The Journal of Medicinal Plants and By-products

Review Article

Traditional Persian Medicinal Plants for Neurological Disorders: A Phytochemical and Ethnobotanical Review

Running Title: Traditional Persian Medicinal Plants for Neurological Disorders

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Article History: Received 14 April 2025/Accepted in revised form 26 August 2025

ABSTRACT

Neurological disorders—including Alzheimer's disease, Parkinson's disease, anxiety, depression, and insomnia—are among the most challenging global health issues. Due to the limitations and side effects of conventional treatments, there is increasing interest in natural, plant-based alternatives. This review aims to evaluate medicinal plants used in Traditional Iranian Medicine (TIM) for neurological disorders and to assess their phytochemical and pharmacological relevance based on both classical texts and modern scientific literature. A total of 52 plant species belonging to 26 botanical families were identified, with Lamiaceae, Apiaceae, Euphorbiaceae, Pinaceae, Asteraceae, and Fabaceae being the most frequently represented. Phytochemical analyses revealed that compounds such as terpenoids (68%), phenolic compounds (52%), and flavonoids (20%)—alongside glycosides, alkaloids, steroids, amines, and saponins—are key contributors to neuropharmacological activity. These metabolites may exert neuroprotective, antioxidant, anti-inflammatory, anxiolytic, and cognition-enhancing effects through various mechanisms, including neurotransmitter modulation (e.g., serotonin, dopamine, GABA), suppression of neuroinflammation, and oxidative stress reduction. Notable species such as *Curcuma longa*, *Cannabis sativa*, *Mentha* spp., *Narcissus jonquilla*, and *Peucedanum officinale* contain well-documented bioactive compounds like curcumin, cannabidiol, linalool, galanthamine, and α-pinene. The phytochemical richness of Apiaceae and Lamiaceae suggests their prominence in traditional neurological care. In conclusion, this review highlights the therapeutic potential of traditional Iranian medicinal plants for neurological disorders and advocates for future bioassay-guided studies, synergistic compound analysis, and formulation standardization to support their integration into evidence-based modern medicine.

Keywords: Botanical therapeutics, Ethnomedicine, Herbal neuroprotective, Natural compounds, Neuropharmacology

INTRODUCTION

Neurological disorders—including neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's disease, as well as mood-related conditions like depression, anxiety, and insomnia—are increasingly prevalent worldwide [1]. These conditions present significant diagnostic and therapeutic challenges, and many conventional pharmacological treatments are associated with limited efficacy and adverse effects [2]. As a result, there is growing global interest in complementary and alternative medicine approaches, particularly those involving natural products [3].

Among these alternatives, Traditional Persian Medicine (TPM), a rich and well-documented system of healing, has long utilized medicinal plants to manage neurological and psychological ailments [4]. These traditional approaches offer insights into therapeutic strategies that are still relevant today and have prompted renewed scientific interest.

The therapeutic properties of medicinal plants are closely linked to their phytochemical constituents [5]. Plants produce a wide range of primary and secondary metabolites; although secondary metabolites are not essential for basic plant survival, they play critical ecological and pharmacological roles [6]. These compounds—including terpenoids, alkaloids, flavonoids, and phenolic acids—exhibit anti-inflammatory, antioxidant, anxiolytic, and neuroprotective effects, making them promising candidates for treating neurological disorders [7, 8].

This review explores medicinal plants traditionally used in TPM for neurological diseases and highlights the secondary metabolites believed to underlie their therapeutic effects on the nervous system. Notable examples include *Cannabis sativa* L., known for its anticonvulsant and anxiolytic effects [9]; *Curcuma longa* L., with established anti-inflammatory and neuroprotective properties [10]; and *Artemisia* spp. L., which have shown potential against neurodegenerative conditions [11]. A more in-depth understanding of these plants and their bioactive compounds may guide the development of novel herbal-based neurotherapeutics [12].

From ancient times, natural products—particularly those derived from plants—have been integral to traditional medical practices worldwide. While many cultures, including Indian, Egyptian, and Chinese systems, have used herbal remedies, Traditional Persian Medicine (TPM) offers a unique and rich pharmacopeia specifically relevant to neurological disorders [13, 14].

In TPM, numerous plants have been historically employed to manage conditions such as seizures, melancholia, insomnia, and nervous agitation. The efficacy of these treatments is closely tied to their phytochemical composition, particularly secondary metabolites such as alkaloids, flavonoids, terpenoids, and phenolic compounds. These compounds contribute to various therapeutic effects including neuroprotection, antioxidant activity, anti-inflammatory responses, and modulation of neurotransmitters like serotonin and dopamine [15, 16].

This review aims to systematically identify and evaluate medicinal plants used in TPM for neurological disorders, focusing on their phytochemical profiles and mechanisms of action. By bridging ethnobotanical records with contemporary pharmacological data, we seek to provide a scientific basis for the integration of these traditional remedies into modern neurotherapeutic strategies [17-19].

Recent scientific studies have revealed that the powerful therapeutic properties of plants are largely determined by their phytochemical compositions [20]. Consequently, understanding plant chemistry is essential for their medicinal applications [21]. Plants produce two major categories of compounds: primary and secondary metabolites [22]. Secondary metabolites are smaller molecules derived from primary metabolites or act as intermediates in their biosynthetic pathways [23]. These compounds do not directly impact the basic cellular processes necessary for growth and reproduction but play critical ecological roles in helping plants adapt to their environments [24]. Additionally, secondary metabolites are known for their wide range of biological activities, including antifungal, antibiotic, and antiviral properties, making them crucial for plant defense against pathogens and their ability to absorb harmful ultraviolet rays [25].

Recent research has demonstrated that secondary metabolites are beneficial not only for plant protection but also for human health, agricultural production, and the cosmetic industry, significantly contributing to economic growth [26]. These compounds are believed to be responsible for the therapeutic effects of plants, with many secondary metabolites being used in modern medicine to treat conditions like cancer and migraines [27].

Despite the progress in medical research, there are still no approved cures for some infections and diseases, and vaccines are limited to certain viral infections [28]. Furthermore, conventional medications can be expensive and often cause adverse effects [29]. As a result, plant-based pharmacotherapy presents a promising alternative for treating various ailments [30].

Neurological disorders, including conditions like Alzheimer's disease, Parkinson's disease, anxiety, and depression, are increasingly prevalent and present significant challenges in modern medicine [31]. Traditional medicine has utilized plants for centuries to manage these disorders [32]. Phytochemical research has indicated that specific plant-derived compounds exhibit beneficial effects on the nervous system [33]. For instance, antioxidants, anti-inflammatory agents, and neuroprotective substances found in plants have shown promise in protecting the nervous system from damage and improving cognitive functions [34].

