ERURJ **2023**, *2*, 3, 502-524
(Mini review)

Phytochemical diversity of genus *Ficus*: A mini-review

Shaimaa E.A. Elish [1,*], Abeer Temraz [2], Mostafa H. Baky [1],

[1]*Department of Pharmacognosy, Faculty of Pharmacy, Egyptian Russian University, Badr City, Cairo-Suez Road, Cairo 11829, Egypt.*
[2]*Department of Pharmacognosy and Medicinal Plants, Faculty of Pharmacy (Girls), Al-Azhar University, Cairo, Egypt.*

*Corresponding author(s):

Shaimaa E.A. Elish, E-mail: shaimaa-essam@eru.edu.eg

Received 6th May 2023, Revised 11h June 2023, Accepted 14th June 2023

DOI:10.21608/ERURJ.2023.310215

ABSTRACT

Genus *Ficus,* belonging to the family Moraceae, comprises more than 1,000 species of woody trees, shrubs, and vines. *Ficus* species, also known as fig trees or figs, are native throughout the tropics, with a few species extending into the semi-warm temperate zone. *Ficus* species are reported to possess an extensive diversity of traditional uses, including expectorants and mild laxatives, anthelmintic, hypoglycemic, and antihypertensive agents, as well as helping in the treatment of rheumatic disease, constipation, dysentery, and dyspepsia. *Ficus* species possess several biological activities *viz*., anti-hypertensive, hypoglycemic, neuroprotective, antioxidant, analgesic, antimicrobial, and anti-inflammatory. Moreover, the leaves of *Ficus carica* were reported as potent antimicrobial and antioxidant owing to their richness in phenolics that can destroy active radicals and chelate prooxidant metal ions. Several phytochemicals were isolated and identified in *Ficus*, including phenolics, saponins, flavonoids, triterpenoids, sterols, and volatiles. This review aims to provide an overview of the major classes of phytoconstituents and the chemical composition of *Ficus* species.

Keywords: Phytochemicals, Moraceae; *Ficus;* flavonoids; saponins

1-Introduction

Plant secondary metabolites are important sources of several phytochemicals and play a pivotal role in human health. Several secondary metabolite compounds, including flavonoids, saponins, alkaloids, steroids, and terpenoids, have been produced by plants to protect themselves from pathogen attacks, and these secondary metabolites can also protect humans against diseases (1). Family Moraceae is composed of more than 60 genera and almost 1,500 species of trees, shrubs, and vines. The genus *Ficus* contains more than 1,000 species distributed on many continents with tropical and subtropical climates (1). Moreover, *Ficus deltoidea* extract has been reported for its analgesic, antihypertensive, and hypoglycemic activities, as well as the protective activity of *F. natalensis* leaves on the testicular impairments induced by cadmium chloride ($CdCl_2$). Numerous studies on the genus *Ficus* reported the presence of various classes of phytochemicals such as flavonoids, alkaloids, glycosides, steroids, saponins, terpenes, and tannins, which have beneficial impacts on human health (2, 3). Hence, the main goal of this review is to present an overview of the chemical composition of *Ficus* species.

2. Review Methodology

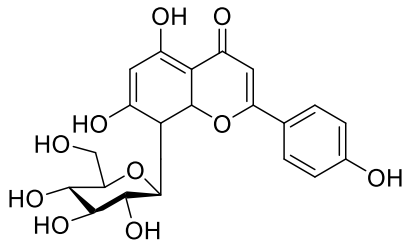
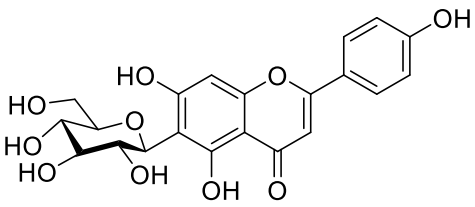
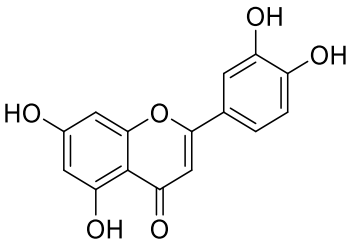
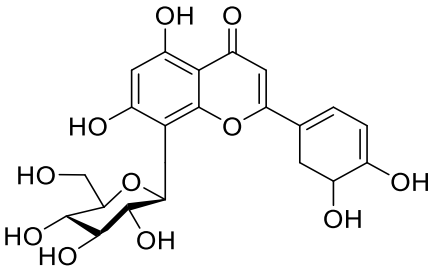
This review was searched in ScienceDirect, Google Scholar, Reaxys, and Scopus databases. The search was accomplished using the keywords "*Ficus*", "phytochemical", "chemical compounds" and "chemical composition", considering published papers from 2000 to May 2023.

