Phyto-Derived Therapeutic Analogs for Neurological Disorders with Prevalence Insights into Metropolitan and Non-Metropolitan Regions of India: A Review

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ABSTRACT

The field of neurological disorders is a growing public health issue, and India has shown this trend in a very uneven distribution between metropolitan and non-metropolitan areas. Air pollution, chronic stress, sedentary lifestyles, and the availability of better diagnosis have become the causes of reported increasing incidence of stroke, migraine, dementia, and Parkinson's disease among metropolitan population. In contrast, non-metropolitan regions have to experience more prevalence of epilepsy, neuroinfections, neurotrauma, and neurological impairment secondary to malnutrition due to late diagnosis and limited specialist care. The current pharmacological treatments are mostly symptomatic with common side effects and potential lack of disease-modifying effects. Neurotherapeutics derived from plants provide a potential, less expensive and culturally rooted alternative. Established medicinal species, including *Withania somnifera, Bacopa monnier* have multi-target effects, which are antioxidant, anti-inflammatory, neuroprotective, and neuromodulatory. Because of their extensive use in treatments, their analogs having similar activities must be found, to extend the spectrum of potential neuroprotective agents and reliance on ecologically endangered species is minimized. Further, this review summarises the metropolitan and non-metropolitan neurological disease incidence in India, where the inducers of neurological disorders might be similar but effects may vary due to availability of diagnosis, treatment and various other environmental and societal conditions. The review points out the therapeutic potential of already known plant compounds and their less-studied structural analogs. Through a combination of phytochemical research and a region-specific medical requirement, plant-based molecules may assist in filling diagnostic gaps and offer more accessible and sustainable treatment for neurological conditions in India.

Keywords: Neurological disorders, Phytochemical analogs, Neuroprotection, Medicinal plants, India

INTRODUCTION

Neurological disorders are among the most critical health problems of the 21st century (Whiteford et al., 2015). On the basis of data from Global Burden of Disease (GBD) 2021, neurological conditions collectively affect over 3.4 billion people worldwide; that is nearly 43% of the global population (Ferrari et al., 2024).

Besides being the most significant contributors to disability, these neurological disorders are among the prominent causes of premature death (GBD, 2021). In India, there has been a worrying upward trend of neurological disorders with 44% increase of burden between 1990-2013 overtaking several other countries in Asia, including China, which had seen a 20% increase (Charlson et al, 2016). According to current estimates, 20 to 30 million persons in India suffer from neurological illnesses, with incidence rates that range from 967 to 4,070 per 100,000 people (Gourie-Devi, 2014).

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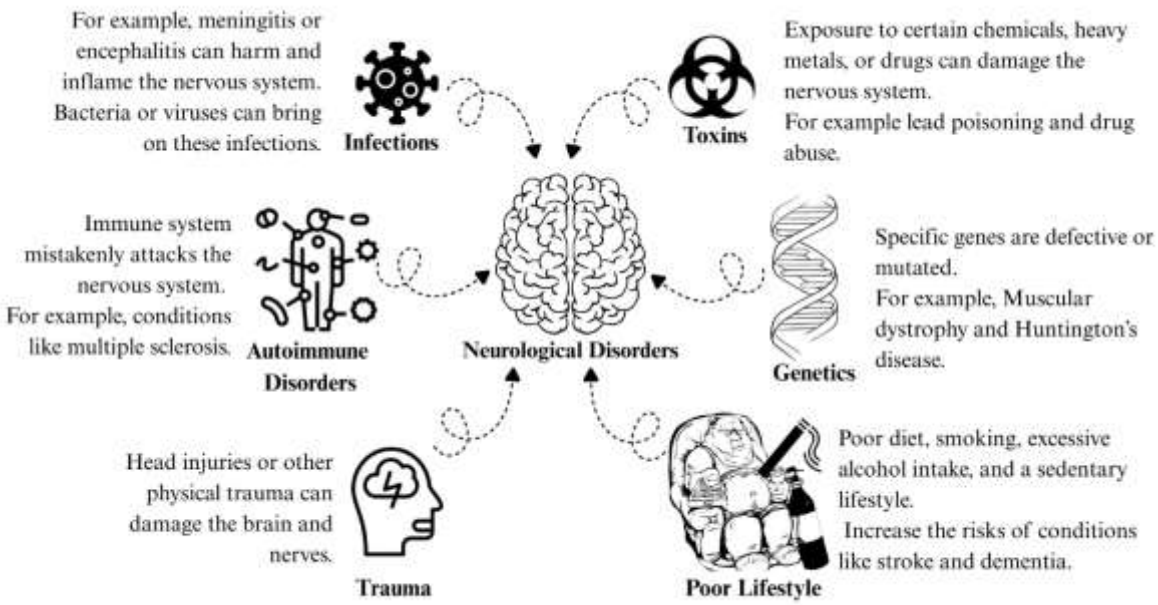
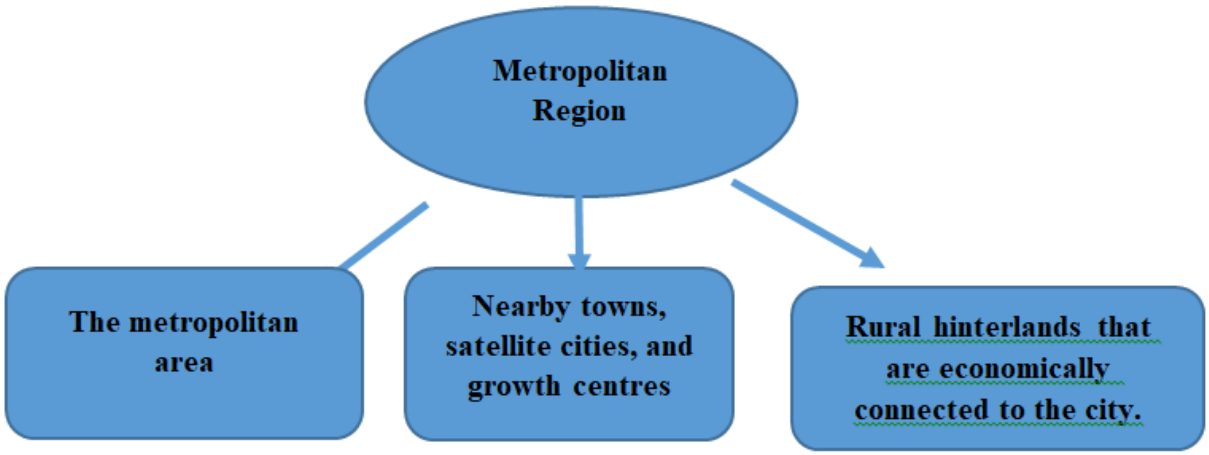
Figure 1: Factors Responsible for Neurological Disorders



Distribution of neurological disorders in India is characterized by a significant distinction between metropolitan and non-metropolitan regions of the country. A metropolitan region represents a significantly broader spatial construct than the metropolitan area, encompassing a diverse set of urban, semi-urban, and rural territories that together form an extended functional system, including the metropolitan area itself, nearby towns, satellite cities, growth centres, peri-urban transition zones, logistics corridors, industrial clusters, and rural hinterlands economically connected to the core city.

In India, a metropolitan region is a larger geographical, economic, and functional territory that includes the metropolitan area, surrounding peri-urban/semi-urban/rural towns, industrial clusters, satellite towns, and regional corridors e.g., Delhi NCR spanning Delhi NCT and districts in Haryana, UP, and Rajasthan (Sharma, 2025). The term "non-metropolitan" is generally used for areas outside metropolitan urban agglomerations or statutory metropolitan jurisdictions that are economically not connected to the city (Balk et al., 2019).

Figure 2: Components of a metropolitan region (Sharma,2025)



This distinction reflects environmental exposures, lifestyle, access to health care, correct diagnosis and the socio-economic realities of both regions. Neurodegenerative and stress-related disorders like dementia, Alzheimer's disease, Parkinson's disease, migraine, stroke are said to have more metropolitan representation. This trend is in significant part due to longer life expectancy, greater survival from other chronic diseases and the cumulative effect of conditions in the urban environment. Chronic exposure to air and noise pollution,

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circadian rhythm disruptions from work in different shifts and high stress levels promote oxidative damage and neuro-inflammatory pathways, leading urban residents to degenerative neurological conditions. For example, exposure to fine particulate matter ($PM_{2.5}$) in metropolitan regions have been strongly related to an increased frequency of stroke and cognitive impairment, emphasizing the critical influence of environmental factors on neurological health (Fu et al., 2018). According to the latest data, several non-communicable risk factors of neurological disorders are stress (44% of the population), low physical activity (67%), an unbalanced diet (55%), and obesity (24%). These risk factors are exponentially greater in metropolitan areas, where modern ways of living encourage prolonged sitting, poor food habits, disrupted sleeping and chronic psychological strain.

In contrast, the neurological disease pattern of non-metropolitan regions of India still reflects the burden of infectious, nutritional and trauma-related conditions. For instance, epilepsy is seen more commonly in non-metropolitan populations because of untreated head injuries often related to agricultural activity or road accidents, perinatal complications and parasitic infections such as neurocysticercosis. Peripheral neuropathies are also common in non-metropolitan communities, where malnutrition, micronutrient deficiencies and exposure to neurotoxic pesticides are common. Stroke is also increasingly recognised in these settings, but unlike in metropolitan areas, the burden in these settings is majorly attributed to uncontrolled hypertension and poor access to timely treatment. This divergence represents the epidemiological transition India is experiencing, where the urban centres are experiencing increasing degenerative disorders and rural parts of the country, belonging to non-metropolitan regions, are still afflicted in their fight against the preventable and infectious neurological conditions. Urban populations in metropolitan areas has the benefits of easy access to neurologists and tertiary hospitals as well as advanced imaging technology that is useful in early detection of conditions such as Parkinson disease. On the other hand, the patients from rural areas of the non-metropolitan regions tend to arrive with advanced stages of the disease due to its lack of awareness, cultural stigma, and access to specialised services. Consequently, the true number of the neurological diseases in the non-metropolitan regions is likely underestimated due to underdiagnosis. Socioeconomic and occupational tendencies also make such a differentiation. The employment in the city, lack of any physical activity, time behind the computer monitors, stress in the offices predisposes people to headaches, insomnia, psychosomatic and neurological disorders.

