

REVIEW

Harnessing Pakistan's Biodiversity for Brain Health: Traditional Medicine and Modern Neuropharmacology

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Competing interests

The authors have declared that no competing interests exist.

Abstract

Medicinal plants have played an integral role in the preservation of healthy brain function through phytochemicals having least adverse reactions as compared to synthetic medicines. In Pakistan, neurological diseases account for a large percentage of the total health burden, with an estimated prevalence of epilepsy is approximately 2%, Alzheimer's disease is ~1%, and schizophrenia is 1.5%. Around 10 percent of the population with neurological disorders is dependent on herbal products.

*Medicinal plants used in the traditional medicine systems of Pakistan possess numerous neuroprotective and cognitive-boosting agents. Four of the most studied plants include *Bacopa pinnata*, *Withania somnifera* (Ashwagandha), *Melissa officinalis*, and *Turmeric*, besides to many other local plants. Each plant contains multiple phytoconstituents (e.g. flavonoids, bacosides, alkaloids, and curcuminoids), that possess antioxidant effects and modulates the inflammation pathways.*

Ethnobotanical research throughout Pakistan has identified over one hundred species of plants reported to be used for treating neurological diseases. These belonged to four plant families: Solanaceae (nightshade), Asteraceae (daisy), Lamiaceae (mint), and Papaveraceae (poppy).

This article elaborates the mode of action of polyphenolic, terpenoidal and alkaloidal compounds that leads to different biological effects, including their antioxidant properties, neuroprotective role, neurogenesis and synaptic plasticity. In addition, the need to support sustainable harvesting and conservation of biodiversity in Pakistan's incredibly diverse but rapidly disappearing flora is highlighted by this review. The combination of validated traditional herbal medicines and validated treatments for cognitive or neurodegenerative disorders may provide an effective and sustainably accessible means of treating these conditions, while also being cost-effective.

Key words: Cognitive enhancement, Ethnopharmacology, Medicinal plants, Neurological disorders, Neuroprotection, Pakistan flora, Phytochemicals

Introduction

Plants have always played a significant role in supplying food, shelter, and medicine to humans. Plants have many bioactive compounds with widespread medicinal properties, and many current pharmaceuticals are derived from plant natural products (Ghosh, 2023). Compared with synthetic drugs, most plant-derived medicines have less toxicity and have fewer adverse side effects than their synthetic counterparts (Khan et al., 2019). In many cultures, herbal preparations continue to be utilized for therapeutic use, and both tradition and the need for access to natural remedies in resource-limited environments have maintained this practice (Rajput, 2023).

Plants classified as nootropic herbs, or those that provide cognitive enhancement and neuroprotection, show promise for treating neurological diseases. Neuroprotection can be defined as the protection of the central nervous system (CNS) against neuronal damage caused by neurodegenerative disorders, such as Alzheimer's, Parkinson's, and stroke, as well as anxiety and epilepsy. It's estimated that these disorders are quickly rising in prevalence, and they are expected to be the second leading cause of death among the elderly (Kumar et al., 2015). The number of individuals afflicted with neurological disease continues to proliferate as a result of the current

demographic and epidemiological transitions. Neurological diseases are currently classified as the leading source of disability and one of the leading causes of mortality on a global scale (Awan et al., 2017). To date, the number of identified neurological diseases has reached approximately 600, which encompasses the categories of mood disorders, depression, paralysis, pain, and cognitive impairment, and represent approximately 6.5% of the overall global burden of disease (Khan et al., 2019). Medicinal plants include a number of different primary and secondary metabolites that exhibit therapeutic potential (Sharma et al., 2022); many of the metabolites provide therapeutic benefits primarily through the mechanisms of glutathione, nitric oxide, and reactive oxygen species production, as well as enhancing and/or modulating the function of key metabolic enzymes, and regulating cellular signaling through alterations in cellular calcium levels (Ahmad et al., 2019).

