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Impact of Phytochemicals on Neuropsychological Health: A Review

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ABSTRACT

Phytochemicals are biologically active compounds produced by plants that can exert diverse effects on the human nervous system. Their influence on neuropsychological health may be beneficial, neutral, or adverse depending on their chemical nature, dose, exposure and biological targets. This review examines the relationship between plant-derived phytochemicals and neuropsychological health, with particular emphasis on neuroactive and neurotoxic mechanisms. Major phytochemical classes and their potential interactions with neurotransmitter systems, oxidative stress, neuroinflammation, receptors and cellular signalling pathways are discussed. Selected neuroactive plants, including *Bacopa monnieri*, *Centella asiatica*, *Withania somnifera* and *Curcuma longa*, are reviewed with respect to their major phytochemicals and reported effects on cognition, memory, stress and neuroprotection. In contrast, neurotoxic plants such as *Datura stramonium*, *Aconitum ferox*, *Strychnos nux-vomica* and *Lathyrus sativus* are examined for their toxic constituents and associated neurological and neuropsychological manifestations. The review highlights the dual nature of plant phytochemicals and emphasizes the importance of understanding their mechanisms, therapeutic potential and toxicity for informed use and future research.

Keywords: phytochemicals; neuroactive plants; neurotoxicity; neuropsychological health; phytochemical mechanism; central nervous system

1. Introduction

Phytochemicals represent a vast and diverse group of plant-derived secondary metabolites that serve critical ecological functions while also offering great potential for human health applications. These compounds, including flavonoids, polyphenols, alkaloids, and terpenoids, have evolved as sophisticated defence mechanisms in plants, protecting against pathogens, herbivores, and environmental stressors. In parallel, their pharmacological properties show remarkable efficacy in addressing chronic diseases such as cancer, cardio-vascular conditions, and neurodegenerative disorders. (Lara Popovic, 2025)

The 'Green' movement in Western civilization has changed public perceptions, with many now feeling that naturally generated substances and extracts are innately safer and more attractive than synthetic chemical products, resulting in increased sales of herbal treatments. About 80% of individuals in poor nations get their primary medical treatment from phytochemistry for both humans and animals.

In traditional medicine, a variety of herbs have been used to treat memory problems and neurodegenerative illnesses including Alzheimer's Disease (AD). Complex blends of organic molecules, herbal products might include fatty acids, sterols, alkaloids, flavonoids, glycosides, the saponins, tannins, terpenes, and more. Herbal medicine proponents contend that the combined advantages of a plant's constituent parts, rather than the individual compounds that pharmacologists isolate, are what provide it therapeutic efficacy; as a result, traditional medicines are said to be efficient and to have few or no adverse effects. (Nagaraju Bandaru et al., 2025)

While dietary phytochemicals (such as polyphenols and flavonoids) are widely studied for their neuroprotective properties, excessive ingestion or specific classes of plant secondary metabolites—particularly toxic alkaloids, cyanogenic glycosides, and high-dose supplements—can exert profound neurotoxic and neuropsychological disturbances by disrupting neurotransmission, inducing oxidative stress, and impairing cellular metabolism. (Tringo, 2023)

1.1. Phytochemicals

Phytochemicals are Low-Molecular-Weight (LMW) substances that hold a diverse array of bioactive compounds produced by plants that have long captivated human interest. These natural substances, often found in fruits, vegetables, herbs, and spices, have been utilized for centuries in traditional medicine systems worldwide. (Saiqali, 2025)

1.1.1. Classification of Phytochemicals

The phytochemicals are mainly classified into two types, Primary and Secondary metabolites. The secondary metabolites are further classified. These bioactive compounds are broadly classified into several categories, including alkaloids, phenolics, terpenoids, glycosides, saponins, lignans, steroids, carotenoids, flavonoids, and anthocyanins. Each category encompasses a wide array of compounds, each exhibiting unique bioactivities.

Primary metabolites are essential compounds produced by living organisms that play a crucial role in their growth, development, and reproduction. These metabolites are involved in the primary metabolic processes such as respiration and photosynthesis, and are typically present in most cells throughout the body. Unlike secondary metabolites, primary metabolites are not involved in ecological interactions but are vital for the physiological functions of the organism.

Table 1. Comparison of primary and secondary metabolites.

Sl. No.	Feature	Primary metabolites	Secondary metabolites
1.	Role in Growth and Development	Directly involved and essential	Not directly involved, but important for survival in a specific context.
2.	Production phase	Growth phase (Trophophase)	Secondary phase (Idiophase) or in response stimuli.
3.	Distribution	Ubiquitous across many species.	Often species-specific or restricted to certain groups.
4.	Amount produced	Large amounts	Small amounts.
5.	Ease of extraction	Relatively easy	Can be challenging.
6.	Primary function	Basic metabolic processes, growth, and reproduction.	Ecological interactions, defence, signalling, etc..
7.	Examples	Carbohydrates, proteins, nucleic acids, and lipids.	Phenolics, alkaloids, terpenoids, and flavonoids.

