Section A-Research paper

# The Role of Polyherbal Drugs as Neuroprotective Agents

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**Abstract**

Neuroprotective agents are capableto protect the peripheral nervous system (PNS) and central nervous system (CNS) against neuronal damage and neurodegenerative conditions. Herbal drugs having both medicinal value and long-term health-promoting. Herbal drugs from different medicinal plant species have various phytochemicals and bioactive compounds with neuroprotective abilities. A wide range of discoveries and studies have proved that medicinal herbs, plant extracts, and their metabolites have strong potential as theneuroprotective agent. Hence the herbal plants may be a valuable source of drugs against neurodegenerative diseases such as Parkinson's disease (PD), schizophrenia, Alzheimer's disease (AD), depression, dementia, seizure, cerebrovascular deficit, and head injury. The present review will highlight the neuroprotective role of herbal drugs and their metabolites against neurodegenerative diseases and other related conditions, targeting their therapeutic potential and mechanism of action.

**Keywords:** Neuroprotection, Neurodegenerative diseases, and Herbal drugs

**Introduction**

Neuroprotection terms as the relative protection of the central and peripheral nervous system from neuronal injury produced by several neuropsychiatric and neurodegenerative conditions like Parkinson's disease~~s~~ (PD), Alzheimer's disease (AD), impairment of cerebrovascular, anxiety, and seizures (Elufioye et al., 2017). Among the plans for neuroprotection, the herbal drugs having bioactive phytochemicals such as phenolics, saponins, alkaloids, terpenoids, flavonoids, and steroids may well specify the best therapy for~~in~~ neurodegenerative diseases (G. P. Kumar et al., 2015). Many groups of synthetic and natural neuroprotective agents have been described in neurodegenerative ailments (Bansal & Singh, 2018). However, synthetic neuroprotective agents have possessed definite side effects like tiredness, sleepiness, a problem with balance, dry mouth, drowsiness, and anxiety. Herbal drug or phytotherapy represents the therapeutic usage of plant parts including seeds, roots, stems, leaves, flowers, and fruits for its curative activities(Alamgir, 2017). Phytotherapy has scientific importance forthe treatment of neuropathological diseases, as they cover many bioactive compounds and phytochemicals which may have neuroprotective actions with producing beneficial health effects between neurodegenerative and neuropsychiatric conditions (da Costa et al., 2017, 2018; G. P. Kumar & Khanum, 2012; H. Xu et al., 2021). Bioactive compounds and phytochemicals from the herbal plant are used as neuroprotective agents in traditional

medicine like the Indian Ayurvedic medicine system, a Korean system of medicine, a Mediterranean system of medicine, and the Chinese medicinal system (Iriti et al., 2010; Y. M. Kang et al., 2017). Herbal-based drugs have extensive awareness from research institutes and industries based at levels of international and national importance (S. Kumar et al., 2012).

Herbal drugs are becoming more common in neurodegenerative diseases as they exhibit the risk of reducing thebrain's degeneration. Their benefits arising from using the treatment of herbal drugs have been very auspicious as they are effective drugs with very few side effects (N. Singh et al., 2011).

Neurodegenerative diseases are progressive dysfunction of the central and peripheral nervous systems. A gradually progressive loss of neurons may produce neurodegeneration (Kovacs, 2014). Many factors are responsible for the initiation of neurodegeneration initiation such as free radical generation by the reactive nitrogen species (RNS) and reactive oxygen species (ROS). Neuro-inflammatory processes are well-known to play a key role inthe development of many neurodegenerative diseases (W. W. Chen et al., 2016). As per the National Institute of Neurological Disorders and Stroke reports, more than 600 neurological diseases have been noted worldwide (Castro et al., 2010; Kehne et al., 2017; Siuly & Zhang, 2016).

Studies have been reported that above 80% of total natural death in middle and low-income countries may be known to stroke **(WHO, 2006).** In the United States countries, the total annual cost of neurological diseasesis approximately $ 800 billion, predictable to rise in the upcoming year due to the elderly population, causing a severe financial problem to human health(Shaw, 2017)**.**

The neurodegeneration process takes place in brain aging and neuropathological disorders. This is identified by the neurodegenerative and cerebrovascular diseases, a second most common cause of death all over the globe among those aged by the 2040s with an incidence of nearly 2/1000 and total death rate around 8% (Ansari et al., 2010; Baquero, 2015). Studies have confirmed that the normal pathology of neurodegeneration is the accumulation of proteins with different physicochemical properties in the brain of a human. These pathological conformers are called misfolded proteins like deposition of amyloid-β (Aβ) protein in Alzheimer's disease (AD), huntingtin protein in Huntington's disease (HD), TDP-43 in amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD), α-synuclein in Parkinson's disease (PD) (Alexander, 2017; Brettschneider et al., 2015).

The present review will highlight the polyherbal drugs from different traditional systems, their phytochemicals on neuroprotective and associated diseases, in certain their mechanism of action, and their therapeutic potential in neurodegenerative diseases (Selvam, 2008)**.**

## Polyherbal agents and their neuroprotective role

Neuroprotective agents are denoted as substances capableto protect the brain structure and function by decreasing and inhibiting oxidative stress, inflammation, mitochondrial dysfunction, and neurotoxicity (Elufioye et al., 2017). Intake of a neuroprotective agent may aid in diminishing the effect of chronic disorders (Meshkini et al., 2019). There is more than 120 medicinal herb which has been used for the treatment of CNS disorders in the Asian countries (V. Kumar, 2006).The following medicinal herbs have shown neuroprotective activities in neurodegenerative diseases in the traditional system:

### 1. *Acorus calamus*

*Acorus calamus* (*A. calamus*),also known as sweet flag belongs to the family Araceae, which act as a rejuvenator of the CNS having beneficial for learning-memory enhancing properties and behavior alteration(V. Sharma et al., 2020)**.***A. calamus* consists of α and β asarone, which can suppress the β-amyloid induced neuronal apoptosis in the brain region through reverse down-regulation of c-Jun N-terminal kinase (JNK) phosphorylation, caspase-3, cytochrome-c, and Bcl-2 activation (Geng et al., 2010). *A. calamus* has possibly improved the function of dopaminergic neurons by the tyrosine hydroxylase expression in substantial nigra and enhancing the level of dopamine in the striatum: hence, it may have an important role in PD. *A. calamus* also rises the expression of DJ-1 gene in the striatum and thus acts as a neuroprotective role in PD (Paterna et al., 2007).

### 2. *Allium sativum*

*Alliumsativum* (*A. sativum*),generally referred to as Garlic belongs to the family Amaryllidaceae, which is most extensively used as an herbal drug primarily for its medicinal abilities in the treatment and inhibition of cardiovascular and other metabolic diseases such as hyperlipidemia, diabetes, atherosclerosis, thrombosis, hypertension, dementia, and cancer (Bayan et al., 2014; Shang et al., 2019). Allicin and alliin are the main bioactive constituents of *A. sativum.* S-allyl cysteine (SAC) is the chief constituent of elderly garlic extract which is widely reported(Pérez-Torres et al., 2016; Tatara et al., 2005). SAC has an indirect and direct antioxidant activity. Elderly garlic extract indirectly and directly triggers gene expression

necessary for neuronal existence (Medina-Campos et al., 2007; Patil et al., 2016). Allyl having sulfides in garlic produces the up-regulation of neuroprotective protein like mitochondrial uncoupling protein. Allicin also stimulates ion channels in the cell membrane of the neuron(G. P. Kumar et al., 2015; G. P. Kumar & Khanum, 2012). Chronic intake of garlic has been revealed to inhibit memory impairment by the drug scopolamine due to the antioxidant and anti-acetylcholinesterase (AChE) activity of the garlic (Mukherjee & Banerjee, 2013).

### 3. *Bacopa monnieri*

*Bacopa monnieri* (*B.monnieri*), commonly known as Brahmi, belongs to the plant family Scrophulariaceaeand is a creeping, perennial herb having medicinal value. It is also well known nervine tonic herbal drugwhich is found in India and adjacent tropical countries(Gohil & Patel, 2010; Khare, 2007; Russo & Borrelli, 2005). It contains bacoside A and B have the main bioactive compound responsible for both learning and memory-enhancing properties (S. Kumar & Mondal, 2016; Rastogi et al., 2012). Several other phytochemical constituents of *B.monnieri* such as alkaloids, phytosterols, herpestine, flavonoids, monnierin, brahmin, saponin acid A as well as bacopa saponins D, E, and F (Mahato et al., 2000; S. K. Singh, 2012).*B.monnieri* has been beneficial for the treatment of memory impairments, insomnia, epilepsy, anxiety, inflammation, pain, fever, sedation, and neurodegenerativeillnesses like PD(Siddique et al., 2014), schizophrenia (Piyabhan & Wetchateng, 2015),AD (Le et al., 2013; Preethi et al., 2014; M. Singh et al., 2013; Uabundit et al., 2010; Vollala et al., 2011).*B.monnieri* extract (BME) exhibits anti-oxidative (S. Kumar & Mondal, 2016), anti-microbial (A. Mathur et al., 2010), neuro-protective (Uabundit et al., 2010), anti-inflammatory(A. Mathur et al., 2010) and memory-enhancing properties(Chaudhari et al., 2017). It also recovers the ATPases activities, retains ionic balance, restoreselenium and zinc levels in the brain.

Studies have reported that neuroprotective effects of *B.monnieri* against 3- NP- induced mitochondrial dysfunction by its antioxidant effect (Shinomol, Bharath, et al., 2012; Shinomol, Srinivas Bharath, et al., 2012). Other studies proved that *B.monnieri*prevents cholinergic degeneration and shown cognitiveenhancing properties in the rat model of AD (Uabundit et al., 2010).Pre-treatment with *B.monnieri* has been shown to improve scopolamine-induced amnesia in the form of retrograde and anterograde by reducing entire brain acetylcholinesterase activity (A. Das et al., 2002; Prabhakar et al., 2008).

**4. *Centella asiatica***

*Centella asiatica* (*C.asiatica*), generally known as Jal Brahmi, Gotu kola, and Indian pennywort, belongs to the family Apiaceae. It is an excellent valuable medicinal and perennial creeping herb located in the sub-tropical and tropical regions of SriLanka, China, Nepal, Indonesia, Madagascar, and India (Shahab Uddin et al., 2017; B. Sun et al., 2020)**.** It has been used as a medicinal herb for a long time for memory enhancement, anti-stress, wound healing, antioxidant, anti-anxiety, anti-cancer, immune booster, and aphrodisiac effects (Puttarak et al., 2017). *C.asiatica* contains a wide range of phytochemicals having triterpenoid saponins, asiaticosides (Morrison et al., 2011), madecassic acid (Randriamampionona et al., 2007), madecassoside, Asiatic acid (Malik et al., 2013), triterpenoid trisaccharides (Z. Y. Jiang et al., 2005)**,** brahminoside, brahmoside (Gohil et al., 2010), triterpenes (B. Sun et al., 2020). It also contains several other components like sasiaticoside, sitosterol, ascorbic acid, centoic acid, tannins, centellic acid, thankuniside, thankunic acid, siatic acid, isothankuniside, vellarin, glycoside, lipids sterols, alkaloids, flavonoids (A. J. Das, 2011; Siddiqui et al., 2007)**.**

*C.asiatica* has been beneficial for treating several ailments such as epilepsy, asthma, depression, mental weakness, body aches, skin illnesses, rheumatism, ulcer, abdominal pain, and also neurodegenerative disorders like AD and PD (Gohil et al., 2010; Khotimah et al., 2015; C. L. Xu et al., 2013). Studies have been suggested that the *C.asiatica* ethanol extract may attenuate Aβ-induced neurotoxicity by increasing the anti-oxidant activity in IMR32 and PC12 cells (C. L. Chen et al., 2016; Soumyanath et al., 2010).Improvement of the colchicine-induced neuronal injury by asiaticoside may also clarify the neuroprotective effect of *C.asiatica*(Jin et al., 2004; V. Kumar, 2006).

**5. *Curcuma longa***

*Curcuma longa* (*C.longa*), commonly referred to as Haldi or Turmeric is a perennial herb, belongs to the family Zingiberaceae. Turmeric is used as the traditional system of medicine in India, Japan, China, and Southeast Asian countries for a long time (Kocaadam & Şanlier, 2017). It has also been used as a normal spice, as a household medicine for the treatment of swelling, skin diseases, sprainon the cause of injury, as an antiseptic and antibacterial(Soleimani et al., 2018; Vaughn et al., 2016). The main bioactive constituent of turmeric is curcumin. *C.longa* exhibits a wide verity of biological and medicinal beneficial effects such as anti-oxidative (Srivastava et al., 2016), neuro-protective, hepato-protective (Razavi & Hosseinzadeh, 2020; H. Zhou et al., 2012), anti-inflammatory (Bundy et al.,

2004)**,** anti-depressant (X.-R. Chang et al., 2016), anti-cancer (Allegra et al., 2017; Chaurasia et al., 2016)and anti-microbial properties (Gunes et al., 2016). Furthermore, C. *longa* is also neuroprotective against neuronal apoptosis, behavioral deficits(Q. Wang et al., 2005), injury of the blood-brain barrier (J. Jiang et al., 2007)and aged rat brain (Bala et al., 2006). The efficacy of Turmeric has been verified in neurodegenerative diseases like AD, HD, and PD (B. Mythri & M. Srinivas Bharath, 2012; Garcia-Alloza et al., 2007; Mohammadi et al., 2022; Monroy et al., 2013).The new promising role of curcumin against the neurodegenerating disease such as glioblastoma and epilepsyhas been reported in brain disease by modulating several pathways in the brain cells(Benameur et al., 2021).

### 6. *Celastrus paniculatus*

*Celastrus paniculatus* (*C. paniculatus*), also known as Jyotishmati, belongs to the family Celastraceae. In the traditional system of medicine, it is used as a brain toznic, emetic, stimulant, and appetite(A. Arya et al., 2022; Nagpal et al., 2022). It contains bioactive phytochemicals having paniculatine A, paniculatine B, sesquiterpene, wifornine F, celapanigine, celastrine, celapagine, celapanine, polyalcohols such as malkanginnol, paniculatadiol, malangunin, triterpenoids, malkanguniol and sterols like β-sitosterol and β-amyrin (Borbone et al., 2007; Lu et al., 2006).*C. paniculatus* extract has possessed both cognition-enhancing and antioxidant activities (Saroya & Singh, 2018). Extract of *C. paniculatus* protected hydrogen peroxide-induced neuronal injury by free-radical scavenging and antioxidant activities(Aleem, 2021). Previous studies have been suggested that *C. paniculatus* prevented neuronal cell injury against glutamate-induced toxicity by modulating glutamate receptor activities that caused improvement in memory and learning performance (Bhanumathy et al., 2010; Godkar et al., 2006).