Sociocultural, environmental, and economic factors, including but not limited to, low socioeconomic status; limited access to health care due to lack of resources (Akter et al., 2025); high rates of unemployment; political instability, etc., as well as genetic predisposition, are among the many underlying factors related to the burden of neurological disease in Pakistan. In rural areas of Pakistan, many individuals rely on folk medicine for their health care, as they perceive folk medicine to be safer and less expensive than traditional medicine, as well as readily available (Yan et al., 2022). Approximately 10% of Pakistan's population is estimated to suffer from neurological disorders, with depression (~5%) (Ullah et al., 2022), epilepsy (~2%) (Khatri et al., 2003), Alzheimer's disease (~1%) (Aggarwal et al., 2012; Phan et al., 2019), and schizophrenia (~1.5%) (Nawaz et al., 2020) being the most prevalent. Given this context, the present review focuses on major neuroprotective medicinal plants traditionally used in Pakistan and their potential mechanisms of action.

Inflammatory Pathway

According to Swarna et al. (2019), inflammation is a bodily protective response that allows the body to remove harmful agents and return to normal tissue balance, or homeostasis. In a healthy person, this will occur in an acute (short term) way and will stop when there is no longer a need for inflammation because the harmful stimulus has been eliminated. However, in people who have chronic inflammatory diseases such as Alzheimer's Disease, or Parkinson's Disease and Multiple Sclerosis, inflammatory signaling continues for long periods of time and can become dysregulated or out of balance. Long-term chronic inflammation results in prolonged microglia and astrocyte activation, increased amounts of the pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6), and prolonged generation of reactive oxygen and nitrogen species. Cytokines, by-products of inflammation and reactive species, negatively impact synapse function, disrupt neuronal membranes, and promote neuronal death over time (Block et al., 2007).

Chronic Neuroinflammation Begins by the Body Recognizing Pathogen-Associated or Damage-Associated Molecular Patterns via Pattern-Recognition Receptors and Results in the Activation of NF- κ B, MAPK and JAK/STAT Pathways which Results in Prolonged Cytokine Release, Increased Oxidative Stress and Disruption of Neuronal Survival Signals (Figure 1).

Numerous medicinal plants protect against neurodegeneration through their action on multiple pathways to reduce chronic inflammation, decrease oxidative load, and inhibit pro-inflammatory signaling (Ayaz et al., 2017; Mohamed et al., 2024). Additionally, phytochemicals (flavonoids, terpenoids, and alkaloids) inhibit the activation of NF- κ B, scavenge reactive oxygen species, and restore the homeostatic balance of antioxidant enzymes, thereby preventing inflammation from damaging the nervous system.

The association between neurodegenerative disease and chronic inflammation supports the notion that medicinal plants may be useful in the treatment of these disorders by the ability of these plant compounds to have multiple targets, which can provide a natural means to alleviate chronic inflammatory signaling, thereby providing neuroprotective effects.

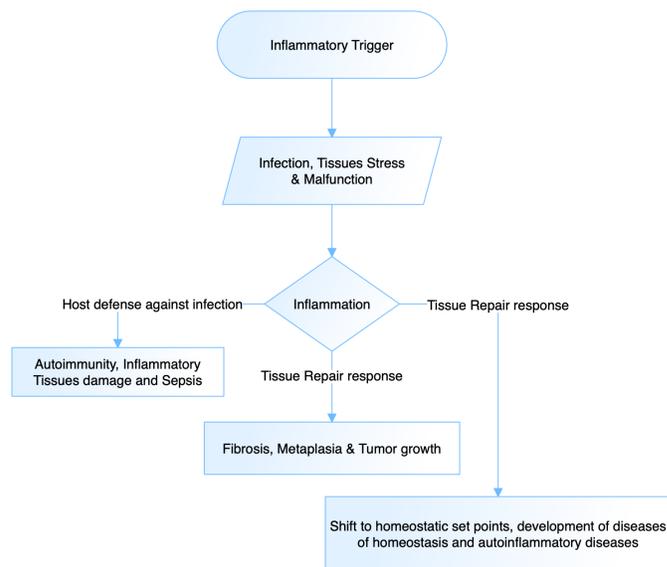


Figure 1. Pathological and physiological pathways of inflammation

Classification of Anti-Inflammatory Drugs:

Neuroinflammation is a key contributor to the development of many neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, multiple sclerosis and Huntington's disease. The chronic activation of resident glial cells (i.e., microglia and astrocytes) leads to the prolonged stimulation of the release of various pro-inflammatory cytokines such as TNF- α , IL-1 β and IL-6.