Secondary metabolites are not directly involved in plant growth and development, but they play important roles in defense against herbivores, pathogens, and environmental stresses. They are often responsible for the flavors, aromas, and colors of plants. Secondary metabolites are further classified into several classes based on their chemical structure and biosynthetic pathways. Some of the major classes include Phenolics, alkaloids, terpenoids, flavonoids and others. They serve as lead compounds for the development of new and novel drugs. They also serve as active ingredients in traditional herbal remedies. Numerous life-saving and health-improving drugs are derived from these secondary metabolites. (Saiqali, 2025)

1.1.2. Classification of Secondary Metabolites

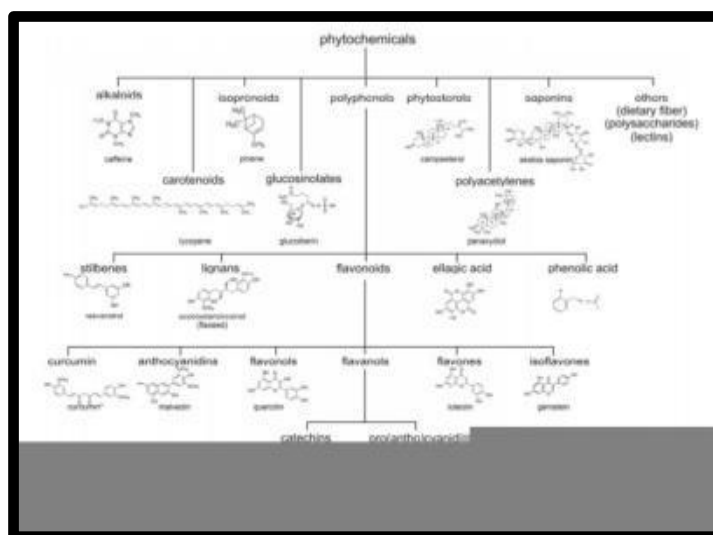


Figure 1. Classification of secondary metabolites.

The structural diversity of phytochemicals, estimated to exceed 100,000 distinct compounds, reflects their evolutionary adaptation to a myriad of ecological challenges. The Chemical classification of phytochemicals organizes these compounds into major categories based on their core structures and biosynthetic pathways, although there is no consensus on a uniform classification system for phytochemicals. Because of the structure-based classification, great diversity in function may exist. Polyphenols including flavonoids (quercetin, catechins) and stilbenes (resveratrol) demonstrate potent antioxidant and anti-inflammatory activities. Terpenoids encompass compounds ranging from volatile monoterpenes to complex carotenoids like lycopene, exhibiting diverse biological activities including antimicrobial effects and vision support. Nitrogen-containing alkaloids such as caffeine and morphine demonstrate potent neurological effects in both plants and humans, while sulphur-containing compounds including glucosinolates release

beneficial hydrogen sulphide with antioxidant and anti-inflammatory properties. The metabolic transformation of these compounds, both by bacterial and host enzymes, often enhances their bioactivity, as seen with curcumin which is converted to tetrahydrocurcumin. The bioavailability of curcumin is greatly enhanced by piperine. (Lara Popovic, 2025)

Table 1 summarizes the distinction between primary and secondary metabolites, while Figure 1 illustrates the major classes of secondary metabolites.

1.1.3. Principles of Phytochemicals

- Foundations and Evolution of Phytochemistry Science
- Extraction Methods and Technological Advances
- Metabolism, Bioavailability, and Clinical Translation
- Biomedical applications

1.2. Neurobiological Mechanisms

Neurobiological mechanisms refer to the physical, chemical, and biological processes inside the nervous system that control how we think, feel, and act.

The growing prevalence of mental health issues and cognitive impairment poses a significant challenge to global public health. Conditions such as depression, anxiety, neurodegenerative diseases, and stress-related cognitive dysfunction are becoming more common, while conventional pharmacotherapies are often limited by suboptimal efficacy, adverse side effects, and concerns about long-term use. Against this backdrop, neurophytochemistry—the study of plant-derived bioactive compounds—has emerged as a promising area of research. (Halina et al., 2025)