Together, these tendencies contribute to bringing out the fact that metropolitan India is becoming increasingly chronic degenerative and lifestyle-related neurological, with the population in the non-metropolitan regions continuing to bear a higher load of infectious, nutritional and trauma-related diseases. This two-sided epidemiology is the image of the accelerating but uneven health transition in India, with the rise in stress in cities and absence of health care in the rural areas. Although the contemporary pharmacological treatments are providing relief but, in most situations, they do not guarantee prevention of the disease progression that is accompanied by its side effects for instance, antiepileptics lead to cognitive dulling, and L-DOPA, that is administered to treat patients of Parkinson's disease, results in dyskinesias akin to involuntary movement (Lane, 2018; Li et al., 2025).

The shortcomings highlight the necessity of exploring plant-based treatments, specifically in the Indian context, where Ayurveda and traditional medicine have long emphasized stress relief and neurological balance. Adaptogenic, antioxidant and neuroprotective medicinal plants, including *Bacopa monnieri*, *Curcuma longa*, *Withania somnifera* as well as *Centella asiatica* have demonstrated potential in alleviating stress pathways as well as the direct action of combating neurological pathology. The cases of the neurologic disorders are increasing worldwide. Therefore, the idea of integration of plant-based neurotherapeutics and region-specific healthcare is necessary to seal the gaps in diagnosis, reduce disparities in therapy, and foster sustainable control of neurological conditions in diverse population groups and guaranteeing long-term control of neurological conditions.

The analogs continue to preserve the core pharmacophores and in addition, have structural variations capable of making them antioxidants, increase blood-brain barrier permeability, or reduce toxicity and serve as a route to more effective and versatile therapy. Their inclusion does not only widen the list of neurotherapies but it also provides an assurance that the population of metropolitan and non-metropolitan regions will have access to affordable, accessible interventions that are scientifically-proven. Therefore, this review aims to (1) describe

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present condition and prevalence of the principal neurological disorders in India, (2) analyse demographic variations between metropolitan areas and other non-metropolitan areas of India, and (3) generalise evidence on medicinal plants with known or suspected neurotherapeutic potential effects.

REVIEW METHODOLOGY

This review was conducted by searching the scientific literature published between 2000 and 2026 to synthesise evidence on the prevalence, epidemiology, and plant-based management of neurological disorders. Major databases, including Scopus, ScienceDirect, PubMed, and Google Scholar, were explored, along with reports from World Health Organisation and Global Burden of Disease Study. Keywords such as “neurological disorders”, “India”, “urban stress”, “metropolitan and non-metropolitan”, “rural India” “epidemiology”, “plant-based treatment”, “Ayurveda”, “medicinal plants”, “phytochemicals”, “neuroprotection”, “Parkinson’s disease” “stroke”, “migraine”, “Alzheimer’s disease”, and “epilepsy” were used in various combinations to refine searches. Only peer-reviewed articles, systematic reviews, meta-analyses, and epidemiological reports available in English were included, while non-English publications, irrelevant studies, and inaccessible full texts were excluded. Plant names and their synonyms were validated using standard taxonomic databases, such as The Plant List and MPNS (Medicinal Plant Names Services, Kew Science). The mentioned phytochemicals were confirmed using PubChem and PubMed databases. Accurate and clear chemical structures of the chosen phytochemicals were made using PubChem Sketcher. The acquired research was critically reviewed to highlight three key points: (i) the world and Indian burden of neurological diseases, (ii) urban and rural disparities in the rate and distribution of the disease in India, and (iii) medicinal plants and bioactive substances, and their hypothetical plant-based alternatives.

Neurological Disorders

The nervous system is impacted by neurological disorders. The neurological system, which works as the body's command centre, sends impulses that govern our movements, thoughts, and physical processes. Any malfunction in this system can cause neurological diseases.

Neurological conditions cover a broad range of ailments impacting the central and peripheral nervous systems, and can generally be classified into:

- **Cerebrovascular disorders** (e.g., stroke, aneurysms, vascular dementia)
- **Neurodegenerative disorders** (e.g., Huntington’s disease, multiple sclerosis, Parkinson’s disease, Alzheimer’s disease)
- **Neuroinfections and inflammatory disorders** (e.g., meningitis, encephalitis, neurocysticercosis, multiple sclerosis)
- **Neuromuscular and demyelinating disorders** (e.g., diabetic neuropathy, amyotrophic lateral sclerosis, myasthenia gravis)
- **Headache and pain-related disorders** (e.g., migraine, cluster headaches, neuropathic pain)
- **Neurodevelopmental disorders** (e.g., autism spectrum disorders, cerebral palsy)
- **Tumours and malignancies** of the nervous system.
- **Trauma-related conditions** (e.g., traumatic brain injury, spinal cord injury)

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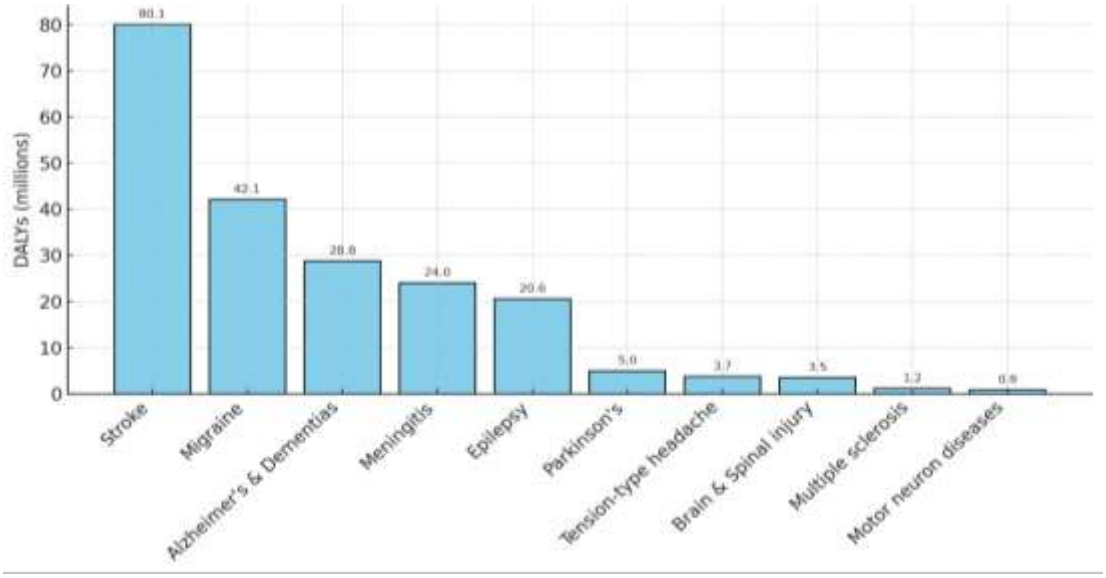
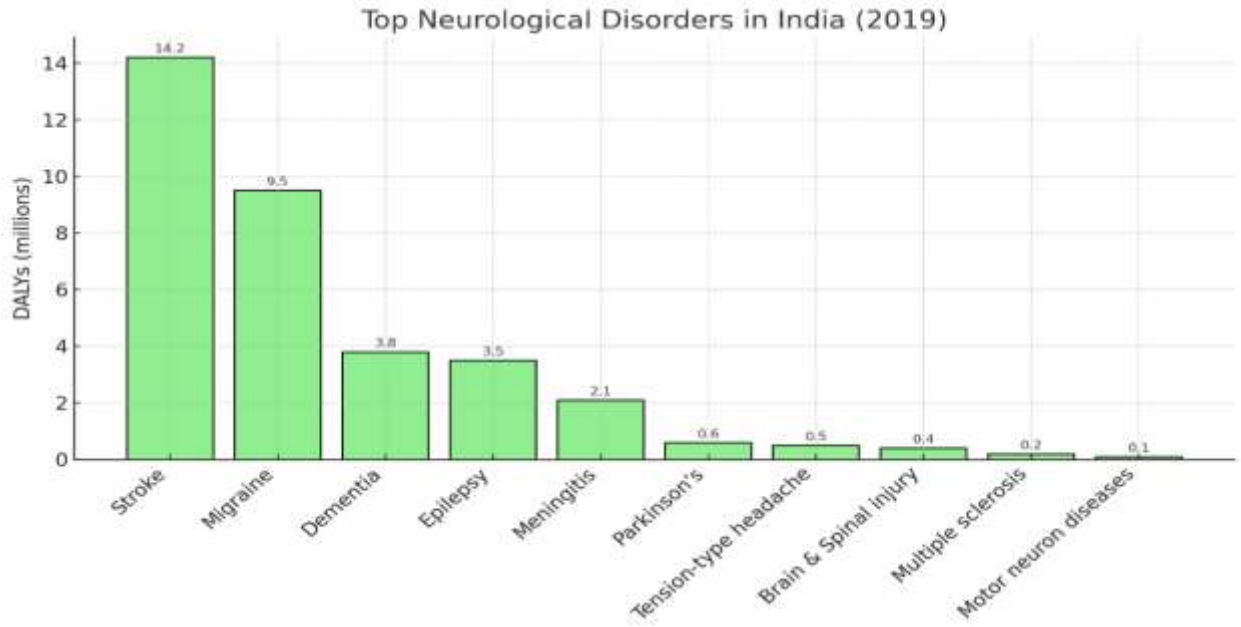
Figure 3: Globally Leading Neurological Disorders as per Global Burden of Disease Study 2019, Expressed as Disability-Adjusted Life Years



*(DALYs depict total years of life lost because of early death (YLLs) and the years lived with a disability (YLDs) resulting from existing instances of the illness or health issue within a population).

