

The Application of *Ficus* Species in the Treatment of Neurological Disorders

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Abstract

Background: Neurological diseases represent a pressing global health concern; the World Health Organization reports that neurological conditions rank as the second leading cause of death worldwide. In the last quarter century, we have witnessed a remarkable 36% surge in global neurological mortality rates. Several factors, including oxidative stress, genetic variability, natural aging process, inflammation, hypertension, diabetes, infections, vitamin deficiencies, metabolic imbalances, chemical exposures, endocrine disorders, and dietary supplements, are implicated in the initiation and progression of various neurological diseases.

Objectives: This comprehensive review aims to shed light on the neuroprotective attributes of distinct *Ficus* and their phytoconstituents that have been harnessed for treating neurological diseases and demonstrating neuroprotective effects.

Methodology: A literature search was conducted to obtain information about the study of neurological disease and their treatment using database and search engine like Google Scholar, ResearchGate, monograph, reference book, SciFinder, PubMed/Medline, Scopus, and ScienceDirect.

Results: *Ficus* species have exhibited remarkable neuroprotective qualities through various mechanisms of action. Moreover, these plants contain a diversity of bioactive such as flavonoids, polyphenols, terpenoids, tannins, alkaloids, glycosides, sterols, and vitamins that proven effective in enhancing memory, reducing anxiety, increasing neurotransmitter levels, mitigating neurodegeneration, and playing pivotal roles in neuroprotection.

Conclusion: This review consolidates the promising potential of *Ficus* species in the treatment of neurological diseases, paving the way for future scientific research in the development of novel herbal neuroprotective medications.

Keywords

Neurological disease, *Ficus*, flavonoids, polyphenols, terpenoids

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Introduction

Neurological disorders encompass a spectrum of conditions primarily affecting the brain and various components of the nervous system, including the central nervous system, autonomic nervous system, and peripheral nervous system. These disorders can manifest due to a range of risk factors contributing to their development, such as oxidative stress, genetic variations, the aging process, inflammation, hypertension, diabetes, infections, vitamin deficiencies, metabolic issues, exposure to certain chemicals, endocrine abnormalities, and dietary supplements, among others (Ding et al., 2022, p. 952161). These factors play pivotal roles in the initiation and progression of neurological diseases. The global impact

of these conditions is substantial, leading to significant disability and loss of life. Notably, the prevalence of neurological diseases is on the rise, making them a major global public health concern. According to the World Health Organization (WHO), neurological conditions rank as the second leading cause of mortality worldwide, resulting in approximately one

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million deaths annually (Wang et al., 2023, pp. e2141–e2154).

As per the survey report of 2021, WHO data revealed that the primary contributors to neurological illnesses included stroke (42.6%), Alzheimer's disease (17.50%), migraine (14.3%), anxiety disorders (4.5%), epilepsy (4.1%), depression (3.4%), Parkinson's disease (1.9%), and meningitis (1.9%) (Figure 1). The analysis indicates that globally, the total burden of disability, illness, and premature death due to neurological conditions, measured in disability-adjusted life years (DALYs), has risen by 18% over the past 31 years. This increase translates to a rise from approximately 375 million years of healthy life lost in 1990 to 443 million years in 2021 (GBD 2021 Nervous System Disorders Collaborators, 2024, pp. 344–381).

In India, the prevalence of neurological disorders has more than doubled over a span of 29 years (1990–2019), thereby affecting a substantial number of individuals, ranging from 967 to 4,070 cases per 100,000 populations, with an average of 2,394 cases. Multiple research studies have emphasized the notable factors contributing to the burden of such disorders in India in 2019, as measured by DALYs (Figure 2). These factors encompass stroke (37.9%), headache disorders (17.5%), epilepsy (11.3%), cerebral palsy, and encephalitis (5.3%) (India State-Level Disease Burden Initiative Neurological Disorders Collaborators, 2021, pp. e1129–e1144).

Methodology

The data on phytochemicals, identification of active compounds, pathophysiological studies of neurological diseases, clinical trials, and studies of neurological activities of 13 Indian *Ficus* species were extended by using various databases and search engines, for example, PhD thesis (unpublished data), Google Scholar, ResearchGate, monograph, reference book, SciFinder, PubMed/Medline, Scopus, and ScienceDirect from 2000 to 2024.

Treatment Approaches of Neurological Disorders by Modern Drug System and Herbal Drug System

Nowadays, the treatment of neurological disorders poses a significant challenge due to their inherent complexity. However, modern prototype drugs such as levodopa (used for Parkinsonism), donepezil (for Alzheimer's), gabapentin (for epilepsy), interferon (for multiple sclerosis), and sumatriptan (for migraines) have been developed for addressing these conditions. It is worth noting that these drugs, while effective, come with a range of side effects, including nausea, dizziness, hallucinations, irregular heartbeats, peripheral edema, chills, muscle aches, redness, chest pain, and shortness of breath (Diener et al., 2003, pp. 1507–1524). Despite these drawbacks, nature has provided us with various medicinal