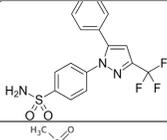
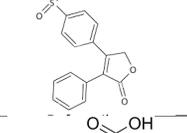
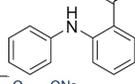
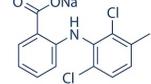
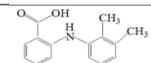
This chronic exposure to pro-inflammatory cytokines damages synapses, increases oxidative stress and impairs mitochondria all leading to the continued death of neurons. The mechanistic relationship between neuroinflammation and the pathogenesis of neurodegenerative disorders has prompted increased interest in modulating inflammatory pathways for therapeutic purposes and thus, to modulate inflammatory pathways in the treatment of neurodegenerative disorders has become an important therapeutic goal. Anti-inflammatory medications are beneficial because they attenuate the effects of too much uncontrolled pro-inflammatory signaling and therefore protect against oxidative damage and also slow or prevent further degradation of the neuronal cell (Nunes et al., 2020). In Table 2, classes of anti-inflammatory medications used in the treatment of

neurodegenerative disorders and neuroinflammatory disorders have been summarized.

Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase (COX-1 and COX-2) and thereby decrease the formation of prostaglandins and activation of downstream in inflammation (Shingala et al., 2021). The potential for neuroprotection with NSAIDs has been widely studied, as COX-2 over-activity may contribute to amyloid pathology and death of dopaminergic neurons, and to neuro-inflammation. Epidemiological results suggest that long-term use of NSAIDs may decrease the chance of developing Alzheimer's disease, however, due to the inconclusive results from clinical trials, these results are not supportive. Some NSAIDs (e.g., ibuprofen, naproxen, and aspirin) may decrease long-term neuro-inflammation; however, the gastrointestinal and cardiovascular adverse effects of these products limit their long-term utility. A list of the common NSAIDs' relevant to brain disorders can be found in Table 1 & 2.

Table 1: NSAIDs used in neuro-inflammatory and neurodegenerative conditions

COX-2 inhibitors	Structures	Diseases
Celecoxib		Spondylitis, Migraine, Adenomatous Polyposis
Rofecoxib		Rheumatoid Arthritis, Osteoarthritis, Pain
Fenamates		
Meclofenamate		Osteoarthritis, Arthritis, Pain
Mefanamic		Dysmenorrhea, Acute Pain, Pain

Corticosteroids

Corticosteroids have powerful anti-inflammatory properties. Corticosteroids affect the inhibition of Nuclear Factor kappa B (NF-kB) and the suppression of cytokines and immune cell infiltration. In practice, corticosteroids such as dexamethasone and methylprednisolone are most commonly used for acute inflammatory episodes in patients with neurological disorders such as auto-immune encephalitis, multiple sclerosis relapses, and cerebral edema. They can cross the blood-brain barrier (BBB) and can rapidly suppress neuroinflammatory pathways. However, the long-term use of corticosteroids is limited by many adverse effects including but not limited to immunosuppression, hyperglycemia, and hormonal imbalance. A list of common corticosteroids used for the treatment of neuro-inflammation can be found in Table 3.

Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

DMARDs have been used traditionally to treat systemic inflammatory diseases such as rheumatoid arthritis; however,