Similarly, as with liver diseases, understanding the role of secondary metabolites in treating neurological conditions is crucial [35]. Research has highlighted the potential of these compounds to not only protect neurons but also enhance mental clarity and combat neurodegenerative diseases [36]. Given the limitations of current treatments and their often-debilitating side effects, exploring natural, plant-based remedies may offer a safer and more sustainable approach for managing neurological health [37].

In conclusion, the use of traditional knowledge from sources like Traditional Persian Medicine (TPM) has long guided the treatment of various disorders [38]. Many herbs, recorded in ancient texts, have demonstrated scientific validity in treating neurological diseases [39]. The present review focuses on identifying these herbs, analyzing their bioactive constituents, and evaluating their potential in treating nervous system disorders based on modern scientific research and traditional Persian medical knowledge [40, 41].

MATERIAL AND METHODS

This review was conducted to document medicinal plants used in Traditional Persian Medicine (TPM) for the treatment of neurological disorders and to examine their phytochemical constituents. The selection of plant species was based on their mention in at least one of three classical TPM texts: *Makhzan al-Advieh*, *The Canon of Medicine (Al-Qanun fi al-Tibb)*, and *Taqwim al-Abdan fi Tadbir al-Insan*. Plants were included if they were explicitly described as treatments for neurological conditions such as anxiety, melancholia, convulsions, insomnia, or other neuropsychological symptoms.

To complement the ethnobotanical data, modern scientific literature was reviewed using online databases including PubMed, Web of Science, Google Scholar, and ScienceDirect. Search terms included combinations of each plant's scientific name with keywords such as “neuroprotective,” “phytochemical,” “antioxidant,” “anti-inflammatory,” and “neurological disorders.”

Only those plants for which at least one phytochemical or pharmacological study related to the nervous system was available were included. Species with insufficient modern scientific evidence or unclear therapeutic indications were excluded.

Information on phytochemical profiles was obtained from peer-reviewed studies involving analytical techniques such as gas chromatography–mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), and nuclear magnetic resonance (NMR), when available. Where such data were not reported, secondary metabolites were identified based on existing phytochemical reviews or monographs.

All identified species were then listed by their scientific names, botanical families, and major classes of bioactive compounds, as presented in the Results section and summary table.

RESULTS

A total of 52 medicinal plant species from 26 botanical families were identified in classical Traditional Persian Medicine (TPM) sources as being traditionally used for the treatment of neurological disorders. These plants were analyzed for their phytochemical profiles based on available scientific literature, resulting in the identification of over 80 bioactive compounds, primarily belonging to classes such as terpenoids, flavonoids, alkaloids, and phenolic compounds. A comprehensive list of these species, including their botanical families and principal phytochemicals, is presented in Table 1. The frequency distribution of plant families is visualized in Figure 1, which demonstrates the taxonomic richness of the dataset. Among the families, Euphorbiaceae was the most represented with 8 species (14.55%), followed by Lamiaceae and Pinaceae (each with 6 species, 10.91%), Asteraceae (5 species, 9.09%), Fabaceae (4 species, 7.27%), and Apiaceae (3 species, 5.45%). Several families, including Cyperaceae, Tamaricaceae, and Rhamnaceae, were each represented by two species (3.64%). The remaining 17 families appeared with only one species each.

These families not only reflect taxonomic diversity but also highlight significant pharmacological potential. For instance, Lamiaceae is notably rich in essential oils with anxiolytic and sedative properties, while Euphorbiaceae contains several diterpenes and alkaloids with reported neuroactive effects.

Among the most studied bioactive compounds are α-pinene, a monoterpene found in Pistacia species shown to enhance cholinergic transmission, and linalool, commonly present in Lavandula species, which modulates GABAergic activity and has anxiolytic effects. These findings support the traditional neurological uses of these plants as documented in TPM.

Despite these promising results, notable gaps remain in the scientific validation of several species. For many traditionally cited plants, detailed pharmacological or toxicological studies are lacking. Additionally, the mechanisms of action for numerous phytochemicals remain poorly understood. These limitations highlight the need for future in vitro and in vivo investigations to fully explore the therapeutic potential of these traditional remedies.

Table 1 Medicinal plants used in Traditional Persian Medicine (TPM) for neurological disorders, along with their scientific names, family affiliations, and key bioactive compounds.

No.	Scientific name	Family name	Organ	Glycoside	Steroids	Tannins	Flavanoids	Phenolic	Terpenoid	Saponins	Alkaloid	References
1.	*Acacia nilotica (L.)* Willd.ex Delile	Fabaceae					Apigenin,Catechin, Kaempferol, Cyanidin-3,4,7-trimethylquercetin	Laricіresinol, Cinnamic acid, 3-hydroxy-4-methoxy, Gallic acid, Pyrocatechol	Lavandulyl acetate, Megastigmatrienone, Cedrane-8,13-diol, Dihydrocitronellol, Neophytadiene, Oxirane, hexadecyl-	Acetylbetacarboline, 3-picoline-2-nitro		42
2.	*Aquilaria malaccensis* Lam.	Thymelaeaceae	agarwood leaves and mature agarwood leaves					Phenol, 2-methyl-, Phenol, 2,6-dimethoxy-, Benzaldehyde, 4-methyl	trans-Farnesol, Cyclohexene, 1-methyl-4-(1-methylethenyl)- (1-P-Mentha-1,8-Diene)			43
3.	*Artemisia absinthium* L.	Asteraceae	Fresh, authentic essential young oil						α-Pinene, β-Pinene, Limonene, Eucalyptol, Linalool, Camphor, Terpinen-4-ol, (E)-β-Caryophyllene, (E)-β-Farnesene, (E)-Nerolidol			44

4.	*Artemisia maritima* L.	Asteraceae	Fresh, authentic essential oil				α-Terpinene, γ-Terpinene, Santolina alcohol, β-Thujone	45
5.	*Artemisia siversiana* Eh.&Wi.	Asteraceae	Fresh, authentic essential oil			Cinnamyl alcohol, Eugenol, Isoeugenol, Benzyl benzoate, Cinnamyl aldehyde, Methyl benzoate, Benzyl alcohol	α-Terpineol, Limonene	46
6.	*Asarum europaeum* L.	Aristolochiaceae	root and aerial parts	Isorhamnetin 3-O-galactoside, Isorhamnetin 3-O-rhamnosyl-galactoside, Kaempferol 3-O-galactoside (Trifolin), Kaempferol 3-O-glucoside (Astragaline), Kaempferol 3-O-β-Sitosterol, Cholesten-5-ol-3β, 24α-Methylcholesten-5-ol-3β, 24α-Aethylcholestadien-5,22-ol-3β, 24α-Gallotannic acid	Isorhamnetin, Kaempferol, Luteolin, Quercetin, Epicatechin, Epigallocatechin gallate	Caffeic acid, Chlorogenic acid, Cichoric acid, Cinnamic acid, n-Coumaric acid, Ferulic acid, Gallic acid, Sinapinic acid, Aristolochic acid-I	Linalool, Limonene, Myrcene, α-Pinene, β-Pinene, Terpinen-4-ol, Terpinolene, α-Copaene, β-Elemene, Germacrene D, α-Humulene, β-Humulene, (E)-Nerolidol, Spathulenol	47