Depression affects over 300 million people worldwide, according to the World Health Organization (WHO), and is identified as the leading cause of disability worldwide. At the same time, neurodegenerative diseases such as Alzheimer's are increasing at an unprecedented rate. Multiple reviews have outlined that aging is the primary risk factor for developing neurodegenerative diseases and their associated comorbidities, including vascular, metabolic, and immune diseases in the elderly. As global life expectancy continues to rise, the prevalence of these diseases is expected to increase, placing a significant burden on health-care systems worldwide. Unfortunately, current therapeutic options are very limited, with no interventions capable of halting or reversing the progression of these diseases. Studies have emphasized the significance of modifiable lifestyle factors, particularly diet, in relation to mental and cognitive health. Plant-derived compounds possess essential antioxidant, anti-inflammatory, anti-cholinesterase, and anti-apoptotic properties for maintaining nervous system integrity. Unlike synthetic drugs that act on a single target, phytochemicals have a variety of effects by modulating neurotransmitter systems, alleviating neuroinflammation, stimulating neurogenesis, and protecting against oxidative stress. This makes them promising agents for preventing and treating mental disorders.

1.2.1. Neuroactive Chemicals

A growing body of recent research has highlighted the therapeutic potential of neurophytochemicals, which are plant-derived compounds that exert biological effects on the nervous system. There is growing interest in using them to treat and prevent neurological disorders, particularly given their diverse mechanisms of action within the central nervous system (CNS). These compounds can modulate a variety of physiological and molecular pathways, making them promising candidates for adjunctive therapies in neurodegenerative, psychiatric, and neuroinflammatory conditions. Furthermore, phytochemicals often have a favorable safety profile compared to conventional pharmacological agents, exhibiting lower toxicity and fewer side effects, which increases their appeal as complementary or standalone therapeutic options. Recent advances in phytoneurology have demonstrated that plant-derived compounds can play an important role in treating nervous system disorders. These natural products can act on neurons at the molecular level to support repair mechanisms and protect against various forms of damage. One well-documented example is *Bacopa monnieri* (L.) Wettst., a key herb in Ayurvedic medicine that contains bacosides, which have been shown to activate the MAPK/ERK signaling pathway. This pathway has been associated with memory enhancement and neuronal survival. Another extensively studied botanical is *Ginkgo biloba*, which is renowned for its neuroprotective properties, primarily due to its flavonoid content. These flavonoids modulate key signaling pathways, such as PI3K/Akt and MAPK, thereby promoting neuronal viability.

Another important area of interest is the regulation of neurotransmitter systems, particularly those involving serotonin, dopamine, and GABA. However, as noted in the aforementioned reviews, findings remain somewhat heterogeneous depending on the disease model and compound studied. Phytochemicals have been shown to influence the balance and activity of these neurotransmitters, thereby contributing to mood stabilization, improved cognitive performance, and the alleviation of anxiety-related symptoms. Consequently, plant-derived compounds such as curcumin, resveratrol, and flavonoids are attracting increasing interest for their potential antidepressant and anxiolytic properties.

The major neuropsychological effects and mechanisms summarized in this review are illustrated in Figure 2.

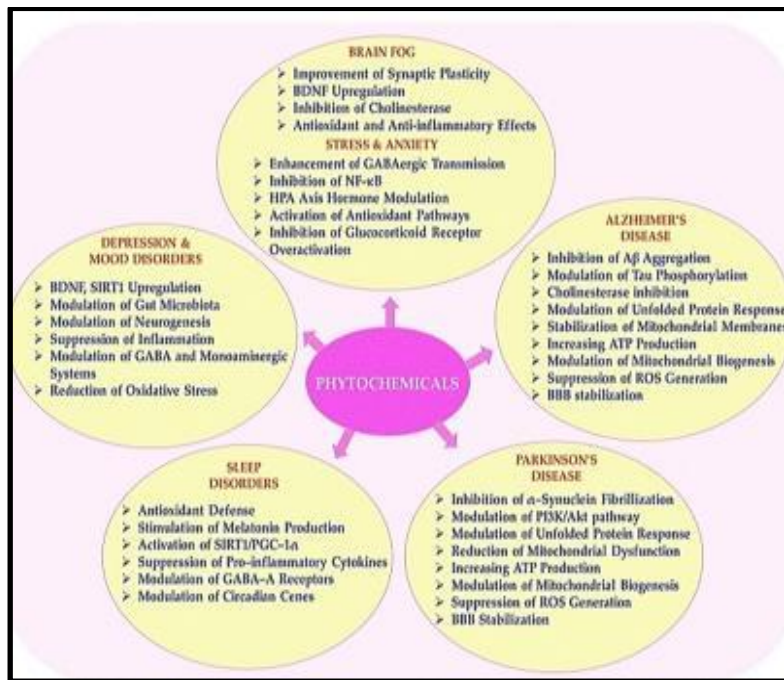


Figure 2. Illustrative neuropsychological effects and mechanisms associated with phytochemicals.