Table 2: NSAIDs used in neuro-inflammatory and neurodegenerative conditions

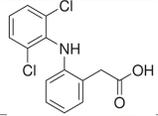
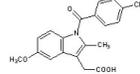
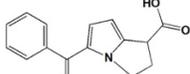
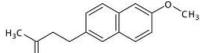
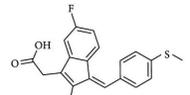
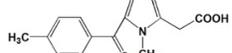
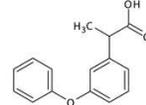
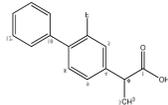
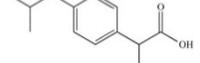
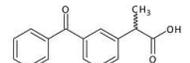
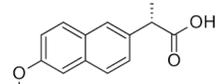
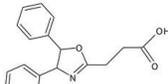
Acetic Acids	Structures	Diseases
Diclofenac		Rheumatoid Arthritis, Osteoarthritis, Dysmenorrhea
Etodolac		Pain, Osteoarthritis, Rheumatoid Arthritis
Indomethacin		Bursitis, Tendinitis, Acute Gouty Arthritis
Ketorolac		Severe Acute Pain
Nabumetone		Arthritis, Osteoarthritis
Sulindac		Gout, Renal Impairment, Hepatic Impairment
Tolmetin		Arthritis, Osteoarthritis, Rheumatoid Arthritis

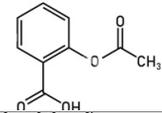
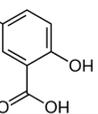
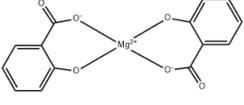
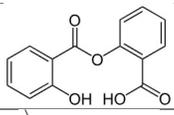
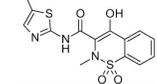
Table 3: Corticosteroids used in neurological inflammation

Propionic Acid's	Structure	Diseases
Fenoprofen		Arthritis, Osteoarthritis, Renal Impairment
Flurbiprofen		Osteoarthritis, Renal Impairment, Rheumatoid Arthritis
Ibuprofen		Dysmenorrhea, Inflammatory Disease, Fever
Ketoprofen		Pain Management, Dysmenorrhea, Arthritis or Osteoarthritis
Naproxen		Ankylosing Spondylitis, Migraine, Gout, Acute
Oxaprozin		Arthritis, Osteoarthritis, Fever

due to DMARDs' ability to modulate chronic inflammation, a medication in the DMARD class is said to have a protective effect on the nervous system. The DMARD medications methotrexate, azathioprine, and leflunomide, for example, are beneficial in various neurodegenerative disorders (multiple sclerosis and neurosarcoidosis) because they inhibit excessive immune activation and the production of pro-inflammatory cytokines. Current evidence suggests that these substances may have a beneficial effect on neurological inflammation. Some

biological DMARD agents, including the TNF- α inhibitors, appear to have a therapeutic benefit in limiting neuroinflammatory processes; however, there are also risks of developing paradoxical demyelination (Table 4).

Table 4: DMARDs with neuroprotective or anti-inflammatory relevance

Salicylates	Structures	Diseases
Aspirin		Acute Coronary Syndrome, Pain and Fever, ASCVD Prevention
Diffenunisal		Hepatic Impairment, Renal Impairment, Arthritis
Magnesium Salicylate		Pain, Mild-to-Moderate Pain, Arthritis
Salsalate		Rheumatoid Arthritis, Osteoarthritis, Pain
Meloxicam		Arthritis, Osteoarthritis, Others

Phytochemical properties of plants:

Plants exert diverse pharmacological effects through their rich repertoire of phytochemicals, including alkaloids, flavonoids, saponins, tannins, phenols, sterols, vitamins, essential oils, and various nutrients. These bioactive compounds possess chemotherapeutic, antibacterial, and neuroprotective properties, making them valuable in the management of numerous diseases, including neurological disorders. Among these, alkaloids such as nicotine and scopolamine have demonstrated antidepressant, anxiolytic, and antiparkinsonian effects (Parvin et al., 2013). Saponins exhibit antiepileptic, anti-amnesic, and anxiolytic activities, while terpenoids have been reported to possess neuroprotective potential. Similarly, flavonoids show antidepressant, anti-Alzheimer's, and memory-enhancing effects, glycosides contribute to sedative and sleep-promoting actions, and steroids are associated with anxiolytic activity (Khan et al., 2019). The major phytochemical classes and their proposed mechanisms of neuropharmacological action are summarized in Table 5.