7.	*Caesalpinia bonduc* L.	Fabaceae	fruit			Kaempferol,TRIAZOLE-3-THIONE, 4-ETHYL-5-(THIOPHEN-2-YL)-2-[1,2,4](9H-	1,2-benzenedicarboxylic acid, mono(2-ethylhexyl) ester	Caryophyllene		Acetyl-9-Butyl-	48
8.	*Calycotome spinosa* L.	Fabaceae								4N-Methylcytosine, tetrahydropyridine, dihydroacridine	49
9.	*Cannabis sativa* L.	Cannabaceae	Aerial parts, female flowersflower (inflorescences)		Condensed tannins	Quercetin, Isorhamnetin	Caffeic acid, Ferulic acid	Terpenes	Saponins	Sparteine, Other quinolizidine alkaloids	50, 51
10.	*Chamaemelum nobile* (L.) All.	Asteraceae	aerial parts					α-Pinene, β-Pinene, β-Myrcene, Limonene, Terpinolene, Linalool, α-Terpineol, β-Caryophyllene, α-Humulene, Caryophyllene oxide			52&53
								Pinocarveol, Pinocarvone, 1R-α-Pinene			

11.	*Citrus aurantium* L.	Rutaceae		γ-Lanosterol, Cycloartenol, 24-Methylenelanosterol, 24-Methylenecycloartanol, Abeo-		Curcumin, Bis-demethoxycurcumin, Demethoxycurcumin, 3,5-Di-tert-butylphenol, 2,4-Di-tert-butylphenol, 5-Methoxypsoralen	α-Pinene, β-Pinene, β-Myrcene, D-Limonene, (Z)-β-Ocimene, γ-Terpinene, Linalool, cis-β-Copaene, Germacrene B, δ-Cadinol, (E)-β-Farnesene, Germacrene D, β-Vetivenene, Linalyl 3-methylbutanoate, Ar-turmerone	54
12.	*Curcuma longa* L.	Zingiberaceae	aerial parts	Stigmasterol, Sitosterol			α-Pinene, D-Limonene, Eucalyptol, α-Terpineol, Caryophyllene, Humulene, β-Farnesene, γ-Muurolene, α-Bisabolene, Caryophyllene oxide, ar-Turmerone	55
13.	*Cyperus longus* L.	Cyperaceae				Dodecanoic Acid, Naphthalene, 1, 2, 3, 4, 4a, 5, 6, 8a, Benzyl Benzoate, Benzenepropanoic Acid, 3, 7-DimethylMethyl 2-(3', 3'-Dimethyl)	Linalool, Geraniol, Borneol, Camphene, Alpha-Terpineol, Citronellyl Propionate, 1S-Alpha-Pinene, Beta-Myrcene, Limonene-1,2-epoxide, Beta-Caryophyllene, Caryophyllene oxide, Alpha-Humulene, Beta-Elemene, Germacrene-D, Nerolidol, Hinesol, Aromadendrenepoxide, Beta-Sesquiphellandrene, Viridiflorol, Spathulenol, Aristolone, Cembrene, Irisone, Retinol acetate, Neophytadiene, Geranyl Acetate, Geranyl Propionate, Geranyl Benzoate, Trans-Beta-Farnesene, Azulene	56
14.	*Cyperus rotundus* L.	Cyperaceae			3-Allylguaiacol (3-Allyl-2-methoxyphenol)	Allylguaiacol (3-Allyl-2-methoxyphenol), Methyl eugenol, Furyl hydroxymethyl ketone, Furanc hydroxymethyl ketone	α-Pinene, β-Pinene, Camphene, Linalool, Eucalyptol, Terpinen-4-ol, α-Terpineol, β-Elemene, Caryophyllene, Caryophyllene oxide, Spathulenol, Dehydrocostuslactone	57

15.	*Equisetum arvense* L.	Equisetaceae	Whole plant (especially latex and leaves).	ethanol, water, the aerial parts		γ-Sitosterol Stigmasta-5,24(28)-dien-3ol Beta-Sitosterol, (Fucosterol),	Kaempferol, Apigenin, Quercetin, Isoquercitrin,	Caffeic acid, Chlorogenic acid, Benzaldehyde, 2-chloro-4-hydroxy-3	Cyclohexene, 4-isopropenyl-1-methoxymethyl, Bicyclo[3.2.1]oct-6-ene-6,8-dimethanol, 1,7-dimethyl-4-isopropyl, Furo[2,3-b]quinoline,4,6,7-trimethoxy, 9,10-Secocholesta-5,7,10(19)-triene-3,24,25-triol, Estra-1,3,5(10)-trien-17β-ol, Stigmastan-3,5-diene	Equisetonin	Nicotine, Palustrine, Palustrinine, Paromomycin	58
16.	*Euphorbia helioscopia L.*	Euphorbiaceae						Thymol (0.46), Chavibetol (0.18)	1,6-Dihydrocarveol (31.39), Carvone (16.79), trans-Dihydrocarvone (5.53), trans-Carveol (3.51), Dihydrocarveol (2.04), β-Caryophyllene (1.23), α-Terpineol (0.47), Pulegone (0.31), α-Copaene (0.19), β-Bourbonene (0.98), γ-Muurolene (0.11), Curcumene (0.33), α-Selinene (0.08), Globulol (0.67).			59
17.	*Euphorbia hirta* L.	Euphorbiaceae					1,2,3-Benzenetriol (3.70)		Phytol (4.78)		2,3-bis(1-methylallyl) pyrrolidine (2.37)	60
18.	*Euphorbia lathyris* L.	Euphorbiaceae	Seeds (commonly used for oil	Whole plant and stems)	D-Glucose, 6-O-α-D-galactopyraosyl	β-Sitosterol, Estra-1,3,5(10)-trien-17β-ol,		3-Allyl-6-methoxyphenol	Estragole, Ascaridole epoxide, Olean-12-ene-3,15,16,21,22,28-hexol	Desulphosinigrin		61