1.2.2. Neurotoxic Chemicals

The term neurotoxicity is defined as any deleterious effect on the structure, function, and chemistry of the nervous system at the time of growth or maturation induced by any chemical or physiological stimuli. The morphological alterations include neuronopathy: a condition of loss of neurons; axonopathy: a condition of degeneration of the neuronal axon; myelinopathy: a condition of loss of the glial cells surrounding the axon, or other gliopathies. It would be considered adverse, even if structural and/or functional changes were mild or transitory. (Nitika Singh, 2021)

In neuroscience experimentation, neurotoxins are generally considered as exogenous substances, administered in order to lesion a particular neural phenotype (i.e., dopaminergic nerves) or subset of neurons with common features (i.e., those with kainate receptors). This narrow definition may have been valid when selective neurotoxins were first discovered approximately 50 years ago, but the concept of a neurotoxin is much more global today. Evolution of the science of neurotoxins has broadened the term to also encompass endogenous substances and metabolites capable of initiating apoptotic, necrotic or necroptotic events leading to neuronal cell death. There are many different stages and pathways capable of provoking neuronal cell death and/or cell injury whereby disruption of normal cellular processes leads to abnormal neural function that can impact neuronal interactions and incite events encompassed in psychiatric and substance use disorders. Nosology of CNS disorders now considers the putative role of environmental factors and an interplay with genes. Accordingly, in this context, the terms "neurotoxins and neurotoxicity" are more global and now encompass a broad spectrum of indigenous neuronal actions all part of the evolution of this area of neuroscience. (JUAN SEGURA - AGUILAR, 2006)

Multiple genes interplay to produce subsets of individuals which perhaps predispose towards psychiatric disorders that manifest under different environmental conditions or on exposure to environmental substances or chemicals. There is still much uncertainty about the gene-environmental interplay, but it is recognized that each person presents differently with a heterogeneous psychiatric disorder, but all nonetheless are globally labeled as having "schizophrenia" or "affective disorder" or "schizoaffective disorder", etc. - according to the prototypical symptom presentation, and unrelated to the pathophysiologic etiology. And all are treated with the same spectrum of agents, i.e., selected among the available antipsychotics or antidepressants, or antimanics, etc. Patients tend to be treated in cookie-cutter fashion. The gene-environmental interplay does position patients as uniquely individual. And mechanistically, this derives from intraneuronal abnormal biochemical process that are evidently neurotoxic.

Moreover, there are recently identified deficits in fast-firing GABAergic neurons containing parvalbumin (a calcium binding protein) in prefrontal cortex and cingulate cortices of postmortem schizophrenics (Benes et al., 1991; Reynolds and Beasley, 2001). When human Parkinson brain specimens were micropunched for isolation of total mRNA and differential display RT-PCR, the differentially expressed cDNAs for complex I (NADH ubiquinone oxidoreductase) and Complex IV (cytochrome oxidase) were reduced. Flotillin-1 (also known as reggie-2), a membrane component of lipid rafts, was expressed to a greater degree in the Parkinson substantia nigra and ventral tegmental area (Jacobowitz and Kallarakal, 2004).

Stress, particularly when experienced during early development, can induce lasting alterations in the amygdala, the brain region central to processing fear and emotional response. Stress activates the hypothalamic-pituitary-adrenal axis (HPA). The hypothalamus releases corticotropin releasing hormone (CRH), which travels to the pituitary that releases adrenocorticotrophic hormone (ACTH), which stimulates the adrenals to release cortisol. The activation of the hypothalamus occurs primarily via norepinephrine (NE) originating in the locus ceruleus (LC). While we commonly think of the actions of CRH being limited to the HPA, in fact, CRH receptors (e.g., CRHR1) are widely distributed across the brain, particularly in stress-responsive regions including

the hypothalamus, hippocampus, amygdala, and locus ceruleus. In parallel with amygdala alterations, early life adversity also affects other key brain regions involved in mood regulation, particularly the prefrontal cortex (PFC) and hippocampus. Both individuals with major depressive disorder (MDD) and animal models of early or chronic stress exhibit reduced volume and neuronal atrophy in these areas. Functional imaging often shows decreased connectivity between the PFC, hippocampus, and associated regions, although increased connectivity in some areas suggests a more complex pattern of dysregulation. For example, adults with PTSD related to childhood maltreatment show heightened amygdala and hippocampal activation during emotional tasks, reflecting increased engagement of affective networks. In the early stage of acute stress, glutamate release in the prefrontal cortex (PFC) enhances focus, vigilance, and executive functioning. However, with prolonged or repeated exposure to stress, this same excitatory signaling becomes maladaptive. Persistently elevated glutamate levels disrupt neural homeostasis, weaken synaptic integrity, and impair cognitive function. (Mina Takahashi, 2025)