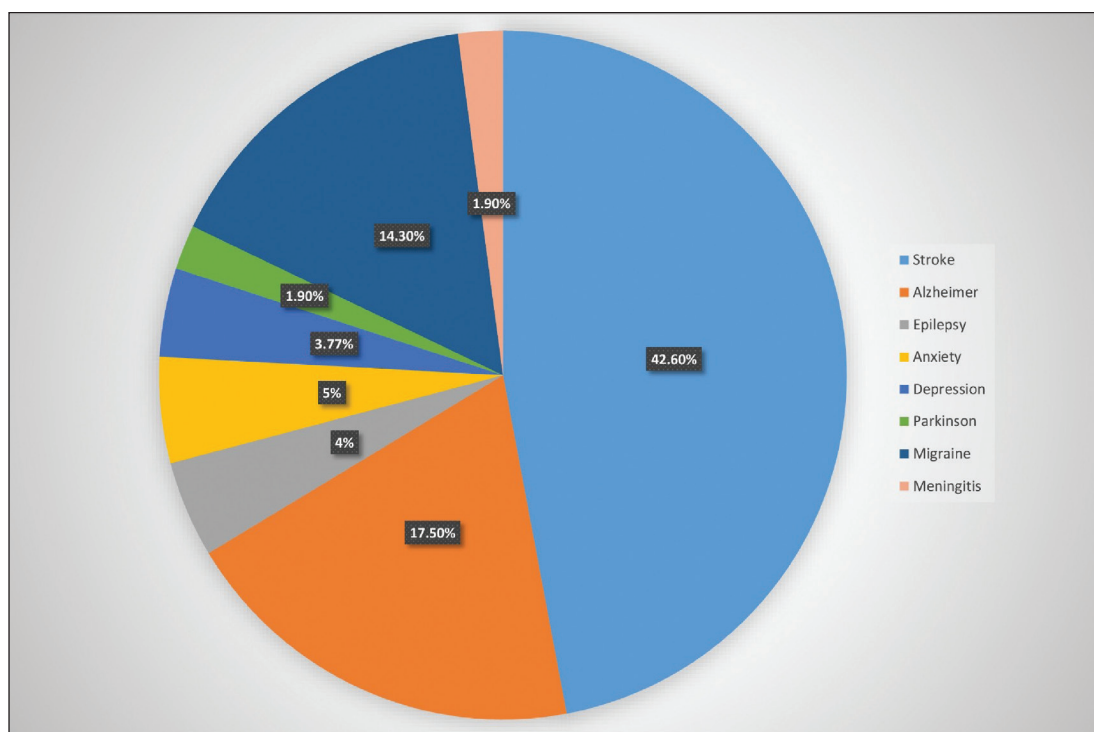


Figure 1. Epidemiological Distribution Graph of Neurological Disease Worldwide.

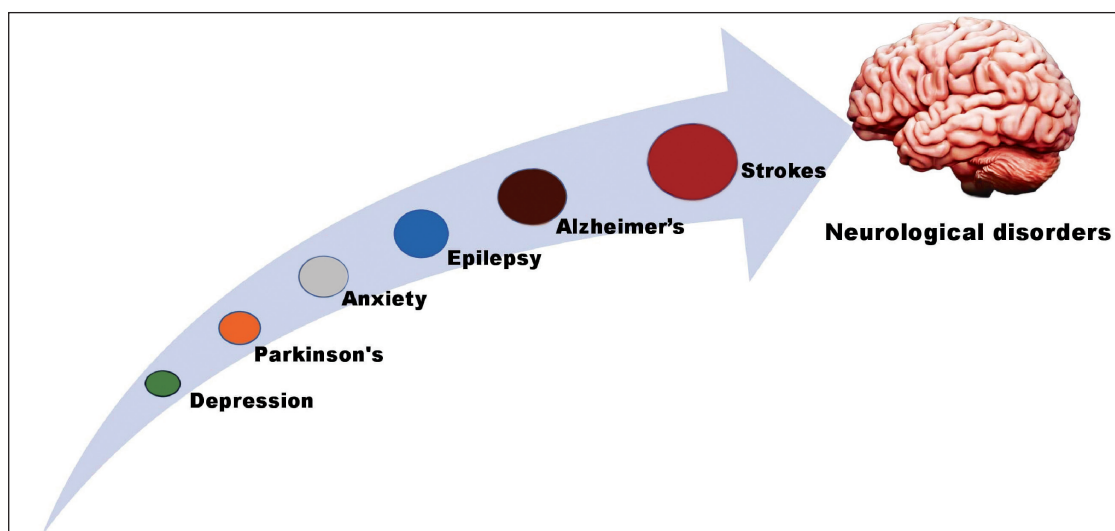


Figure 2. Types of Prevalent Neurological Diseases.

plants that are extensively utilized to treat a wide array of diseases, including neurological complications. Some of these medicinal plants, such as *Ginkgo biloba* (for Alzheimer's) (Singh et al., 2019, pp. 666–674), *Curcuma longa* (for Parkinsonism) (Ma & Guo, 2017, pp. 1799–1805), *Passiflora incarnata* (for anxiety), *Withania somnifera* (for depression), and *Valeriana officinalis* (as a sedative), have shown promise in addressing neurological conditions. However, it is essential to be aware that these herbal remedies may also have side effects, such as bleeding disorders, gastrointestinal discomfort, drowsiness, heartburn, nausea and vomiting, headaches, and potential liver toxicity (Cock, 2015, pp. 2–50).