19.	*Euphorbia milii* Des Moul.	Euphorbiaceae	Stems (latex extraction), flowers	6-YL hexofuranoside (2.74%)	Beta-amyrin (2.11%), Lanosterol (0.21%), Cholestan-3-one (0.15%), Ergost-5-en-3-ol (0.29%), Squalene	Neryl linalool isomer (0.75%) , 7-DI-O-glucoside (1.51%)	-٢Pentanone, 1-(2,4,6-trihydroxyphenyl)-, Aspidinol, 4-Methyl-2,5-dimethoxybenzaldehyde	(S)-Cembrene (0.09%) , Podocarp-7en-3-one, 13. beta-methyl-13-vinyl (1.59%) ,D: A-Friedooleanan-3-ol, (3. beta) (12.69%) ,Lupeol (0.17%)	Beta-amyrin (2.11%)	62
20.	*Euphorbia parviflora* L.	Euphorbiaceae	Whole plant (especially leaves)					Chloroform extract: Presence (+), Methanol extract: Presence (+), Ethyl acetate extract: Presence (+)		63

21.	*Euphorbia retusa* Forssk.	Euphorbiaceae	Latex and aerial parts	Absence (-)	Stigmasterol, Sarveroside (1.13%), Ethyl 3,7,12-trihydroxycholan-24-oate (2.43%),	Considerable Presence	Qualitative Screening Result: Presence (+), 2-(3,4-Dimethoxyphenyl)-3,5-dihydroxy-7-methoxy-4H-chromen-4-one (1.23%)	4-(3,3-Dimethylbut-1-yn-1-yl)-4-hydroxy-2,6,6-trimethylcyclohex-2-en-1-one, Qualitative Screening Result: Considerable Presence	3-O-trans-Caffeoylisomyricadiol, 3α-(3",4"-Dihydroxy-trans-cinnamoyloxy)-D-friedoolean-14-en-28-oic acid	Abundance (+++)	6-Chloro-N2-ethyl-1,3,5-triazine-2,4-diamine (2.01%), Qualitative Screening Result: Presence	64
22.	*Glossostemon bruguieri* Desf	Malvaceae	Aerial parts	Benzyl Benzoate, Geranyl Benzoate, 3-Hexene-1-ol, 3-Buten-1-ol, Benzenepropanoic Acid, 3,7-Lanosterol, Cycloartenol, 24-Methylenelanosterol, cholestan-8-one,	Sucrose Cholesterol, Abeo-Campesterol, Squalene, Lupeol Norlup20-	Apigenin, Kaempferol, Physcion	Chlorogenic Acid, Hydrocinnamic acid, Carvone, 4,6-di-tert-Butylresorcinol.	Pinene, Carvone, Phytol			65
23.	*Glycyrrhiza glabra* L.	Fabaceae				Estragol, Geraniol, Linalool L, Alpha	Beta-Myrcene, 1H-Cycloprop [E] Azulene, Azulene, 1, 4-Dimethyl-7-(1-Methylene), 2-Naphthalenemethanol, Naphthalene, Decahydro-4a-Methyl, Naphthalene, 1, 2, 3, 4, 4a, 5, 6, 8a	Alpha-Pinene, Beta-Caryophyllene, Alpha-Caryophyllene, Beta-Santalene, Beta-Eudesmol, (-)-Caryophyllene Oxide, Geranyl Acetate, Neryl Acetate, Geranyl Propionate, Citronellyl Propionate, Lavandulyl Acetate, Trans-Beta-Farnesene,	Peplusol Obtusifolio	Caffeine, Theobromine	-(-) Anymol 4-[1'-Hydroxy], Beta-Sesquiphellandrene	66

					Terpineol, Nerolidol		Camphene, Borneol L, Pinocarvone, Caryophyllene, Theaspirane A, Hinesol	
24.	*Laurus nobilis* L.	Lauraceae	Seed and leaf			Eugenol, Eugenol methyl ether, Isoeugenyl methyl ether, Estragole	α-Pinene, β-Pinene, Camphene, Myrcene, α-Phellandrene, 1,8-Cineole (Eucalyptol), α-Limonene, Linalool, α-Terpineol, Bornyl acetate, α-Terpinyl acetate, β-Caryophyllene, Caryophyllene oxide, Spathulenol	67& 68
25.	*Matricaria chamomilla* L.	Asteraceae	capitula	Apigenin, Quercetin, Luteolin		Caffeic acid, Chlorogenic acid		69
26.	*Mentha* × *piperita* L.	Lamiaceae	Aerial parts, leaves				Pinene, Limonene, Eucalyptol, Linalool, Menthol, Caryophyllene, (E)-β-Farnesene	70
27.	*Mentha aquatica* L.	Lamiaceae	Aerial parts, leaves				Pinene, Sabinene, β-Pinene, Limonene, Menthol, Pulegone, β-Caryophyllene, Germacrene-D, Viridiflorol, α-Pinene, Terpinolene, Germacrene D, Caryophyllene Oxide, Y-Eudesmol	71

28.	*Mentha longifolia* (L.) Huds.	Lamiaceae	Aerial parts, leaves	Campesterol, Phytosterols, Stigmasterol, β-Sitosterol	Phenyl ethylalcohol	Linalool, Menthol, α-Terpineol, 1,8-Cineole, β-Ocimene, α-Terpinolene, Eucalyptol, β-Caryophyllene, α-Caryophyllene, Germacrene D, Caryophyllene oxide	72
29.	*Mentha pulegium* L.	Lamiaceae	Aerial parts, leaves		3-Methoxy-5-propyl-phenol	α-Pinene, D-Limonene, Menthone, Pulegone, α-Elemene, Piperitone, Caryophyllene, α-Humulene, Caryophyllene oxide, 3-Carene, β-Pinene, β-Myrcene, Eucalyptol, Isopulegon, L-alpha-Terpineol, Carvone, Thymol	73

30.	*Momordica charantia* L.	Cucurbitaceae	Leaves and Seeds	Flavonoids such as catechin, epicatechin	Charantin, kuguacins A – S, momordicine I, II and III, Karavilagenin A, B, C, D, E, saponins (triterpenoid glycosides), goyasaponins, sapogenins such as diosgenin	74&75

31.	*Narcissus jonquilla* L.	Amaryllidaceae		Compound (fresh)	- alpha-D-Glucopyranoside, O, alpha D-glu (listed twice)	Galanthamine, Haemanthamine, Galanthine, Narcissidine			Lycoramine, Narwedine, Eugenine, Hippeastrin, Assoanine, Carasnine, Arinatine, Incartine, Lycorine, Pluviine, Norpluviine, Demethylpluviine, Tortuosin, Vasconine	76&77
32.	*Nauclea latifolia* Sm.	Rubiaceae			- Stigmast-5-en-3-ol, oleate, Campesterol, Stigmasterol, gamma-Sitosterol, Spirost-8-en-11-one, 3-hydroxy-, (3β,5α,14β,20β…)		-2-Methoxy-4-vinylphenol	Phytol, acetate, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, 3,7,11-Trimethyl-2,4-dodecadiene		78
33.	*Nerium oleander* L.	Apocynaceae	leaves,Leaves	Latex, flowers	- gamma Sitosterol			Camphene, beta-Myrcene, D-Limonene-Cymene, Squalene, Caryophyllene oxide, Verbenone, dl-Isoeugenol, Phytol, Phytol acetate	8-Quinolinol, 4-methyl	79