1.3. Neuroactive Plants – Phytochemical Description and Outcomes

- 1) **Bacopa monnieri** - The name *B. monnieri* (Brahmi) is derived from "Brahma", the legendary "creator" in the Hindu pantheon. Since the cerebrum is responsible for creative activity, any material that enhances the mind capability is called *B. monnieri* (Brahmi), which additionally signifies "bringing information on the incomparable reality" in India. The plant comes under the endangered category due to its overexploitation for the medicine. It has various medicinal properties like an anti-inflammatory, analgesic, antipyretic, sedative, antiepileptic and antioxidant, immuno-modulatory, memory enhancing, anti-stress, antianxiety, and anti-cancer. In a new report, *B. monnieri* comes under the second position in Indian therapeutic plants based on medicinal significance, business esteem and research and development. (Shailaja et al., 2021)

Table 2. Taxonomic classification of Bacopa monnieri (Brahmi).

Taxonomical Rank	Taxon
Kingdom	Plantae
Division	Anthophyta
Class	Dicotyledoneae
Order	Scrophulariales
Family	Scrophulariaceae
Genus	<i>Bacopa</i>
Species	<i>monnieri</i>
Common name	Brahmi



Figure 3. Bacopa monnieri (Brahmi).

In Ayurvedic medicine, *Bacopa monnieri* is a widely known herbal medicine and a Medhya Rasayana (memory-enhancing) plant. Its leaves contain bioactive saponins (bacosides A and B), flavonoids, alkaloids, and other phenolics, which confer their pharmacological effects. Bacopa extracts have been demonstrated to have a wide neuroprotective effect: they protect cholinergic neurons, promote synaptic plasticity (i.e., increasing NMDA receptors and Brain-Derived Neurotrophic Factor (BDNF) expression), scavenge free radicals, prevent Ab fibril formation and toxicity. Bacopa also suppresses neuroinflammatory signaling in vitro and in animals. For example, Bacopa therapy suppresses LPS-induced microglial TNF- α and IL-6 release and stimulates antioxidant responses via nuclear factor erythroid 2-related factor 2 (Nrf2). Such joint effects in inhibition of oxidative stress, suppression of inflammation, and regulation of neurotransmission have been linked with enhanced learning and memory in preclinical models of cognitive impairment.

In the study conducted by (Abosede et al., 2026) examined the impact of BM extract which was extracted from *Bacopa monnieri*, a medicinal plant known to have neuroprotective and antioxidant activity, on cognitive performance in a model of LPS-induced dementia. BM extraction was done using standardized alcoholic method followed by experiments which were done for the determination of “Total Phenolic Content”, “Total Flavonoid Content”, “Antioxidant capacities”, “Phytochemical compounds” and later Evaluation of the Effects of BME on Neuroinflammatory Markers in LPS-Induced Rats was done. The results of the study indicate that BM extract can be useful in the preservation of cognitive abilities and neuroinflammation, which means that it can be used as a preventive or as an adjunctive treatment of dementia. Phytochemical studies revealed that ethanolic BM extract contained phenolic and flavonoid compounds, which are significant sources of antioxidant activity. As anticipated, the total phenolic content was more than the total flavonoid content since flavonoids form a subgroup in the general phenolic group. The observation in phytochemical profiles made in this study, as opposed to the previous reports, could be due to variations in the plant part, harvesting conditions, and the solvent of choice. Polar solvents (acetone or methanol) tend to extract phenolic compounds more efficiently than ethanol, which was used in the current study. Since phenolics and flavonoids can neutralize free radicals, give electrons or hydrogen atoms, and chelate metals, their appearance has a great biochemical explanation of the antioxidant effects shown in this study. BM extract has an antioxidant profile that was verified using a variety of in vitro assays. The DPPH and ABTS outcomes indicated that the extract can counteract free radicals via hydrogen atom transfer reaction, as well as single electron transfer reaction, in agreement with phenolic antioxidant behavior. The reduced IC₅₀ in ABTS compared to DPPH could be due to the fact that ABTS has a higher solvent range and a higher rate of reaction. This activity was further supported by further mechanistic activity: FRAP revealed electron-donating ability by reduction in ferric ions, NBT revealed scavenging of superoxide, and OARC revealed scavenging of peroxyl radical by hydrogen donation. These results indicate that BM extract works primarily by radical scavenging and reducing actions, thus preventing the extent of oxidative destruction of lipids, proteins, deoxyribonucleic acid (DNA), and other cellular molecules.