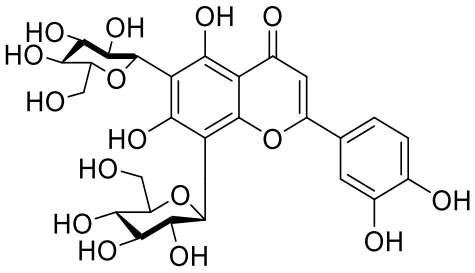
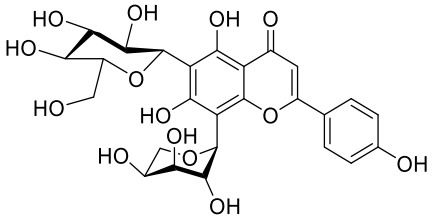
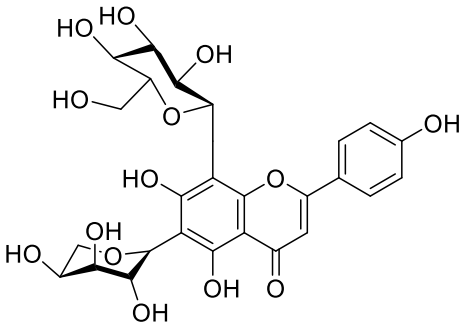
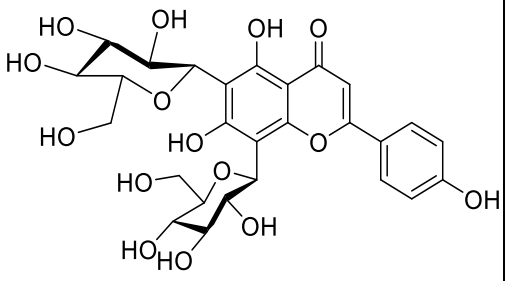
3. Bioactive metabolites of *Ficus*

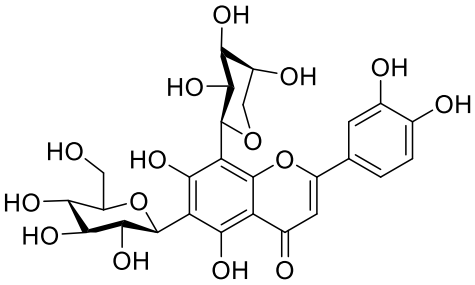
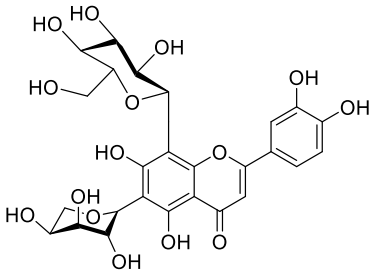
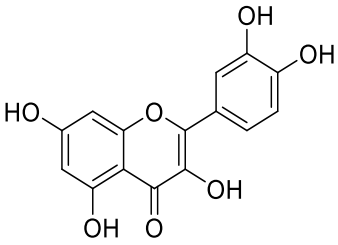
3.1. Flavonoids

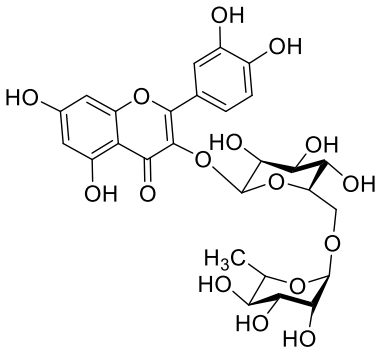
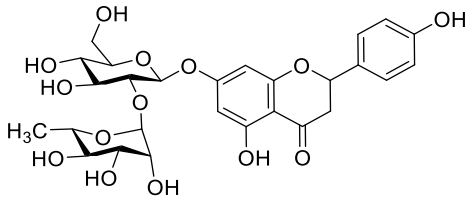
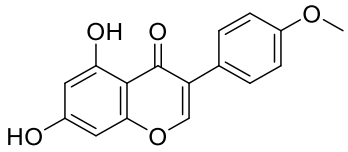
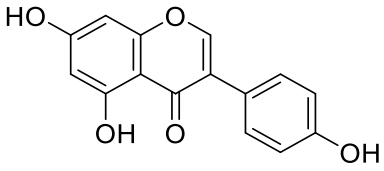
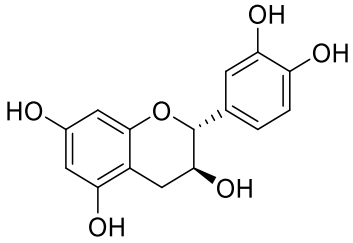
Flavonoids are a class of organic compounds with variable phenolic structures; they are extensively found in the plant kingdom. They possess antioxidant potential, and widely known for their positive health impacts (4). Based on their structures, flavonoids are classified into six major classes: flavones, flavan-3-ols, flavonols, isoflavones, flavanones, and anthocyanins (5). Many flavonoids and their glycosides were isolated and identified from several *Ficus* species, such as *Ficus hirta, Ficus microcarpa, Ficus nymphaeifolia, Ficus formosana, Ficus deltoidea, Ficus carica, and Ficus natalensis* (6). There is a list of flavonoids that have been previously isolated and identified from the genus *Ficus* in (Table 1).