Ficus, a predominant species found in Southeast Asian countries, has been identified as having medicinal properties that are effective in treating various diseases with fewer side effects and great structural diversity. These species are rich sources of polyphenols, flavonoids, and terpenes, particularly focusing on neurological complications. In this review, we delve into the chemical constituents of *Ficus* and their respective properties, demonstrating their potential efficacy in the treatment of diverse neurological disorders.

Description and Distribution of *Ficus* Species

The Moraceae family encompasses the *Ficus* genus, which comprises both deciduous and evergreen trees. *Ficus*, with its impressive 800 species and 2,000 varieties, is widely spread throughout tropical and subtropical regions (Deepa et al., 2018, pp. 210–232). Different parts of this plant, such as leaves, roots, barks, fruits, and latex, have a long history of traditional use for medicinal, dietary, decorative, and religious purposes (Donia et al., 2013).

The majority of *Ficus* species, which accounts for roughly 66% of all species globally, are concentrated in the Asian–Australian region. The highest diversity of this genus can be found in the Asian mainland (170 species), New Guinea (132 species), and Borneo (129 species). *Ficus* species exhibit a wide distribution across various biogeographic zones, primarily in lowland areas, but some can also be found at elevations of up to 2,000 m (Berg & Corner, 2005, pp. 1–702).

Around 115 taxa of *Ficus* species have been documented in India. They are dispersed across the entire country, extending from the southern to the northern regions, including the Himalayas, reaching altitudes of approximately 2,000 m. The northeastern region of India stands out as a hotspot due to its remarkable presence of around 43 *Ficus* species (Chaudhary et al., 2012, pp. 193–216).

The present review summarizes and discusses the updated knowledge of active constituents and neurological activities of 13 Indian *Ficus* species, but they have not been evaluated for their clinical research. No information is available in the literature about how these species showed a protective effect in neurological conditions. This review also provides some critical insights into current scientific knowledge of pharmacokinetic and pharmacodynamics profiles and its future potential in pharmaceutical research.

Studies Using *Ficus* Species in Alzheimer's Disease

According to a literature review, researchers have identified that several *Ficus* species, including *Ficus bengalensis*, *Ficus carica*, *Ficus erecta*, and *Ficus racemosa*, have been used for the treatment of Alzheimer's disease. Studies have demonstrated that the aqueous bark and aerial root extract of *Ficus benghalensis* possess notable antioxidant effects and acetylcholinesterase inhibitory effects for treating Alzheimer's disease (Ramasamy et al., 2022, pp. 291–299). A study involving

Swiss albino Wistar mice investigated the cognitive effects of the hexane extract of *F. carica*, finding that higher dosages led to significant behavioral improvements and enhanced learning outcomes (Vasundhara et al., 2013, pp. 109–113). Another study conducted on male Albino rats examined the effect of ethanolic extract of *F. carica* leaf extract on the hippocampus of aged rats that possess antioxidant, anti-inflammatory, and neuroprotective properties that ameliorate age-related diseases like Alzheimer's disease (Zeair et al., 2024, p. 15). Additionally, the investigation of an ethanolic leaf extract derived from *F. erecta* on the aggregation of amyloid- β in mice indicated that the extract was associated with the activation of the CREB/BDNF signaling pathway and an increase in inflammatory cytokines, holding promise for the treatment of Alzheimer's disease and related neurodegenerative conditions (Sohn et al., 2021, p. 607403). In a Wistar rat model, orally administered aqueous extract of *F. racemosa* bark significantly increased acetylcholine (ACh) levels in the hippocampi of the rats, with statistically significant implications for its memory-enhancing activity, which may be attributed to the inhibition of acetylcholinesterase (Ahmed et al., 2011, pp. 246–249).

Studies Using *Ficus* Species in Anxiety

The literature indicated that *Ficus thonningii*, *F. benghalensis*, *F. carica*, *Ficus hispida*, and *Ficus sycomorus* alleviate anxiety. In an animal study, ethanolic leaf extract of *F. thonningii* significantly reduced anxiety-related behaviors,

such as stretch-attend posture and head dipping, and increased the frequency and duration of entries into the open arms of the elevated plus maze test, indicating a strong anxiolytic effect (Wadioni et al., 2019, pp. 121–127). Similarly, oral administration of aqueous extract from *F. benghalensis* aerial roots demonstrated anxiolytic effects in mice assessed via the Open Field Test (Panday et al., 2016, p. 429). Research on *F. carica* using the elevated plus maze and staircase tests suggested that its aqueous acetonc extract enhances chloride channel opening through GABA receptors, highlighting its potential antianxiety mechanism (Bhanushali et al., 2014, pp. 89–96). Additionally, *F. hispida* leaf extracts showed anxiolytic effects in Swiss albino mice with corticosterone-induced anxiety (Sivaraman et al., 2012, pp. 467–471). Furthermore, *F. sycomorus* extract significantly elevated glutathione (GSH) content and reduced the levels of malondialdehyde (MDA) that indicated its neuroprotective and anxiolytic potential in stress-induced behavioral changes and oxidative stress in the rat (Foyet et al., 2017, p. 502).