34.	*Ocimum basilicum* L.	Lamiaceae	Leaves		amma-Sitosterol, Stigmasterol	Condensed tannins	Orientin, Vicenin-2, Quercetin, Apigenin	Rosmarinic acid, Caffeic acid, Chlorogenic acid, Eugenol, Methyleugenol. Resorcinol, Benzoic acid,Benzoic acid, 4-hydroxy-, Salicylic acid, Phenol	Linalool,Geraniol, Terpinene,Beta-caryophyllene,1,8-ineole (Eucalyptol), Camphor,Phytol,Phytol acetate, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, Lupeol, Beta-Amyrin	80
35.	*Opopanax chironium* (L.) W.D.J.Koch	Apiaceae	Gum (resinoid part)					Coumarins Eugenol,Myristicin, 1,3-Benzodioxole, Methoxsalen, Psoralen derivatives	Gaudichaudin, Columbianadin, Peucedanin, Officinalin, isobutyrate, Umbelliprenin, Imperatorin, Xanthotoxin,Bergapen Heraclenin HeraclenolSuberosinMarmesin Dehydromarmesin methyl ether, Prantschimgin, Smirniorin	81
36.	*Pastinaca sativa* L.	Apiaceae	Aerial parts					Angelicin, Bergaptene, Xanthotoxin, Psoralen, Coumarins: Osthol, Umbelliferone, Hydroxycinnamic acids: (No specific compounds listed), Polyphenols: (No specific compounds listed).	α-Pinene, β-Pinene, Myrcene, Limonene, Linalool, Terpinen-4-ol, (E)-Caryophyllene, α-Humulene, (E)-β-Farnesene, Germacrene D, Caryophyllene oxide, γ-Terpinene, Camphene, Sabinene, α-Copaene, β-Bourbonene, γ-Muurolene, Bicyclogermacrene, Spathulenol, Caryophyllene oxide, Humulene epoxide II, E-β-Ocimene, Z-β-Ocimene, α-Terpinolene, Lavandulyl acetate, β-Ocimene, β-Farnesene, α-Zingiberene, (E)-Nerolidol.	82

37.	*Peucedanum officinale* L.	Apiaceae					α-Pinene, β-Pinene, Myrcene, Limonene, Linalool, Terpinen-4-ol, (E)-Caryophyllene, α-Humulene, (E)-β-Farnesene, Germacrene D, Caryophyllene oxide, γ-Terpinene, Camphene, Sabinene.	83
38.	*Picea orientalis* (L.) Peterm.	Pinaceae	Fruits Seed Cone			Carvacrole Carvone, Camphor, Borneol, Pinocarvone, Myrtenol, Terpinen-4-ol	α-Pinene, β-Pinene, Camphene, Limonene, Myrcene, β-Phellandrene, Terpinolene, Caryophyllene, α-Copaene, Humulene, Squalene, α-Fenchol, Borneol, camphor, Caryophyllene oxide	84
39.	*Pinus cembera* L.	Pinaceae	heartwood ethanolic extract	Aromadendrin, Naringenin, Chrysin, Pinocembrin, Apigenin, Pinostrobin,		Stilbene: Stilbene: Pinosylvin, Stilbene: Pinosylvin monomethyl ether b, Stilbene: Pinosylvin dimethyl ethe	α-Pinene, β-Pinene, β-Myrcene, Limonene, γ-Terpinene, Terpinolene, Linalool, α-Terpineol, Linalool acetate, Isobornyl acetate, α-Copaene, β-Cubebene, (E)-caryophyllene, α-Humulene, (E)-β-farnesene, α-amorphene, Germacrene D, α-muurolene, Germacrene, δ-Cadinene, (E)-nerolidol, Caryophyllene oxide, α-Cadinol, (2E, 6E)-farnesyl acetate, Manool oxide, Abietic acid	85

40.	*Pinus eldarica Medew*	Pinaceae	Aerial parts, Needles, Bark Pollen			Thymol, Verbenol	Camphene, β-Pinene, Limonene, Linalool, Thymol, Verbenol, Bornnly acetae, α-Pinene, Caryophyllene	86
41.	*Pinus nigra* J. F. Arnold	Pinaceae	heartwood ethanolic extract				α-Pinene, β-Pinene, β-Myrcene, δ-3-Carene, Limonene, c-Terpinene, Terpinolene, Linalool, a-Terpineol, Linalool acetate, Isobornyl acetate, a-Copaene, b-Cubebene, (E)-caryophyllene, α-Humulene, (E)-β-Farnesene, a-amorphene, Germacrene A, Germacrene D, a-muurolene, d-Cadinene, erolidiol (E), Caryophyllene oxide, a-Cadinol, (2E, 6E)-farnesyl acetate, Manool oxide	87
42.	*Pinus sylvestris* L.	Pinaceae		Androst-5-en-4-one	Naringenin	2,4-Dimethoxybenzo[h]quinazoline	α-Pinene, Camphene, Sabinene, p-Cymene, dl-Limonene, Cineole-1.8, Pinole, Fenchone, D-Fenchyl alcohol, Isopinocarveol, Camphor, Trans-sabinene hydrate, Borneol, α-Fenchyl alcohol 3, -Caren-10-al, Eucarvone, Fenchyl acetate, Bornyl acetate Geranyl isovalerate, 1-(3,3-dimethylbutenyl)-2-formyl-1-cyclohexen Cembrene, Abietic acid, α-Pimaric acid, Palustric acid	88
43.	*Pinus sylvestris* L.	Pinaceae	Fruit,Woodand Bark Needles, Bark			Thymol methyl ether, Phenol, 2,4-bis(1,1-dimethylethyl),Caryophylleneoide	α-Pinene, β-Pinene, Limonene, Sabinene, Longifolene Caryophyllene, Humulene, Germacrene-D, Caryophyllene oxide	89

44.	*Piper nigrum* L	Piperaceae	White Pepper Seed		Ethyl iso-allocholate, Methyl glycocholate, 3TMS derivative			Caryophyllene	Pyrrolidine, Piperidine, Piperine, Piperlonguminine		90
45.	*Plantago ovata* Forssk.	Plantaginaceae	Seeds	Lactose, Homovanilic acid hexoside, 4-O-caffeoyl-quinic acid, Phloretin-C-diglycoside, Rutin (quercetin-3-o-rutinoside).		Luteolin, Quercetagetin, Kaempferol, Cyanidin	Forsythoside, Acteoside, Caffeic acid derivatives	α-Amyrin, β-Amyrin		Indican, Plantagonin	91
46.	*Rosa canina* L.	Rosaceae	Fruit		14-Beta-H-pregna	Naringenin, Rutin	Chlororesorcinol, Eugenol, Methyl salicylate,Quinic acid, Citric acid, Caffeic acid, Chlorogenic acid.	Limonene, Caryophyllene, α-Pinene, Thymol, Carvacrol, Lycopene or -carotene			92, 93