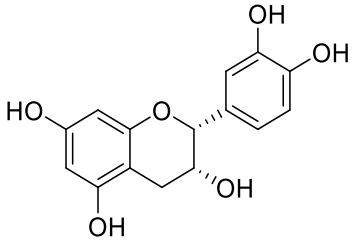
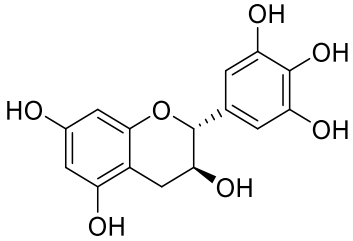
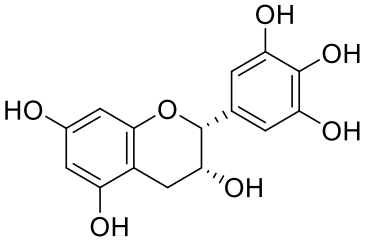
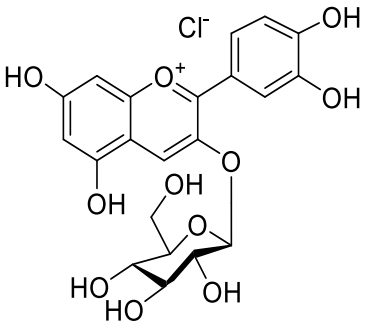
Table 1. Flavonoids reported from genus *Ficus*

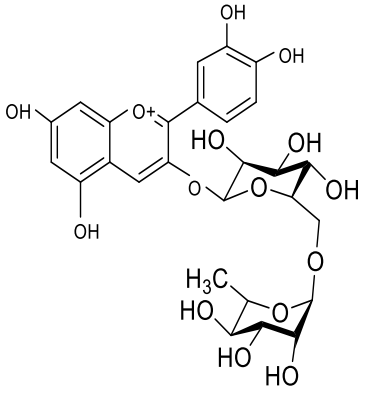
Compound	Species	Investigated part (analysis)	Reference
 Vitexin	*F. deltoidea*	Leaf (HPLC)	(7-20)
	F. vasta	Leaf (HPLC-PDA/ESIMS)	(2)
	F. exasperate	Leaf, Stem (HPLC –DAD–ESI/MS)	(2)
		Bark (UPLC–ESI–QTOF–MS)	
	F. carica	Leaf, Fruit (UHPLC−DAD-QTOF-MS)	(21)
 Isovitexin	*F. deltoidea*	Leaf (HPLC), (HPLC-DAD-TOF-MS)	(7-20, 22)
	F. carica	Leaf (TOF-LC-MS-MS)	(2)
 Luteolin	*F. carica*	Leaf (HPLC), (UHPLC−DAD-QTOF-MS)	(2, 21, 23-25)
	F. deltoidea	Leaf (UPLC-QTOF-MS/MS)	(26)
	*F. deltoidea*	Leaf (HPLC), (UPLC-QTOF-MS/MS)	(8, 15, 26)
	F. carica	Leaf, Fruit (UHPLC−DAD-QTOF-MS)	(21, 25)

Orientin			
 lucenin-2	*F. deltoidea*	Leaf (HPLC), (UPLC-QTOF-MS/MS)	(8, 15, 26)
 Schaftoside	*F. deltoidea* *F. carica*	Leaf (HPLC), (UPLC-QTOF-MS/MS) Leaf (HPLC-DAD-TOF-MS), (UHPLC−DAD-QTOF-MS)	(8, 15, 26) (2, 21)
 Isoschaftoside	*F. deltoidea* *F. carica*	Leaf (HPLC) Leaf (UHPLC−DAD-QTOF-MS)	(8, 15) (2)
 Vicenin-2	*F. deltoidea*	Leaf (HPLC), (UPLC-QTOF-MS/MS)	(8, 15, 26)

 Luteolin-6-C-glucosyl-8-C-arabinoside	*F. deltoidea*	Leaf (HPLC)	(8, 15)
 Luteolin-6-C-arabinosyl-8-C-glucoside	*F. deltoidea*	Leaf (HPLC)	(8, 15)
 Quercetin	*F. carica* *F. deltoidea* *F. capensis* *F. microcarpa* *F. microcarpa* *F. vasta* *F. auriculata*	Leaf (HPLC) Leaf (HPLC) Leaf (HPLC-DAD) Leaf (HPLC-DAD and FT-IR) Root (HPLC-DAD and FT-IR) Leaf (HPLC-PDA/ESI-MS) Aerial parts (NMR)	(2, 23) (27) (2) (2) (2) (2) (24)