On the base of the available literature *Ficus* species showed anxiolytic properties by enhancing chloride channel opening, elevated GSH content, and reducing the MDA levels (Figure 3).

Studies Using *Ficus* Species in Convulsion

A review of the existing literature highlights the use of various parts of *Ficus* species in managing convulsions,

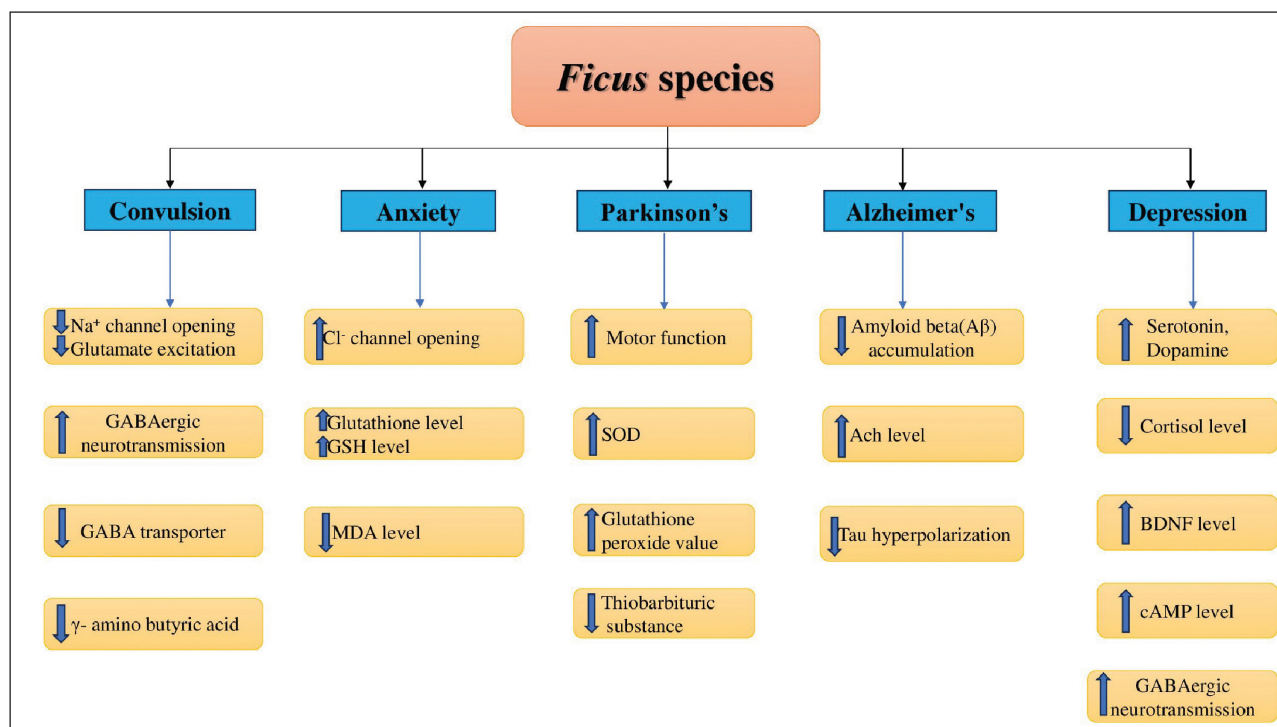


Figure 3. Scientific Evaluation of *Ficus* Species in Various Neurological Disorders and Their Tentative Mechanism.

including *Ficus abutilifolia*, *F. carica*, *F. hispida*, *Ficus platyphylla*, *F. racemosa*, *Ficus religiosa*, *F. sycomorus*, and *Ficus sur*. For instance, the aqueous ethanolic extract of *F. abutilifolia* showed 40% protection against maximal electric shock-induced seizures in chicks (Danmalam et al., 2012, pp. 234–237). Similarly, the aqueous extract of *F. carica* fruit exhibited notable effects by inhibiting voltage-dependent Na⁺ channels and blocking NMDA receptor-mediated glutamergic excitation (Bhat et al., 2022, pp. 162–165) (Figure 3). *F. racemosa* bark and methanolic extract of *F. hispida* altered the GABAergic and glycinergic pathways to show anticonvulsant activity (Chavan et al., 2021). *F. platyphylla* extract showed central depressant effects and protection against strychnine-induced seizures (Bum et al., 2009). The zinc-rich aqueous root extract of *F. religiosa* demonstrated anticonvulsant properties by modulating glycine receptors and GABA transporters (Patil et al., 2011, pp. 92–96). *F. sycomorus* bark extract protected against pentylenetetrazole-induced seizures (Sandabe et al., 2003, pp. 103–110) and *F. sur* extract exhibited significant anticonvulsant effects, likely involving multiple neurotransmitter pathways (Ishola et al., 2013, pp. 1287–1294).