Key Medicinal Plants of Pakistan with Neuroprotective Properties:

Pakistan hosts a rich diversity of medicinal plants, distributed across its mountainous and plain regions. Several high-value species, such as *Glycyrrhiza glabra*, *Commiphora wightii*, *Ephedra intermedia*, *Saussurea lappa*, *Ferula foetida*, *Valeriana wallichii*, *Colchicum luteum*, *Bergenia ciliata*, *Paeonia emodi*, and *Morchella* spp., are increasingly overexploited, leading to a significant decline in their natural populations and productivity. The ecological and climatic conditions of these regions play a vital role in the distribution and phytochemical composition of these plants ("Plants as Anti-Inflammatory Drugs," 2021). The geographical features of Pakistan and climatic conditions which are made up of four

distinct seasonal environments, provide ideal conditions for growing many medicinal plants in Pakistan's diverse geography, and particularly, large populations of medicinal plants are found in Pakistan's mountainous regions, as they have a more favorable environment and very stable microclimates (Akhtar 2022).

The unnatural harvesting process of many medicinal herbs drastically affects biodiversity and the ability to regenerate various species of medicinal herbs in Pakistan. There is an urgent need to promote the study and ultimately develop an ethnobotany research program for Pakistan's herbal industry, in addition to encouraging and focusing research and development activities regarding plant biodiversity conservation efforts, plant cultivation and propagation practices, phytochemical analysis, product quality control and improvement, product value-added processing, and the formulation of medicinal herbal industry growth policies at both national and provincial levels. Although many of the following species of medicinal herbs are known historically to possess medicinal properties, I will highlight only the most important and ecologically relevant medicinal plants from the various geographic regions of Pakistan, noting how each plant has been traditionally used for medicinal purposes (Adebayo et al., 2015).

Crude extracts of these plants have historically been the source of many of today's medicines in both developed and developing nations (Adebayo et al, 2015). Recent advancements in chemical and microbial synthesis have allowed for more complete isolation and production of many bioactive components isolated from traditional medicinal plants, including aloin from *Aloe vera*, santonin from species of the genus *Artemisia*, glycyrrhizin from *Glycyrrhiza*, ephedrine from *Ephedra*, berberine from species of *Berberis*, and silymarin from *Milk Thistle*. One of the best examples from a nutritional standpoint is *Phyllanthus emblica* (amla), which contains a high concentration of vitamin C; *Allium sativum* (garlic), another example of a widely used medicinal plant in Pakistan, is recognized for its hypolipidemic, antidiabetic, and antifungal properties (Akhtar, 2022). The active compound found in garlic, ajoene, has significant antiplatelet effects and is responsible for most of these benefits. *Cichorium intybus* (chicory) has also been used traditionally to treat various medical issues. This plant exhibits, among others, anti-inflammatory, demulcent, diuretic, and depurative properties (Street et al., 2013).

Mechanism of Actions:

Phytochemical Mechanisms of Neuroprotection:

Plant-derived phytochemicals exert neuroprotective effects through diverse molecular pathways, including modulation of neurotransmitter systems such as adrenergic and cholinergic signaling, activation or inhibition of receptor systems like GABA and N-methyl-D-aspartate (NMDA), and regulation of ion channels, including sodium, potassium, and calcium channels (Khan et al., 2019).

Polyphenols:

Polyphenols, such as resveratrol, catechins, quercetin and epigallocatechin gallate (EGCG), exhibit very potent neuroprotective effects related to their antioxidant, anti-inflammatory and anti-amyloid properties. Several studies have demonstrated that polyphenols effectively scavenge free radicals; stimulate the expression of antioxidant enzymes (SOD, CAT, GPx) and inhibit NF- κ B activation and the production of

pro-inflammatory cytokines (Li et al., 2026). Studies show that both resveratrol and EGCG can also inhibit the aggregation of A β , enhance mitochondrial function, and enhance synaptic

plasticity. Thus, resveratrol and EGCG may have therapeutic value in experimental models of Alzheimer's disease (Aggarwal et al., 2012).

Table 5: Classification of Phytochemicals and their mode of Actions.