 Rutin	*F. deltoidea*	Leaf (HPLC)	(27-29)
	F. vasta	Leaf (HPLC-PDA/ESI-MS)	(2)
	F. carica	Leaf (TOF-LC-MS-MS), (UHPLC−DAD-QTOF-MS), (HPLC)	(2, 6, 21, 24, 25)
	F. carica	Fruit (HPLC)	(20)
	F. auriculata	Leaf (HPLC)	(2)
	F. beecheyana	Roots (HPLC)	(2)
	F. capensis	Leaf (HPLC-DAD)	(2)
 Naringin	*F. deltoidea*	Leaf (HPLC)	(27, 28)
	F. deltoidea	Stem (LC-MS)	(30)
	F. vasta	Leaf (HPLC-PDA/ESI-MS)	(2)
	F. sycomorus	Leaf (GC-MS, HPLC)	(2)
	F. benghalensis	Leaf (NMR)	(24)
 Biochanin A	*F. carica*	Leaf (UHPLC−DAD-QTOF-MS), (HPLC)	(21, 23-25)
	F. carica	Fruit (UHPLC−DAD-QTOF-MS)	(21, 25)
 Genistein	*F. palmate*	Leaf (CC- NMR, IR, Mass, UV)	(31)
	F. carica	Leaf (UHPLC−DAD-QTOF-MS)	(21)
 Catechin	*F. deltoidea*	Leaf (UHPLC, UV-Vis), (HPLC), (UPLC-QTOF-MS/MS)	(2, 8, 11, 15, 18, 26)
	F. palmate	Leaf (CC- NMR, IR, Mass, UV)	(31)
	F. capensis	Leaf (HPLC-DAD)	(2)
	F. vasta	Leaf (HPLC-PDA/ESI-MS)	(2)

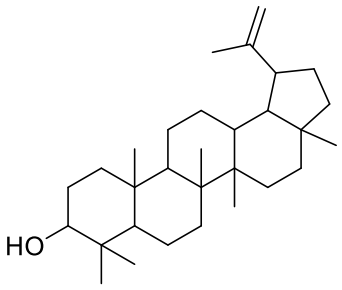
		Stem bark (LC/MS)	
	F. sycomorus	Leaf, Fruit (UHPLC−DAD-QTOF-MS)	(2)
	F. carica		(21, 25)
 Epicatechin	*F. deltoidea*	Leaf (HPLC), (UPLC-QTOF-MS/MS)	(8, 15, 18, 26)
	F. beecheyana	Roots (HPLC)	(2)
	F. capensis	Leaf (HPLC-DAD)	(2)
 Gallocatechin	*F. deltoidea*	Leaf (HPLC), (UPLC-QTOF-MS/MS)	(8, 15, 18, 26)
 Epigallocatechin	*F. deltoidea*	Leaf (HPLC)	(8, 15)
	F. auriculata	Aerial parts (NMR)	(24)
 Cyanidin-3-*O*-glucoside	*F. carica*	Fruit (UHPLC−DAD-QTOF-MS), (RP-LC)	(6, 21, 32)
	F. carica	Leaf (TOF-LC-MS-MS)	(2)

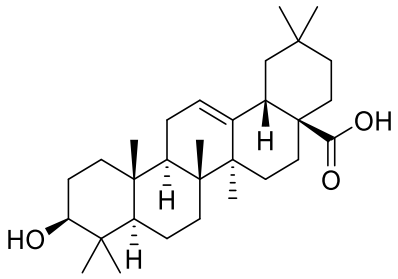
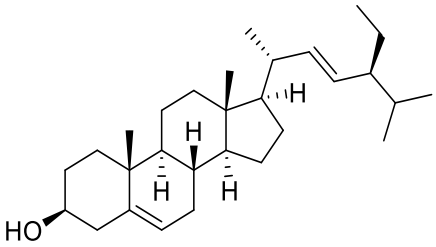
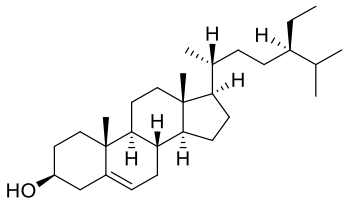
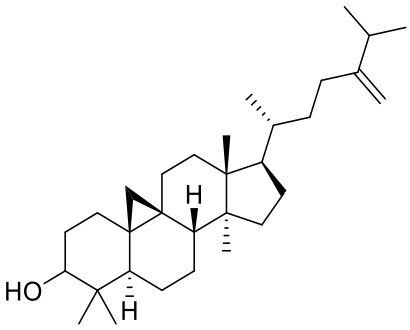
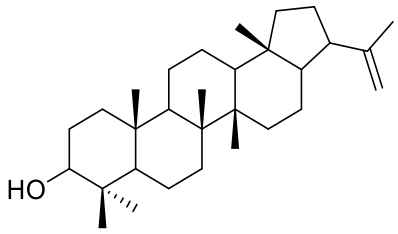
 Cyanidin-3-*O*-rhamnoglucoside	*F. carica*	Fruit (UHPLC−DAD-QTOF-MS), (RP-LC)	(6, 21, 32)