These findings underscore the potential of *Ficus* species in developing novel anticonvulsant therapies primarily by enhancing GABAergic neurotransmission and reducing the expression of GABA transporter, as shown in Figure 3.

Studies Using *Ficus* Species in Depression

The previous literature revealed the use of notable species of *Ficus* like *F. benghalensis*, *F. carica*, and *Ficus elastica* in curing depression. In a study by Malik et al. (2020), the methanolic extract of *F. benghalensis* showed significant antidepressant potential. Additionally, *in vivo* studies of ethanolic extract of *F. carica* fruits proved antidepressant, anxiolytic, and stress-relief effects at different doses (Gul et al., 2018). Further research involving the administration of aqueous, methanol, and chloroform extracts of *Ficus elastica* in mice demonstrated potent antidepressant activities in the forced swim test and tail suspension test, as well as anxiolytic activity in the elevated plus maze test and rotarod activity (Koley et al., 2023, pp. 1–10).

Based on these findings, *Ficus* species exhibit antidepressant activity by modulating levels of cortisol, serotonin, and dopamine (Figure 3). Also, it regulates IL-1 β , IL-6, and TNF- α expressions, inhibits pro-inflammatory cytokine expression and NF- κ B signaling, and decreases NLRP3 inflammasome activation (Liu et al., 2017, pp. 128–134).

Studies Using *Ficus* Species in Parkinson's Disease

The existing literature revealed that various components derived from *F. religiosa*, *Ficus exasperata*, and *Ficus*

deltoidea have been employed in the management of Parkinson's disease. According to Bhangale and Acharya (2016, p. 9436106), the administration of petroleum ether extracts of *F. religiosa* leaves suppressed disease-related symptoms like cataleptic scores, muscle stiffness, and locomotor activity when compared with marketed medications in rats. Furthermore, the neurorestorative and motor function ameliorating efficacy of saponins-rich fraction of *F. exasperata* was explored by Adekeye et al. (2020, pp. 183–193) in a vanadium-induced Parkinson mice model. Another study on diabetic rats revealed that oral administration of *F. deltoidea* leaf extract significantly increased the superoxide dismutase (SOD) and glutathione peroxidase (GPx) values, while notably decreasing oxidative stress (Figure 3). Therefore, a simultaneous enhancement of cortical gyrification, spatial learning, and memory performance was observed (Gautam et al., 2015, pp. 331–339; Nurdiana et al., 2018, pp. 190–202).

According to available literature, *Ficus* species have been shown to aid in Parkinson's disease treatment by increasing Park2 mRNA levels and reducing Lrrk2 mRNA levels, protecting dopaminergic PC12 cells and safeguarding dopaminergic neurons by activating the ER-mediated signaling pathway (Elmazoglu et al., 2020, pp. 96–103; Siddique et al., 2021, pp. 198–206).

Common Flavonoids, Polyphenols, and Triterpenoids Present in *Ficus* Species

Structures of some common flavonoids, polyphenols, and triterpenoids isolated from different *Ficus* species have been compiled in Figure 4.

Pharmacokinetic Profile of Common Phytoconstituents Present in *Ficus* Species

Pharmacokinetic data of common phytoconstituents present in *Ficus* species demonstrate their absorption, distribution, metabolism, and excretion (ADME) characteristics with the help of an extensive literature survey and using the SwissADME online tool (Table 1). This profiling is essential for understanding the therapeutic potential, safety, and clinical of these phytoconstituents. Moreover, this information will also help to establish their efficacy and toxicity profiles, thereby guiding their rational use in traditional and modern medicine.

Effect of Phytoconstituents from *Ficus* Species on Neurological Activities

The different neurological activities that are treated by different chemical constituents obtained from various *Ficus* species have been enumerated and compiled in Table 2.