### 7. *Coriandrum sativum*

*Coriandrum sativum* (*C.sativum*) is an annual herb that belongs to the family Apiaceae, generally called Dhanya.*C.sativum*is found in the region of Mediterranean and widely grown all over the world (Bower et al., 2016; Kabak & Dobson, 2017).*C.sativum* having major phytochemical includes polyphenolics such as caffeic acid glycitin, protocatechinic acid, and flavonoids such as quercetin 3-glucoronide. The seed extract of *C.sativum* has been used in shampoos and lotions and leads to anti-rheumatoid and anti-microbial effects (Khazdair et al., 2018).In the Iranian traditional system of medicine, *C. sativum* has been proposed to improve insomnia and anxiety (Mahendra & Bisht, 2011). It exhibits a wide range of learning and

memory-enhancing effects due to its cholesterol-lowering, anti-inflammatory, and antioxidant activities (Kajal & Singh, 2019).

### 8. *Ferula assafoetida*

*Assafoetida* (*F.assafoetida*) belongs to the family Apiaceae, and is isolated from the plants live tap roots or rhizome. In Iran,*F.assafoetida* is commonly called gum-resin, anguzakoma, anghouzeh, and khorakoma (Iranshahy & Iranshahi, 2011).*F.assafoetida* has been used in traditional system of medicine, as a spice in many foods in Nepal and India. It contains major bioactive constituents like germacrene B and E-1-propenyl sec-butyl disulfide (Khajeh et al., 2005).*F.asafoetida* has been used for the treatment of many diseases such as epilepsy, asthma, stomach ache, weak digestion, influenza, intestinal parasites, and flatulence in traditional medicine (Y. K. Lee et al., 2009). It has been reported that *F.assafoetida* possesses a wide verity of biological and pharmacological like antioxidant, antihypertensive, ant-diabetic, contraceptive, sedative, laxative, antispasmodic, anti-inflammatory, antifungal, molluscicidal, anti-epileptic, antiviral effects (Bagheri et al., 2014; Khazdair et al., 2018). It also acts as a nerve simulative and neuroprotective agent in central and peripheral neuropathy (Homayouni Moghadam et al., 2014). Hence, *F.assafoetida* may be used in the treatment of neurodegenerative diseases like Alzheimer's and Parkinson's diseases (Zarmouh et al., 2016).

### 9. *Thymus vulgaris*

*Thymus vulgaris* (*T.vulgaris*) belongs to the family Lamiaceae, which are strongly aromatic. They consist of about 38 species found in subtropical countries (Azaz et al., 2004). The main bioactive constituents of *T.vulgaris* are thymol, carvacrol. It exhibits antimicrobial, antioxidant, antitussive, and antispasmodic effects(Dogu-Baykut et al., 2014; Javed et al., 2019).The bioactive monoterpene thymol obtained from *T.vulgaris has been* neuroprotective and improved effects on amyloid β or scopolamine-induced cognitive deficit in rats (Deng et al., 2015).

### 10. *Zataria multiflora*

Zataria multiflora (*Z.multiflora*) belongs to the family Lamiaceae (Shaiq Ali et al., 2000)**.** The main bioactive constituents of *Z.multiflora* are β-caryophyllene, thymol, PARA-cymene, carvacrol, and γ-terpinene (Sharififar et al., 2007). It also contains many compounds like luteolin, di, tri, and tetra-ethoxylated and 6-hydroxyluteolin glycosides, which may be

responsible for the beneficial effect (Boskabady & Gholami Mhtaj, 2014). In the traditional Iranian system of medicine, which is used as an antiseptic, analgesic, and carminative effects (Boskabady & Gholami Mhtaj, 2014). It has been reported that the *Z.multiflora* essential oil shown anti-bacterial (Dadashi et al., 2016), anti-inflammatory (Khazdair et al., 2018), immunoregulatory (Kianmehr et al., 2017; Shokri et al., 2006), anti-oxidant and anti-fungal properties (Dadashi et al., 2016; Eskandari-Roozbahani et al., 2019). Further, it has also been reported that the Aβ produced learning and memory deficits and was restored by intake of essential oil of *Z.multiflora* in rats. Thus *Z.multiflora* essential oil reduces cognitive symptoms of AD (Majlessi et al., 2012).

**11. *Galanthus nivalis***

*Galanthus nivalis* (*G.nivalis),* usually called Sarpagandha/snowdrop, belongs to Amaryllidaceae family. The major bioactive constituent of *G.nivalis is* galantamine located in flower and bulb, which is a tertiary alkaloid isoquinoline (Benedec et al., 2018). Galantamine may well decay the neuro-degenerative faults in AD through the processes of neuro-protection and neuro-genesis (Hussain et al., 2018).*G.nivalis* can excite nicotinic receptors which further increase memory and cognition (Wattmo et al., 2013).

**12. *Ginkgo biloba***

Ginkgo biloba (*G.biloba*) among the ancient living species on this globe, belongs to the Ginkgoaceae family, also called a living fossil (Yuan et al., 2017). It shows medicinal importance and has been noted in the oldest Chinese herbal drug(Chan et al., 2007).Extract of *G.biloba* is one of the topmost best 10 selling herbal drugs in the United States and has been used in several studies to assess the effect of ginkgo (Gold et al., 2002). *G.biloba* extract consists of flavonoids having three flavonols, isorhamnetin, kaempferol, quercetin and terpenic lactones including diterpenic lactones such as ginkgolides- A, B, C, J and M(Nucifora et al., 2001; Rubinsztein, 2005) and sesquiterpene tri-lactone-bilobalide (Birks & Grimley Evans, 2009). The main bioactive components of *G.biloba* are bilobalide responsible for the multifunctional role such as learning-memory enhancement and neuroprotective (Bedir et al., 2002; Chandrasekaran et al., 2001; Nakanishi, 2005; B. Singh et al., 2008).*G.biloba* is well known to have anti-inflammatory, anti-oxidant properties(S. K. Singh et al., 2019), anti-apoptotic, anti-aging (S.-K. Hsieh et al., 2016), and neuro-protective (Kuchta et al., 2016; C. Rojas et al., 2016; X. Zhou et al., 2017).Studies have reported that *G.biloba* extract denoted as EGb 761 is responsible for neuroprotection in an animal model of

PD (El-Ghazaly et al., 2015; Fei & Sun Sheng-Gang, 2013; P. Rojas et al., 2008). Also, EGb 761 having a low molecular weight is capable to pass the BBB (Shi et al., 2010).Numerous clinical and preclinical studies have also reported the neuroprotective effect of EGb 761 against neurodegenerative diseases like schizophrenia (Deng et al., 2015),PD(P. Rojas et al., 2012), and AD (Mahadevan & Park, 2008).

**13. *Camellia sinensis (Tea plant)***

*Camellia sinensis* (*C.sinensis*), commonly called Tea Plant is known for a variety of tea products such as white tea, green tea, oolong tea, and black tea. The most important form of black tea account for more than 70% of total tea production (Sharangi, 2009). Tea plant shows medicinal value based on their flavonoid and antioxidant constituents (Saeed et al., 2017). In these studies, the significance of green and black tea has been reported in neurodegenerative diseases (S.-Q. Chen et al., 2018).

**14. *C.sinensis***

**Green tea**

Green tea is obtained from dried and steamed leaves of *C.sinensis* and is common for human health benefits (Cabrera et al., 2006).*C.sinensis* contain polyphenol (N. Khan & Mukhtar, 2019) having anti-inflammatory (B.-T. Chen et al., 2012)**,** anti-oxidative (Malar et al., 2020), anti-carcinogenic(Filippini et al., 2020; Ravindranath et al., 2006), neuroprotective(Boadas-Vaello & Verdú, 2015), anti-microbial (Chan et al., 2011; Thakur et al., 2015),anti-arthritic activities(Hong et al., 2008). Studies reveal that supplement of *C.sinensis* diminishes the risk of PD (Tanaka et al., 2011). The main bioactive constituent of green tea is catechin and provides neuroprotection in the MPTP-induced mouse model of PD through its iron-chelating and anti-oxidative properties (Levites et al., 2001).

***Black tea***

Black tea is generally an oxidized form of tea made up from the fermentation process (Sharangi, 2009). It contains theaflavin with medicinal value. The antioxidant properties of theaflavin are like catechin found in black tea (Leung et al., 2001). Black tea exhibits a variety of biological activities like anti-oxidative and neuroprotective (S.-Q. Chen et al., 2018). The chlorogenic acid present in black tea which is shown to increase the total plasma level of homocysteine in humans(Olthof et al., 2001). The increased homocysteine level is related to PD patients(Blandini et al., 2001; Dos Santos et al., 2009)and may cause

mitochondria-mediated apoptosis (Mattson & Shea, 2003). Thus, black tea supplements should be taken in upcoming studies.

**15. *Glycyrrhiza glabra***

*Glycyrrhiza glabra* (*G.glabrais*) are generally referred to as licorice, belonging to the family Leguminosae (Also known as Fabaceae). It includes linalool oxide, pentanol, tetramethyl pyrazine, hexanol, terpinene, geraniol, terpinol, benzoic acid, propionic acid, methyl ethyl ketone, ethyl-linolenate, butanediol, furfuraldehyde, furfuryl formate, trimethyl pyrazine, maltol, glycyrrhizin, tannin, and glycyrrhizic acid (Rekha & Parvathi, 2012). *G.glabrais* is commonly used in throat problems, gastric ulcer, hoarseness, and lung congestion (Dastagir & Rizvi, 2016). The main flavonoid of *G.glabra* is Glabridin which showed several pharmacological and biological activities such as anti-ulcer, anti-viral, anti-diabetic, anti-cancer,anti-inflammatory, anti-oxidant, anti-convulsant, anti-microbial and immunomodulatory activities (Karthikkeyan et al., 2020; Pastorino et al., 2018). Memory enhancing activities of *G.glabrais* has been reported in scopolamine-induced dementia in mice (Ambawade et al., 2001; Dhingra et al., 2004). Extract of *licorice* has also been shown to reverses the amnesia caused by scopolamine and improve memory and learning activities due to cholinergic neurotransmission in mice.

**16. *Hypericum perforatum***

*Hypericum perforatum* (*H. perforatum*), commonly called hypericum or millepertuis, belongs to the family Hypericaceae. It is world-wide distribution mainly found in western Asia, northern Africa, and Europe. *H. perforatum* having bioactive constituents like hyperoside, kaempferol, quercetin, hypericin, and biapigenin in which hyperoside is the major active constituent (Shrivastava & Dwivedi, 2015). Ethanolic extract of *H. perforatum* may recover microglial viability by decreasing amyloid-β protein-mediated toxicity in AD (Butterfield et al., 2007). Thus, it also acts as an antioxidant, anti-inflammatory, neuroprotective (Oliveira et al., 2016)and the capability to interact with iron ions (Alía et al., 2006).

**17. *Lycopodium serratum***

*Lycopodium serratum* (*L. serratum*) is also known as club mosses, creeping cedar, and ground pines, belonging to the family Lycopodiaceae (fern-allies). *L. serratum* contains an bioactive constituent huperzine A, which has been widely studied for the therapy of AD(Ding et al., 2014). Huperzine- A isolated from *L. serratum* and has been used to treat inflammation, fever, schizophrenia, and blood-related diseases for a long time (D. Bai, 2007).

It is a highly reversible, selective, powerful AChE inhibitor and its AChE inhibition potency is similar to that of donepezil, galanthamine, tacrine, and physostigmine (D. Chu et al., 2007). Huperzine A has a protective role against Aβ mediated cell death, mitochondrial dysfunction, and oxidative stress as well as anti-inflammation (Ohba et al., 2020).

**18. *Melissa officinalis***

*Melissa officinali*s (*M. officinalis*), commonly called lemon balm which is used in the traditional system of medicinefor its spasmolytic, nerve-calming, and soothing effect (João et al., 2017). *M.officinali*s contains some phytochemical components like phenolic acids, flavonoids having apigenin, quercitrin and luteolin. These derivatives scavenges the free radicals and inhibit the enzymes AChE, monoamine oxidases (MAO), in addition to cell death (Mahboubi, 2019). The inhibition of these enzymes causes improvement in a symptom like depression (Timonen & Liukkonen, 2008). *M. officinali*s ethanolic extracthas been capabletoimprove the scopolamine-induced amnesia by inhibition of the enzyme AChE (Soodi et al., 2014). Studies have also suggested that *M. officinalis* possess protective activities in vitro PC12 cell line and may protect the neurons (Akhondzadeh et al., 2003a).

**19. *Ocimum sanctum***

*Ocimum sanctum* (*O.sanctum*) is also called Tulsi / Holy Basil, belongs to the family Labiatae. This herb contains several compounds such as glycosides, tannins, saponins, alkaloids, vitamin C, tartaric acid, and maleic acid (Cohen, 2014). Ethanolic extract of *O. sanctum* may restore and activate the expression of choline acetyltransferase in aged humans, It protects nerve cells and high production of acetylcholine neurotransmitters may improve the cognitive and memory capability(Hening et al., 2018; Kusindarta et al., 2016). Studies have also revealed that hydro-alcoholic extract of *O. sanctum* exhibited potent antioxidant activities against hydroxyl radicals and DPPH because of the large number of flavonoids and polyphenols components (Venuprasad et al., 2013).

**20. *Panax ginseng***

*Panax ginseng* (*P. ginseng*) belongs to the family Araliaceae. This herb is distributed in Korea Japan and China, which is generally used for several beneficial effects like energy booster, elevating mood, and inhibiting age-related diseases in the traditional Chinese system of medicine for a long time (Nah et al., 2007; Pan et al., 2013). *P. ginseng* contains active constituent ginsenoside, is a member of tetracyclic triterpenoid saponin glycosides (Van Kampen et al., 2014).*P. ginseng* extract powder and constituent ginsenosides Rd (Lin et al.,

2007), Rg1, Re, Rg3 (R. Wang et al., 2006; L. Xu et al., 2009), Rh2 and Rg5 (S. Chu et al., 2014)have been found beneficial neuroprotective effects against AD and PD by multiple mechanisms in vitro andin vivo models (Cho, 2012; Heo et al., 2008; H. J. Kim et al., 2013; Radad et al., 2006; Tu et al., 2009; X. Zhang et al., 2014).A large number of the memory-enhancing and cognition effects of *P. ginseng* has been reported in clinical studies (Ru et al., 2015; Smith et al., 2014).

**21. *Rosmarinus officinalis***

*Rosmarinus officinalis (R. officinalis)* commonly called Rosemary and Satapatrika belong to the family Lamiaceae. It covers many essential oils such as oleanolic, carvacrol, thymol, ursolic acid, eugenol acid, and antioxidant constituents like ferulic acid, carnosic acid (Papajani et al., 2015). Carnosic acid is the main bioactive constituent and extracted from the *R. officinalis* exhibited a neuroprotective effect on cyanide induced brain damage in vitro and in vivo models(D. Zhang et al., 2015). The neuroprotective mechanism plays part in AChE inhibition, amyloid-β deposit, and anti-butyryl-cholinesterase activities (Habtemariam, 2016). Apart from these activities, it takes anti-inflammatory, and anti-apoptotic in addition to its neuroprotective mechanism (Rasoulian et al., 2019).