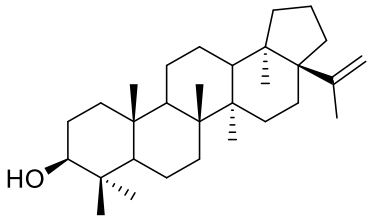
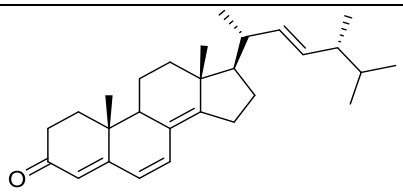
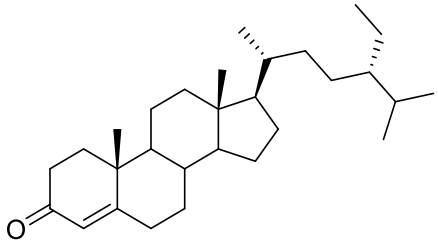
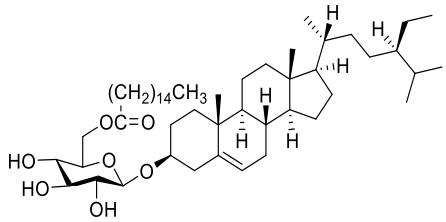
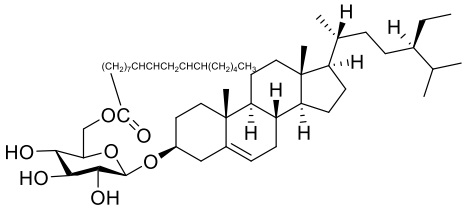
3.2. Saponins

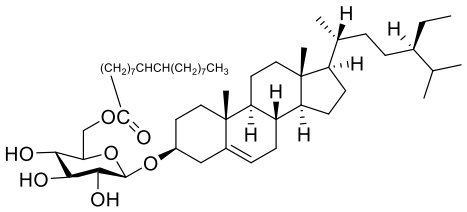
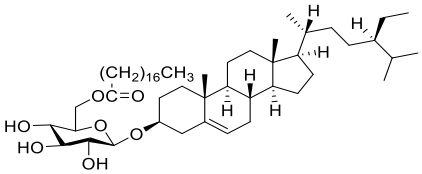
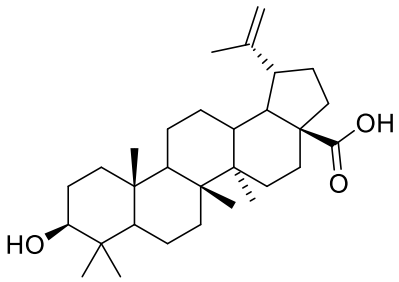
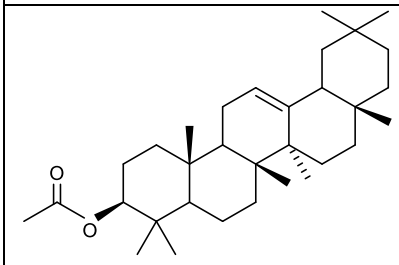
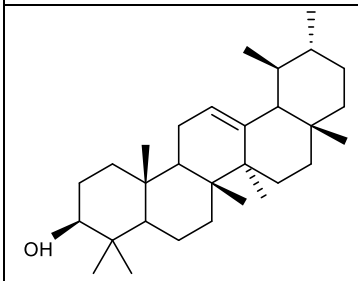
Saponins are a diversified group of compounds abundant in the plant kingdom. Saponins are classified either as steroids or triterpenoids according to the aglycone skeleton present in their structure, attached to one or more sugar moieties (33). Steroidal glycosides are sugar conjugates of C-27 steroidal compounds with either furostanol or spirostanol aglycone types. Recently, steroidal saponins received a lot of attention, not only as biologically active compounds but as economically important raw materials for the production of different steroidal hormones in the pharmaceutical industry (34). Triterpenoids are formed by the cyclization of one of the two linear C-30 isoprenoid precursors, oxidosqualene and squalene. They play a pivotal role in cell membrane maintenance, signal transduction, ecological interactions, and biological defence (33). Saponins and their aglycons that have been previously isolated and identified from genus *Ficus* are listed in (Table 2).

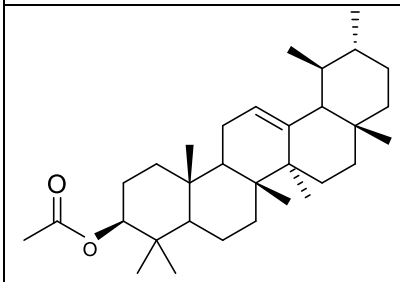
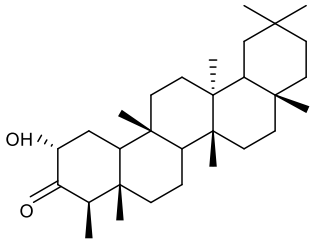
Table 2. Saponins and their aglycons reported from the genus *Ficus*

Compound	**Species**	**Investigated part (analysis)**	**Reference**
 Lupeol	*F. deltoidea* *F. carica*	Leaf (HPLC), (LC-MS) Leaf (CC- NMR, IR, Mass, UV)	(15, 30) (6, 35)