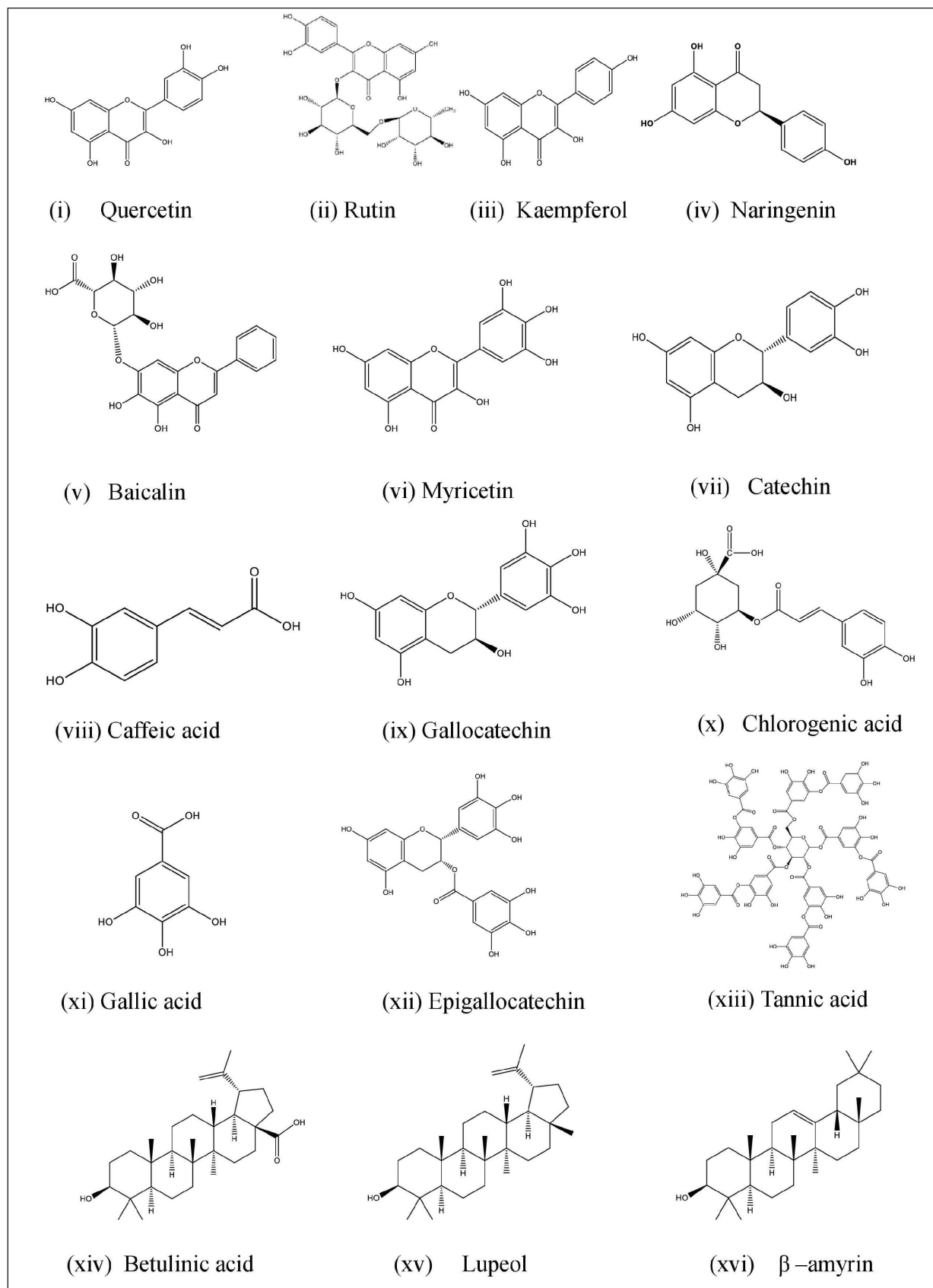


Figure 4. Structure of Some Common Compounds Present in Different *Ficus* Species.

Table 1. Pharmacokinetic Parameters of Some Common Phytoconstituents Isolated from Different *Ficus* Species.

Sl. No.	Common <i>Ficus</i> Compound	Dose (mg/kg)	GI Absorption	BBB Permeation	T_{max} (h)	C_{max} (ng/ml)	$t_{1/2}$ (h)	References
1	Betulinic acid	100	Low	No	0.15	509.31	5.95	Godugu et al. (2014)
2	Caffeic acid	20	High	No	0.33	7,870.58	1.25	Wang et al. (2015)
3	Catechin	200	High	no	0.75	1,636.69	–	Varia et al. (2021)
4	Chlorogenic acid	50	Low	No	0.48	5,542.45	1.70	Qi et al. (2011)
5	Ferulic acid	100	High	Yes	0.3	8,174.55	0.7	Li et al. (2021)
6	Gallic acid	100	High	No	1.5	1,712.29	3.10	Yu et al. (2018)
7	Kaempferol	100	High	No	1.5	2,539.48	3.5	Barve et al. (2009)
8	Lupeol	200	Low	No	6.44	8,071	13.56	Cháirez et al. (2019)
9	Myricetin	100	Low	No	5.2	2,611.76	3.79	Dang et al. (2013)
10	Quercetin	120	High	No	2.75	1,105.34	0.89	Zhao et al. (2011)
11	Rutin	400	Low	No	0.1	1,546.65	0.358	Ou-yang et al. (2013)

Table 2. Isolated Phytoconstituents from Various Parts of *Ficus* Species and Their Use in the Treatment of Neurological Disorders.