**22. *Salvia officinalis***

*Salvia officinalis (S. officinalis*) belongs to the family Lamiaceae. Itimproves memory retention by binding with cholinergic and muscarinic receptors, which have been involved in the memory retention process for a long time and use as a memory-enhancing (Eidi et al., 2006; Imanshahidi & Hosseinzadeh, 2006). The main active constituents of *S. officinalis* are carnosic acid and rosmarinic acid having strong pharmacological and biological effects like anti-oxidant, anti-inflammatory as well as weak AChE inhibitor(Ghorbani & Esmaeilizadeh, 2017; Sallam et al., 2016). Previous studies showed the efficacy of S. officinalis in treating memory impairments with AD (Akhondzadeh et al., 2003b).

**23. *Terminalia chebula***

*Terminalia chebula* (*T. chebula*), the King of Medicine in Tibet, belongs to the family Combretaceae. It is the most popular medicinal herb used in the medicine of Unani, Siddha, Ayurveda, and Homeopathy (D. Y. Lee et al., 2017). *T. chebula* contains many components like sarjun-glucoside- 1, triterpene, arjungenin, tannins, chebulosides-1 & 2, chebulic acid, punicalaginter-flavin A, tannic acid, chebulinic acid, gallic acid, 2,4-chebulyi–β-D-glucopyranose, ethyl gallate, terchebin, ellagic acid, flavonoids having rutins, quercetinetc

and luteolin (Upadhyay et al., 2014). Gallic acid obtained from *T. chebula* shows anti-inflammatory activities by the downregulation of nuclear factor kappa B (NF-κB) pathway in the growth of inflammatory diseases in vitro and in vivo studied (Afshari et al., 2016; Shen et al., 2017). It acts as an antioxidant activity as compared to those of standard radical scavengers like quercetin, which exhibit 95% activity with inhibitory concentration (IC) of 2.2 μg/ml (V. Arya et al., 2011). The fruit extract of *T. chebula* may probably protect the neurons against ischemia, decreases death rate, and NO level of microglial cell activated by lipopolysaccharide (Gaire et al., 2013).

**24. *Tinospora cordifolia***

*Tinospora cordifolia* (*T. cordifolia*) is also known as Giloe, belongs to the family Menispermaceae. *T. cordifolia* contains phytochemical components such as steroids, lactones, aliphatics, diterpenoid, glycosides, and alkaloids (Rawal et al., 2004). It possesses biological and pharmacological activities including anti-oxidant, immuno-modulating, anti-fertility, and memory-enhancing (P. Sharma et al., 2019) by its immuno-stimulation and elevated level of acetylcholine (Kosaraju et al., 2014; Reddy & Reddy, 2015). *T. cordifolia* has been shown to inhibit neurodegenerative alterations and improve cognition, memory, and learning in AD patients of AD.

**25. *Withania somnifera***

*Withania somnifera* (*W. somnifera*), generally called Ashwagandha, Indian ginseng, belongs to the family Solanaceae. It is extensively found in sub-tropical and tropical areas covering Northern Africa, Canary Island, and the Mediterranean region to East-south Asia (A.Ramachandran, M.Senthil Kumar, K.paneerselvam, 2013). *W. somnifera* is the most essential Indian medicinal herb and has been widely used in Ayurvedic medicine to increase vitality, immunity, and longevity for a long time (Mirjalili et al., 2009). It contains different chemical constituents such as somniferine, withananine, somnine, withanine, somniferinine, withanolide A, withanoside IV, withanoside VI and withaferin A.(R. Mathur & Mishra, 2021; Tohda, 2008). The main essential bioactive constituents of *W. somnifera* are withanoside IV, withanoside VI, withaferin A, and withanolide A (Tohda, 2008), which are responsible for the treatment of neurodegenerative diseases (Gupta & Rana, 2007; Misra et al., 2008).*W. somnifera* root extractexhibits a wide variety of pharmacological and biological activities such as anti-inflammatory(G. Y. Sun et al., 2016), anti-depressant (Bhattacharya et al., 2000), anti-carcinogenic (Rai et al., 2016), anti-oxidant (G. Y. Sun et al., 2016), memory and

cognition-enhancing (Shivamurthy et al., 2016), neuroprotective in many studies (P. Kumar & Kumar, 2009; Preeti et al., 2010).*W. somnifera* has been reported as a potentialaphrodisiac and nerve tonic which improves memory and learning activities (Ernst, 2010; S. Sharma et al., 2011). It has also been reported that the neuroprotection against paraquat (PQ) and maneb (MB) induced-nigrostriatal dopaminergic neurodegeneration by an elevated level of anti-apoptotic (Bcl-2) protein and reduced level of pro-apoptotic (Bax) protein(Prakash et al., 2013; S. P. Singh, 2015). Thus, it improved biological and catecholamine abnormalities in the PD model of mice (RajaSankar et al., 2009).

**26. *Mucuna pruriens (Velvet bean)***

*Mucuna pruriens*(*M. pruriens*), commonly known as Kapikacho or Kevach, belongs to the family Fabaceae. It is an annual climbing legume herb native to subtropical and tropical regions of southern China and eastern India (Pugalenthi et al., 2005). This herb has been long time used in Ayurvedic medicine as a potent aphrodisiac to treat brain diseases, arthritis, and Parkinsonism (Sathiyanarayanan & Arulmozhi, 2007). *M. pruriens* contains phytochemical having alkaloids like prurieninine, prurienidine, prurienine. Severalamino acids along with proteins, Zn, Se, carbohydrate, fatty acids having palmitic acid, oleic acid, and linoleic acid are rich in the seed of *M. pruriens* (Divya et al., 2017). Triterpenes and sterols are also found in both seed and root of *M. pruriens*. Some studies have been reported that the *M. pruriens* seed extract contains Coenzyme Q10, NADH, and Levodopa (Katzenshlager et al., 2004). Levodopa (L-dopa) is a precursor of the neurotransmitter dopamine and is referred to as the gold standard drug for PD treatment (Sinha et al., 2018). All parts such as seed, root, and stem of*M. pruriens* have valuable medicinal properties i.e. anti-inflammatory, anti-ulcer, anti-helminthiasis, and anti-nephropathy (Suresh et al., 2013). Studies show that the *M. pruriens* recovers redox status by reducing oxidative stress(Poddighe et al., 2014). through its metal chelating and ant-oxidative properties (Dhanasekaran et al., 2008). Furthermore, *M. pruriens* seed extract has also improved synaptic and mitochondria function essential for neuronal existence, recover TH expression in Drosophila and mice model of PD(Poddighe et al., 2014; Yadav et al., 2014). In vitro and In vivo studies of *M. pruriens* extracts have exhibited a wide variety of pharmacological and biological effects such as anti-neoplastic, anti-microbial, anti-diabetic, aphrodisiac, anti-epileptic(Sathiyanarayanan & Arulmozhi, 2007), anti-helminthic (Jalalpure et al., 2006), anti-venom (Guerranti et al., 2008), anti-oxidative, neuroprotective and anti-inflammatory activities, possibly due to the presence of L-dopa (Pathania et al., 2020).

**27. *Emblica officinalis***

Emblica officinalis (*E. officinalis*), commonly known as Amla, belongs to the family Euphorbiaceae. It is widely found in Bangladesh, Sri Lanka, Southern China, Southern India, Pakistan, and Malaysia. Amla fruit has been used in traditional systems of Unani such as brain tonic, hair tonic, cardiac tonic, anti-diarrhoeal, hemostatic, tranquilizer, and astringent (Vasudevan & Parle, 2007). The therapeutic potential of *E. officinalis* has also been used for cerebral asthenia, palpitation, cardiac asthenia, hair fall, neurasthenia, and diminished vision (Shamsi et al., 2019; Vasudevan & Parle, 2007). It exhibited improvement in memory scores of young and aged mice in a dose-dependent manner, also reversed the scopolamine and diazepam induced amnesia (Golechha et al., 2012; Vasudevan & Parle, 2007). Memory enhancer and antioxidant activities of *E. officinalis* play a key role in the treatment of AD and amnesia (Husain et al., 2019; S et al., 2013).

**28. *Lepidium meyenii***

*Lepidium meyenii* (*L.meyenii*), commonly known as Black Maca, belongs to the family Brassicaceae. *L. meyenii* aqueous and hydro-alcoholic extract hasbeen shown to recover scopolamine-induced amnesia by inhibiting AChE activity in the mouse model (Rubio et al., 2007). It has also exhibited memory and learning enhancing activity in Alzheimer's patient by raising the acetylcholine level (Rubio et al., 2007; Yu et al., 2020).

**29. *Nardostachys jatamansi***

*Nardostachys jatamansi* (*N. jatamansi*) belongs to the family Caprifoliaceae. It contains main active components like valeranone and sesquiterpene, which have been used to treat stress-induced memory deficit (Lyle et al., 2009). *N. jatamansi* has been shown to enhancememory and learning capabilities (M. B. Khan et al., 2012) in young and aged mice, also improved diazepam, scopolamine, and aging-induced amnesia by cholinergic transmission (Joshi & Parle, 2006c; Karkada et al., 2012).

**30. *Pueraria lobata***

*Pueraria lobata (P. lobata*)is a Chinese herbal drug, belonging to the family Leguminosae. It has been commonly used as a traditional system of medicine for the treatment of several diseases like gynecological, cardiovascular, and cognitive impairment (O. H. Kang et al., 2015; Xiao et al., 2017). The major bioactive constituent of *P. lobata* is puerarin (daidzein). This constituent prevented scopolamine-induced amnesia in the Y-maze test by working as a

choline acetyl-transferase enzyme for the synthesis of acetylcholine (Y. Chang et al., 2009; Han et al., 2007; M.-T. Hsieh et al., 2002).

**31. *Prunus amygdalus***

*Prunus amygdalus* (*P. amygdalus*), commonly called Almond/Badam, belongs to the family Rosaceae, which is distributed in East and South Asia. It has been cultured in China and Greece, also cultured mostly in Indian Kashmir, the region of the Mediterranean, and California (Esfahlan et al., 2010). In Unani medicine, it is regarded as a brain tonic and used in cerebral aberrations like headache, insomnia, and loss of memory (K. S. Kulkarni et al., 2010). Badam supplementation inhibited scopolamine-induced amnesia in mice (Sahib, 2014) and enhanced learning and memory abilities (Nandgopal & Ali Khan, 2020)in HFD-fed rats model.

**32. *Zingiber officinale***

*Zingiber officinale* (*Z. officinale*), belongs to the family Zingiberaceae. It has been used in the treatment of stomach trouble, headache, rheumatism, memory impairment, and AD (Mao et al., 2019). Extract of *Z. officinale* has improved memory and learning abilities in mice and recovered the scopolamine-induced amnesia by inhibiting acetylcholinesterase activity (Joshi & Parle, 2006e).

**33. *Commiphora whighitii***

*Commiphora whighitii* (*C. whighitii*) belongs to the family Burseraceae. It has improved mice's memory and learning abilities and recovered scopolamine-induced amnesia (G. Saxena et al., 2007). The Guggul is the major constituent of *C. whighitii*, significantly inhibited AChE activity of exposed mice, and showed an anti-amnesic effect (Ajay J Parikh, 2013; Kunnumakkara et al., 2018; Nazir et al., 2020).

**34. *Convolvulus pluricaulis***

*Convolvulus pluricaulis* (*C. pluricaulis*), generally known as Shankhpushpi, belongs to the family Convolvulaceae. It is an Ayurvedic drug used as a neuro-protective and memory-enhancing activity for a long time (Malik et al., 2011; Sethiya et al., 2019).*C. pluricaulis* contain many chemical constituents such as scopolin, ayapanin scopoletin-glycoside, fatty acids, kaempferol-glycoside, β- sitosterol, aliphatic compounds, and secondary metabolites having flavonol-glycosides, steroids, anthocyanins, and tri-terpenoids which are responsible for nootropic and memory-enhancing activities (Malik et al., 2016). Extract of *C. pluricaulis*

significantly improved memory and learning capabilities in rat's model (Bihaqi et al., 2012; Nahata et al., 2008). Among the constituents, scopolin andscopoletin have exhibited memory-enhancing activity, also attenuated scopolamine-induced amnesia by the inhibition of AChE activity in mice(Bates et al., 2015; Evans et al., 2013; Malik et al., 2016).

**35. *Ficus carica***

*Ficus carica* (*F. carica*) belongs to the family Moraceae. The major active constituent of *F. carica* is quercetin which may play an essential role in AD and memory deficit due to its anti-oxidant activity(Avneet et al., 2018). At a low dose, *F. carica* shows mild memory-enhancing activity and at a high dose, it shows behavior changes, better memory, and learning capability (V. Saxena et al., 2013). This study suggested the potential of *F. carica* treat memory deficits in Alzheimer's disease (Essa et al., 2015).

**36. *Acori graminei***

The extract of *Acori graminei* (*A.graminei*) has been shown to improve scopolamine-induced amnesia by reducing acetylcholinesterase (AChE) activity in the whole brain (Park et al., 2008). It also exhibited neuroprotective, antioxidant, anti-hyperlipidemic, anti-apoptosis, anti-inflammatory and antibacterial activities (Y. Li et al., 2020).

**37. *Anacyclus pyrethrum***

Ethanolic extract of *Anacyclus pyrethrum* (*A. pyrethrum*) has been capable to recover scopolamine-induced amnesia models by improving central cholinergic neurotransmission (Sujith et al., 2012). It has also shownneuroprotective, antiepileptic, anti-inflammatory and antioxidant effects

**38. *Angelica gigashas***

*Angelica gigashas* (*A. gigashas*) has been capable of significantly improving the scopolamine-induced amnesia in passive avoidance and Morris water maze test by inhibiting AChE activity in the hippocampus of treated mice and shown the anti-amnesic effect (S. Y. Kang et al., 2003).

**39. *Asparagus recemosus***

*Asparagus recemosus(A. recemosus)* methanolic extract significantly reversed scopolamine-induced amnesia by an increase in transfer latency on the elevated plus-maze. Further, *A. recemosus* methanolic extract dependently inhibited AChE enzyme in particular brain regions indicative of anti-amnesic activities (Ojha et al., 2010).

**40. *Caesalpinia crista***

*Caesalpinia crista* (*C. crista*) extract has been exhibited to improve the amnesic activity of Scopolamine in mice models (Kshirsagar, 2011).

**41. *Carica papaya***

*Carica papaya* (*C. papaya*) ethanolic seed extract has been capable to recover the Scopolamine induced amnesia by its activity of antioxidant (A. Sharma et al., 2022).

**42. *Clitoria ternatea***

The anti-amnesic activity of *Clitoria ternatea*(*C. ternatea*) alcoholic extracthas been revealed against scopolamine-induced amnesia in the passive avoidance task model in rats by reducing AChE activity which reduces the level of the acetylcholine in the brain (Vyawahare et al., 2006).

**43. *Corydalis tuber***

*Corydalis tuber* (*C. tuber*) is one of the most essential medicinal plants in the traditional system of medicine. The main bioactive constituents are pseudocoptisine and benzyl-isoquinoline obtained from *C. tuber.* It has been shown that the anti-amnesic activity of *C. tuber* against scopolamine-induced learning and memory deficit (Hung et al., 2008).

**44. *Desmodium gangeticum***

*Desmodium gangeticum* (*D. gangeticum*) extract has been exhibited to improve scopolamine-induced amnesia by reduction of AChE activity in the brain (Joshi & Parle, 2006a).