As per the data on the global burden of neurological disorders in 2019, stroke clearly emerges as the most significant contributor, accounting for approximately 80.1 million DALYs, reflecting its high prevalence and severe long-term disability outcomes. Migraine, despite being non-fatal, occupies the second position with 42.1 million DALYs, emphasising the considerable years lived with disability it generates. Alzheimer's disease and other dementias rank third (28.8 million DALYs), underscoring the growing challenge of neurodegenerative conditions in ageing populations worldwide. Infectious causes like meningitis (24.0 million DALYs) and chronic conditions such as epilepsy (20.6 million DALYs) further highlight the diverse etiological spectrum contributing to neurological disease burden. In contrast, rarer disorders such as multiple sclerosis (1.2 million DALYs) and motor neuron diseases (0.9 million DALYs) contribute relatively less at a global scale, but remain highly debilitating at the individual level. This distribution demonstrates that both high-mortality conditions (e.g., stroke) and non-fatal disabling disorders (e.g., migraine) dominate the global neurological health landscape (Feigin et al., 2019; Huang et al., 2023).

Figure 4: Leading Neurological Disorder DALYs in India as per Global Burden of Disease Study, 2019



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India contributes a substantial share of South Asian neurological disease burden. Stroke and migraine dominate, mirroring the global picture but at a particularly high absolute scale due to India's large population. Dementia and epilepsy are also prominent, indicating that both ageing-related and long-standing neurological conditions contribute significantly. Meningitis remains more prominent in India compared to high-income countries, reflecting persistent challenges with infectious disease control. Parkinson's disease and tension-type headache contribute moderately, while conditions such as multiple sclerosis and motor neuron diseases account for smaller proportions but remain clinically important (Gourie-Devi et al., 2004). This India-specific profile underscores the need for targeted strategies addressing both vascular and infectious neurological disorders, alongside preparation for the rising tide of dementia and other age-associated diseases.

Prevalence of Neurological Disorders in Metropolitan and Non-Metropolitan Regions

The epidemiological footprint of neurological disorders in India reveals a sharp urban-rural divide. In the case of stroke, there has been a concerning increase in the cases among younger adults (20-45 years) in metropolitan hospitals, which is attributed to the effect of stress, sedentary lifestyle, and poor quality of sleep. Indicatively, the number of stroke cases among IT professionals has increased many times over the last few years in Hyderabad. On the same note, urban women aged 30-45 years are significantly more susceptible to migraine with stress and hormonal fluctuations being synergistic conditions. According to the national statistics, migraine affects 15-18 percent of women and 6-8 percent of men, and it was more detected in urban healthcare systems (WHO Neurological Disorders Report, 2021). In contrast, epilepsy has increased prevalence in rural India because it is perinatally injured, neuro-infected, whereas metropolitan centres have higher rates of drug resistant cases subject to tertiary care. Both dementia and Parkinson disease are also disproportionately identified in urban populations, which is partly explained by the fact that better diagnostic facilities and longer life expectancy in cities are detected. Notably, stress in urban living conditions is a precipitating factor via vascular and metabolic risk and an exacerbating factor enhancing cognitive deterioration and motor symptoms. Although the incidence of neurological diseases in the world has shown significant disparities by region, India depicts a very intricate epidemiological picture, owing to its high rates of urbanisation and population heterogeneity. As over one-third of the population has moved into metropolitan regions and it is estimated that half of India will be urban by 2050 (WHO, 2021), the distribution of neurological disorders is a growing culture of the duality of urban stress-related disorders and rural under-diagnosis with high treatment gaps. Stroke and migraine exhibit an increase in their prevalence in metropolitan regions, especially in younger adults with the rise of exposure to sedentary jobs, lengthy commuting distances, and chronic psychosocial stress. Conversely, epilepsy and dementia tend to be more problematic in rural areas and indicates a lack of specialised care, untreated vascular and infectious risk factors and socioeconomic obstacles to prompt diagnosis. Parkinson disease exists between two worlds, as the prevalence is more detected in urban areas, yet there is an environmental exposure, pesticide use that may lead to rural prevalence (Janardhana et al., 2023). These tendencies take place against the background of alarming national prognoses: neurological diseases affect 20-30 million Indians, with the prevalence rate ranging between 967 to 4070 per hundred thousand people, and the overall burden is also projected to increase by 23 percent by 2025 (WHO, 2021). More so, comprehensive state-level analysis of Global Burden of Disease Study (1990-2019) indicates non-communicable neurological disorders share in total DALYs increased in India by 4.0% to 8.2% in 1990 and 2019, respectively, with injury-related DALYs increasing by 0.2 to 0.6. Communicable neurological diseases went down to 4.1 to 1.1. In 2019, headache disorders (17.5%), stroke (37.9%) and epilepsy (11.3%) were the leading causes with considerable state discrepancies (Singh et al., 2021). These tendencies altogether highlight the fact that the crisis of neurological health in India is not only increasing but also fragmented by the metropolitan tendency to over-diagnose stress-related illness and rural tendencies to ignore preventable and curable neurological diseases. The variations in metropolitan and non-metropolitan trends are condensed in Table 1, which identifies the prevalence, patterns, and major differences of major neurological disorders in India.

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Table 1: National Prevalence and Key Causes of Neurological Disorders

Disorder	National Prevalence	Metropolitan and Non-Metropolitan Trends	Key Causes	References
Stroke	Stroke is a significant neurological disorder in India, with prevalence rates varying widely across urban and rural settings, ranging from 44.54 to 487 per 100,000 population.	Impacts approximately 33-123/100,000 of the population. Increasing incidence among younger adults (20–45 yrs), especially IT professionals in cities like Hyderabad and Bengaluru. Rural areas have reported around 123.57/100,000 cases of stroke. Worse outcomes occur due to limited acute care and rehab access.	Hypertension, diabetes, obesity and sedentary lifestyle.	Hedau et al., 2024
Migraine	Migraine prevalence in India ranges between 14% and 26% nationally, with significant regional variations and a strong female predominance.	Multiple regional studies provide robust evidence of migraine's epidemiology. The Delhi and NCR study found a 26.3% one-year migraine prevalence, whereas an Eastern India study reported a prevalence of 14.12%. Rural areas consistently show higher prevalence rates, with females experiencing significantly higher rates (35.7% vs. 15.1% in males)	Environmental exposure, education levels and oral contraceptives account for about 75% of migraine cases.	Chowdhury et al., 2024
Dementia (incl. Alzheimer's)	Dementia affects approximately 20 per 1,000 people in India, with an estimated 4.1 million current cases expected to double by 2030.	Prevalence rates appear similar across rural and urban populations	Rapidly rising with ageing, Low education levels, Family history, and Hypertension	Kumar et al., 2019
Epilepsy	Epilepsy affects approximately 10-12 million people in India, with a national occurrence of 4.7 per 1,000 population.	Studies reveal that neurological problems are twice as common in rural as in urban settings, indicating a significantly higher incidence in rural communities.	Neuroinfections, Neurocysticercosis, Neurotrauma, Birth injuries,	Dhiman et al., 2021
Parkinson's Disease	Shows significant regional variation, with incidence rates between 42.3 to 52.85 per 100,000 population, increasing dramatically to 308.9 per 100,000 in populations over 60 years old.	Metropolitan cities like Kolkata demonstrate slightly higher prevalence rates compared to rural areas. While specific national-level data remains limited, studies consistently show that PD prevalence increases with age for both genders	Potential genetic and environmental factors, though no definitive links have been established.	Je et al., 2021, Khurana et al., 2025.

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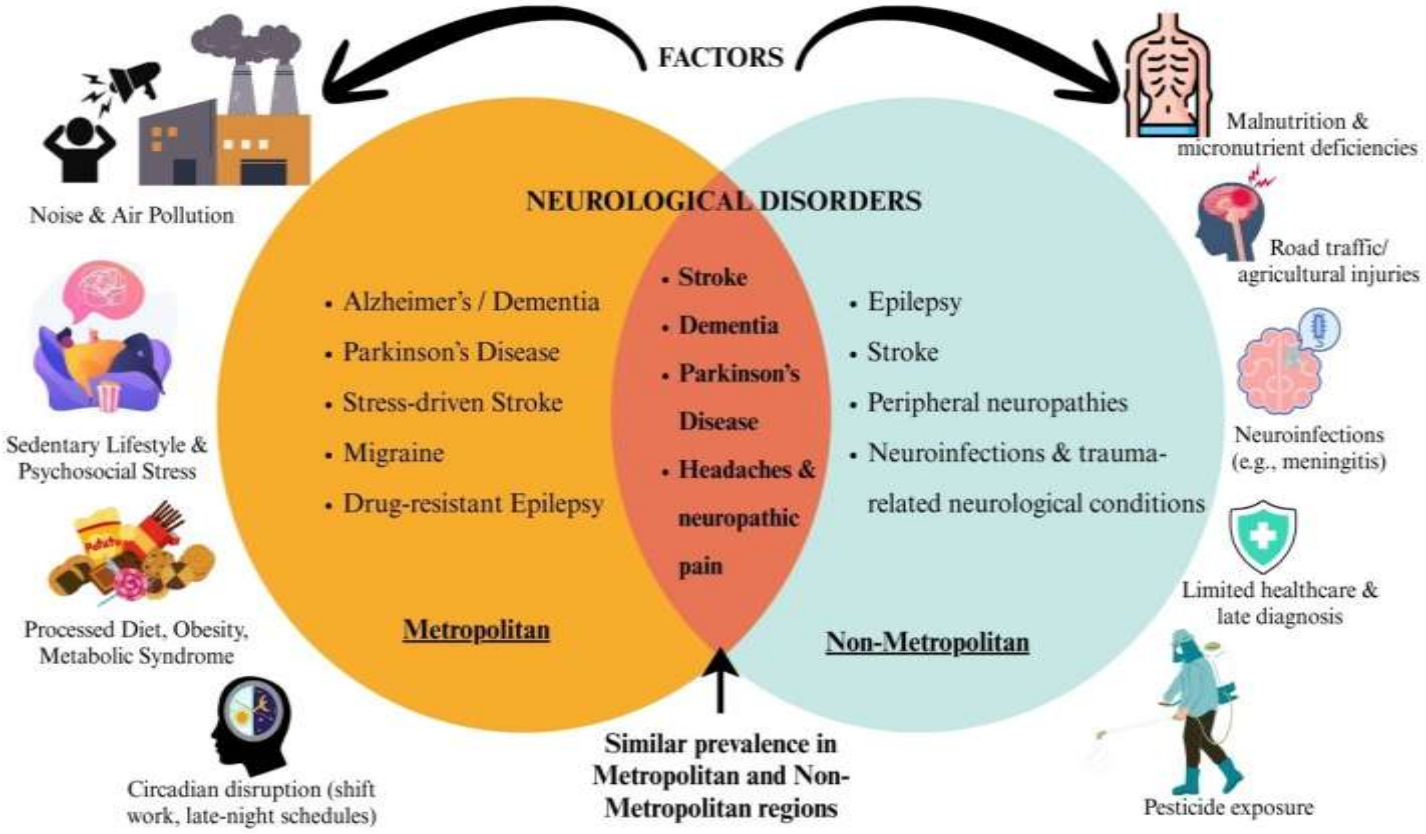
Figure 5: Prominent Neurological Disorders in Metropolitan and Non-Metropolitan Areas