 Oleanolic acid	*F. deltoidea*	Stem (LC-MS)	(30)
 Stigmasterol	*F. palmate* *F. deltoidea* *F. crocata* *F. ulmifolia*	Leaf (CC- NMR, IR, Mass, UV) Leaf (RP-HPLC), (LC-MS) Leaf (GC-MS) Leaf (NMR)	(31) (29, 30) (2) (36)
 *β*- Sitosterol	*F. natalensis* *F. carica*	Leaf, Stem bark, Fruit (NMR) Root bark (NMR)	(37, 38) (24)
 24-Methylenecycloartanol	*F. carica*	Leaf (NMR)	(6, 39)
	*F. natalensis*	Leaf, Stem bark, Fruit (NMR)	(38, 40)

3*α*-Hydroxy-21*α*-H-hop-22(29)-ene			
 Moretenol	*F. deltoidea*	Leaf (HPLC), (NMR)	(15, 41)
 Ergosta-4,6,8(14),22-tetraen-3-one	*F. natalensis*	Leaf, Stem bark, Fruit (NMR)	(38, 42)
 Stigma-4-en-3-one	*F. natalensis*	Leaf, Stem bark, Fruit (NMR)	(38, 43)
 6-*O*-Palmitoyl-*β*-D-glucosyl-*β*-sitosterol	*F. carica*	Latex (NMR)	(6, 44)
 6-*O*-Linoleyl-*β*-D-glucosyl-*β*-sitosterol	*F. carica*	Latex (NMR)	(6, 44)

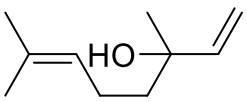
 6-*O*-oleyl-*β*-D-glucosyl-*β*-sitosterol	*F. carica*	Latex (NMR)	(6, 44)
 6-*O*-stearyl-*β*-D-glucosyl-*β*-sitosterol	*F. carica*	Latex (NMR)	(6, 44)
 Betulinic acid	*F. pandurata*	Stem bark, Leaf (UV, IR, MS, ^{1}H- and ^{13}C-NMR)	(36)
 *β*-Amyrin acetate	*F. pandurate* *F. Pseudopalma* *Ficus racemosa*	Stem bark, Leaf (UV, IR, MS, ^{1}H- and ^{13}C-NMR) Leaf (NMR) root bark (NMR)	(36) (36) (45)
	*F. pandurata*	Stem bark, Leaf (UV, IR, MS, ^{1}H- and ^{13}C-NMR)	(36)

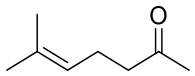
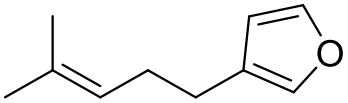
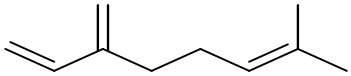
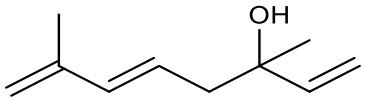
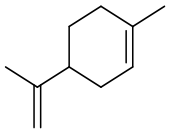
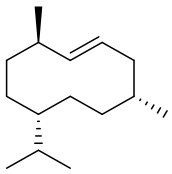
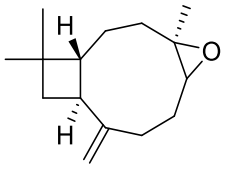
α-Amyrin			
 *α*-Amyrin acetate	*F. pandurate* *F. Pseudopalma* *Ficus racemosa*	Stem bark, Leaf (UV, IR, MS, ^{1}H- and ^{13}C-NMR) Leaf (NMR) root bark (NMR)	(36) (36) (45)
 *β*-Amyrone	*F. pandurata*	Stem bark, Leaf (UV, IR, MS, ^{1}H- and ^{13}C-NMR)	(36)

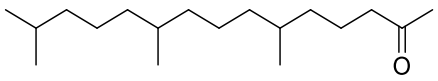
3.3. Essential oil component

One of the most significant secondary metabolites biosynthesized by plants is essential oils. Such compounds have high vapor pressures at room temperature and low molecular weight, released from flowers, leaves, fruits, stems, and even roots. They play a crucial role in plant evolution and its climatic adaptation (46). Moreover, they have diverse therapeutic activities, such as their capability to enhance sleep, protective effect against viral pneumonia, as well as other activities including hypolipidemic, anti-cancer, anti-oxidative, anti-inflammatory, anti-asthmatic, and anti-*Trypanosoma* effects, as well as industrial uses such as oil for aromatherapy, flavoring agents, and commercial chemicals for many food products, perfume, and soaps (47). There is a list of volatile compounds that have been previously isolated and identified from genus *Ficus* in (Table 3).