Phytochemical	Plants Source	Type	Disease treatment	Action	Reference
Epigallocatechin-3-Galate	Tea leaves	Polyphenol	Alzheimer's disease (AD)	Reduce Amyloid plaques by its cleavage by α -secretase	(Velmurugan B et al., 2018)
Berberine	<i>Berberis species, Goldenseal (Hydrastis canadensis), and Coptis chinensis</i>	Alkaloid	Alzheimer's Disease, Neurotoxicity, Hypoxia	Inhibit Enzymes involved in the progression of AD and Scavengers of ROS	
Curcumin	Turmeric	Phenol	Alzheimer's disease. Cognitive impairment	Inhibit NF- κ B and reducing the pathogenesis of AD. Cognitive impairments improved because of an increase in CREB and BDNF levels	
Resveratrol	Grapes, Peanut, tea	Phenol	Cognitive impairment. Neurotoxicity	Cognitive impairment by inhibiting TNF- α and IL-1 β levels and elevating BDNF.	
Quercetin	Apple, Onion, buck wheat, green tea	Flavonoids	Neurodegenerations	Anti-proliferative, cytotoxic and genotoxic activities	
Limonoids	<i>Melia toosendan,</i>	Terpenoids	Stroke, Alzheimer Disease	Involved in neuronal differentiation and growth by increasing NGF levels	
Sulforaphane	Cruciferous vegetables	Isothiocyanate	Stroke	In stroke, it reduced the amount of brain damage, brain edema and protected retinal pigment epithet.	
Hypericin and pseudo hypericin	<i>Hypericum perforatum</i>	Naphthodianthrone	Depression and anxiety	Inhibition of monoamine oxidase. block synaptic re-uptake of serotonin, dopamine, and norepinephrine	
Allicin	Garlic and onion	Organo sulfur compound.	Improve cognitive function	activate stress-response pathways, result in upregulation of neuroprotective proteins such as mitochondrial uncoupling proteins	

Table 6 : Key Medicinal Plants of Pakistan with their local names and traditional uses.

Botanical name	Common name	Parts used	Traditional uses
<i>Caralluma tuberculata</i>	Marmooth	Tubers	Jaundice, dysentery, stomach pain, constipation
<i>Carthamus tinctorius Linn</i>	Safflowers, Saffron Thistle	Flowers, Seeds	Food flavoring
<i>Crataegus oxycantha</i>	Hawthorn, Ghunza	Berries	Heart problem, blood pressure
<i>Cassia fistula Linn.</i>	Amaltas	Seed, Root, Bark	Hepatitis, jaundice, constipation
<i>Cassia senna Linn.</i>	Sana, Sana-i-Makki	Pods, Seeds	Blood purification and abdominal discomfort
<i>Citrus aurantifolia Christm.</i>	Lime, Limun	Fruit Juice	Vomiting, burning in chest, diarrhea
<i>Cichorium intybus Linn.</i>	Chicory, Kasni	Leaves, Seeds, Roots	Digestion, asthma, spleen problems
<i>Coriandrum sativum Linn</i>	Coriander, Dhaniya	Leaves, Seeds	Fresh flowers and dry seeds are used in many cooking dishes
<i>Commiphora wightii</i>	Gumgugul, Guggal	Gum	Resin to treat piles, plant fumigants used to keep snakes away from homes
<i>Crocus sativus Linn.</i>	Saffron, Zafran	Flowers (Stigmas)	Food flavoring, tonic, heart problem
<i>Cuminum cyminum</i>	White Cumin	Seeds	Condiment or spice in curries, pickles and flavor in confectionery
<i>Curcuma longa</i>	Turmeric, Haldi	Tubers, Rhizomes	Wound healing, major ingredient of many foods

Curcuminoids:

Turmeric-derived curcuminoids possess many pharmacological functions that are relevant to the development of neurodegenerative diseases, including potent actions as anti-amyloid, antioxidant, and anti-inflammatory agents. In an Alzheimer's disease model, curcumin has demonstrated to be able to inhibit A β aggregation, reduce tau phosphorylation, inhibit ROS production, and decrease microglial activation (Mahmood et al., 2011). Additionally, curcumin appears to promote neurogenesis and improve memory via modulation of BDNF/CREB signaling pathways.