Burden of Neurological Disorders in Metropolitan and Urban regions of India

According to recent reports, the number of stroke cases is growing significantly in young adulthood in metropolitan areas like Bengaluru, Hyderabad, and Delhi, especially among IT professionals and corporate workers who work long hours, are exposed to chronic stress, and lack sleep. The incidence of migraine also varies in urban areas, with 15 to 18% of women and 6 to 8% of men experiencing it, and urban women aged 30 to 45 being the most susceptible group of people because of the combination of stress and hormonal changes and disrupted regularities (WHO, 2021). Metropolitan populations have higher rates of dementia and Parkinson disease not only due to the increased life expectancy but also to the increased number of special diagnostic facilities and care (Janardhana et al., 2023). Moreover, the prevalence of drug-resistant epilepsy is also rising in urban India in tertiary hospitals, indicating better detection and lifestyle factors including sleep deprivation and comorbid mental disorders (Dhiman et al., 2021)

Burden of Neurological Disorders in Non-Metropolitan and Rural regions of India

In non-metropolitan regions of India, the prevalence of epilepsy is higher, and surveys show a combined prevalence of 11.9 per 1,000 people in rural regions as opposed to 5.7 per 1,000 in urban regions (Dhiman et al., 2021). This gap is closely attributed to perinatal injuries, neurocysticercosis which has not been treated and increased rates of traumatic brain injuries due to road accidents and farm hazards. There is also a possibility of underdiagnosis of dementia in non-metropolitan areas because the vascular risks (hypertension and diabetes) are not well controlled, thereby increasing the true prevalence, which is higher than the reported one. Pesticide exposure and agricultural activity have been suggested as risk factors for higher prevalence in some rural groups, despite the fact that cases of Parkinson's disease are disproportionately reported in metropolitan areas (Janardhana et al., 2023). The fact that neuroinfections and malnutrition-induced neurological morbidity persist in non-metropolitan regions elucidates the contribution of the socioeconomic inequities to disease distribution.

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The differences in the prevalence of neurological disorders between metropolitan and non-metropolitan regions should be cautiously interpreted to account for potential epidemiological variability and to identify disparities in diagnostic accessibility (Gourie-Devi, 2014). Magnified rates of migraine (26.3% in the metropolitan regions versus 14.1% in the Eastern India rural cohort) (Chowdhury et al., 2024) and Parkinson disease (Janardhana et al., 2023) are the main indicators of better diagnostic infrastructure such as the presence of neurologists, access to MRI/CT, and awareness of the disease instead of actual increase in incidence (WHO, 2021). Conversely, the prevalence of epilepsy (11.3% DALY share) and neuroinfections in non-metropolitan regions represent increased burden due to untreated perinatal insults, pesticide exposure, and neurocysticercosis, in which underdiagnosis causes relative rural inequities (Singh et al., 2021). This diagnostic gradient is the reason why stroke is consistently prevalent on a national level (44-487/100,000) in all regions because its sudden and severe symptom onset requires emergency care regardless of the location (Hedau et al., 2024).

Plant-based Treatments of Neurological Disorders

The available pharmacological therapies in the treatment of neurological disorders are symptomatic but are still insufficient in the prevention of diseases. Symptoms can be treated with drugs like antiepileptics, dopaminergic, and cholinesterase inhibitors, but they have serious side effects, including drowsiness, dyskinesias, nausea, and cardiovascular factors (Singh et al., 2021; Feigin et al., 2021). Additionally, most neurological diseases do not have disease-modifying therapies, and therefore their medical need has not been met sufficiently. Within the Indian context, the problem is aggravated by differences in accessibility to healthcare between metropolitan and non-metropolitan areas, expensive healthcare and a high number of individuals that depend on traditional healthcare systems like Ayurveda. Plant-based therapies are a cheap, culturally acceptable, and sustainable alternative. Medicinal plants are also source of a variety of bioactive phytochemicals that can directly act on the pathophysiological pathways of neurodegeneration, ischemia and synaptic dysfunction with anti-inflammatory, antioxidant, adaptogenic, neurotrophic and anti-apoptotic effects. Phytochemicals are particularly helpful in multifactorial disorders like stroke, dementia, and epilepsy because, unlike single-target synthetic medications, they often act on multiple biological pathways simultaneously (Janardhana et al., 2023). The *Bacopa monnieri* (brahmi), *Withania somnifera* (ashwagandha), *Curcuma longa* (turmeric) and *Centella asiatica* (gotu kola) are traditional Indian herbs already known to have an adaptogenic effect as well as neuroprotective properties, and have been incorporated into folk and Ayurvedic preparations. These effects are increasingly being confirmed by modern pharmacological studies, which offers a chance to reconcile conventional knowledge with the evidences of neurology. Plant-based therapies have multi-target effects (anti-inflammatory, anti-apoptotic, antioxidant, neurotrophic, modulation of synapses) and these are in line with the intricate pathobiology of major neurological disorders.

Plant-derived compounds such as polyphenols, terpenoids, curcuminoids have antioxidant and anti-inflammatory properties, blocking COX-2 production, nuclear factor kappa B signalling and proinflammatory cytokines for example IL-1β and TNF-α (Gawrysz et al., 2025; Fan & Lei, 2022). These agents also support mitochondrial integrity and anti-apoptotic pathways, evidenced by modulation of the Bcl-2/Bax ratio, suppression of caspase-3, and stabilisation of neuronal membranes (Gawrysz et al., 2025). Their influence on neurotransmission and synaptic plasticity encompasses GABAergic facilitation, cholinesterase inhibition, modulation of glutamate and NMDA, and upregulation of BDNF (Gawrysz et al., 2025; Semwal et al., 2014). Additionally, endothelial stabilisation and antiplatelet effect aid cerebrovascular protection, especially in a situation of ischemic injury (Fan & Lei, 2022).

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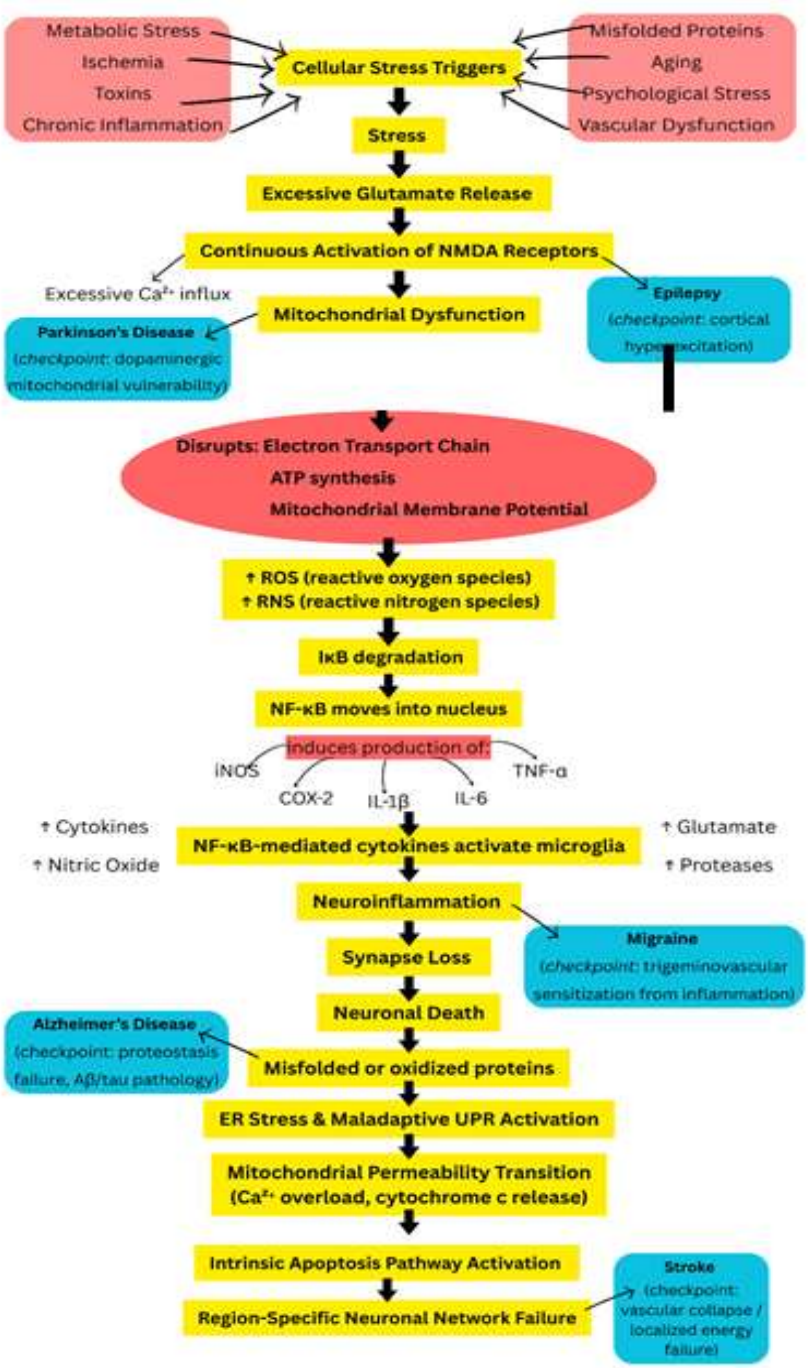
Figure 6: Major inflammatory pathways of neurological disorders



*Checkpoints mark the stages in the shared pathway where each neurological disorder emerges based on its dominant underlying mechanism.