S. No.	<i>Ficus</i> Species	Neurological Disease	Parts of Plant	Chemical Constituents			References
				Flavonoids	Phenols	Terpenes	
1.	<i>Ficus abutilifolia</i>	Convulsion	Root	Quercetin, epigallocatechin, kaempferol, quercetin, and myricetin	Gallic acid Caffeic acid Rutin Ferulic acid Morin	α -Pinene β -Pinene Limonene Myrcene Caryophyllene Linalool Terpinolene Geraniol Camphene	Aliba et al. (2018) Madeleine et al. (2020)
2.	<i>Ficus benghalensis</i>	Alzheimer, anxiety, depression	Bark, root, leaves	Naringenin, quercetin, bengalensinone, alpinumisoflavone, and 4-hydroxyacetophenone	Gallic acid Caffeic acid Ferulic acid Theaflavin-3,3'-digallate Leucocidin Gallocatechin	Bergapten, stigmasterol, friedelin, lupeol, β -amyrin, 3-friedelanol, sitosterol, ergosterol acetate, furostano, 4,22-stigmastadiene-3-one protodioscin	Afzal et al. (2020) Gopukumar and Praseetha (2015)

(Table 2 continued)

(Table 2 continued)

S. No.	Ficus Species	Neurological Disease	Parts of Plant	Chemical Constituents			References
				Flavonoids	Phenols	Terpenes	
3.	<i>Ficus carica</i>	Alzheimer, convulsion, anxiety, depression	Fruit	Quercetin Luteolin Biochanin A Caffeoylmalic acid Rutin Schafatoside Quercetin 3-O-glucoside Quercetin 3-O-malonylglucoside Kaempferol 3-O-glucoside Benzopyran-2-one	Chlorogenic acid Caffeoylmalic acid Caffeic acid Isoschaftoside Schafatoside Psolaric acid glucoside Quercetin 3-O-rutinoside Ferulic acid Quercetin-3-O-glucoside	Psoralen Bergapten Psolaren α -Amyrin β -Sitosterol β -Sitosterol- β -D-glucoside Baueranol Lupeol acetate Methyl maslinate Calotropenyl acetate Oleanolic acid 15-octadecatrienoic acid, methyl ester, ferruginol	Joseph and Raj (2011) Mawa et al. (2013)
4.	<i>Ficus deltoidea</i>	Parkinson	Leaves	Vitexin Isovitexin Caffeic acid Catechin Rutin Quercetin Naringenin Chrysoeriol-7-O- α -rhamnoside Lucenin-2 Vicenin-2 Luteolin-6-C-hexosyl-8-C-pentoside Luteolin-6-C-glucosyl-8-C-arabinoside Isoschaftoside Luteolin-6-C-arabinosyl-8-C-glucoside Schafatoside Orientin Apigenin-6-C-pentosyl-8-C-glucoside Apigenin-6-C-glucosyl-8-C-pentoside	Gallic acid Gallocatechin Epigallocatechin Catechin Epiafzelechin Epicatechin Apigenin-6,8-C-dipentose isomer 4-p-Coumarolyquinic acid	Lupeol Stigmasta-5,8-dien-3 β -ol 1,1,2,3,3-Pentamethylindane 6-Methyl-5-hepten-2-one Myrcene Linaloolcis-Pyranoid linalool oxidetrans-Pyranoid linalool oxide Hotrienol Limonene Dendrolasine Alloaromadendrene Aciphyllene Germacrene D D-cadinene Cadina-1,4-diene Germacrene B Caryophyllene oxide	Musapha and Harun (2015) Omar et al. (2011)
5.	<i>Ficus erecta</i>	Alzheimer's	Leaves	Rutin and kaempferol-3-O-rutinoside	Chlorogenic acid Vanillic acid p-Hydroxybenzoic acid Syringic acid Methyl p-hydroxybenzoate Methyl vanillate	β -Sitosterol α -Amyrin acetate Ethyl linoleate	Jung et al. (2018)
6.	<i>Ficus exasperata</i>	Parkinson's	Leaves	Quercetin Kaempferol Luteolin Apigenin Myricetin Rutin Morin Isorhamnetin Fisetin Galangin Genistein Quercetin-3,7-dihexoside Kaempferol-3 hexoside Apigenin-8-C-glucoside	Gallic acid Catechin Epicatechin Caffeic acid Chlorogenic acid Ferulic acid Bergapten Oxypeucedanin hydrate	β -Sitosterol Sitosterol-3-O- β -D-glucopyranoside β -Amyrin acetate Friedelin Lupeol hexanoate Lupeol acetate Dehydroferreirine	Amponsah (2012) Bafar et al. (2013)

(Table 2 continued)

(Table 2 continued)