Flavonoids:

Flavonoids are an important class of phytochemicals that have antioxidant and anti-apoptosis properties. They reduce the formation of reactive oxygen species (ROS) and shield against rotenone-induced mitochondrial damage and boost ATP production. The beneficial properties of flavonoids on neurological function indicated by experimental models demonstrate how flavonoids protect mitochondrial integrity and neuronal viability (Li et al., 2012).

Terpenoids:

On the other hand, the neuroprotective effects of specific terpenoids (ginkgolides, bilobalide, asiaticoside, and ursolic acid) are mediated through multiple biochemical mechanisms. Terpenoids have been demonstrated to protect against oxidative stress by restoring endogenous antioxidant enzyme levels:

- i. Protect against oxidative stress via restoration of endogenous antioxidant enzyme levels
- ii. Protect against neuroinflammation by inhibiting TNF- α , IL-1 β , and IL-6
- iii. Protect against NF- κ B and MAPK signaling pathways
- iv. Regulate apoptotic markers by increasing Bcl-2, downregulating Bax, preventing cytochrome-c release and preventing the activation of caspase-3 (Khatri et al., 2003; Sharma et al., 2022).

The protective effects of terpenoids on models of Alzheimer's disease, Parkinson's disease, and ischemic brain injury may enhance neuronal survival and reduce the neurotoxicity associated with these diseases.

Alkaloids:

Galantamine, an alkaloid, has been shown to have effects on synaptic plasticity through its dual mechanism of action: it inhibits the activity of acetylcholinesterase (AChE) and acts on nicotinic acetylcholine receptors (nAChRs). Inhibition of AChE increases the amount of acetylcholine available at the synapse, which enhances cholinergic neurotransmission. By acting as an allosteric modulator of nAChRs, galantamine enhances synaptic plasticity and cognition. These properties make galantamine a potential therapy for several neurodegenerative and mental illness conditions including Alzheimer's disease, schizophrenia and major depression (Colović et al., 2013).

Limitations and Future Perspectives

While this review outlines several medicinal plants that have demonstrated neuroprotective properties, as well as their respective mechanisms of action, important limitations need to be acknowledged. The incidence of neurological diseases is on the rise in Pakistan because of ageing population, pressures due to urbanization and environmental pollution, and inadequate

access to appropriate mental health services. Many of the available studies regarding cannabis have been conducted using either preclinical or animal models, and the therapeutic efficacy of the medicinal plants on humans has not been validated by many region-specific randomized placebo-controlled clinical trials. There are also differences in the chemical composition and physical characteristics of the plants used, and differences in the extraction techniques used to prepare the plant extracts for administration, which affects their ability to be reproduced and compared to one another. Most of the studies conducted have only examined the effects of a single component, whereas traditional herbal medicine typically utilizes multiple components, and their synergistic interactions have not been well-characterized in scientific literature.

In summary, a greater emphasis on conducting standardized randomized placebo-controlled clinical trials using well-characterized plant extracts, particularly those that have been traditionally utilized in Pakistan, is required as a priority for future research. Genotyping of these plants will assist in the identification of putative bioactive compounds that provide neuroprotective effects, as well as elucidate their pharmacokinetic properties, ability to penetrate the blood-brain barrier, and long-term safety.

Conclusion

The review presents Pakistan's extensive biological diversity as well as its ethnopharmacological background for exploring neuroprotective herbal medicines. Combining traditional/herbal knowledge with modern day neuroscience may produce low-cost, multi-target medicines to treat neurodegenerative diseases and cognitive disorder. Future studies need to focus on clinical validation of herbal formulations as well as standardize herbal formulations and support sustainable harvesting of plants harvested sustainably to preserve both therapeutic and biological topicality.

Author contributions

NS: Data acquisition and manuscript write-up; MA: Data acquisition and manuscript write-up; HA: Data acquisition and manuscript write-up; ZA: Data acquisition and manuscript write-up; NN: Conceived the idea, Intellectual input, manuscript review

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