In stroke, curcumin from *Curcuma longa* provides potent antioxidant, anti-inflammatory, and anti-apoptotic actions, reducing clot size and cerebral oedema, while enhancing mitochondrial and endothelial function (Gawrysz et al., 2025; Fan & Lei, 2022; W. Wang & Xu, 2020). Ginkgolides and bilobalide from *Ginkgo biloba* serve as an antagonist to platelet-activating factor and are used for treating inflammation, supporting microcirculation and mitochondrial health, and act as a supplement in stroke recovery. Traditional neuroprotective agents, such as *Acorus calamus* and *Nardostachys jatamansi*, exhibit antioxidative and anti-apoptotic effects. In migraine, *Withania somnifera* modulates the HPA axis and reduces neuroinflammation (Pandit et al., 2024), while *Centella asiatica*, through asiaticoside and madecassoside, supports neurotrophy and suppresses inflammation-induced neurodegenerative markers (Ansari et al., 2025). *Curcuma longa* also contributes to anti-inflammatory effects relevant to nerve-blood vessel system activation. For dementia and Alzheimer's disease, bacosides and bacosaponins from *Bacopa monnieri* enhance synaptic plasticity and

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memory, while anti-amyloid and antioxidant effects ((Eraiah et al., 2024; Gościniak et al., 2025). Withanolides and sitoindosides from *Withania somnifera* offer anti-inflammatory, anti-amyloidogenic, and neuroprotective benefits and stress-ameliorating properties. Curcumin and demethoxycurcumin from *Curcuma longa* modulate neuro-inflammatory pathways making it a promising long-term therapeutic (Gawrysz et al., 2025). In Parkinson's disease, *Mucuna pruriens* acts as a source of L-DOPA for dopaminergic support and reducing motor fluctuations. *Withania somnifera* demonstrates antioxidant, anti-apoptotic, and dopaminergic stabilisation effects including a favourable Bcl-2/Bax balance and α-synuclein aggregation attenuation (Prakash et al., 2014). *Bacopa monnieri* can further support anti-inflammatory and antioxidant defences. In epilepsy, *Centella asiatica* and *Bacopa monnieri* offer GABAergic facilitation and antioxidant protection, which may complement anticonvulsant therapies (Gościniak et al., 2025). *Nardostachys jatamansi* provides experimental anticonvulsant effects likely through GABA modulation and membrane stabilisation. For neuropathic pain and diabetic neuropathy, both *Curcuma longa* and *Withania somnifera* provide anti-inflammatory and neurotrophic support targeting sensitisation in peripheral and central pathways. In traumatic brain injury (TBI), curcumin alleviates oxidative stress, decreases inflammatory cytokines (e.g., IL-1β, IL-6, TNF-α), reduces cerebral oedema, enhances BDNF, synapsin-I, and CREB expression, and optimises apoptotic markers (Farkhondeh et al., 2019). *Withania somnifera* and *Centella asiatica* add complementary anti-inflammatory, anti-oedema, and neurotrophic support, aiding recovery and rehabilitation. Collectively, these phytochemicals offer multi-targeted neuroprotection through antioxidant, anti-apoptotic, anti-inflammatory, synaptic plasticity, neurotrophic and cerebrovascular pathways. As adjuncts, not substitutes to standard care, they hold promise when supported by clinical validation for safety, dosing, and efficacy. Table 2 compiles commonly investigated medicinal plants, their major phytochemicals, and their proposed mechanisms of neuroprotection across neurological disorders.

Table 2: Commonly used plants for the treatment of neurological disorders

Plant	Key Phytochemicals	Proposed Mechanisms	Target Neurological Disorders	References
Curcuma longa	Curcumin, demethoxycurcumin	Antioxidant (↓ ROS), anti-inflammatory (↓ NF-κB, TNF-α), anti-amyloid, neurogenesis, cerebrovascular protection	Stroke, dementia/AD, migraine, neuropathic pain, TBI	Garodia et al., 2023, Genchi et al., 2024
Withania somnifera	Withanolides, sitoindosides	Adaptogenic (HPA modulation, ↓ cortisol), neurotrophic, GABA-mimetic, antioxidant	Stress-linked migraine, dementia/AD, PD, neuropathic pain, TBI	Lerose et al., 2024,
Bacopa monnieri	Bacosides A & B	Synaptic plasticity, cholinesterase inhibition, antioxidant, anti-amyloid	Dementia/AD, epilepsy, PD	Prabhakar et al., 2020
Centella asiatica	Asiaticoside, madecassoside	Neurotrophic, anxiolytic, GABAergic, cerebrovascular protection	Migraine, epilepsy, dementia, PD	Ansari et al. 2025, Mando et al., 2024
Mucuna pruriens	Natural L-DOPA, alkaloids	Dopaminergic support, antioxidant	Parkinson's disease	Hammoud et al., 2025
Ginkgo biloba	Ginkgolides, bilobalide	PAF antagonism, ↑ cerebral blood flow, mitochondrial protection, antioxidant	Stroke recovery, dementia/AD	Singh et al., 2019
Nardostachys	Jatamansone	GABA modulation,	Epilepsy, stroke,	Pathak & Godela,

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jatamansi	(valeranone), sesquiterpenes	anticonvulsant, antioxidant, anti-apoptotic	anxiety	2024
Acorus calamus	α- and β-asarone	Neuroprotective, antioxidant, anti-apoptotic	Stroke, epilepsy, cognitive disorders	Balakrishnan et al., 2022

AD- Alzheimer's Disease, PD- Parkinson's Disease, ROS- Reactive Oxygen Species, GABA- Gamma-Aminobutyric Acid, L-DOPA- L-3,4-Dihydroxyphenylalanine, TNF-α- Tumor Necrosis Factor-alpha, HPA-Hypothalamic-Pituitary-Adrenal, NF-κB-Nuclear Factor Kappa-light-chain-enhancer of activated B cells, TBI-Traumatic Brain Injury, PAF-Platelet Activating Factor, ↑: increase; ↓: decrease.

Phytochemicals in Neurological Disorders

Plant-derived compounds have long played an important role in the management of neurological disorders, with many already incorporated into modern therapeutic regimens. For instance, galantamine, an Amaryllidaceae alkaloid derived from *Galanthus* and *Narcissus* species, is approved by FDA for Alzheimer's disease due to its acetylcholinesterase inhibitory activity. Similarly, huperzine A from *Huperzia serrata* is a potent reversible acetylcholinesterase inhibitor that has shown promise in improving cognitive function, although its clinical application remains limited outside China. Resveratrol, a stilbene from grapes, *Vitis vinifera*, exerts neuroprotective effects by antioxidant and anti-inflammatory mechanisms and has been investigated for its role in Alzheimer's, Parkinson's, and cerebrovascular diseases. Another widely studied phytochemical is Curcumin from *Curcuma longa* that is known for its pleiotropic antioxidant, anti-inflammatory, and anti-amyloidogenic effects. Beyond these, withanolide A from *Withania somnifera*, asiaticoside from *Centella asiatica*, ginkgolide B from *Ginkgo biloba*, cannabidiol from *Cannabis sativa*, bacoside A from *Bacopa monnieri*, and lycopene from *Solanum lycopersicum* represent diverse structural classes including terpenoids, alkaloids, flavonoids, and carotenoids. Collectively, these phytochemicals show the therapeutic versatility of plant secondary metabolites in neurological disorders. The diverse classes of neuroactive phytochemicals and their neuroprotective roles are outlined in Table 3.

Table 3: Various Classes of Phytochemicals and Their Neuroprotective Roles

Class	**Representative Compounds with Plant Sources**	**Neuroprotective Role**	**References**
Alkaloids	Huperzine A (*Huperzia serrata)*	A reversible acetylcholinesterase inhibitor that enhances memory in Alzheimer's disease.	Callizot et al., 2021, Suvaiv et al., 2025
	Galantamine (*Galanthus* species)	FDA-approved for Alzheimer's disease, it enhances cholinergic neurotransmission.	Varadharajan et al., 2023.
	Morphine, Codeine (*Papaver somniferum)*	Pain control in neurological conditions.	Bharti et al., 2023
	Berberine (*Berberis* species)	Neuroprotective, anti-inflammatory, and anti-amyloidogenic in Parkinson's and Alzheimer's disease models.	Cheng et al., 2022, Tian et al., 2023
Flavonoids	Quercetin (Onions, apples)	Reduces oxidative stress, prevents neuroinflammation, and improves cognition.	Chiang et al., 2023
	Kaempferol (Green tea, *Ginkgo*	Neuroprotection via antioxidant	Nezhad Salari et

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	biloba)	mechanisms.	al., 2024, Santos et al. 2022
	Apigenin (*Chamomilla recutita)*	Anxiolytic and neuroprotective.	Olasehinde & Olaokun, 2024
	EGCG (Epigallocatechin gallate) (*Camellia sinensis* (green tea))	Modulates amyloid-beta aggregation, prevents neuronal apoptosis.	Mokra et al., 2022
Polyphenols (Non-flavonoids)	Curcumin (*Curcuma longa)*	Reduces amyloid-beta, inhibits alpha-synuclein aggregation and exhibits strong antioxidant properties.	Xu et al., 2022
	Resveratrol (Grapes, red wine, *Polygonum cuspidatum)*	SIRT1 activation, improves mitochondrial function, and demonstrates neuroprotective properties.	Shaito et al., 2023
	Caffeic & Ferulic acids (Various medicinal plants)	Antioxidant and anti-inflammatory neuroprotection.	Singh et al., 2022
Saponins	Bacosides (*Bacopa monnieri)*	Enhance memory, synaptic plasticity, extensively studied in Alzheimer's disease; and guard against oxidative damage.	Valotto Neto et al., 2024
	Ginsenosides (*Panax ginseng)*	Modulate neurotransmission, reduce oxidative stress, and improve cognition; clinical evidence supports its use in stroke and dementia recovery.	Feng et al., 2022, Lee et al.,2024
Glycosides	Salidroside (*Rhodiola rosea)*	Adaptogen reduces stress-induced neuronal damage.	Liang et al., 2024
	Stevioside (*Stevia rebaudiana)*	Antioxidant and neuroprotective (experimental stage).	Wang et al., 2025
Essential Oils / Aromatic Compounds	Linalool (*Lavandula angustifolia)*	Anxiolytic, anticonvulsant (GABAergic modulation).	Bavarsad et al., 2023
	Menthol (*Mentha* species)	Analgesic, anti-migraine.	Li et al.,2022, De Oliveira Koren et al., 2024
	Thymol, Carvacrol (*Thymus vulgaris*, *Origanum vulgare)*	Neuroprotective via antioxidant/anti-inflammatory pathways.	Gago et al., 2025
Coumarins	Umbelliferone, Scopoletin (*Ferula*, *Angelica* species)	Neuroprotection through anti-inflammation and antioxidation.	Lin et al., 2023
Steroidal Compounds	Diosgenin (*Dioscorea* species)	Enhances memory and neurite outgrowth.	Yang and Tohda, 2023