Table 3. Essential oil component reported from genus *Ficus*

Compound	**Species**	**Investigated part (analysis)**	**Reference**
	*F. deltoidea*	Fruit (GC-MS)	(15, 48)

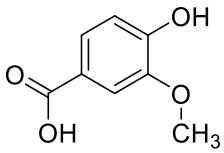
Linalool			
 6-Methyl-5-hepten-2-one			
 Perillene			
 Myrcene			
 Hotrienol			
 Limonene			
 Germacrene D			
 Caryophyllene oxide			

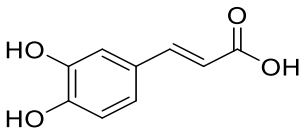
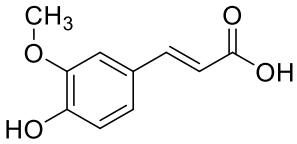
 6,10,14-trimethyl-2-pentadecanone	*F. natalensis* *F. deltoidea*	Leaf (GC-MS) Leaf (GC-MS)	(38, 49, 50) (20)

3.4. Phenolic acids

Phenolic acids are secondary metabolites widely distributed across the plant kingdom. They are compounds consisting of a phenolic ring and at least one organic carboxylic acid function, occurring in food plants as glycosides or esters conjugated with other compounds such as alcohols, flavonoids, sterols, hydroxy fatty acids, and glucosides (45). Fruits and vegetables have unique tastes, flavors, and health-promoting properties due to the presence of phenolic compounds. They have antioxidant properties that cause free radical scavenging, anti-aging, and can reduce the risk of cancer (51, 52). There is a list of phenolic acids that have been previously isolated and/or identified from genus *Ficus* in (Table 4).

Table 4. Phenolic acids reported from genus *Ficus*

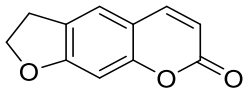
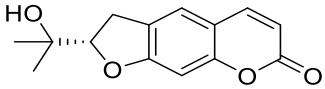
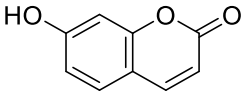
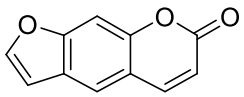
Compound	**Species**	**Investigated part (analysis)**	**Reference**
 Vanillic acid	*F. deltoidea* *F. carica* *Ficus palmata*	Leaf (UPLC-QTOF-MS/MS) Leaf, Fruit (UHPLC−DAD-QTOF-MS) aerial parts (NMR)	(26) (21, 25) (45)

 Caffeic acid	*F. deltoidea* *F. beecheyana* *F. capensis* *F. carica* *F. microcarpa* *F. racemose* *F. carica*	Stem (LC-MS) Roots (HPLC) Leaf (HPLC-DAD) Latex (HPLC) Root (HPLC-DAD and FT-IR) Leaf (HPLC) Fruit (UHPLC−DAD-QTOF-MS)	(11, 30) (2) (2) (2) (2) (2) (21)
 Ferulic acid	*F. carica*	Leaf (HPLC-DAD-QTOF-MS)	(25)

3.5. Coumarins

Coumarins are secondary metabolites produced by plants, a few microorganisms (fungi and bacteria), and sponges. Regarding the chemical structure, they are phenolic compounds composed from the fusion of a benzene ring and an α-pyrone ring (47). They are found in plants in free forms as well as glycosides. Based on their chemical structure, coumarins are classified into seven types: simple coumarin, furanocoumarin, dihydrofuran coumarin, phenyl coumarin, pyranocoumarin linear type, pyranocoumarin angular type, and bicoumarin. They can be found in the leaves, fruits, flowers, stems, seeds, and roots of plants. Coumarins have anti-inflammatory, antithrombotic, and vasodilatory activities. Some of the coumarin compounds have antimicrobial and antiviral activities (53, 54). There is a list of coumarins that have been previously isolated from genus *Ficus* in (Table 5).

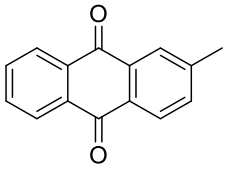
Table 5. Coumarins reported from genus *Ficus*

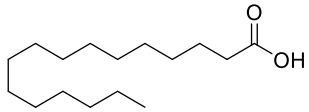
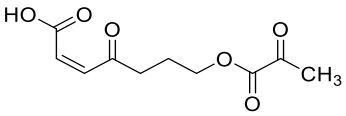
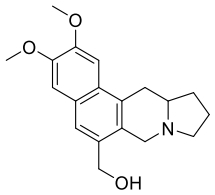
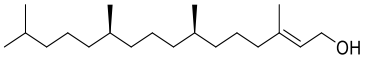
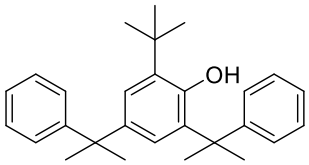
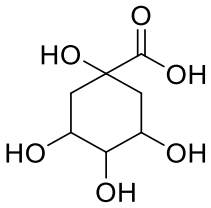
Compound	Species	Investigated part (analysis)	Reference
 4',5' -Dihydropsoralen	*F. carica*	Leaf (UHPLC−DAD-QTOF-MS), (HPLC)	(6, 21, 55)
 Marmesin	*F. carica*	Leaf (UHPLC−DAD-QTOF-MS), (HPLC)	(6, 21, 55)
 Umbelliferone	*F. carica*	Leaf (UHPLC−DAD-QTOF-MS), (HPLC)	(6, 21, 55)
 Psoralen	*F. carica* *Ficus palmata*	Leaf, Fruits (UHPLC−DAD-QTOF-MS) aerial parts (NMR)	(21) (45)