47.	*Saccharum officinarum* L.	Poaceae		Kaempferol-3-O-glucuronide, Kaempferol-3-O-glucoside, Quercetin-3-O-β-D-glucopyranuronide, 1,2,6-Tri-O-Nilocitin,	Nilotinin M1, Nilotinin M2, Nilotinin M4, Nilotinin M5, Nilotinin D1, Nilotinin D9 Gallic acid, Ellagic acid, 3,3'-Di-O-methylellagic acid,		Caryophyllene oxide, Spathulenol, Eudesm-4(14)-en-11-ol	Morphinan-4,6-diol, N-formyl-6-acetate (ester) N-trans-Feruloyltyramine	94
48.	*Tamarix gallica* L.	Tamaricaceae	Branches, leaves		Tamarix gallica (50% tannins	Hispidulin, Luteolin, Quercetin, Kaempferol-3-O-Kaempferide, Tamarixetin, Tamarixin, Quercetol (methylic ester), Tamarixetin, Anthocyanins, Flavanones, Isoflavones, Resveratrol	Phenol, 2,6-dimethoxy, Phenol, 4-(2-propenyl)-2,6-dimethoxy, Phenol, 2-methoxy-Phenol, Creosol, Methyl gallate, Methyl gallate methyl ether, Gallic acid, Ferulic acid, Caffeic acid, Ferulic acid sulfate derivative	9-Hexadecenoic acid, methyl ester, (Z) ,Hexadecanoic acid, methyl ester (methyl palmitate), N-Hexadecanoic acid	2-Fluorenamine, 4-Methoxymethyl-6-methyl-1H-pyrazolo [3,4-b] pyridin-3-ylamine	95
49.	*Tamarix nilotica* (Ehrenb.) Bunge	Tamaricaceae	Leaves, branches, flowers	β-Sitosterol		Hispidulin, Luteolin, Quercetin, Kaempferol, Kaempferide, Tamarixetin, Tamarixin, Quercetol (methylic ester), Tamarixetin, Anthocyanins, Flavanones, Isoflavones, Resveratrol	Phenol, 2,6-dimethoxy-, Vanillin, Benzaldehyde, 4-hydroxy-3,5-dimethoxy- ,3,5-Dimethoxy-4-hydroxycinnamaldehyde ,Benzoic acid, 4-hydroxy-3,5-dimethoxy- ,Benzoic acid, 4-hydroxy-3,5-dimethoxy-, hydrazide ,Ethanone, 1-(3-hydroxyphenyl)- ,2-Pentanone, 1-(2,4,6-trihydroxyphenyl)- , Aspidinol ,4-Methyl-2,5-dimethoxybenzaldehyde Methyl gallate ,1,6-Di-O-galloyl-D-glucose (Nilocitin) ,Gallic acid , Ferulic acid ,Caffeic acid ,Dehydrodigallic acid ,Coniferyl alcohol 4-O-sulphate , Syringaresinol , 1,2,6-Tri-O-galloyl-β-D-glucose , Ellagic acid , Methyl ferulate 3-O-sulphate , Isoferulic acid ,Isoferulic acid methyl	Tamarixoic acid ,3α-(3'',4''-Dihydroxy-trans-cinnamoyloxy)-D-friedoolean-14-en-28-oic acid		96

								ester , Methyl gallate methyl ether, 3,3',4-Trimethylellagic acid, Tellimagrandin I & II				
50.	*Vitis vinifera* L.	Vitaceae	Peels			Tannins: 0.640 ± 0.02 c	.	Phenol: 0.710±0.05d	Chloropyridin-2-ol, Cyclopentanone, 2-methyl-, 4,5-Dihydro-2-methylimidazole-4-on, 1-Methylimidazole-4 carboxaldehyde, Benzeneacetaldehyde, 2-(tert-Butylamino) ethanol, Methylazoxymethanol acetate, 5-Hydroxyuridine, Hydrouracil, 1-methyl-, 2-Furancarboxylic acid, Methyl-2-furoate			97&98
51.	*Ziziphus spina-christi* (L.) Willd.	Rhamnaceae	fruit	Beta-Sitosterol, γ-Sitosterol, Unsaturated sterol	Steroidal Saponins,	Campesterol, Stigmasterol, β-SterolsCampeSitosterol, Betulin	Quercetin Rutin Quercetin, Kaempferol, Apigenin, Luteolin	Phenol, 2,5-bis(1,1-dimethylethyl), Butyl hydroxytoluene,	Phytol, Neophytadiene,8,11-Octadecadienoic acid, methyl ester		Aspidospermidin-17-ol, 1-acetyl-16-methoxy-C22H30N2O3	99& 100
52.	*Zizyphus lotus* (L.) Lam.	Rhamnaceae				Catechic tannins, Gallic tannins		Caffeic acid, Chlorogenic acid, Benzenecarboxylic acid	Squalene, Neophytadiene, Phytone, Apiole	Equisetonin, Soponosides		101

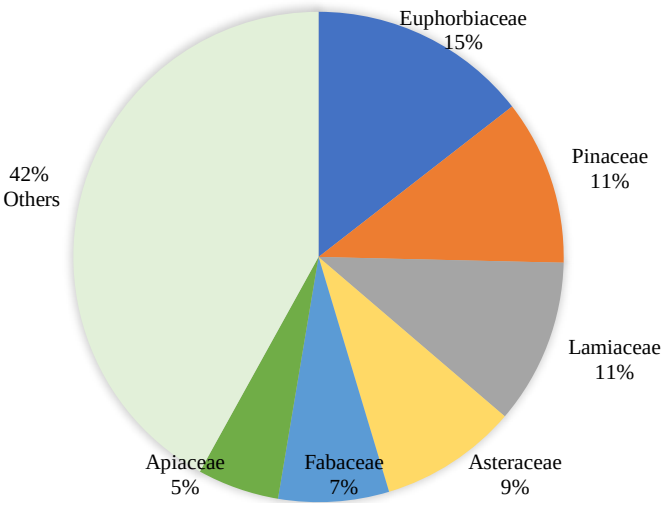

Fig. 1 Relative Abundance of Medicinal Plant Families Used in Traditional Persian Medicine for Neurological Disorders
Phytochemical Profile of Medicinal Plants Used for Neurological Disorders

Further analysis of the 52 medicinal plant species revealed a wide array of secondary metabolites implicated in neurological health. Terpenoids emerged as the most prevalent phytochemical class, present in approximately 68% of the species. These compounds, especially monoterpenes such as α-pinene, are recognized for their neuroprotective, anti-inflammatory, and antioxidant properties. They play a critical role in preventing neurodegeneration by enhancing cholinergic neurotransmission and mitigating oxidative stress and inflammation.