**45. *Foeniculum vulgare***

All parts of *Foeniculum vulgare* (*F. vulgare*) extract have significantly improved the amnesic effect of scopolamine by reducing AChE activity in the mice model (Joshi & Parle, 2006b).

**46. *Geissospermum vellosii***

The ethanolic stem extract of *Geissospermum vellosii (G. vellosii)* has been exhibited to improve scopolamine-induced memory deficit as proved in passive avoidance and Morris water maze tests by decreased AChE activity(Baradaran et al., 2012).

**47. *Hibiscus sabdariffa***

*Hibiscus sabdariffa* (*H. sabdariffa*) extract has been shown to significantly attenuate scopolamine-induced amnestic deficits by decreased AChE activity in mice model (Joshi & Parle, 2006d).

**48. *Hippophae rhamnoides***

*Hippophae rhamnoides* (*H.rhamnoides*), also called Seabuckthorn. The leaf extract of *H.* rhamnoides has exhibited a possible therapeutic effect against scopolamine-induced cognitive impairment by the regulation of AChE and antioxidant activity in the brain (Attrey et al., 2012).

**49. *Mimusops elengi***

*Mimusops elengi* **(***M. elengi*) has significantly attenuated scopolamine-induced amnesia by reducing transfer latencies and elevating down latencies, also decrease AChE activity in the whole brain (Joshi & Parle, 2012).

**50. *Murraya koenigii***

*Murraya koenigii* (*M. koenigii*) leaves have been capable to improve scopolamine-induced amnesia in aged and young mice by inhibition of cholinesterase activity in the brain (Tembhurne & Sakarkar, 2011).

**51. *Nelumbo nucifera***

*Nelumbo nucifera* (*N. nucifera*) has been exhibited to reduce scopolamine-induced memory deficit by ACHE activity (Oh et al., 2009).

**52. *Phyllanthus amarus***

*Phyllanthus amarus* (*P. amarus***)** hasimproved memory scores of aged and young mice in passive avoidance, elevated plus maze, and reversed effectively scopolamine-induced amnesia by reducing AChE activity (Joshi & Parle, 2007).

**53. *Scrophularia buergeriana***

*Scrophularia buergeriana* (*S. buergeriana*)has been shown to significantly enhance cognitive actions against scopolamine-inducedamnesia in mice by using the Morris water maze test (Jeong et al., 2009). *Iridoid* glycoside is the main constituent isolated from *S. buergeriana*.

**54. *Teucrium polium***

*Teucrium polium* (*T. polium*) ethanolic extract has improved the scopolamine-induced amnesia by decreased central cholinesteraseactivity (Orhan & Aslan, 2011).

**55. *Thespesia populnea***

*Thespesia populnea* (*T. populnea*) ethanolic extract has revealed significantly improved scopolamine-induced amnesia by decreasing the brain cholinesterase activity in mice (Vasudevan & Parle, 2006).

**56. *Vigna radiate***

*Vigna radiate* (*V. radiate*) seed extract has been shown to improve the amnesic effect of Scopolamine in the mouse by using Morris water maze and radial arm maze test(Aruna et al., 2012).

**57. *Vitex negundo***

*Vitex negundo* (*Vitex negundo*) has been shown to decrease scopolamine-induced amnesia by diminishing AChE and antioxidant activities (Kanwal et al., 2010).

**58. *Zizyphus jujube***

*Zizyphus jujube* (*Z. jujube*) contains an oleamide compound. It is used in traditional system of medicine like Chinese and Korean to reduce anxiety, stomach, and gastrointestinal problems (L. Bai et al., 2016). *Z. jujube* also contains large quantities of phenyl glycosides, flavonoid, terpenoid, sugar, organic minerals, mucilage, protein, citric acid, vitamin-C, and malic acid (Koetter et al., 2009). It recovers learning- memory deficit, motor coordination, behavioral disorder and mild to moderate cognitive effects (Jivad & Rabiei, 2014).

**59. *Ilex paraguariensis***

*Ilex paraguariensis* (*I. paraguariensis*), commonly called Yerba Matic Tea, belongs to the family Aquifoliaceae. Itcontains Vitamin C, B12, and B1. It has a memory-enhancing activity in different rat's model and is widely used as an anti-dementia agent (Bastos et al., 2007; Kujawska, 2018). *I. paraguariensis* has also been exhibited to improve short-term and long-

term memory loss (Prediger et al., 2008). The studies show that the *I. paraguariensis* is effective in treating neurodegenerative diseases like AD (Heck & De Mejia, 2007).

**60. *Delphinium denudatum***

*Delphinium denudatum* (*D. denudatum*), commonly known as Jadwar, belongs to the family Ranunculaceae, it is a perennial herb located in Western Himalaya from Kumaon to Kashmir (Nizami & Jafri, 2006). In the Unani system of medicine, Jadwaris also called the nervine-tonic, brain-tonic, common tonic, cardio-tonic, and tonic for teeth, exhilarant, stomach, viscera, sedative (S. Chen et al., 2020; Shamsi et al., 2019). It has been suggested for the treatment of migraine, insanity, hysteria, paralysis, convulsion, epilepsy, and mania (M. Ahmad et al., 2006).

**61. *Magnolia officinalis***

*Magnolia officinalis* (*M. officinalis*), belongs to the Magnoliaceae family. *M. officinalis* ethanolic extractcontains active constituents such as magnolol and honokiol, which have been reported to possess anti-inflammatory, anti-oxidant, and neuroprotective activities in vitro and in vivo models (Ge et al., 2017). *M. officinalis* plays an essential role in the treatment of memory deficits and AD (Y. L. Chen et al., 2001; Liou et al., 2003).

**62. *Punica granatum***

*Punica granatum (P. granatum),*belongs to the Punicaceae family. *P. granatum* contains many active constituents like punicafolin, punicacortein A, corilagin, pedunculagin, and granatin. It is mainly used in dysentery and diarrhea (Rahimi et al., 2012). Flower of *P. granatum* has effectiveness in memory and learning performance diminished by diabetes mellitus in rats model (Cambay et al., 2011).

**63. *Crocus sativus***

Crocus sativus (*C. sativus*), generally known as Saffron, belongs to the family Iridaceae. It is grown in various countries such as Afghanistan, Kashmir, Spain, Iran, and Turkey (Kafi et al., 2018). *C. sativus* has mainly used as herbal medicine to treat reduce smooth muscle and cognitive disorder in many areas of the world (Abu-Izneid et al., 2022; Gorginzadeh & Vahdat, 2018; Hosseinzadeh et al., 2007; Jalali-Heravi et al., 2009; Khazdair et al., 2015; Mokhtari-Zaer et al., 2015). It contains several biomolecules like lipids, minerals, polypeptides, vitamins, carbohydrates. The major biologically active constituents of *C. sativus* are safranal, crocetin, crocins, and picrocrocin (Bathaie & Mousavi, 2010). Extract of

*C. sativus* has been reported to exhibit anti-Alzheimer and anti-convulsant properties in animal and human models (Bian et al., 2020).

**64. *Nigella sativa***

*Nigella sativa* (*N. sativa*) is an annual medicinal plant, belongs to the family Ranunculaceae, which is generally cultivated in the Mediterranean countries like Eastern Europe and Western Asia. The seed extract of *N. sativa* has mainly been used as a spice in Persian foods like sauces, bread, salads, and pickle (Hajhashemi et al., 2004). It contains many chemical constituents such as protein, fiber, carbohydrate, and fatty acids having Palmitic acid, Myristic acid, Linoleic acid, Arachidic acid, Oleic acid, Stearic acid, and Eicosadienoic acid (Hussein El-Tahir & Bakeet, 2006). The *N. sativa* seed also contains major phenolic compounds such as thymoquinone, thymol, p-cymene, and carvacrol with potential anti-oxidant effects(A. Ahmad et al., 2013; Venkatachallam et al., 2010). It recovered scopolamine-induced memory and learning deficit in addition to reduced activity of AChE and oxidative stress of rat's brain (Hosseini et al., 2015).

**65. *Cissampelos pareira***

*Cissampelos pareira* (*C. pareira*),belongs to the Menispermaceae family. *C. pareira* extracts improved scopolamine-induced amnesia by increased activities of anti-inflammatory, anti-oxidant (Akram & Nawaz, 2017) and reduced activity of the acetyl-cholinesterase enzyme (P. D. Kulkarni et al., 2011).

**66. *Mellisa officinalis***

*Mellisa officinalis* (*M. officinalis*),belongs to the Lamiaceae family. *M. officinalis* is an anti-depressant, anti-inflammatory, and anxiolytic activities (Moacă et al., 2018). It has been used significantly in managing AD (Akhondzadeh et al., 2003a).

**67. *Moringa oleifera***

*Moringa oleifera* (*M. oleifera*), belongs to the Moringaceae family. The leaf extract of *M. oleifera* contains Vitamin-E and C, which is involved in the memory-enhancing process in AD (Pakade et al., 2013). *M. oleifera* ameliorates colchicine-induced AD byaltering monoamine levels like serotonin-norepinephrine anddopamine(Obulesu & Rao, 2011).

**68. *Myristica fragrans***

*Myristica fragrans* (*M. fragrans*),belongs to the Myristicaceae family. *M. fragrans* contain many chemical constituents such as myristic acid, oleic acid, palmitic acid, lauric acid, stearic

acid, penta-decanoic acid, heptadecanoic acid, camphene, safrol, elemicin, b-sitosterol, sabinene, d-borneol, b-pinene, cymene, linalool, myristicin, phenyl-propane derivative, garaniol and terpineol (Maeda et al., 2008). It has been used in the digestive disorder, body ache, leukemia, nervous disorder, memory disturbances, dizziness, vomiting and tachycardia. It exhibits a wide range of anti-oxidant, anti-depressant, anti-bacterial and hypo-lipidemic activities(Ha et al., 2020).

**69. *Evolvulus alsinoides***

*Evolvulus alsinoides* (*E. alsinoides*),belongs to the family Convolvulaceae. *E. alsinoides* ethanol extract has a beneficial effect on memory enhancement and learning behavior in rodent models (Nahata et al., 2010).

**70. *Scutellaria baicalensis***

*Scutellaria baicalensis* (*S. baicalensis*), belongs to the family Labiatae. The bioactive compound baicalein is isolated from *S. baicalensis* dried root. Baicalein prevents ROS generation, mitochondrial membrane disruption, ATP depletion, and apoptosis on rotenone-induced neurotoxicity in the cell of PC12 (X. X. Li et al., 2012).

**71. *Erythrina velutina***

*Erythrina velutina* (*E. velutina*), is mainly found in Brazil and generally used as a traditional system of medicine for the management of brain-related diseases (Ximenes et al., 2019). *E. velutina* ethanol extract has a neuroprotective effect and may be therapeutic potential in PD (Silva et al., 2016).

**72. *Peganum harmala***

The extract of *Peganum harmala* (*P. harmala*) may reduce oxidative stress and inhibit symptoms of PD in rat's model (Rezaei et al., 2016). The neuroprotective effect of *P. harmala* can prevent the angiotensin-II activity that protects dopaminergic neurons and reduces oxidative stress(Lopez-Real et al., 2005).

**73. *Carthamus tinctorius***

*Carthamus tinctorius* (*C. tinctorius*), commonly called Safflower. It contains flavonoids, widely used as herbal medicine to treat cerebrovascular diseases (Delshad et al., 2018). In an animal study, *C. tinctorius* has a beneficial effect on rotenone-induced PD(Ablat et al., 2016; Ren et al., 2016).

**74. *Juglandis Semen***

*Juglandis Semen* (*J. Semen*), commonly known as Walnut. *J. Semen* extract has shown a potential neuroprotective activity in PD mice model by its capability to reduce the NO and ROS generations and inhibit the striatal DA depletion (J. G. Choi et al., 2016; Essa et al., 2015).

**75. *Lycium barbarum***

The major chemical constituent *barbarum* polysaccharides isolated from the *Lycium barbarum* (*L. barbarum*) fruit. It is referred to as a potent anti-oxidant and has been a beneficial effect in the PD model by reducing the level of NO, ROS (Gao et al., 2014).

**76. *Paeoniae Alba Radix***

*Paeoniae Alba Radix*(*P. Alba Radix***)** is generally used as Chinese herbal medicine for different health problems such as epistaxis, sores, and wounds (H. Q. Liu et al., 2006). The major bioactive constituents of *P. Alba Radix* is paeoniflorin reversed the 6-OHDA induced neurological deficits in rat's model (D. Z. Liu et al., 2005, 2007).

**77. *Gynostemma pentaphyllum***

*Gynostemma pentaphyllum* (*G. pentaphyllum*), belongs to the family Cucurbitaceae. It is mainly used as an herbal tea and has several protective effects on hyperlipidemia, depression, oxidative stress, diabetes, and fatigue (Ji et al., 2018). Studies have reported that the *G. pentaphyllum* ethanol extract improved the concentrations of 3, 4-dihydroxy- phenylacetic acid, norepinephrine, DA, and homovanillic acid in PD of rats (H. S. Choi et al., 2010).

**78. *Gastrodia elata***

*Gastrodia elata* (*G. elata*) is generally used as a traditional herbal medicine to treat neurological disorders (Jang et al., 2015). *G. elata* has been shown a wide range of strong anti-oxidant and treatments for PD by reducing the level of Bcl-2/Bax ratio and ROS (An et al., 2010; I. S. Kim et al., 2011).

**79. *Cuscutae semen***

*Cuscutae semen*(*C. semen*) is generally used in herbal medicine because of its beneficial effect on immune diseases having osteoblast and oxidative stress in the brain (J. H. Liu et al., 2003; X. M. Wang et al., 2001; Yang et al., 2011). *C. semen* has improved the MPTP-induced

loss of dopaminergic neurons by reducing the generation of ROS and increasing the GPx activity in PD of mice model (Ye et al., 2014).

**80. *Macrosphyra longistyla***

A species of shrub belonging to the Rubiaceae family is called *Macrosphyra longistyla*. They have plain, large leaves. This shrub found in various tropical country.A better alternative for the treatment of Alzheimer's and other neurological illnesses is the *M. longistyla* shrub, which possesses bioactive components. The concentration of antioxidants and anticholinesterase components is found highest in the polar fractions(Elufioye et al., 2019)

## Phytochemical functional groups of polyherbal drugs in neuroprotection

Many phytochemicals have been reported to exert a neuroprotective role in vitro and in vivo models(Velmurugan et al., 2018). Poly-phenols (proanthocyanidins, phenolic acids, tannins anthocyanins, and flavonols), isoprenoids (triterpenes, saponins, diterpenes, steroids, and sesquiterpenes), alkaloids (lysergic acid diethylamide, indole alkaloids, ergot, and tropane alkaloids), and fatty acid are phytochemical constituents found in various medicinal herbs **(Fig. 1)**, which control a variety of cell receptor as well as enzyme(Chau et al., 2011; Facchini, 2001).