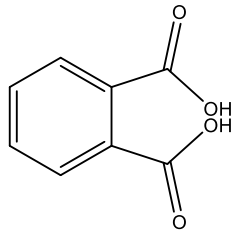
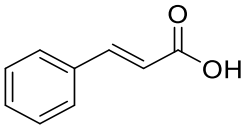
3.6. Miscellaneous compounds

There is a list of miscellaneous compounds that have been previously isolated from the genus *Ficus* in (Table 6).

Table 6. Miscellaneous compounds reported from genus *Ficus*

Compound	Species	Investigated part (analysis)	Reference
	*F. natalensis*	Leaf, Stem bark, Fruit (NMR)	(38, 56)

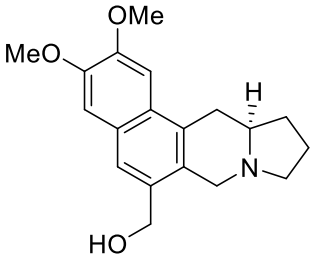
Tectoquinone			
 Hexadecanoic acid	*F. deltoidea*	Stem (LC-MS)	(30)
 Glutaric acid dimer	*F. deltoidea*	Leaf (UPLC-QTOF-MS/MS)	(26)
 Fistulosine	*F. deltoidea*	Leaf (LC-MS)	(30)
 *E*- Phytol	*F. natalensis*	Leaf (GC-MS)	(50)
 2,4-Bis (dimethylbenzyl)-6-t-butylphenol	*F. deltoidea*	Leaf (GC-MS)	(20)
 Quinic acid	*F. deltoidea* *F. carica*	Leaf (UPLC-QTOF-MS/MS) Leaf (TOF-LC-MS-MS), (UHPLC−DAD-QTOF-MS)	(26) (2, 21)

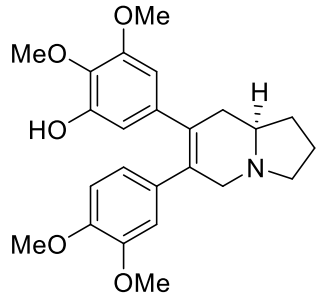
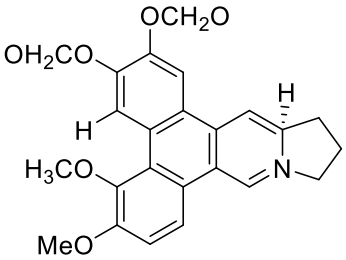
 Phthalic acid	*F. deltoidea*	Leaf (GC-MS)	(20)
 Cinnamic acid	*F. deltoidea* *F. microcarpa* *F. sycomorus* *F. sycomorus*	Stem (LC-MS) Leaf, Root (HPLC-DAD and FT-IR) Latex (HPLC) Leaf (GC-MS, HPLC)	(30) (2) (2) (2)

3.7. Alkaloids

Plant alkaloids, one of the largest groups of natural products, represent a highly diverse group of chemical compounds. The principal requirement for classification as an alkaloid is the presence of a basic nitrogen atom at any position in the molecule, which does not include a peptide bond or nitrogen in an amide. Many alkaloids possess potent pharmacological effects. For example, the narcotic analgesics morphine and codeine, apomorphine used in Parkinson's disease, the muscle relaxant papaverine, and the antimicrobials sanguinarine and berberine (57). There is a list of alkaloids that have been previously isolated from genus *Ficus* in (Table 7).

Table 7. Alkaloids reported from genus *Ficus.*

Compound	**Species**	**Investigated part (analysis)**	**Reference**
 fistulosine	*F. fistulosa*	Stem bark (NMR)	(58)

 Fistulopsine A		Bark (NMR)	(59)
 Ficuseptine B	*Ficus septica*	Stem (NMR)	(60)

4. Conclusion

Ficus species have attracted the attention of several scientists due to their beneficial properties for human health. *Ficus* leaves, fruits, stem bark, roots, and latex are rich with different classes of high-value compounds such as flavonoids, glycosides, steroids, saponins, terpenes, tannins, coumarins, phenolic acids, alkaloids, and volatile compounds. Owing to their richness in phytochemical bioactive metabolites, *Ficus* species possess several biological activities, such as anti-hypertensive, hypoglycemic, neuroprotective, antioxidant, analgesic, and anti-inflammatory effects. Such a review introduces the genus *Ficus* as a good source of bioactive phytochemicals with higher health benefits for pharmaceutical formulation.

- **Conflict of Interest**

The authors declare no conflict of interest.

5. References

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