Phenolic compounds, identified in 52% of the plants, are potent free radical scavengers that protect neurons from oxidative damage. Their neuroprotective activity is linked to improved cognitive function and modulation of cellular signaling pathways related to neuronal survival.

Flavonoids were found in 20% of the species and are known to enhance synaptic plasticity, regulate neuroinflammatory responses, and improve learning and memory processes. These compounds contribute to the restoration of neuronal function under stress conditions.

In addition, several other classes of secondary metabolites were identified:

- Glycosides (16%): Exhibit anti-inflammatory and analgesic effects, beneficial for conditions like neuropathic pain.
- Alkaloids (15%): Possess diverse neurological activities, including anticonvulsant and neuroprotective effects, often mediated through neurotransmitter modulation.
- Steroids (12%), amines (10%), and saponins (8%): Provide complementary roles such as hormonal balancing, neurotransmitter regulation, and immune modulation—factors essential for maintaining nervous system equilibrium.

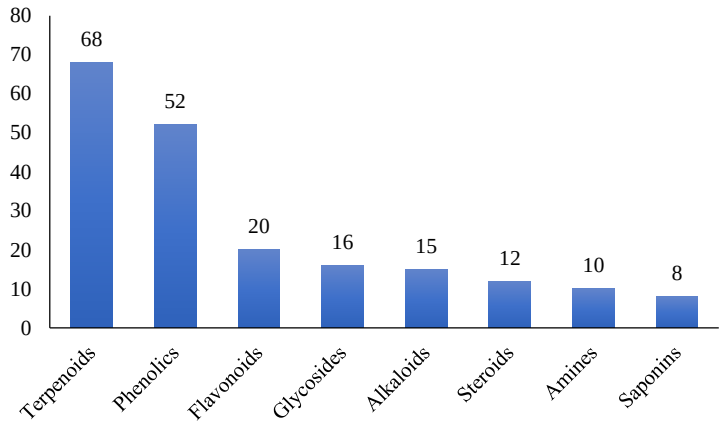

Fig. 2 Percentage of occurrence of main bioactive compounds, including terpenoids, phenolic compounds, flavonoids, glycosides, alkaloids, steroids, amines, and saponins in medicinal plants used for treating neurological disorders based on traditional medicine sources and phytochemical findings. Terpenoids, with 68%, show the highest frequency, followed by phenolic compounds and flavonoids at 52% and 20%, respectively.

Taken together, these findings underscore the synergistic potential of multiple phytochemical classes in TPM-based medicinal plants. The predominance of terpenoids, phenolic compounds, and flavonoids suggests that these metabolites are key contributors not only to direct neuroprotection but also to the regulation of complex molecular pathways implicated in neurodegenerative and neuropsychiatric disorders.

Nevertheless, it is important to note that for many of these compounds, the exact mechanisms of action remain incompletely understood, and further experimental validation is necessary. Future research should aim to isolate and characterize individual constituents, assess their interactions, and evaluate their efficacy through bioassay-guided in vivo and clinical studies.

Additionally, to visually support the botanical diversity of the most frequently cited neuroactive plants in Traditional Persian Medicine, a composite illustration (Figure 3) was included. This figure presents four key species—*Lavandula angustifolia*, *Curcuma longa*, *Glycyrrhiza glabra*, and *Mentha piperita*—that are frequently used for their neuroprotective, anxiolytic, and cognitive-enhancing properties.

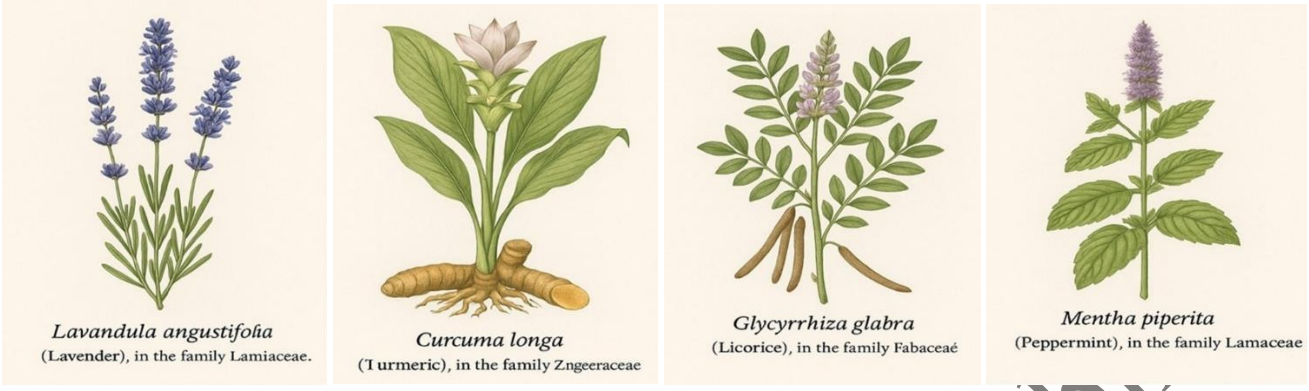

Fig. 3 Representative medicinal plants commonly used in Traditional Persian Medicine for neurological disorders. Clockwise from top left: *Lavandula angustifolia* (Lamiaceae) – anxiolytic and sleep-inducing properties; *Curcuma longa* (Zingiberaceae) – anti-inflammatory and neuroprotective effects; *Mentha piperita* (Lamiaceae) – stress-reducing and cognitive-enhancing effects; *Glycyrrhiza glabra* (Fabaceae) – mood-regulating and antioxidant activities. All illustrations are based on public-domain botanical references.

DISCUSSION

Overview of Phytochemical Classes and Their Neurological Roles

In this study, medicinal plants used in Traditional Iranian Medicine (TIM) for neurological disorders were analyzed for their phytochemical composition. The main bioactive classes identified include flavonoids, terpenoids, alkaloids, glycosides, phenolic acids, and volatile compounds, all of which are known for their diverse pharmacological activities on the central nervous system.

Terpenoids and Mood Regulation

Terpenoids such as glabridin from *Glycyrrhiza glabra* L. and citrulline from *Jasminum sambac* (L.) Aiton modulate neurotransmitters serotonin and dopamine, exerting notable antidepressant and anxiolytic effects [102]. Volatile terpenoids, like linalool and linalyl acetate from *Lavandula angustifolia* Mill., and α-pinene from *Rosmarinus officinalis* L., improve sleep quality and reduce anxiety via central nervous system modulation [103, 104].