## Mechanism of action of polyherbal drugs in correlation with neuroprotection

Polyherbal drugs have phytochemicals that trigger the pathway of cellular response, causing the neuroprotective gene's upregulation(J. Lee et al., 2014; Naoi et al., 2019). Many pieces of evidence have revealed that the neurotrophic factors' neuroprotective effect is generally mediated by preventing the pathway of neuronal cell death shown in **Fig. 2**(Haddad, 2002; Naoi et al., 2017). Phytochemicals may stimulate the transcription factor NF-kB by inducing the expression of the anti-apoptotic and anti-oxidant enzymes. Some phytochemicals may trigger several signaling pathways through ligands which interact with various receptors such as growth factor receptor (GFR), G-protein coupled receptor (GPCR), and insulin receptor (IR)(Mattson & Cheng, 2006).These receptors initiate kinase cascades which participate in mitogen-activated protein kinase (MAPK), phosphatidylinositol-3 kinase (PI3K), and protein kinase-C (PKC)(Suvarna et al., 2017).

## Medicinal properties of herbal drugs and their clinical significance

Herbal drugs exhibited anti-inflammatory, anti-oxidant, antiapoptotic and neuroprotective effects which may have a therapeutic effect in various brain disorders (G. P. Kumar & Khanum, 2012). Other phytochemicals like flavonoids trigger the PI3K mTOR-cascade and the cAMP-response element-binding protein (CREB) pathways leading to synaptic plasticity alterations (Bakoyiannis et al., 2019). Bioactive constituents such as insoles, isothiocyanates, terpenes, curcuminoids, and diallyl sulfides have been revealed to activate more than one pathway of nuclear factor erythroid 2-related factor-2 (NRF-2) (G. P. Kumar et al., 2015). Ellison produces transient receptor potential (TRP) ion channels in the neuronal membrane, causing $Ca^{2+}$ influx, which also activates neuroprotective kinase cascade by CREB and MAPK (Gees et al., 2010; Vrenken et al., 2016). CREB causes the expression of brain-derived neurotrophic factor (BDNF), which may initiate MAPK and PI3K pathways by binding to its tyrosine receptor kinase B (TrkB) and thus cause the downstream molecule which may help cell survival and neurogenesis (H. Wang et al., 2018).

The studies have also proposed that beneficial effects of the herbal drugs on neurodegenerative disorders such as Parkinson's and Alzheimer's diseases are generally due to correlation with a glutamatergic, cholinergic, and dopaminergic system (Khazdair et al., 2018). The medicinal properties of herbal drugs have been concisely depicted in **Fig. 3.** The significance of herbal drugs on various diseases as clinical studies have been indicated in **Fig. 4.**Medicinal properties of the herbs and their active constituents along with their functions has been given in **Table 1.**

The detail of physicochemical properties of phytoconstituents is given in **Table 2**.

## Conclusion

The management of neurodegenerative diseases remains a challenge among modern herbal drugs due to their complex neuropathogenesis. The pharmacological action of many herbal extracts and phytochemicals have been reported to exert neuroprotective and antioxidant effects against neuronal apoptosis induced by exposure to excitatory toxins, toxic products of the amyloid precursor protein, free radicals, and other neurotoxins. Herbal drugs are considered effective and good sources of neuroprotective agents due to their cognitive benefits, their mechanism of action associated with the physiopathology of the diseases. The evidence collected in this review on several herbal extracts and constituents possess therapeutic effects in various animal models of neurodegenerative diseases, may be used in a search for novel therapies from medicinal herbs for these diseases. Our review has putative the many herbal drugs with potential neuroprotective effects for neurodegenerative diseases. It is expected that the information given by this review would assist the researchers to give some information and concept of the benefit of a wide variety of herbal drugs as neuroprotective agents.

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**Figure legends**

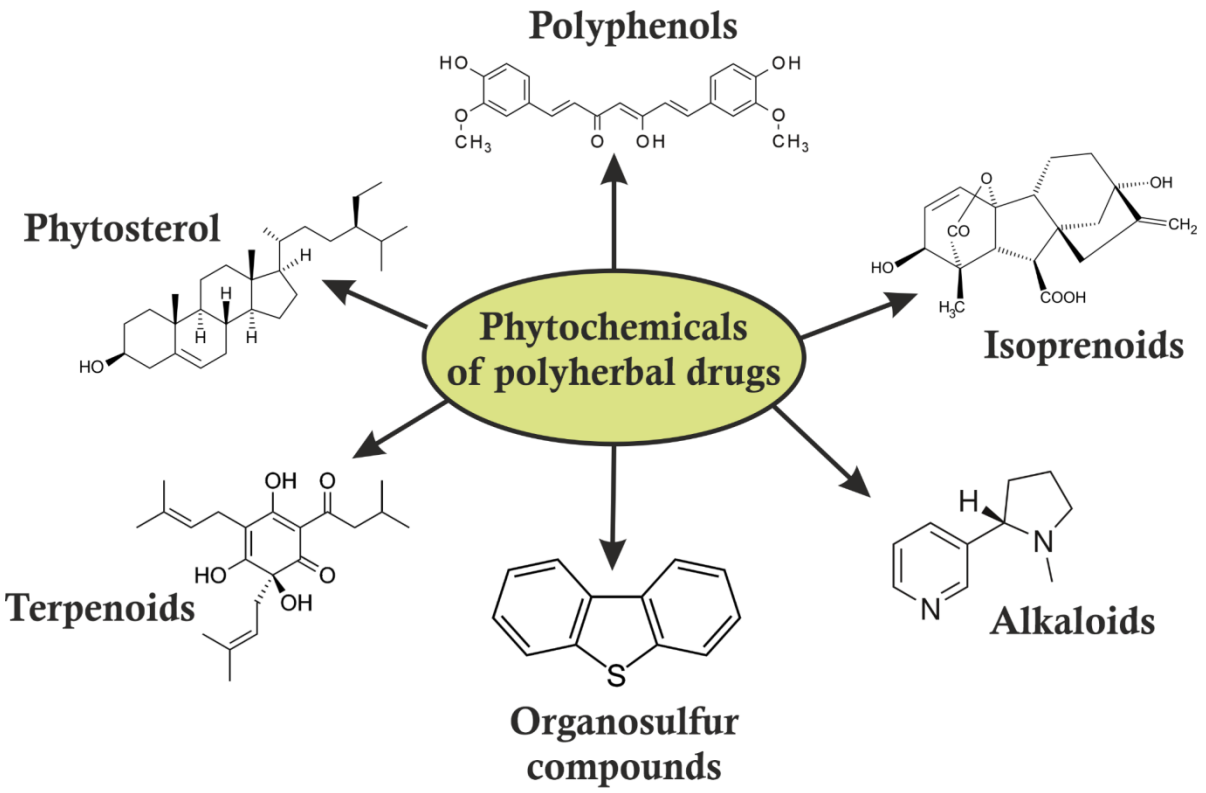


**Figure 1.**Phytochemical components of polyherbal drugs.

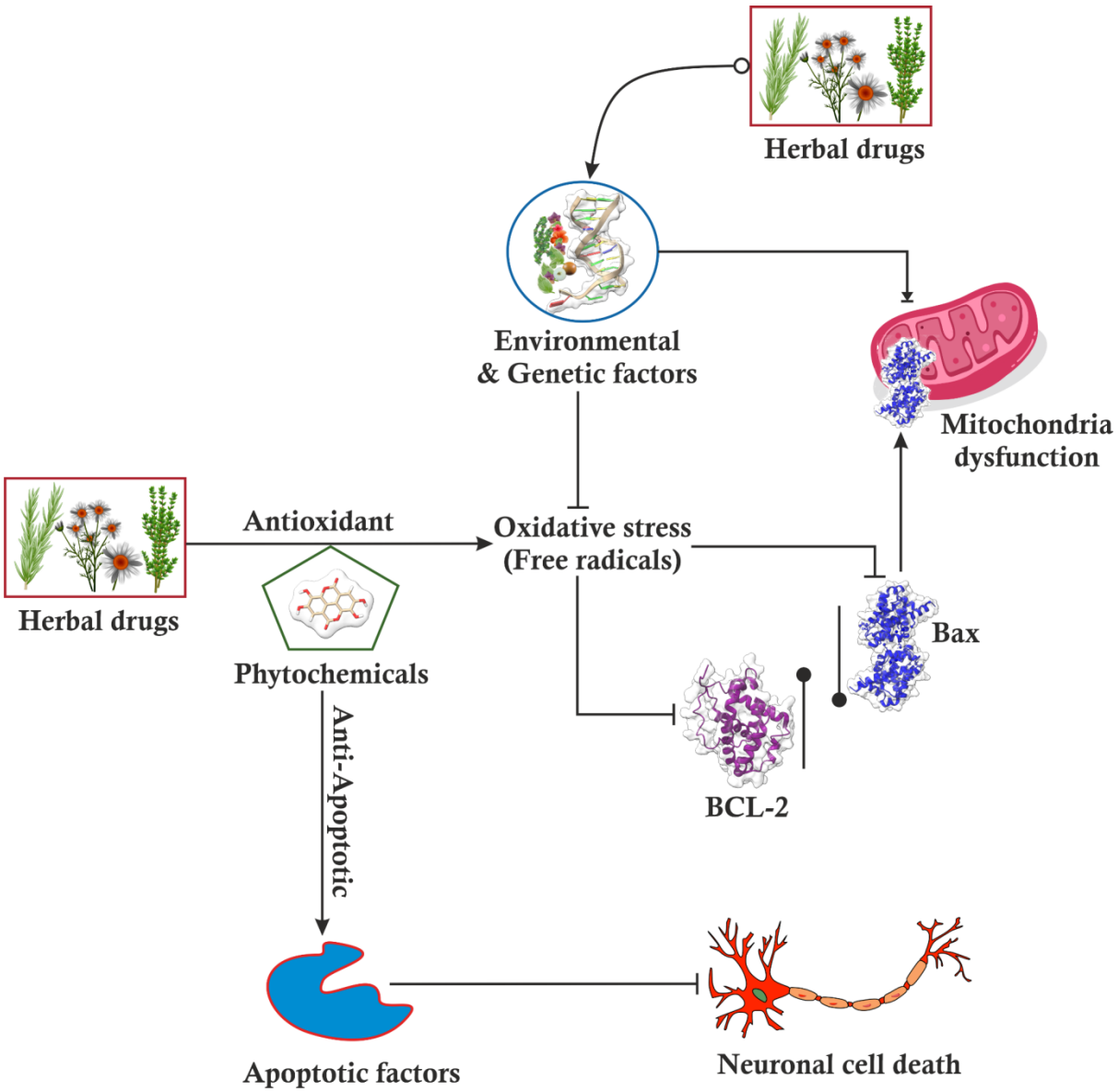


**Figure 2.** Mechanism of action of polyherbal drugs and the possible cellular targets in neurodegenerative diseases therapy.