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	β-sitosterol (Various medicinal plants)	Reduces oxidative stress, neuroprotective.	Tang et al., 2023
Lignans	Schisandrin B (*Schisandra chinensis)*	Improves cognition, antioxidant.	Lee et al., 2012
	Sesamin (Sesame seeds)	Protect neurons from oxidative stress.	Ruankham et al., 2019
Cannabinoids	Δ9-Tetrahydrocannabinol (THC), Cannabidiol (CBD) (*Cannabis sativa)*	Modulate endocannabinoid system; neuroprotective, anticonvulsant; studied in epilepsy, multiple sclerosis, and neurodegeneration.	Yousaf et al., 2022
Terpenoids – Monoterpenoids (C10)	Linalool (*Lavandula angustifolia)*	Anxiolytic, anticonvulsant via GABAergic potentiation; potential in anxiety, epilepsy.	Santos et al., 2022
	Menthol (*Mentha* species)	Analgesic and anti-migraine effects via TRP channel modulation.	Dillon et al., 2022
Terpenoids – Sesquiterpenoids (C15)	β-Caryophyllene (*Cannabis sativa*, Clove)	CB2 receptor agonist, anti-inflammatory and neuroprotective; potential in Alzheimer's and Parkinson's disease.	Zhang et al., 2022
	Parthenolide (*Tanacetum parthenium* (feverfew))	Historically linked to migraine prophylaxis; NF-κB pathway modulation.	Kashkooe et al., 2024
Terpenoids – Diterpenoids (C20)	Ginkgolide B, Bilobalide (*Ginkgo biloba)*	Protects against ischemic injury, supports cognitive function, and aids stroke recovery.	Cao et al., 2022
	Andrographolide (*Andrographis paniculata)*	Anti-inflammatory, neuroprotective, and modulates mitochondrial pathways.	Shan et al., 2025
Terpenoids – Triterpenoids (C30)	Withanolides (*Withania somnifera)*	Enhance synaptic plasticity, reduce stress-induced cognitive deficits; potential in cognitive ageing and Alzheimer's disease.	Vittal and Vinciguerra, 2025
	Asiaticoside (*Centella asiatica)*	Promotes neurite growth, improves memory, and has antioxidant activity.	Tan et al., 2021
Terpenoids – Tetraterpenoids (C40)	Lycopene (*Solanum lycopersicum* (tomato))	Potent antioxidant, protects dopaminergic neurons, adjunct in post-stroke recovery and Parkinson's disease.	Prema et al., 2015
	β-Carotene (Carrots, sweet potatoes)	Strong antioxidant, protective against cognitive decline.	Wang et al., 2023

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Plant-Derived Structural Analogs with Untapped Potential

The phytochemicals listed in table 3 have analogs with similar structures present in related plant species that are yet to be fully explored. For example, narwedine from *Narcissus pseudonarcissus* and sanguinine from *Galanthus woronowii* share the Amaryllidaceae alkaloid structure of galantamine but display stronger acetylcholinesterase inhibition in vitro (Armengol et al., 2011). Lycodoline, fawcettimine are structurally related to huperzine A and thus have a potential to give cholinesterase inhibitors a unique pharmacological property (Kitajima & Takayama, 2011; Ma & Gang, 2004). Oxyresveratrol of *Morus alba* and piceatannol of *Passiflora edulis* are among the extension of the neuroprotective family of resveratrol owing to their better anti-apoptotic and antioxidative properties (Shen et al., 2009). Curcumin analogs that are more stable like yakuchinone A from *Alpinia oxyphylla*; and dehydrozingerone from *Zingiber officinale*, provide better stability and different neuroprotective characteristics (Chun et al., 2002c). Other steroidal lactones like physalin B of *Physalis angulata* and withanolide E of *Physalis peruviana* have early potential in the control of neuroinflammation (Kuo et al., 2006; Mirjalili et al., 2009). Similarly, triterpenoid saponins such as aescin from *Aesculus hippocastanum* and glycyrrhizin from *Glycyrrhiza glabra* have the same neuroprotective effects as asiaticoside (Asl & Hosseinzadeh, 2008).

Andrographolide (*Andrographis paniculata*) and tanshinone IIA (*Salvia miltiorrhiza*) of the diterpenoid category replicate the vascular and mitochondrial protective effects of ginkgolides (Islam et al., 2018b; Lee et al., 2013). Cannabinoid-related products such as perrottetinene from *Radula marginata* and daurichromenic acid from *Rhododendron dauricum* increase the range of therapeutic opportunities in addition to cannabidiol (Chicca et al., 2018). In the same fashion, ginsenoside Rg1 (*Panax ginseng*) and jujuboside A (*Ziziphus jujube*) resemble the synaptogenic potential of bacosides (Kennedy et al., 2002; Wu et al., 2013), and carotenoid intermediates such as phytofluene (*Citrus paradisi*) and neurosporene (*Zae mays*) are analogous of lycopene antioxidant activity (Fraser & Bramley, 2004; Meléndez-Martínez et al., 2015).

The importance of the investigation of these analogs goes beyond pharmacological novelty. Many medicinal plant species producing frontline neuroprotective compounds are globally threatened due to habitat destruction, overharvesting, and climate change, while only a few are cultivated sustainably. Even under cultivation, the phytochemical makeup is frequently not the same as wild ones and, therefore, restricting consistency in therapy (Pammi, 2026). Structurally similar analogs propose a long-term and scientifically sound solution, as they retain the main pharmacophores and improve the characteristics, including bioavailability, blood-brain barrier diffusion, or safety profiles. Examples include oxyresveratrol, that has a greater antioxidative activity than resveratrol and narwedine that outperforms galantamine in acetylcholinesterase inhibition (Shen et al., 2009). The analogs not only guarantee the continuation of therapeutic effects but also help to preserve the biodiversity and promote equal neuropharmacological health of the metropolitan and non-metropolitan community by expanding the chemical repertoire and reducing the risk of dependence on endangered species. Table 4 lists the documented phytochemicals and their structural analogs to have neuroprotective and neurotherapeutic potential, while Table 5 highlights less-studied potential neuroprotective phytochemical analogs.

Table 4: Plant-Derived Analogs of Already Established Phytochemicals with Their Chemical Structures

Phytochemical (Plant Source)	**Plant-Derived Analogs (with source)**	**Structural Similarity**
Galantamine **(***Galanthus* spp.) Chemical Formula: $C_{17}H_{21}NO_3$	Narwedine *(Narcissus pseudonarcissus)* Chemical Formula: $C_{17}H_{19}NO_3$	Amaryllidaceae alkaloid sharing tetracyclic benzoazepine core; oxidation and O-methylation pattern variations (Armengol et al., 2011).

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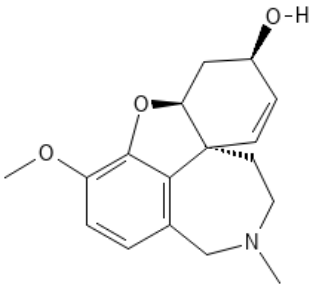
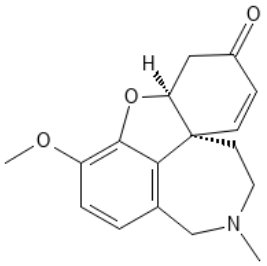
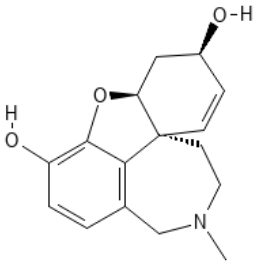
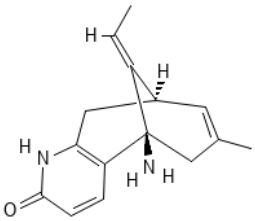
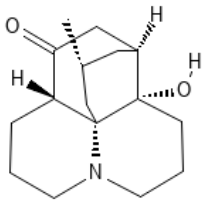
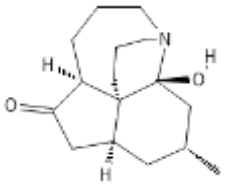
		
	Sanguinine *(Galanthus woronowii)* Chemical Formula: $C_{16}H_{19}NO_3$ 	Close Amaryllidaceae congener with the same polycyclic skeleton; substitution differences at aromatic positions (Georgiev et al., 2024).
Huperzine A **(***Huperzia serrata*) Chemical Formula: $C_{15}H_{18}N_2O$ 	Lycodoline *(Lycopodium clavatum)* Chemical Formula: $C_{16}H_{25}NO_2$ 	Lycopodium alkaloid with compact polycyclic nitrogenous scaffold; potential acetylcholinesterase inhibitor (Ma & Gang, 2004).
	Fawcettimine *(Lycopodium fawcettii)* Chemical Formula: $C_{16}H_{25}NO_2$ 	Shares bicyclic cage-like skeleton and tertiary nitrogen; differs in ring fusion/oxidation (Kitajima & Takayama, 2011).
Resveratrol Grapes (*Vitis vinifera*), *Polygonum cuspidatum* Chemical Formula: $C_{14}H_{12}O_3$	Oxyresveratrol *Morus alba* Chemical Formula: $C_{14}H_{12}O_4$	Stilbene backbone with an additional hydroxyl group; enhances antioxidant profile (Shen et al., 2009).