Alkaloids in Neurodegeneration

Alkaloids such as huperzine A from *Huperzia serrata* (Thunb. ex Murray) Trevis. and quinine from *Cinchona officinalis* L. act by inhibiting enzymes like acetylcholinesterase or modulating dopamine pathways, thereby alleviating symptoms of Alzheimer's and Parkinson's diseases [105, 106]. Another key alkaloid, galanthamine from *Narcissus jonquilla* L., is clinically approved for Alzheimer's treatment, demonstrating the empirical efficacy of TIM [107].

Flavonoids and Alzheimer's Disease

Flavonoids, like quercetin found in *Allium cepa* L. and *Malus domestica* Borkh., and EGCG from *Camellia sinensis* (L.) Kuntze, inhibit amyloid plaque formation and oxidative stress, protecting neurons from degeneration [108, 109]. Species such as *Asarum europaeum* L. are rich in flavonoids (kaempferol, quercetin, luteolin) with potent antioxidant and anti-inflammatory effects, contributing to neuroprotection and cognitive support [110]

Glycosides and Anti-inflammatory Effects

Glycosides, such as senoside A from *Senna alexandrina* Mill., display strong anti-inflammatory properties essential for mitigating neurodegenerative inflammation [126]. Other secondary metabolites, like steroids and saponins, also contribute to reducing neuroinflammation and supporting neuronal health [111, 112].

Volatile Compounds in Stress and Sleep Regulation

Compounds such as linalool, linalyl acetate from *Lavandula angustifolia* Mill., and α-pinene from *Rosmarinus officinalis* L. enhance sleep and alleviate anxiety by modulating neurotransmitter systems in the brain [103, 104]. Plants like *Mentha piperita* L. and *Ocimum basilicum* L. contain menthol and rosmarinic acid, which help regulate mood and reduce stress [113].

Phytochemical Diversity and Plant Families in TIM

The therapeutic potential of TIM plants arises from the complex mixture of bioactive compounds. Notably, families such as Apiaceae, Asteraceae, Lamiaceae, Fabaceae, and Euphorbiaceae dominate the pharmacopeia for neurological disorders.

- In Apiaceae, species like *Opopanax chironium* (W.D.J. Koch) G. Karrer and *Peucedanum officinale* L. are rich in coumarins and volatile terpenoids that may act through calcium channel inhibition and GABA receptor modulation, effective for seizures and nervous tension relief [114].
- The Asteraceae family includes *Matricaria chamomilla* L. and *Artemisia absinthium* L., which contain apigenin, luteolin, and eucalyptol with anxiolytic and anti-inflammatory properties [115].
- Lamiaceae species such as *Mentha piperita* L. and *Ocimum basilicum* L. provide linalool, menthol, and rosmarinic acid, which aid in stress reduction and sleep improvement [116].
- Families Fabaceae and Euphorbiaceae, including *Glycyrrhiza glabra* L. and *Euphorbia ipecacuanha* L., offer flavonoids, alkaloids, and saponins that contribute to mood regulation and neuroprotection. Although several species of the Euphorbiaceae family are well known for their dermatological applications and contain diterpenes with recognized toxic potential, some of these plants—such as *Euphorbia ipecacuanha*—have also been traditionally prescribed in Persian Medicine for neurological conditions. Their inclusion in this review is based on combined ethnobotanical evidence and the presence of neuroactive phytochemicals. Nevertheless, the potentially toxic nature of diterpenes warrants further toxicological validation before therapeutic use [117, 118].

Future research should aim to isolate and characterize active constituents through bioassay-guided methods, investigate compound synergies, and conduct controlled clinical trials. Integrating traditional knowledge with rigorous pharmacological research may lead to novel, effective, and safer neurotherapeutic agents derived from medicinal plants [119].

In our previous phytochemical investigations on medicinal plants traditionally used for liver and kidney disorders in Persian Medicine, we identified several bioactive compounds—such as flavonoids, terpenoids, and phenolic acids—with proven antioxidant and anti-inflammatory effects [120, 121]. These classes of compounds, frequently found in plants like *Scrophularia striata*, *Berberis integerrima*, and *Rheum ribes*, have shown significant potential in modulating oxidative stress and immune responses. Given the shared pathophysiological mechanisms between hepatic/renal inflammation and neuroinflammation, these findings further support the potential role of such phytochemicals in neurological protection. Thus, integrating knowledge from phytochemical studies on liver and kidney therapeutics may offer new insights into neuropharmacological applications of Persian medicinal plants.

CONCLUSION

This study underscores that Traditional Iranian Medicine (TIM), with its centuries-long empirical knowledge, has identified numerous plant species now validated by modern phytochemical research for their promising therapeutic potential in neurological disorders. The frequent presence of bioactive compounds such as flavonoids, volatile terpenoids, coumarins, and alkaloids in these plants highlights their significant role as sources of neuroprotective agents.

These phytochemicals act via multiple mechanisms—including modulation of neurotransmitter systems, antioxidative effects, and anti-inflammatory actions—offering potential benefits for conditions such as Alzheimer's disease, Parkinson's disease, anxiety, and depression. The growing evidence supports integrating these natural compounds as complementary options alongside conventional treatments.

The fusion of traditional ethnobotanical knowledge with contemporary phytochemical research creates a fertile ground for discovering and developing safe, natural, and effective neuropharmacological agents. However, to fully realize this potential, focused and multidisciplinary efforts are urgently needed.

We strongly encourage future research to:

Employ bioassay-guided isolation and characterization of active constituents, especially from species within the Apiaceae and Lamiaceae families.

Investigate synergistic and antagonistic interactions among plant compounds to better understand combined effects.

Conduct rigorous in vitro and in vivo neuropharmacological evaluations, including standardized clinical trials, to validate efficacy and safety.

Explore chemical variability within species (intraspecific diversity) and standardize herbal formulations for reproducible therapeutic outcomes.

Integrate traditional knowledge with modern pharmacology and toxicology to innovate novel, effective, and safer neurotherapeutics.

By prioritizing these research directions, the scientific community can accelerate the development of novel neuroprotective agents derived from medicinal plants, ultimately improving treatment options for neurological disorders worldwide

Acknowledgment

The authors would like to express their sincere gratitude to Mr. Ahmad Reza Okhovat (Herbarium Curator, University of Tehran) for his valuable guidance in plant identification and for providing access to key herbarium specimens. We also appreciate the support of the University of Tehran Herbarium (TUH) for facilitating botanical consultations. Special thanks are extended to the Semnan Province Elite Foundation for their academic and logistical support throughout this research.

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