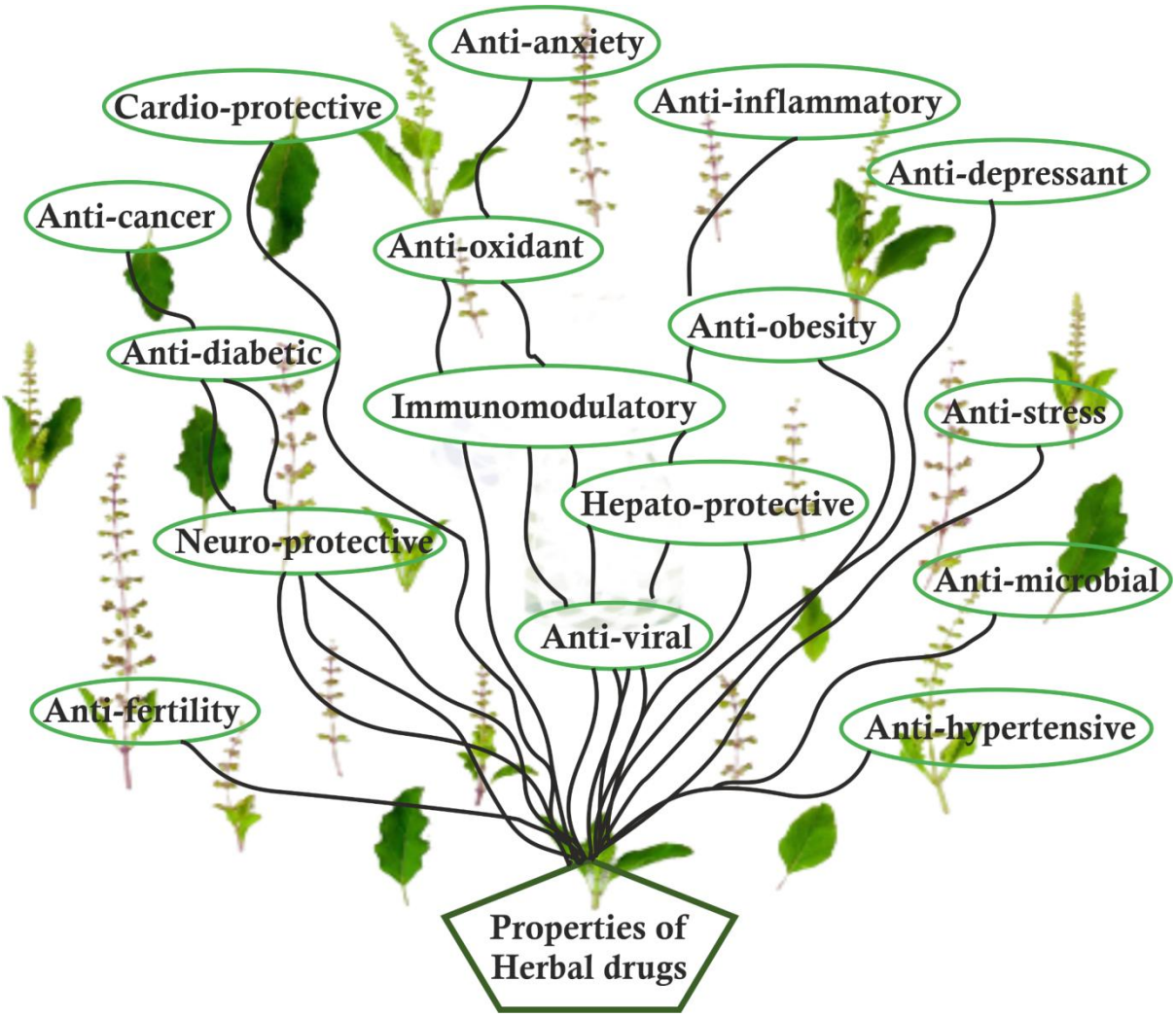


**Figure 3.** Pharmacological properties of herbal drugs.

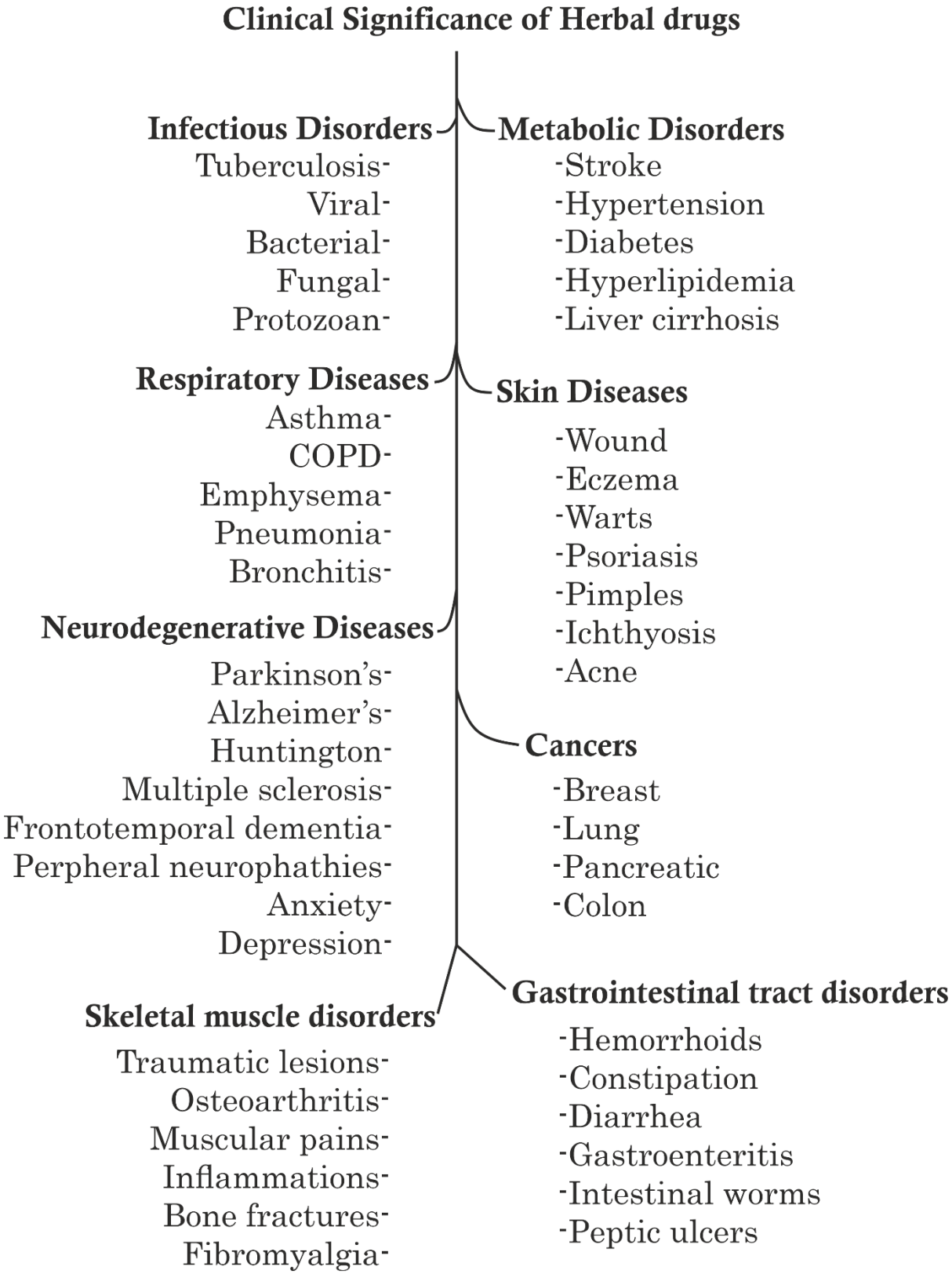


**Figure 4.**Clinical significance of herbal drugs on several diseases.

**Table 1.** Medicinal herbs, their phytochemical groups, active constituents, and functions.

| Name of medicinal herbs | Common name | Family | Phytochemical groups | Active constituents | Plant parts used | Functions | References |
|---|---|---|---|---|---|---|---|
| ***Acorus calamus*** | Sweet flag/ Vacha | Araceae | Phenylpropanoids, sterols, triterpene glycosides, triterpenoid saponins, sesquiterpenoids, monoterpenes, and alkaloids | α and β asarone, eugenol, isoeugenol, calamendiol, pregabalin | Rhizome, leaves | -Shows anticonvulsant, antidepressant, antihypertensive, anti-inflammatory, immunomodulatory, neuroprotective, cardioprotective, and anti-obesity effects | **Sharma et al., 2020** |
| ***Allium sativum*** | Garlic | Amaryllidaceae | Organosulfur compounds, flavonoids | Allicin, alliin, S-allyl cysteine, allixin | Garlic extract | -Exhibits antioxidant, anti-inflammatory, antibacterial, antifungal, immunomodulatory, cardiovascular protective, anticancer, hepatoprotective, digestive system protective, anti-diabetic, anti-obesity, neuroprotective and renal protective properties. | **Shang et al., 2019** |
| ***Bacopa monnieri*** | Brahmi | Scrophulariaceae | Saponins, alkaloids, flavonoids and glycosides | Bacoside A, B and bacopaside | Whole plant | - Possesses antioxidant, anti-inflammatory, neuroprotective, anticonvulsant, cardiotonic, bronchodilator, and peptic ulcer protection | **Chaudhari et al., 2017** |
| ***Centella asiatica*** | Jal brahmi/ Gotu kola | Apiaceae | Saponins, triterpenoid, sesquiterpene, sterols, flavonoids | Asiaticoside, asiatic acid, centelloside, brahmoside and brahminoside | Leaves, roots and rhizomes | - Shows antioxidant, neuroprotective, antipyretic, wound healing, anti-wrinkle, anti-inflammation, memory-enhancing, antidepressive, anti-stress, anxiolytic effects | **Puttarak et al., 2017** |
| ***Curcuma longa*** | Haldi/ Turmeric | Zingiberaceae | Tannins, alkaloids, phenols, steroids, flavonoids, terpenoids, triterpenes, saponin | Curcumin, d-sabinene, cinol, borneol, zingiberene, sesquiterpenes | Rhizome/ Root | - Possesses neuroprotective, anti-amyloid, antioxidant, anti-inflammatory, antiseizure, memory enhancer, antianxiety, antidepressant, analgesic, antimicrobial, and anticancer effects | **Razavi and Hosseinzadeh, 2020** |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| ***Celastrus paniculatus*** | Jyotishmati | Celastraceae | Alkaloids, tannins, flavonoids and phenolics | Celastrine and paniculatin | Whole plant | -Shows anti-amnesic, anti-arthritic, antianxiety, hypolipidemic, antioxidant, neuroprotective, antifertility, analgesic, anti-inflammatory and cardioprotective activities | **Saroya and Singh, 2018** |
| ***Coriandrum sativum*** | Dhanya | Apiaceae | Alcohols, hydrocarbons, ketones and esters | Linalool, γ-terpinene, camphor and geranyl acetate | Mostly leaves and seeds | -Exhibits antioxidant, asantidyslipidemic, anti-inflammatory, cardioprotective and neuroprotective | **Kajal and Singh, 2019** |
| ***Ferula assafoetida*** | Gum-resin/ Anghouzeh | Apiaceae | Glycosides | E-1-propenyl sec-butyl disulphide, germacrene B | Roots and Rhizome | -Shows neuroprotective, antioxidant, antiviral, antifungal, anti-diabetic, molluscicidal, sedative, analgesic, antiperiodic, antipyretic, laxative, anti-inflammatory, anti-epileptic, antispasmodic and antihypertensive effects | **Khazdair et al., 2018** |
| ***Thymus vulgaris*** | Thyme | Lamiaceae | Monoterpenes, flavonoids and phenolic | Thymol, carvacrol, thymol methyl ether | Leaves and flowering tops | -Having neuroprotective, anti-microbial, anti-spasmodic, antioxidant, expectorant, anti-septic, anti-helmintic anti-viral, astringent, anti-inflammatory, antimutagenic and analgesic effects | **Javed et al., 2019** |
| ***Zataria multiflora*** | Avishan-e-Shirazi | Lamiaceae | Monoterpenes | Carvacrol, thymol and linalool | Leaves, flower and dried aerial parts | -Exhibits antioxidant, neuroprotective antimicrobial, antifungal, anti-seizure, anti-nociceptive, anti-candida, anti-septic, anti-aphtous, analgesic, carminative and anti-inflammatory effects. | **Eskandari-Roozbahani et al., 2019** |
| ***Galanthus nivalis*** | Sarpagandha/Snowdrop | Amaryllidacea | Alkaloids | Isoquinoline galantamine, lykorine and tazetine | Whole plant (mainly flower and bulb) | -Enhances memory and cognition, antioxidant, neuroprotective, anti-tumor, anti-aging, anti-viral, anti-fungal activities. | **Benedec et al., 2018** |
| ***Ginkgo biloba*** | Maidenhair tree/Living fossil | Ginkgoaceae | Terpenoids, flavanoids and steroids | Bilobalide, ginkgolides, kaemferal, quercetin, isorhamneting sitosterol and | Leaves, seeds and fruit | -Exhibits antioxidant, neuroprotective, anti-asthmatic, antidepressant, anti-anxiety, wound healing, anti-inflammatory, radical-scavenging and anti-apoptosis effects | **Singh et al., 2019** |

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| | | | | stigmasterol | | | |
| ***Camellia sinensis*** | Green tea | Theaceae | Alkaloid, polyphenol, caffeine, steroids flavonoids, terpenoids and Tannin | Catechin, epicatechin gallate, epigalloca-techin, epigallocatechin gallate | Leaves and flowers | -Shows antioxidant, anti-inflammatory, antidepressive, neuroprotective, anti-aging and anti-stress activities | **Malar et al., 2020** |
| ***Camellia sinensis*** | Black tea | Theaceae | Tannin, flavonoid, Alkaloid, polyphenol, caffeine, steroids and terpenoids | Theaflavins, theaflavin-3-gallate | Leaves and flowers | -Possesses antioxidant, neuroprotective, anti-inflammation, anti-carcinogen, antibacterial, anti-viral and anti-apoptotic effects | **Chen et al., 2018** |
| ***Glycyrrhiza glabra*** | Liquorice/ Yashtimadhu | Leguminosae | Triterpenoid, saponins | Glycyrrhizin | Root/ Rhizomes | -Exhibits neuroprotective, hepatoprotective, antidepressant, antioxidant, memory enhancer, anti-inflammation, antiviral, antibacterial, anti-tumour, anti-ulcer, anti-HIV and anti-osteoporotic activities | **Karthikkeyan et al., 2020** |
| ***Hypericum perforatum*** | Perforate St. John's-wort | Hypericaceae | Flavonoids | Hyperoside, Rutin | Flowers, leaves and stems | -Shows antioxidant, anti-inflammatory, neuroprotective, anti-depressant, wound healing and anti-nociceptive effects | **Oliveira et al., 2016** |
| ***Lycopodium serratum*** | Club mosses | Lycopodiaceae | Triterpenoids | Huperzine A, caffeic acid and ferulic acid | Spores, Whole herb | -Having antioxidant, anti-convulsant, neuroprotective, anti-inflammatory, anti-nociception and anti-apoptosis effect. | **Ohba et al., 2020** |
| ***Melissa officinalis*** | Lemon balm | Lamiaceae | Flavonoids, polyphenols, monoterpene | Rosmarinic acid, ursolic acid | Leaves | -Enhances sedative, carminative, antispasmodic, antibacterial, antiviral, anti-inflammatory, antioxidant, and neuroprotective effects | **Mahboubi, 2019** |
| ***Ocimum sanctum*** | Tulsi | Lamiaceae | Alkaloids, flavonoids, phenolics, essential oils, tannins and saponins | Oleanolic acid, rosmarinic acid, ursolic acid, eugenol, β-elemene β-caryophyllene | Leaves and roots | -Shows antioxidant, neuroprotective, antidiabetic, antiulcer, anticancer, antifungal antimicrobial, antifertility, hepatoprotective, antispasmodic, analgesic and antiemetic effect. | **Hening et al., 2018** |

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| | | | | and germacrene | | | |
| ***Panax ginseng*** | Asian ginseng /Chinese ginseng/ Korean ginseng | Araliaceae | Triterpenoidal, saponins, poly-saccharides and phenolic | Ginsenoside | Roots and rhizomes | -Enhances anti-aging, anti-diabetic, immunoregulatory, anti-cancer, neuroprotective, wound and ulcer healing activities. | **Ru W et al., 2015** |
| ***Rosmarinus officinalis*** | Rosemary/ Satapatrika | Lamiaceae | Flavonoids, phenolic, essential oil | Carnosic acid, carnosol, caffeic acid | Leaves | -Exhibits neuroprotective, antioxidant, anti-carcinogenic, cognition-enhancing, antinociceptive, anti-inflammatory, anti-apoptotic activities | **Rasoulian et al., 2019** |
| ***Salvia officinalis*** | Sage | Lamiaceae | Flavonoids, polyphenols, monoterpene | Ellagic acid, rosmarinic acid | Flowers, leaves and stem | -Having anticancer, anti-inflammatory, neuroprotective anti-nociceptive, antioxidant, antimicrobial, antimutagenic, antidementia, hypoglycemic and hypolipidemic effects | **Ghorbani and Esmaeilizadeh , 2017** |
| ***Terminalia chebula*** | Harar/ Chebulic myrobalan | Combretaceae | Triterpenoid, phenolic, tannin | Ellagic acid, gallic acid | Dried fruit | -Shows antioxidant anti-inflammatory, neuroprotective and hepatoprotective | **Shen et al., 2017** |
| ***Tinospora cordifolia*** | Giloe | Menispermaceae | Terpenoid, alkaloid, glycosides, lignans, steroids | Tinosporiside, palmitoside F,cardioside, tinosporaside | Root, stem and leaves | -Possesses anti-oxidant, neuroprotective, anti-hyperglycemic, anti-stress, immuno-modulating, anti-neoplastic, anti-fertility, anti-cancer and memory-enhancing effects | **Sharma et al., 2019** |
| ***Withania somnifera*** | Ashwagandha | Solanaceae | Steroidal lactones, alkaloids, flavonoids and tannin | Sitoindoside, Withanoside IV, VI, Withaferin A and Withanolide A | Root, leaves | -Exhibits Memory enhancer, Antioxidant, neuroprotective, immunomodulator, free radical scavenger, anti-stress and anti-cancer agent. | **Shivamurthy et al., 2016** |
| ***Mucuna pruriens*** | Kapikacho/ Kevach | Fabaceae | Alkaloids, phytosterols, triterpenes | Glycoside, gallic acid, glutathione, Levodopa | Seed, Root and Stem | -Possesses anticholesterolemic, neuroprotective, antioxidant, antidiabetic, sexual enhancing, anti-inflammatory, anticancer antimicrobial and antivenom activities | **Pathania et al., 2020** |
| ***Emblica*** | Amla | Euphorbia | Tannins, flavonoids, | Gallic acid, | Fruit, seed, | -Having memory enhancer, antioxidant, | **Husain et al.,** |