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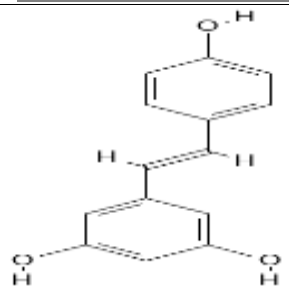
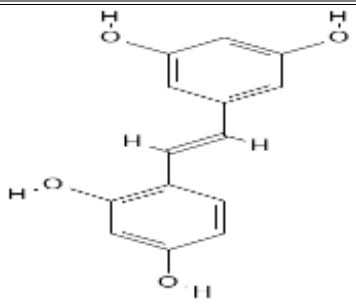
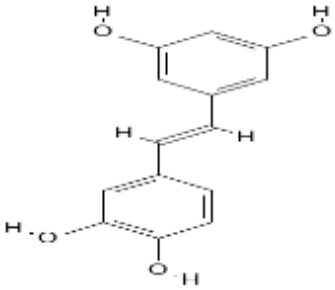
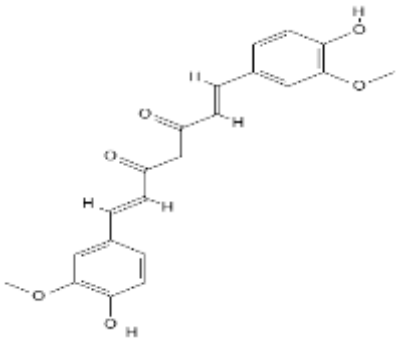
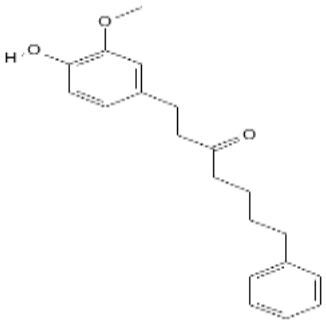
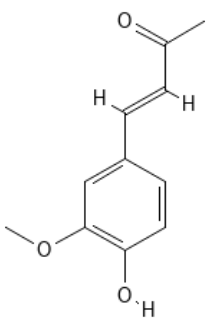
		
	Piceatannol *Passiflora edulis* Chemical Formula: $C_{14}H_{12}O_4$ 	Stilbene analog with extra hydroxylation; retains neuroprotective stilbene scaffold (Piotrowska et al., 2012).
Curcumin **(***Curcuma longa*) Chemical Formula: $C_{21}H_{20}O_6$ 	Yakuchinone A *Alpinia oxyphylla* Chemical Formula: $C_{20}H_{24}O_3$ 	Diarylheptanoid sharing conjugated enone linker; Michael acceptor conserved (Chun et al., 2002c).
	Dehydrozingerone *Zingiber officinale* Chemical Formula: $C_{11}H_{12}O_3$ 	"Half-curcumin" motif with vanillyl group and enone; common pharmacophore (Priyadarsini, 2014).

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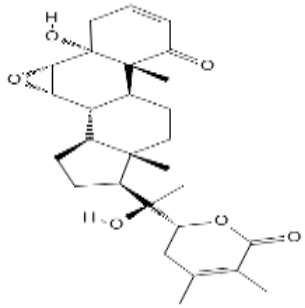
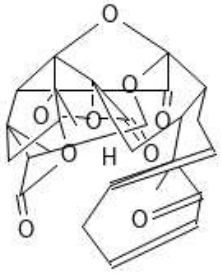
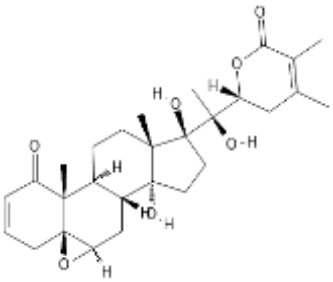
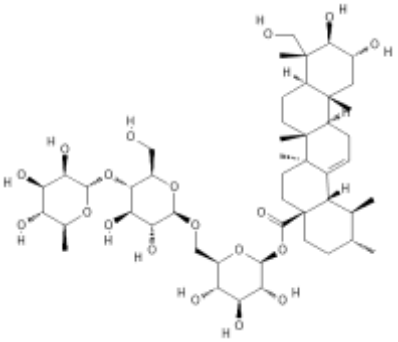
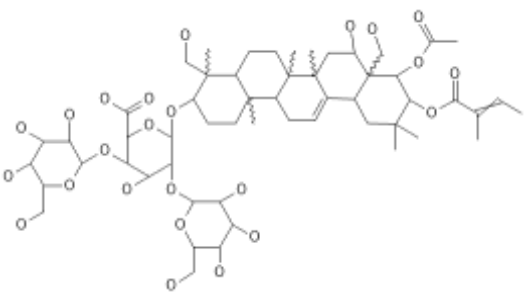
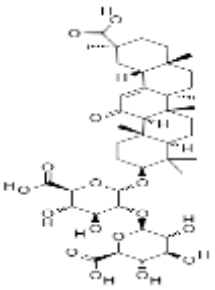
Withanolide A *Withania somnifera* Chemical Formula: $C_{28}H_{38}O_6$ 	Physalin B *Physalis angulate* Chemical Formula: $C_{28}H_{30}O_9$ 	Steroidal lactone with ergostane-derived framework and δ-lactone, akin to withanolides (Kuo et al., 2006).
	Withanolide E *Physalis peruviana* Chemical Formula: $C_{28}H_{38}O_7$ 	True withanolide congener with steroidal backbone; differs in stereochemistry and oxidation (Mirjalili et al., 2009).
Asiaticoside *Centella asiatica* Chemical Formula: $C_{48}H_{78}O_{19}$ 	Aescin *Aesculus hippocastanum* Chemical Formula: $C_{55}H_{86}O_{24}$ 	Triterpenoid saponin with oleanane aglycone and sugars, structurally similar to asiaticoside (Chindo et al., 2012).
	Glycyrrhizin *Glycyrrhiza glabra* Chemical Formula: $C_{42}H_{62}O_{16}$ 	Triterpenoid saponin with glycosylated pentacyclic triterpene, same class (Asl & Hosseinzadeh, 2008).

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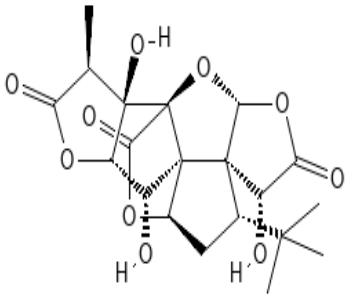
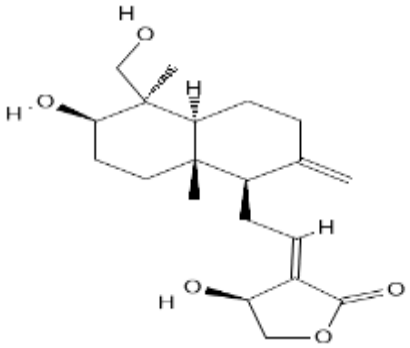
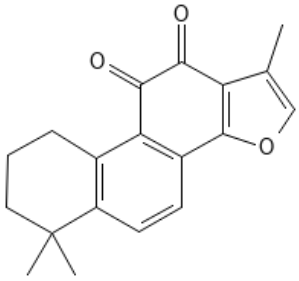
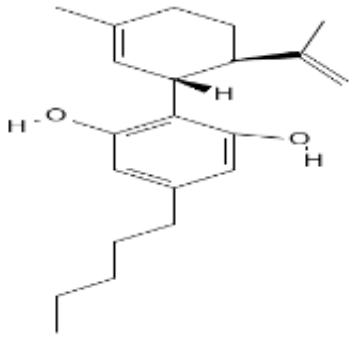
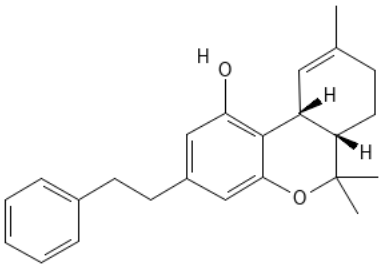
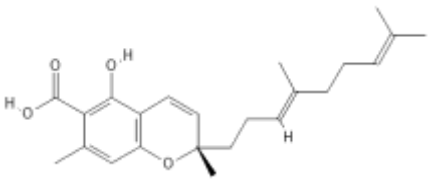
Ginkgolide B *Ginkgo biloba* Chemical Formula: $C_{20}H_{24}O_{10}$ 	Andrographolide *Andrographis paniculata* Chemical Formula: $C_{20}H_{30}O_5$ 	Diterpenoid lactone, oxygen-rich with lactone rings and hydroxyl groups (Islam et al., 2018b).
	Tanshinone IIA *Salvia miltiorrhiza* Chemical Formula: $C_{19}H_{18}O_3$ 	Abietane diterpenoid with conjugated quinone core; functional-class similarity (Lee et al., 2013).
Cannabidiol (CBD) *Cannabis sativa* Chemical Formula: $C_{21}H_{30}O_2$ 	Perrottetinene *Radula marginata* Chemical Formula: $C_{24}H_{28}O_2$ 	Cannabinoid-like meroterpenoid with resorcinyl aromatic ring and terpene chain (Chicca et al., 2018).
	Daurichromenic acid *Rhododendron dauricum* Chemical Formula: $C_{23}H_{30}O_4$ 	Prenylated chromene carboxylic acid; cannabinoid-like scaffold (Iijima et al., 2017).
Bacoside A	Ginsenoside Rg1	Dammarane-type