- 2) ***Curcuma longa*** - *Curcuma longa* is a perennial herb erect, leafy, belongs to the Zingiberaceae family, that measures up to 1 m high with a short stem, having oblong, pointed leaves and funnel-shaped yellow flowers. It is spread throughout tropical and subtropical regions of the world that are generally cultivated in Asiatic countries, mainly in India and China. Medicinal properties of turmeric are innumerable. Its use as an antiseptic and healing wounds of all kinds are very ancient in India. This has been recorded and well documented. However, in spite of its vast use as a folk-medicine, two non-resident Indians, Dr. Suman K Das and Dr. Hari Har P Cohly, University of Mississippi Medical Center, Mississippi, filed a patent application in the US Patent Office in December 1993 for “use of turmeric in wound healing”. The patent was granted in March 1995. It claimed that the administration of an effective amount of turmeric locally and orally to enhance the wound healing process, was a novel finding. The claims were challenged by the Council of Scientific and Industrial Research (CSIR), India in March 1995 locating 32 references, some of them more than 100 years old, which showed that this finding was well known in India prior to the patent being filed. It then filed a formal request for re-examination of the patent at USPTO in October 1996. It was done and after protracted techno-legal arguments, in March 1997 unequivocally rejected all six claims, ruling that turmeric's medicinal properties were not patentable and the patent on turmeric has been revoked on the grounds of lacking the novelty requirement. The CSIR then Director General Dr R A Mashelkar described the development as one of far-reaching consequences for the protection of traditional Indian knowledge in the public domain. India has developed a multi-pronged approach to tackle IPR disputes by way of implementing Geographical Indications Bill, Plant Varieties Bill and Traditional Knowledge Digital Library. (K C Velayudhan, 2012)

Table 3. Taxonomic classification of *Curcuma longa* (Turmeric).

Taxonomic Rank	Taxon
Kingdom	Plantae
Division	Magnoliophyta
Class	Zingiberidae
Order	Zingiberales
Family	Zingiberaceae
Genus	<i>Curcuma</i>
Species	<i>longa</i>
Common name	Turmeric



Figure 4. *Curcuma longa* (Turmeric).

(Sayatani Chanda, 2019) reviewed phytochemistry of turmeric by compiling previously published standard literature about PRELIMINARY PHYTOCHEMICAL SCREENING which includes qualitative chemical tests which have been used for identification of various phytoconstituents present in the powdered crude drug. The Preliminary phytochemical investigations of aqueous extract, acetone extract, ethanolic extract, chloroform extract and methanolic extract of *Curcuma longa* rhizome using commonly employed precipitation and coloration reactions were performed by various researchers which reveals the presence such as carbohydrates, proteins, alkaloids, glycosides, terpenes, steroids, flavonoids, tannins and saponins. Test for Alkaloid was conducted by Mayer's Test, Wagner Test and Dragendroff's Test. Test for Glycosides was conducted by Legal's Test and Keller-Killani Test. Test for Flavonoids was conducted by Shinoda Test, Alkaline Reagent Test and Zn Test. Test for Tannins was conducted by Ferric Chloride Test and Gelatin Test. Test for Saponins was conducted by Foam test. Test for Fats and Fixed Oils was conducted by Stain Test. Test for proteins and amino acids was conducted by Millon's Test and Ninhydrin Test. Test for Carbohydrates was conducted by Molish Test, Fehling Test, Benedict's Test and Iodine Test.

Curcuma longa exhibit potent anti-inflammatory effects due to volatile oils and curcumin. One half of curcumin if taken as oral is effective for Chronic inflammation, was found to be as helpful as cortisone or phenylbutazone in instances of acute inflammation. Turmeric is credited with hot potency and anti-inflammatory action with specific lipoxygenase- and COX-2-inhibiting properties. Rheumatic complaints are often connected with inflammatory changes of joints. It cures the etiological factors and pathological changes of inflammation. Turmeric have significant role in diabetes. It has been observed that a hexane extract (containing ar-turmerone), ethanolic extract (containing ar-turmerone, curcumin, demethoxycurcumin and bisdemethoxycurcumin) and ethanolic extract from the residue of the hexane extraction (containing curcumin, demethoxycurcumin and bisdemethoxycurcumin) are dose-dependent stimulation of adipocyte differentiation. The result shows that the extract of turmeric ethanolic is the composition of curcuminoids and sesquiterpenoids is more strongly hypoglycemic than either curcuminoids or sesquiterpenoids. The effects of turmeric on postprandial plasma glucose and insulin are remarkable. The constituents of *Curcuma longa* namely Sodium curcumin and p-tolymethylcarbinol have several protective effects on the gastrointestinal tract. Sodium curcumin exhibits the characteristics of inhibition of intestinal spasm and p-tolymethylcarbinol, increases gastrin, secretin, bicarbonate, and pancreatic enzyme secretion. Turmeric has also been seen that it can inhibit ulcer formation caused by stress, alcohol, indomethacin, pyloric ligation, and reserpine.