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|---|---|---|---|---|---|---|---|
| ***officinalis*** | | ceae | saponins, terpenoids | ellagic acid, rutin, quercetin, and catechol | leaves, root bark, flower | antimicrobial, anti-inflammatory, neuroprotective hepatoprotective | **2019** |
| ***Lepidium meyenii*** | Black maca | Brassicaceae | Alkaloids, fatty acids, carbamic acid | Glucosinolates, macamides, macaenes | Hypocotyl, root, stem, leaves | -Exhibits antifatigue, neuroprotective, anti-depressant, anti-inflammatory and antioxidant | **Yu et al., 2020** |
| ***Nardostachys jatamansi*** | Jatamansi/ Spikenard | Caprifoliaceae | Glycosides, flavanoids, steroids, saponins, phenolic, alkaloids | Valeranone, sesquiterpene and coumarins | Root and rhizome | -Enhances learning and memory, sedative, anti-stress, antioxidant and meuroprotective | **Khan et al., 2012** |
| ***Pueraria lobata*** | Kudzu | Leguminosae | Flavonoid, Polyphenol, glycoside and terpenoid | Puerarin genistin | Root, flower and leaves | -Having anti-oxidative, neuroprotective, anti-inflammatory, anti-hypertension, antidepressant effects | **Xiao et al., 2017** |
| ***Prunus amygdalus*** | Almond/ Badam | Rosaceae | Polyphenolic, flavonoid | Biochanin A, genistein, daidzein, glycitein and formononetin | Nuts and oil | -Shows enhance learning-memory, antistress, antioxidant, neuroprotecctive activities | **Nandagopal and Ali khan, 2020** |
| ***Zingiber officinale*** | Ginger/ Adrak | Zingiberaccae | Phenolic and terpene | Gingerols, shogaols, paradols and essential oils | Dried rhizomes, root | -Exhibits antioxidant, anti-inflammatory, antinausea, cardiovascular protective, antimicrobial, anticancer, antiobesity, antidiabetic, neuroprotective, respiratory protective, and antiemetic activities | **Mao et al., 2019** |
| ***Commiphora whighitii*** | Guggal/ Indian bdellium | Burseraceae | Terpenoidal, steroids, flavonoids, guggultetrols, lignans, sugars, and amino acids | Guggulsterone-E & Z | Oleo-gum resin | -Possesses activities like hypolipidemic, antiobesity, anti-inflammatory, anti-tumor, cardioprotective, neuroprotective, hepatoprotective, and anti-amnesic effects | **Kunnumakkara et al., 2018** |
| ***Convolvulus pluricaulis*** | Shankhpushpi | Convolvulaceae | Alkaloids, terpenoids, phenolics, flavonoids and coumarins | Scopolin andScopoletin | Whole plant | - Having memory booster, anti-amensic, anti-depressant, anti-stress, antioxidant, anti-fungal, anti-bacterial, anti-diabetic, anti-ulcer, anti-catatonic, hypolipidemic, immunomodulatory, analgesic, cardiovascular protective and anxiolytic activities | **Sethiya et al., 2019** |
| ***Ficus carica*** | Anjeer | Moraceae | Flavonoids, phenolic acids, | Quercetin, rutin | Fruit, root, | -Exhibits anti-oxidant, neuroprotective | **Essa et al.,** |

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|---|---|---|---|---|---|---|---|
| | | | coumarins, sterols and volatiles | | leaves | antibacterial, anti-fungal, antispasmodic, antiplatelet, antipyretic, anti-HSV, hypoglycemic, anticancer, hepatoprotective, antituberculosis and hypo-lipidemic and memory enhancing activities | **2015** |
| ***Acori graminei*** | - | Acoraceae | Phenols, flavonoids, lectins and saponins | Eugenol and beta-asarone | Rhizome | -Shows neuroprotective, antioxidant, anti-hyperlipidemic, anti-apoptosis, anti-inflammatory antibacterial activities | **Yan et al., 2020** |
| ***Anacyclus pyrethrum*** | AkkarKarha/ Tigandizt | Asteraceae | Polyphenols, tannins, coumarins, sterols, triterpenes and alkaloids | Pellitorin, anacyclin, phenyl-ethyl amine, inulin and sesamin | Roots | -Possesses neuroprotective, antiepileptic, anti-inflammatory and antioxidant effects | **Manouze et al., 2019** |
| ***Angelica gigashas*** | Chora | Apiaceae | Polysaccharide, phenolics, alkaloids, essential oils, steroids, lignins, resins and tannins | Decursin, decursinol angelate and decursinol | dried root | -Exhibits antimicrobial, anticancer, antitumour, anti-inflammatory, hepatoprotective and nephroprotective effects | **Park et al., 2020** |
| ***Asparagus recemosus*** | Shatavari/ Shatamull | Asparagaceae | Flavonoids, alkaloids, steroids, terpenoids, glycosides, tannins, terpenoids, and saponins | Adscendi-B, racemofuran, asparanin-A, Shatvarin and sarsapogenin | Root, fruits and leaves | - Possesses antiulcer, antioxidant, antidiarrhoeal, antidiabetic, neuroprotective and immunomodulatory activities | **Alok et al., 2013** |
| ***Caesalpinia crista*** | Kantkarej/Bonducella nut | Fabaceae | Flavonoids, alkaloids, tannins, triterpenoids, coumarin and glycosides | Natin, bonducin | Dried seed, leaves | -Shows anti-microbial, anti-inflammatory, anti-oxidant and neuroprotective | **Ravi et al., 2018** |
| ***Carica papaya*** | *Papaya/Pawpaw* | Caricaceae | Alkaloids, saponins, tannins and terpenoids | Papain, chymopapain | Leaves, fruit, seed, flower, and root | - Possesses antitumor, immunomodulatory, antibacterial, antioxidative, anti-inflammatory and neuroprotective | **Savla et al., 2017** |
| ***Clitoria ternatea*** | Aparajita/ Butterfly Pea | Fabaceae | Triterpenoids, flavonol glycosides, anthocyanins and steroids | Cliotides, ternatins, taraxerol and taraxerone | Seed, leaves and root | -Exhibits memory enhancing, anti-acetylcholinesterase, antiasthmatic, anti-inflammatory, antipyretic, and antiamnesic activities | **Wu et al., 2020** |

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|---|---|---|---|---|---|---|---|
| ***Corydalis tuber*** | YuanHu | Papaveraceae | Alkaloids and terpenoids | Pseudocoptisine and Benzyl-isoquinoline | Root/tuber | -Having sedative, anti-epileptic, antidepressive, anti-anxiety, anti-myocardial infarction, anti- antithrombotic, antimicrobial, anti-inflammation, and anticancer effects | **Tian et al., 2020** |
| ***Desmodium gangeticum*** | Salaparni/ Anshumati | Fabaceae | Alkaloids, tannins, phenols, flavonoids and terpenoids | Pterocarpenoid, gangetin, gangetinin and desmodin | Whole plant/ root | -Shows antioxidant, antiemetic, anti-inflammatory, anti-depressant and anti-leishmanial activities | **Mahesh et al., 2012** |
| ***Foeniculum vulgare*** | Sweet fennel/ Moti saunf | Apiaceae | Volatile compounds, flavonoids, phenolic compounds, fatty acids, and amino acids | Anethole, estragole, fenchone and limonene | Whole plant | -Possesses antimicrobial, anti-inflammatory, antipyretic, antispasmodic, antithrombotic, antitumor, hepatoprotective and memory enhancing | **Shamkant et al., 2014** |
| ***Geissospermum vellosii*** | Pao pereira | Apocynaceae | Indole alkaloids | Flavopereirine, geissoschizolin, geissoschizone and geissospermine | Stem bark | -Exhibits antioxidant anticholinesterase, anti-neuroinflammatory, antinociceptive and neuroprotective | **Lima et al., 2020** |
| ***Hibiscus sabdariffa*** | Roselle | Malvaceae | Anthocyanins, terpenoids, steroids, alkaloids, quinones, naphthalene and polyphenols | Protocatechuic acid and quercetin | Red calyxes | -Having antioxidant, antidepressant, sedative, anti-inflammatory, antiproliferative, antimicrobial and neuroprotective | **El-Shiekh et al., 2020** |
| ***Hippophae rhamnoides*** | Seabuckthorn | Elaeagnaceae | Flavonoids, phenolic acids, tannins, polyprenols, dolichols, triterpene and sterols | Kaempferol, quercetin, isorhamnetin, catechin, procyanidins and gallic acid | Leaves, fruits | -Shows antioxidant, immunomodulatory, anti-atherogenic, anti-stress, hepatoprotective and neuroprotective | **Ma et al., 2020** |
| ***Mimusops elengi*** | Spanish cherry/ Maulsari | Sapotaceae | Saponins, tannins, sterols, mannitol, triterpenoids, fatty oil | β-amyrin, bassic acid, taraxerone, taraxerol, α-spinasterol, sodium ursolate betulinic acid and quercitol | Leaves, root, fruit, seed, flower, stem bark | -Exhibits activities like antibacterial, antifungal, anticariogenic, free radical scavenging, anti hyperglycemic, gastro-protective, anti-nociceptive antiviral, memory and cognitive enhancing | **Gami et al., 2012** |

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| ***Murraya koenigii*** | Curry patta/ Kari patta | Rutaceae | Terpenoids, flavonoids, phenolics, carbohydrates, carotenoids, vitamins and nicotinic acid | Mahanine, mahanimbine, isolongifolene, koenimbine, girinimbine, isomahanine, koenoline and O-methylmurrayamine | Leaves, fruit, roots, bark | -Shows antioxidant, antidiabetic, anti-inflammatory, antimicrobial, antitumor, and neuroprotective activities | **Balakrishnan et al., 2020** |
| ***Nelumbo nucifera*** | Indian Lotus/ Kamal | Nelumbonaceae | Alkaloids, flavonoids, triterpenoid, saponins, polyphenolics | Catechin, nuciferine, lotusine, pronuciferine, rutin, kaempferol, quercetin and linalool | Whole plant | -Having antidiabetic, anti-inflammatory, antioxidant and neuroprotective | **Paudel and Panth, 2015** |
| ***Phyllanthus amarus*** | Bhui-amla | Phyllanthaceae | Tannins, terpenes, alkaloids, glycosidic compounds, saponins, and flavones | Hypophyllanthin, phyllanthin, Quercetin, gallic acid, gallotannins | Leaves, stems and fruit | -Shows good antibacterial, antiviral, antioxidant, anti-inflammatory, antidiabetic, anticancer, immunomodulatory, neuroprotective, hepatoprotective, nephroprotective and anti-amnesic activities | **Ismail et al., 2020** |
| ***Scrophularia buergeriana*** | Bei xuan shen/Figworts | Scrophulariaceae | Glycoside esters, alkaloids, flavonoids, triterpenoids, iridoids and resin glycosides | Iridoid, crypthophilic acids | Root | -Exhibits antioxidants, hepatoprotective, antitumor, anti-inflammatory, antiprotozoal, neuroprotective and anti-amnestic effects | **Pasdaran and Hamedi, 2017** |
| ***Teucrium polium*** | Felty germander/ Jaada | Lamiaceae | Terpenoids and flavonoids | α-pinene, germacrene, γ-cadinene, and α-cadinol | Whole plant | -Shows antioxidant, neuroprotective, anticancer, anti-inflammatory, hypoglycemic, hepatoprotective, hypolipidemic, antibacterial and antifungal activities | **Atki et al., 2019** |
| ***Thespesia populnea*** | Indian tulip tree | Malvaceae | Carbohydrate, protein, amino acids, phenol, flavonoids, glycosides, | Kaempferol, Quercetin, thespesin, | Stem bark, leaves | -Possesses antifertility, antibacterial, anti-inflammatory, antioxidant, hepatoprotective and memory enhancing activities | **Mohini et al., 2017** |

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| | | | polyphenols | gossypol, Gallic acid, catechin, and myricetin | | | |
| ***Vigna radiate*** | Mung bean | Fabaceae | Polyphenols, Polysaccharides, Peptides | Vitexin and isovitexin | Seed, leaves and seedpod | -Shows antihypertensive, anticancer, anti-melanogenesis, hepatoprotective, immunomodulatory and neuroprotective activities | **Hou et al., 2019** |
| ***Vitex negundo*** | Nirgundi | Verbenaceae | Flavonoids, lignans, terpenoids and steroids | α-pinene, 1,8-cineole, linalool, caryophyllene oxide | Whole plant | -Possesses antimicrobial, anti-androgenic, anti-osteoporotic, and anti-tumour, anti-cancer, anti-inflammatory, anti-oxidant, anti-hyperglycemic, hepatoprotective and neuroprotective | **Siddiqui et al., 2018** |
| ***Zizyphus jujube*** | Jujube/Bada ber | Rhamnaceae | Phenyl glycosides, flavonoid, terpenoid, sugar, organic minerals and vitamin C | Ziziphin, pomonic acid, benthamic acid, terminic acid, oleanic acid, betulinic acid, apigenin, jujuboside B, traumatic acid | Fruit, seed and leaves | -Exhibits anti-tumor, antioxidant, anti-inflammatory, hepatoprotective, neuroprotective, gastrointestinal protective, sedative effects | **Bai et al., 2016** |
| ***Ilex paraguariensis*** | Yerba mate | Aquifoliaceae | Phenolic compounds, xanthines, alkaloids, flavonoids, tannins, triterpenoid, saponins, minerals and vitamins | Caffeic acid, chlorogenic acid, quercetin, kaempferol, and rutin | Leaves | -Possesses antioxidant, anti-obesity, chemopreventative, anti-inflammatory, antimicrobial, cardioprotective and neuroprotective | **Kujawska, 2018** |
| ***Delphinium denudatum*** | Jadwar | Ranunculaceae | Alkaloids, flavonoids, phenolic compounds, fatty acids, terpenoids, and steroids | Delphocurarine, staphisagrine, delphine, condelphine, denudatin, diterpenoid, β-sitosterol | Root | -Shows sedative, neuroprotective, anti-bacterial, analgesic, anti-inflammatory, anti-depressant and anti-cancer | **Sitan et al., 2020** |

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| ***Magnolia officinalis*** | Houpu magnolia/ Him champa | Magnoliaceae | Neolignans, lignans, sesquiterpenes, alkaloids, and phenylethanoid glycosides | Magnolol, honokiol, magnolianone, erythro-honokitriol, and threo-honokitriol | Bark, Whole herb | -Exhibits anti-bacterial, anti-oxidant, anti-inflammatory, anti-anxiety, anti-gastric ulcer, antitumor, neuroprotective, and cardiovascular protection activities | **Ge L et al., 2017** |
| ***Punica granatum*** | Pomegranate | Punicaceae | Phenolic acids, flavonoids, tannins | Gallic acid, apigenin, luteolin, rutin, punicafolin, corilagin and granatin | Whole herb | -Exhibits antioxidant, neuroprotective, anti-inflammatory, antidiabetic, anti-allergic and antiplatelet activities | **Singh et al., 2018** |
| ***Crocus sativus*** | Saffron | Iridaceae | Phenolics, flavonoids, monoterpenoids and Saffron | Crocin, crocetin, picrocrocin and safranal | Fruits, seeds flowers, leaves, stem and roots | -Possesses antioxidant, anti-inflammatory, hepato-protective, cardi-protective, anti-diabetic, neuroprotective and anti-tumour activity | **Bian et al., 2020** |
| ***Nigella sativa*** | Black Cumin/Kalonji | Ranunculaceae | Alkaloids, triterpene saponin, protein, carbohydrates, vitamins, fatty oil and minerals | Thymoquinone, thymohydroquinone, dithymoquinone, p-cymene and carvacrol | Seed | -Exhibits antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepato-protective, renal protective, gastro-protective, neuroprotective and antioxidant activities | **Ahmad et al., 2013** |
| ***Cissampelos pareira*** | Laghu patha/ abuta | Menispermaceae | Saponins, gums, carbohydrates, alkaloids, terpenoids, tannins and proteins | Tetrandrine, magnoflorine, magnocurarine, curine, Magnoflorine and magnocurarine | Root, stem, seed, bark and leaves | -Shows memory enhancing, analgesic, antioxidant, anti-inflammatory, antipyretic, antitumor and antileukemic activities | **Akram and Nawaz, 2017** |
| ***Mellisa officinalis*** | Lemon balm/ common balm | Lamiaceae | Phenolic acids, tannins, flavonoids, terpenes and volatile compounds | Neral, geranial, citronellal, geraniol, luteolin, caffeic | Leaves and stem | -Exhibits antioxidant, antidepressant, hepatoprotective, antimicrobial, antiviral, anti-inflammatory, anti-nociceptive, anti-diabetic, antispasmodic and sedative effects | **Elena-Alina et al., 2018** |