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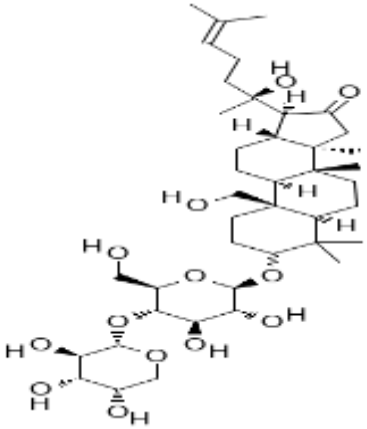
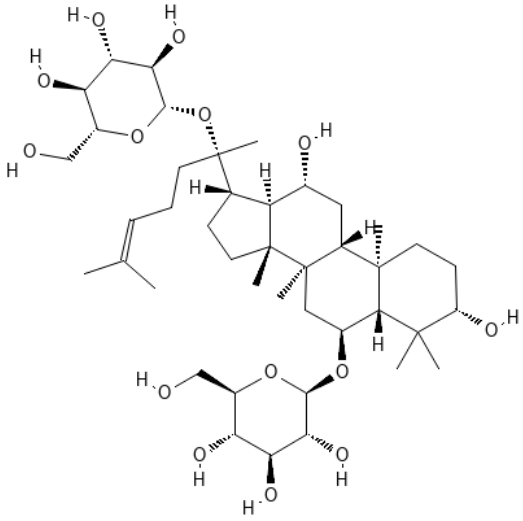
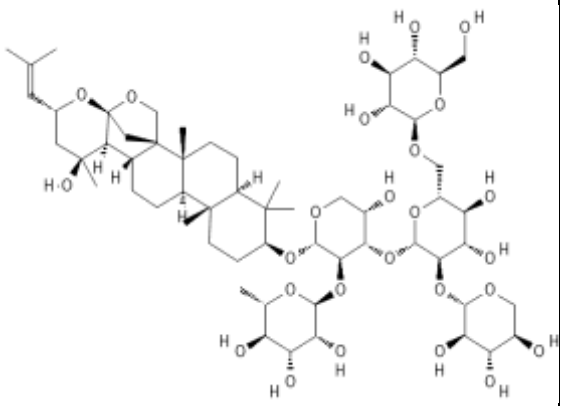
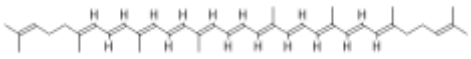
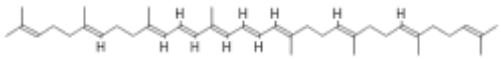
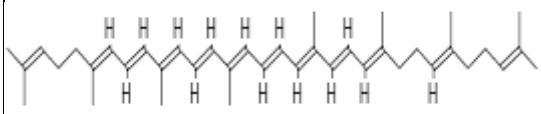
Bacopa monnieri Chemical Formula: $C_{41}H_{68}O_{13}$ 	*Panax ginseng* Chemical Formula: $C_{42}H_{72}O_{14}$ 	triterpenoid saponin with sugar chains; same amphiphilic scaffold (Kennedy et al., 2002).
	Jujuboside A *Ziziphus jujube* Chemical Formula: $C_{58}H_{94}O_{26}$ 	Triterpenoid saponin with oleanane core and oligosaccharides (Wu et al., 2013).
Lycopene *Solanum lycopersicum* Chemical Formula: $C_{40}H_{56}$ 	Phytofluene *Citrus paradise* Chemical Formula: $C_{40}H_{62}$ 	C_{40} carotenoid with fewer double bonds but same polyene chain (Meléndez-Martínez et al., 2015).
	Neurosporene *Zea mays* Chemical Formula: $C_{40}H_{58}$ 	C_{40} carotenoid, biosynthetic precursor to lycopene, differing by one double bond (Fraser & Bramley, 2004).

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Table 5: Neurological disorder-specific possible analogs for established compounds with their potential neuroprotective role

Neurological Disorder	Key Established Compound	Promising Analogs with Source Plant	Potential Neuroprotective Role
Alzheimer's disease	Galantamine (*Galanthus* spp.)	Narwedine (*Narcissus pseudonarcissus*); Sanguinine (*Galanthus woronowii*)	Enhanced acetylcholinesterase inhibition, improved cholinergic neurotransmission (Bastida et al., 2019)
	Huperzine A (*Huperzia serrata*)	Lycodoline (*Lycopodium clavatum*); Fawcettimine (*Lycopodium fawcettii*)	Potent cholinesterase inhibition, possible cognitive enhancement (Kitajima & Takayama, 2011; Ma & Gang, 2004)
	Resveratrol (*Vitis vinifera*, *Polygonum cuspidatum*)	Oxyresveratrol (*Morus alba*); Piceatannol (*Passiflora edulis*)	Stronger antioxidant, anti-apoptotic and anti-amyloidogenic effects (Piotrowska et al., 2012; Shen et al., 2009)
Parkinson's disease	Curcumin (*Curcuma longa*)	Yakuchinone A (*Alpinia oxyphylla*); Dehydrozingerone (*Zingiber officinale*)	Mitochondrial protection, inhibition of α-synuclein aggregation (Chun et al., 2002c)
	Withanolide A (*Withania somnifera*)	Physalin B (*Physalis angulata*); Withanolide E (*Physalis peruviana*)	Neuroinflammation modulation, dopaminergic neuron protection (Kuo et al., 2006; Mirjalili et al., 2009)
Stroke & Vascular Cognitive Impairment	Ginkgolide B (*Ginkgo biloba*)	Andrographolide (*Andrographis paniculata*); Tanshinone IIA (*Salvia miltiorrhiza*)	Anti-ischemic effects, mitochondrial stabilization, improved vascular function (Islam et al., 2018b; Lee et al., 2013)
Epilepsy & Seizure Disorders	Cannabidiol (CBD) (*Cannabis sativa*)	Perrottetinene (*Radula marginata*); Daurichromenic acid (*Rhododendron dauricum*)	Anticonvulsant potential, endocannabinoid system modulation (Chicca et al., 2018).
Cognitive Decline / Memory Disorders	Bacoside A (*Bacopa monnieri*)	Ginsenoside Rg1 (*Panax ginseng*); Jujuboside A (*Ziziphus jujuba*)	Synaptogenic support, improved learning and memory (Wu et al., 2013).
Migraine / Oxidative Stress-Linked Disorders	Lycopene (*Solanum lycopersicum*)	Phytofluene (*Citrus paradisi*); Neurosporene (*Zea mays*)	Antioxidant carotenoids, neurovascular protection (Meléndez-Martínez et al., 2015)

Pharmacokinetic Limitations and Standardization Challenges

Despite the promising structural analogy of these phytochemicals in extending neuroprotective efficacy, pharmacokinetic limitations persist, such as, poor bioavailability, rapid metabolism and limited blood-brain barrier penetration. Phytochemicals exhibit potent neuroprotective effects in vitro but face significant pharmacokinetic challenges in vivo, including low aqueous solubility, poor intestinal absorption, rapid first-

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pass metabolism via glucuronidation and sulfation, and quick systemic elimination (Amri et al., 2011; Anand et al., 2007; Kim et al., 2023).

Many compounds also show limited blood-brain barrier (BBB) penetration due to P-glycoprotein efflux and poor lipophilicity, hindering central nervous system targeting essential for disorders like Alzheimer's or Parkinson's (Bartels, 2011). These limitations underscore the need for targeted formulation strategies.

Analogs (e.g., yakuchinone A, oxyresveratrol) may offer modest improvements in stability or uptake, but overall, strategies like piperine co-administration (boosts curcumin AUC 20-fold by inhibiting metabolism), nanoparticles, or liposomes are needed to enhance bioavailability without toxicity (Kodli et al., 2025).

Phytochemical extracts exhibit significant compositional variability due to genetic diversity, edaphic factors, harvest timing, and post-harvest processing (Lu & Luthria, 2014). Unlike synthetic pharmaceuticals with defined molecular uniformity, botanical extracts have complex chemical matrices, making standardization essential for reproducibility and therapeutic predictability (Dawoud & Abdalbagi, 2025b). The identification of standardized phytochemical markers and validated chemical fingerprinting approaches is therefore critical to ensure batch-to-batch consistency, dosage accuracy, and pharmacological stability. Only then analogs can achieve clinical reliability comparable to synthetic neurotherapeutics.

Future Directions

The neurological disorders are increasingly affecting the global health and economy; hence the market of neurological drugs is expected to grow swiftly. Despite the continuous introduction of new neurological drugs, an enormous gap in effective therapeutics in terms of provision of such therapeutics still exist. The available therapies are expensive, in many cases have side effects, and are not widely available to a majority population, especially in rural and resource-constrained areas. This disequilibrium highlights the necessity of low cost, safer, and more sustainable alternatives.

Here, phytochemical analogs have the transformational potential. Analogs not only serve the purpose of supplementing the current drugs but additionally address the existing shortcomings like; restricted bioavailability, therapeutic inconsistency, and dependency on threatened medicinal plant species through the provision of structurally similar, though functionally superior molecules. Their pharmacological retention capability, coupled with stability and accessibility, makes them worthy alternatives for filling the demand-supply gap.

The future lies in identifying such analogs in a systematic manner as low-cost neurotherapeutic leads and establishing their validity. There is a strong demand to diversify the drug pipelines with cost-effective plant-derived analogs. Future research should prioritize pharmacokinetic optimization of these phytochemical analogs through advanced delivery systems such as nanoparticles, liposomes and metabolism inhibitors. Phytochemistry, computational modeling, and clinical validation can be strategically integrated to speed up the conversion of these analogs to clinically relevant drugs. The utilization of analogs would not only solve the worldwide problem of the lack of neurological therapeutics but also provide equal access to treatment, especially in such a country as India where the metropolitan dwellers are exposed to the risks of stress and develop neurological disorders and the residents of the non-metropolitan regions who are underdiagnosed and lack adequate treatment choices.

CONCLUSION

The therapeutic arena for neurological disorders is expanding beyond synthetic drugs and includes a wide range of plant-derived compounds. This review illuminates the differences in epidemiology of neurological disorders in the metropolitan and non-metropolitan areas of India and presents the therapeutic potential of known phytochemicals and their structural analogs produced by sustainable plant sources.

Although these plant-derived analogs have structural potential as neuroprotective systems but the pharmacokinetic challenges continue to hinder their potential application in clinical practice. Subsequent

studies ought to focus on pharmacokinetic enhancement using novel delivery methods such as nanoparticles and liposomes, and localized clinical trials which consider the metro and non-metropolitan differences in the Indian physiology, genetic polymorphisms in the metabolism of phytochemicals, and high-throughput screening of analogous compounds using a model based on Indian patient-derived neurons. Such systematic exploration and clinical trials of structurally related phytochemical analogs can pave the way forward as potential neurotherapeutics.

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