3) *Centella asiatica*

The Asiatic pennywort is also known as the Indian pennywort, marsh pennywort, water pennywort, pennyweed, and, occasionally, sheep rot. *Centella* is comprised of about 20 species, found mainly in South Africa (Mabberley, 1987), belonging to the family Apiaceae (also known as Umbelliferae). *Centella asiatica* is a perennial herb with long slender horizontal stolons, characterized by long internodes, from which arise a cluster of ascending petiolate leaves at each node. Leaf size and margins vary; the latter can be smooth, crenate, or slightly lobed. Inflorescences of one to four simple umbels per node contain one to four flowers per umbel and form throughout the growing season. The petals are white, often tinged with rose; the calyx teeth are obsolete; the fruit are ellipsoid, 3 to 4 mm long, and 3 to 5 mm broad (broader than long) (Correll and Correll, 1982). *Centella asiatica* has been used for several centuries in folk medicine, and extracts were used as a drug in France in the late 1800s. Health claims range from enhanced memory and longevity to the treatment of leprosy (Kartnig, 1988; Turton, 1993). The perception of the plant as beneficial to general health may, likewise, be a contributing factor in its popularity as a vegetable in Sri Lanka. Clinical tests and case studies have substantiated many of the positive benefits of *C. asiatica* extracts or asiaticoside in the healing of skin wounds (Kiesswetter, 1964), burns (Boiteau and Ratsimamanga, 1959; Gravel, 1965), and skin diseases (Blettry, 1980; Lythgoe and Trippett, 1949); in the treatment of stomach and duodenal ulcers (Ravokatra et al., 1974); and in the treatment of leprosy, lupus, scleroderma, and diseases of the veins. (Kays, 1996)

Table 4. Taxonomic classification of *Centella asiatica* (Indian pennywort).

Taxonomic Rank	Taxon
Kingdom	Plantae
Division	Tracheophyta
Class	Magnoliopsida
Order	Apiales
Family	Apiaceae
Genus	<i>Centella</i>
Species	<i>asiatica</i>
Common name	Indian pennywort



Figure 5. *Centella asiatica* (Indian pennywort).

(Mech P et al., 2024) Studied phytochemical composition of *Centella asiatica* using in vitro methodology by testing Carbohydrates using (Molish test, Benedict test and Fehling test), Alkaloids using (Dragendorff test, Wagner's test and Hager's test), Amino acid using (Ninhydrine test), Protein using (Biuret test, Xanthoprotic test and Millon test) Saponin using (Foam test), Glycosides using (Borntrager's test), and Phenolic compounds using (Phenolic test). For the screening of phytochemical dried sample was used. Five grams of the dried sample was weighed and homogenized with 50 ml of water, HCL (1%) and ethanol separately. The extracts was boiled for 1 hour, cooled and filtered. The filtrate was used to screen for phytochemical activity. The plant material was examined using powder microscopy, which showed the presence of oil globules and vessels two characteristics that are specific to *Centella asiatica*. Safranin and methylene blue are two examples of staining reagents that were used to help clearly visualize these microscopic traits, which further aided in the plant material's authentication. The quality and purity of the *Centella asiatica* samples were assessed using the physicochemical criteria, which included loss on drying, total ash, acid-insoluble ash, and water-soluble ash. After drying, the percentage of loss was 6.95%, which is within permissible bounds and suggests a low moisture content and a decreased chance of microbial contamination. The findings indicate that silica is present, as indicated by the total ash value of 11.65% and the acid-insoluble ash value of 4.10%, respectively. In order for the plant to have therapeutic potential, water-soluble minerals must be present, as indicated by the water-soluble ash value of 6.78%. Numerous bioactive substances, including as carbohydrates, alkaloids, saponins, glycosides, phenolic compounds, and tannins, were found during the qualitative phytochemical screening. The diverse pharmacological actions of these substances are well-known. For example, it's especially significant to include triterpenoid saponins like madecassoside and asiaticoside since they have anti-inflammatory and wound-healing characteristics.