S. No.	Ficus Species	Neurological Disease	Parts of Plant	Chemical Constituents			References
				Flavonoids	Phenols	Terpenes	
7.	<i>Ficus hispida</i>	Convulsion, anxiety	Leaves, bark	Quercetin Rutin Kaempferol Myricetin Luteolin	Chlorogenic acid Vanillic acid Gallic acid Caffeic acid Myricetin Fisetin Resveratrol	Ursolic acid α -Amyrin Betulinic acid Lupeol Stigmasterol β -Sitosterol	Ali and Chaudhary (2011)
8.	<i>Ficus platyphylla</i>	Convulsion	Bark	Chrysoeriol Rutin Astilbin	Phenoxyphenethylamine Triphenylacetic acid Methylmalonic acid Succinic acid Butanoic acid 4-Chlorophenyl ester Herniarin	β -Sitosterol α -Amyrin β -AmyrinCeryl alcohol Ursolic acid 2,4-Dimethoxyamphetamine Hexadecanoic acid Oleic acid Lanosterol Octadecadienoic acid Triacontylbenzene Octaethylene glycol Nicothanol Sarcosine	Hasan et al. (2022) Kubmarawa et al. (2009)
9.	<i>Ficus racemosa</i>	Alzheimer, convulsion	Bark	Quercetin, kaempferol, catechin, and epicatechin	Quercetin, kaempferol, catechin, epicatechin, bergenin, bergapten, and psoralens	Stigmasterol, β -sitosterol, β -sitosterol-D-glucoside, lupeol, lupeol acetate, α -amyrin acetate, gluanol acetate, friedelin, and glaucol	Shiksharathi et al. (2011) Yadav et al. (2015)
10.	<i>Ficus religiosa</i>	Convulsion, Parkinson	Root, leaves	Leucoanthocyanidin Leucoanthocyanin Quercetin Myricetin Kaempferol	Tannic acid Eugenol Leucoanthocyanidin Leucoanthocyanin 2,6-Dimethoxyphenol 4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl 2,4-bis(1,1-dimethylethyl)	α -Amyrin Lupeol Stigmasterol <i>n</i> -Nonacosane <i>n</i> -Hentricontane Campesterol Hexacosanol Isofucosterol <i>n</i> -Octacosane Lanosterol Lupen-3-one β -Sitosterol β -Sitosterol-D-glucoside Lupeol acetate α -Amyrin acetate	Manorenjitha et al. (2013) Chandrasekar et al. (2010)
11.	<i>Ficus sur</i>	Convulsion	Leave, barks	Gallocatechin Rutin Quercetin Kaempferol Luteolin Apigenin	Quinic acid Citric acid Caffeic acid Gallic acid Hydroxybenzoic acid Coumaric acid Ferulic acid	11- <i>oxo</i> - β -Amyrin acetate Olean-12-en-3-one β -Amyrin palmitate β -Amyrin β -Amyrin acetate Lupeol acetate Ergosterol peroxide (22R)-3 β -stigmast-5-ene-3,22-diol β -Sitosterol Palmitic acid	Dongmo et al. (2022) Odusanmi et al. (2017)

(Table 2 continued)

(Table 2 continued)

S. No.	Ficus Species	Neurological Disease	Parts of Plant	Chemical Constituents			References
				Flavonoids	Phenols	Terpenes	
12.	<i>Ficus sycomorus</i>	Anxiety, convulsion	Leaves, bark	Quercetin-3-rutinoside Isoquercitrin Myricetin Quercetin Naringenin Kaempferol	Cinnamic acid Rosmarinic acid Vanillic acid Pyrogallolp-Hydroxy benzoic acid Chlorogenic acid Gallic acid Glucopyranoside 1,2-Benzenedicarboxylic acid	β -Sitosterol Caffeine Oleic acid Piperidine Methyl oleate	Romeh (2013) Sandabe et al. (2006)
13	<i>Ficus thonningii</i>	Anxiety	Leaves	Rutin Morin Thonningiol Gancaonin G Alpinumisoflavone Wighteone Taxifolin Conrauiiflavanol Shuterin Luteone	Gallic acid Caffeic acid Ferulic acid Protocatechuic acid	β -Sitosterol β -Sitosterol 3-O- β -d-glucopyranoside β -Amyrin acetate Friedelin Lupeol hexanoate Lupeol acetate Stigmasterol	Omosa et al. (2022) Adamu et al. (2018)

Conclusion

Ficus species are widely distributed throughout the world, and approximately all parts of the plant are used in folklore medicine. There is currently a worldwide increase in interest in herbal remedies, as well as increased laboratory research into the pharmacological properties of bioactive components and their ability to treat various disorders. Recent studies have highlighted the ability of pharmacologically relevant constituents of *Ficus* species to treat neurological disorders. Hence, this review provides a scientific basis for further studies in association with developing effective neurological drugs from plant sources, especially *Ficus* species.

Abbreviations

Ach: Acetylcholine; ADME: Absorption, distribution, metabolism, and excretion; BDNF: Brain-derived neurotrophic factor; CREB: Cyclic AMP response element-binding protein; DALYs: Disability-adjusted life years; GABA: Gamma-aminobutyric acid; GPx: Glutathione peroxidase; IL-1 β : Interleukin-1 β ; IL-6: Interleukin-6; iNOS: Inducible-NO synthase; L-DOPA: Levodihydroxyphenylalanine; Lrrk2: Leucine rich repeat kinase 2; MDA: Malondialdehyde; NLRP3: Nucleotide-binding domain; leucine-rich-containing family, pyrin domain-containing-3; NMDA: *N*-methyl-D-aspartate; PC12: Pheochromocytoma-12; SOD: Superoxide dismutase; TAC: Total antioxidant capacity; TNF- α : Tumor necrosis factor alpha; WHO: World Health Organization.

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