <i>et al.</i> , 2019
<i>Morus nigra</i> L.	Fruit	Chiang Mai, Thailand	Ultrapure water	0.40 ± 0.033 µmol TE/100 g DW	—	21.33 ± 0.35 µmol TE/100 g DW	—	—	—	—	—	Suttisansanee <i>et al.</i> , 2020

Continued

Genus <i>Morus</i>											
Species	Part	Location	Extraction solvent	DPPH	ABTS	FRAP	HRSA	Antioxidant assay			Reference
								Lipid peroxidation	RP	SAS	
<i>Morus nigra</i> L.	Leaf	Santa Catarina, Brazil	Distilled water	83.85 ± 0.99%	—	—	—	—	—	—	Zeni <i>et al.</i> , 2017
<i>Morus nigra</i> L.	Leaf	Bahia, Brazil	95% ethanol	IC ₅₀ 69.10 ± 1.88 µg/ml	—	—	—	—	—	—	Souza <i>et al.</i> , 2018
Genus <i>Ficus</i>											
Species	Part	Location	Extraction solvent	DPPH	ABTS	FRAP	HRSA	Antioxidant assay			Reference
								Lipid peroxidation	RP	SAS	
<i>Ficus hirta</i> Vahl.	Fruit	Jiangxi, China	Ethyl acetate	IC ₅₀ 2.52 mg/ml	IC ₅₀ 3.06 mg/ml	—	—	—	—	—	Chen <i>et al.</i> , 2020
<i>F. exasperata</i> Vahl.	Leaf	Bingserville, Ivory Coast	Distilled water	IC ₅₀ 222.5 ± 8 µg/ml	—	—	—	—	—	—	Mouho <i>et al.</i> , 2018
<i>F. deltoidea</i>	Leaf	Negeri Sembilan, Malaysia	Double-distilled water, ethyl acetate fraction	IC ₅₀ 182 µg/ml	—	—	—	—	—	—	Abraham <i>et al.</i> , 2018
<i>Ficus vasta</i> Forssk.	Leaf	Giza, Egypt	80% methanol	IC ₅₀ 67.2 ± 3.8 µg/ml	—	—	—	—	3.65 ± 0.48 ASE/ml	—	Taviano <i>et al.</i> , 2018
<i>F. carica</i>	Fruit	Bragança, Portugal	80% ethanol	IC ₅₀ 1.13 ± 0.05 mg/ml	—	—	—	—	IC ₅₀ 3.58 ± 0.03 mg/ml	—	Palmeira <i>et al.</i> , 2019
<i>F. carica</i>	Fruit	Cosenza, Italy	70% ethanol	IC ₅₀ 41.3 ± 1.7 µg/ml	IC ₅₀ 8.2 ± 0.9 µg/ml	IC ₅₀ 32.7 ± 3.9 µmol/L Fe(II) g	—	—	—	—	Loizzo <i>et al.</i> , 2014
<i>F. racemosa</i>	Fruit	Khulna, Bangladesh	Methanol	IC ₅₀ 8.59 µg/ml	—	—	SC ₅₀ 91.353 µg/ml	RC ₅₀ 40.443 µg/ml	—	SC ₅₀ 122.264 µg/ml	Sumi <i>et al.</i> , 2016
<i>F. racemosa</i>	Leaf	Khulna, Bangladesh	Methanol	IC ₅₀ 10.28 µg/ml	—	—	SC ₅₀ 103.163 µg/ml	RC ₅₀ 45.564 µg/ml	—	SC ₅₀ 130.104 µg/ml	Sumi <i>et al.</i> , 2016
Genus <i>Artocarpus</i>											
Species	Part	Location	Extraction solvent	DPPH	ABTS	FRAP	HRSA	Antioxidant assay			Reference
								Lipid peroxidation	RP	SAS	
<i>Artocarpus altalis</i>	Fruit	Kuantan, Malaysia	Methanol	IC ₅₀ 55 ± 5.89 µg/ml	—	—	—	—	—	—	Jalal <i>et al.</i> , 2015

DPPH: 2,2-diphenyl-1-picrylhydrazyl, ABTS: 2,2'-azino-bis-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, IC₅₀: half maximal inhibitory concentration, TE: Trolox equivalent, DW: dried matter, ASE: ascorbic acid equivalent, SC₅₀: half maximal scavenging concentration, RC₅₀: 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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