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| | | | | acid, hesperidin, naringin, coumarinic acid, rosmarinic acid, oleanolic and ursolic acid | | | |
| ***Moringa oleifera*** | Drumstick tree/ horse radish tree | Moringaceae | Phenolic acids, flavonoids, alkaloids, saponins, phytosterols, natural sugars, vitamins, minerals and organic acids | Rutin, quercetin, kaempferol, myricetin, procyanidins, all- E- lutein and vanillin | Leaves, roots, seed, bark, fruit, flowers and immature pods | -Possesses hepatoprotective, anti-inflammatory, antinociceptive, anti-atherosclerotic, antitumor, antioxidant, cardioprotective, antimicrobial and neuroprotective activities | **Dhakad et al., 2019** |
| ***Myristica fragrans*** | Nutmeg | Myristicaceae | Vitamins, carotenoids, terpenoids, alkaloids, flavonoids, lignans and phenolics | Eugenol, methyleugenol, methylisoeugenol, elemicin, myristicin, Sabinene, carvacrol | Seed and aril | -Shows memory enhancer, aphrodisiac, antioxidant, neuroprotective, antimicrobial, antidiarrheal, anti inflammatory and anti-cancer effects | **Ha et al., 2020** |
| ***Evolvulus alsinoides*** | Dwarf morning-glory/ Vishnukranti | Convolvulaceae | Steroids, reducing sugars, alkaloids, phenolic compounds, saponins, tannins, flavonoids, amino acids, terpenoids and cardioglycosides | Scopoletin, umbelliferone, scopolin and 2-methyl-1,2,3,4-butanetetrol | Whole plant | -Having hepatoprotective, neuroprotective, Chemopreventive, anticancer, anti-microbial, antioxidant and antidiabetic activities | **Sundaramoorthy et al., 2020** |
| ***Scutellaria baicalensis*** | Baikal skullcap/Chinese skullcap | Labiatae | Lignins, flavones and amides | Catechin, baicalein wogonoside, aglycones and wogonin | Root and rhizomes | -Possesses anticancer, anti-inflammatory, hepatoprotective, antibacterial, antiviral, antioxidant, anticonvulsant and neuroprotective | **Billah et al., 2019** |
| ***Erythrina velutina*** | Mulungu | Fabaceae | Alkaloids, terpenes, flavonoids and phenolic acids | Hesperidin, abssinine, homoesperidin, sigmoidin C, | Leaves, bark | -Shows neuroprotective, anxiolytic, sedative, anticonvulsant, antinociceptive, antioxidant and anti-inflammatory | **Silva et al., 2016** |

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| | | | | rizonic acid | | | |
| ***Peganum harmala*** | Syrian rue | Zygophyllaceae | Alkaloids, saponins, flavonoids, tannins, glycosides, terpenoids and steroids | Harmine, peganine, harmaline, β-carbolines and quinazoline | Seeds, leaves, fruit, flower, bark and root | - Exhibits neuroprotective anticancer, antihypertensive, antidepressant, hallucinogenic and antimicrobial activities | **Iranshahy et al., 2019** |
| ***Carthamus tinctorius*** | Safflower | Asteraceae | Flavonoid, alkaloid, fatty acid, polyphenolic, phytosterols, free sugar and mineral | Carthamin, carthamidin, isocarthamidin, daucosterol, beta-sitosterol hydroxysafflor | Flowers, seed oil | -Shows antibacterial, anticoagulant, antioxidant, analgesic, anti-inflammatory, antidiabetic and neuroprotective effects | **Mani et al., 2020** |
| ***Juglandis Semen*** | Walnut | Juglandaceae | Alkaloids, flavonoid, saponins and pheonols | Ellagic acid, caffeic acid, chlorogenic, p-coumaric, ferulic, sinapic, and syringic acid | Seed, leaves, fruits, bark, flowers | -Exhibits anti-inflammatory, antioxidants, neuroprotective, antimicrobial , antitumor activities | **Chauhan and Chauhan, 2020)** |
| ***Lycium barbarum*** | Goji berries/ Matrimony vine | Solanaceae | Flavonoids, lignan, sterols, phenolic acids, alkaloids, glycosides, polysaccharide, terpenoids and essential oil | Scopoletin, beta-sitosterol, p-coumaric acid, lutein, zeaxanthin, daucosterol and betaine | Root bark, leaves and fruit | -Shows antioxidant, neuroprotective, hepatoprotective and antitumor activities | **Benchennouf et al., 2017** |
| ***Paeoniae radix alba*** | Bai shao/ Chinese peony | Ranunculaceae | Terpenoids, polyphenolic compounds, monoterpene glycosides and volatile oils | Paeoniflorin, albiflorin, oxypaeoniflori, benzoyl paeoniflorin, and benzoyl hydroxy paeoniflorin | Root | -Exhibits antioxidant, hepatoprotective, anti-inflammatory, neuroprotective, antidepressant, sedative, analgesic and anti-tumor anticonvulsant activities | **Tan et al., 2020** |

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| ***Gynostemma pentaphyllum*** | Sweet tea vine/ Jiaogulan | Cucurbitaceae | Phenolic, saponin, sterols, flavonoid, polysaccharides | Rutin, quercetin, gallic acid and gypenoside | Leaves and stems | -Shows antioxidant, anti-inflammatory, anticancer, antiproliferative, immunomodulatory, hepatoprotective, antifatigue, antimicrobial, antiaging, antiulcer, lipid metabolism regulatory and neuroprotective effects | **Xiaolong et al., 2018** |
| ***Gastrodia elata*** | Tianma | Orchidaceae | Phenolics, polysaccharide, organic acids, sterols | Gastrodin | Tuber/ rhizome | -Possesses neuroprotective, analgesic, anti-vertigo, antispasmodic, anti-epileptic, anti-convulsive, antidepressant, hypnotic, anxiolytic, sedative, lowering blood pressure, memory-improving and anti-aging effects | **Liu et al., 2018** |
| ***Cuscutae semen*** | Cuscuta seed/ Chinese dodder seed | Convolvulaceae | Flavonoids, phenolic compounds, polysaccharide, alkaloids | Hyperoside, quercetin, astragalin, kaempferol, isorhamnetin, vanillin, | Seed | -Shows immunomodulatory, hepatoprotective, antioxidant, anti-inflammatory, antiaging, and memory enhancing activities | **Song et al., 2016** |

**Table 2.** List of phytoconstituents drugs with physicochemical properties.

| S. No. | Name of Phytoconstituents | Status | Formula | Pubchem CID | PDB | LogP | Mw | TPSA (Å²) | MR | Rings | Target | Role |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1.** | Andrographolide | Investigational | C20H30O5 | 5318517 | - | 2.2 | 350 | 87 | 94.93 | 2 | - | Anti-Inflammatory |
| **2.** | Apigenin | Experimental | C15H10O5 | 5280443 | 5UQT | 3.02 | 270 | 87 | 73.02 | 3 | Transferase | Antineoplastic Agent |
| **3.** | Artemisinin | Investigational | C15H22O5 | 17396660 | - | 4.5 | 282 | 53.99 | 68.68 | 4 | Kinases | Antiparasitic |
| **4.** | Atropine Sulphate | Approved | C17H23NO3 | 174174 | - | 1.83 | 289 | 49.77 | 80.82 | 3 | - | Anticholinergic |
| **5.** | Bargapten | Investigational | C12H8O4 | 2355 | - | 2.12 | 216 | 48.67 | 56.85 | 3 | - | Atopic Dermatitis |
| **6.** | Berberine | Approved | C20H18NO4 | 2353 | 1JUM | -0.18 | 336 | 40.8 | 93.52 | 5 | Transcriptional Repressor | Parasitic And Fungal Infections |
| **7.** | Betulinic Acid | Approved | C30H48O3 | - | - | 5.34 | 456.7 | 57.53 | 132.63 | 5 | - | - |
| **8.** | Caffeine | Approved | C8H10N4O2 | 2519 | 1C8L | -0.24 | 194.1 | 58.44 | 49.83 | 2 | Adenosine Receptor | - |
| **9.** | Capsaicin | Approved | C18H27NO3 | 1548943 | 2N27 | 3.75 | 305.4 | 58.56 | 90.32 | 1 | Trpv1 Receptor | Analgesic Agent |
| **10.** | Chlorogenic Acid | Investigational | C16H18O9 | - | - | 0.17 | 354.3 | 164.75 | 83.23 | 2 | - | Cancer Treatment |
| **11.** | Cholesterol | Approved | C27H46O | 5997 | 1LRI | 7.02 | 386.6 | 20.23 | 120.62 | 4 | - | Cardiovascular |
| **12.** | Colchicine | Approved | C22H25NO6 | 2833 | 3E22 | 1.59 | 399.4 | 83.09 | 111.38 | 3 | Tubulin Beta | Relief Of Pain |
| **13.** | Curcumin | Approved | C21H20O6 | 969516 | 6HDR | 3.62 | 368.3 | 93.06 | 103.81 | 2 | - | - |
| **14.** | Diosmetin | Experimental | C16H12O6 | 5281612 | 6M8D | 3.06 | 300 | 96.22 | 79.38 | 3 | Trkb Receptor | - |

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| **15.** | Diosmin | Approved | C28H32O15 | 5281613 | - | 0.08 | 608.5 | 234.2 | 58.93 | 5 | Tnf Alpha, Vegf-C, Il-6 | Vascular Health |
| **16.** | Ellagic Acid | Investigational | C14H6O8 | 5281855 | 2ZJW | 1.59 | 302.1 | 133.5 | 70.6 | 4 | - | Antioxidant |
| **17.** | Emodin | Investigational | C15H10O5 | 3220 | 1F0Q | 2.66 | 270.2 | 94.83 | 72.13 | 3 | - | - |
| **18.** | Ephedrine | Approved | C10H15NO | 9294 | - | 1 | 165.2 | 32.26 | 49.69 | 1 | - | Beta-Adrenergic Agonist |
| **19.** | Epigallo Catechin Gallate | Investigational | C22H18O10 | - | 6DHL | 2.55 | 442.3 | 177.1 | 109.7 | 4 | - | Multiple Sclerosis |
| **20.** | Esculin | Approved | C15H16O9 | 5281417 | 7VL7 | -0.53 | 340.2 | 146.9 | 77.65 | 3 | - | Vasoprotective Agent |
| **21.** | Ferulic Acid | Experimental | C10H10O4 | 445858 | 1GKL | 1.58 | 194.1 | 66.76 | 51.5 | 1 | - | - |
| **22.** | Forskolin | Experimental | C22H34O7 | 47936 | 1AB8 | 1.28 | 410.5 | 113.2 | 104.4 | 3 | - | Antihypertensive |
| **23.** | Hesperidin | Approved | C28H34O15 | 10621 | - | -0.27 | 610.5 | 234.2 | 140.7 | 5 | Kinase B | Bioflavonoid |
| **24.** | Inositol | Approved | C6H12O6 | 347829280 | 1AOD | -2.6 | 180.1 | 121.3 | 35.7 | 1 | - | Nutritional Products |
| **25.** | Kaempferol | Experimental | C15H10O6 | 5280863 | 1H1M | 1.99 | 286.2 | 107.2 | 74.8 | 3 | - | - |
| **26.** | Lawsone | Experimental | C10H6O3 | 46509125 | 2D0E | 0.99 | 174.1 | 54.3 | 16.42 | 2 | - | - |
| **27.** | Lupeol | Investigational | C30H50O | 259846 | | 5.97 | 426.7 | 20.23 | 130.9 | 5 | - | - |
| **28.** | Luteolin | Experimental | C15H10O6 | | 3SZ1 | 2.73 | 286.2 | 107.2 | 74.89 | 3 | - | - |
| **29.** | Naringenin | Experimental | C15H12O5 | 439246 | 1CGK | 2.47 | 272.2 | 86.9 | 71.2 | 3 | - | - |
| **30.** | Quercetin | Experimental | C15H10O7 | 5280343 | 1E8W | 1.81 | 302.2 | 127.4 | 76.8 | 3 | Quinone Reductase | Antioxidant |
| **31.** | Quinine Sulphate | Approved | C20H24N2O | 3034034 | 4UIL | 2.82 | 324. | 45.5 | 94.69 | 4 | | Alkaloid |

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| | | | 2 | | | | 4 | 9 | | | | |
| **32.** | Reserpine | Approved | C33H40N2O9 | 5770 | | 4.05 | 608.6 | 117.7 | 161.4 | 6 | Norepinephrine | Alkaloid |
| **33.** | Resveratrol | Investigational | C14H12O3 | 445154 | 1CGZ | 2.57 | 228.2 | 60.69 | 67.46 | 2 | Nf-Kappab | Stilbenoid |
| **34.** | Rutin | Approved | C27H30O16 | 5280805 | 1RY8 | 0.15 | 610.5 | 265.5 | 140.15 | 5 | - | Vitamin Supplements |
| **35.** | Silibinin | Experimental | C25H22O10 | 31553 | - | 2.35 | 482.4 | 155.1 | 120.29 | 5 | - | Flavonolignan |
| **36.** | Strychnine | Experimental | C21H22N2O2 | | 2XYS | 1.68 | 334.4 | 32.78 | 94.51 | 7 | - | - |
| **37.** | Taxifolin | Experimental | C15H12O7 | 439533 | 1GP5 | 0.95 | 304.2 | 127.4 | 76.61 | 3 | - | - |
| **38.** | Ursolic Acid | Experimental | C30H48O3 | | 5K3M | 6.35 | 456.7 | 57.53 | 133.7 | 5 | - | - |
| **39.** | Vinblastin | Approved | C46H58N4O9 | 13342 | 1Z2B | 3.70 | 810.9 | 154.1 | 222.4 | 9 | - | Antitumor Alkaloid |
| **40.** | Yohimbine | Approved | C21H26N2O3 | 8969 | - | 2.73 | 354.4 | 65.56 | 99.63 | 5 | - | Alpha-2-Adrenergic Blocker |