4) *Withania somnifera*

Winter cherry, Indian ginseng, and Ajagandha, Queen of Ayurveda, called by so many names, *Withania somnifera* Dunal (Ashwagandha; Family-Solanaceae), is a plant used in ayurvedic medicine in the traditional system and indicated for the management of several neurological disorders. Ashwagandha (ASH) is a Rasayana of Ayurveda – a real potent regenerative tonic possessing several pharmacological properties, such as neuro-protective, anti-stress, anti-arthritis, antitumour, analgesic and anti-inflammatory. Fresh root of the Ashwagandha herb 'smells like horse' so-called Ashwagandha, because there is the belief that anyone who consumes the herb is given the power and strength of a horse). It is also referred to as a 'royal herb' possessing multiple therapeutic effects in the different human body systems: immune system, neurological and endocrinal system, the aerobic energy-production system, as well as the reproductive system. Ashwagandha as a whole plant including each part serves therapeutic uses. Several therapeutic properties of ashwagandha are associated with presence of chemical constituents in the herb. In the era of evidence-based medicine research and innovation is a practical phenomenon. Ashwagandha has been also used successfully in ayurvedic research. Ashwagandha as a herb promotes the health of body and brain by increasing stress tolerance and reinforcing the immune system. Ashwagandha is available as churna, a fine powder that can be mixed with water or ghee honey which has various medicinal benefits. It improves the memory and increases the function of the central nervous system (CNS). Ashwagandha is a plant used in Ayurveda, the ancient system of Indian medicine. Ashwagandha is a rasayana, adaptogen as well as nervine tonic. The plant has also been widely studied for its various pharmacological activities, such as antioxidant, anxiolytic, adaptogen, memory enhancing, anti-parkinsonian, anti-inflammatory, anti-tumour properties. Various other effects, e.g. immunomodulation, hypolipidaemic, antibacterial, cardiovascular protection, and sexual behaviour have also been studied. Although the effects of the herb are quite promising for use as a multi-purpose medicinal agent, several limitations exist in the current literature. There is a need to explore more about the herb, and more clinical trials are required to support its safe therapeutic use. (Sonu Gupta et al., 2021)

Table 5. Taxonomic classification of *Withania somnifera* (Ashwagandha).

Taxonomic Rank	Taxon
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Solanales

Taxonomic Rank	Taxon
Family	Solanaceae
Genus	<i>Withania</i>
Species	<i>somnifera</i>
Common Name	Ashwagandha



Figure 6. *Withania somnifera* (Ashwagandha).

(Dr. Bargale Sushant Sukumar, 2019) studied phytochemical analysis of *Withania somnifera* Dunal roots using various studies such as Macroscopic study, Microscopic study, Preliminary phytochemical studies and Physicochemical studies and tests for Carbohydrates using Molisch Test, Fehling's test and Benedict's test ; Proteins using Xanthoprotein test and Precipitation test ; Tannins using Ferric chloride test and Lead acetate test ; Alkaloids using Mayer's test, Wagner's test, Ehrlich's test and Dragendroff's test ; Flavonoids using Shinoda Test , Alkaline reagent test, Zinc–hydrochloride test, Lead acetate test, Ammonia test and Ferric chloride test. The quantitative determination of some pharmacognostic parameters is useful for setting standards for crude drugs. The physical constant evaluation of the drugs is an important parameter in detecting adulteration or improper handling of drugs. The moisture content of the drug is not too high, thus it could discourage bacterial, fungi or yeast growth. Equally important in the evaluation of crude drugs, is the ash value and acid-insoluble ash value determination. The total ash is particularly important in the evaluation of purity of drugs, i.e. the presence or absence of foreign inorganic matter such as metallic salts and/or silica. They concluded that the result shown were 2% foreign matter was determined. Loss on drying 1.6%, total ash obtained was 9 %, acid insoluble ash was 1% and water soluble extractive was 12 % and Alcohol soluble extractive was 13 %. The phytochemical investigation revealed the presence of various phytochemical constituents such as alkaloids, flavonoids, carbohydrate, Steroids and Saponin Glycoside.

1.4. Neurotoxic Plants – Phytochemical Description and Outcomes

- 1) ***Datura stramonium*** - *Datura stramonium* is commonly known as jimson weed or thorn apple. It grows to a height of 2-4 feet and commonly reaching a diameter of 4-6 feet. The flowers are large and corollas are 6 cm long. The fruit is a large, four-lobed ovate capsule, very thorny and contains numerous black to dark brown seeds. The stems are simple, stout and mostly erect. The leaves are large, approximately 20 cm long and oval like with a wavy and coarsely dentate margin. The root is long, thick and tapering and somewhat branched. The species of *Datura* can be found throughout the world. The plant grows in sandy flats, plains, areas up to 2,500 feet above sea level. The origin of *Datura Stramonium* is disputed. The Sanskrit dhatura and the Hindustani dhatur formed the basis of the general name, the origin of Jimson weed could be Asiatic. Some sources report a probable Central American origin, due to *Datura's* habitation of most temperate and Subtropical parts of the world. It is indigenous to India and grows abundantly throughout the Himalayas from Kashmir to Sikkim. (Langonjam Rajeev Singh, 2013) . The consumption of any part of *Datura* plant may lead to the severe anticholinergic effect that may cause toxicity. In fact, the entire plant is toxic to some extent, but the seeds are found to be the most toxic; neither drying out nor boiling destroys the toxic properties. Ayurvedic system of medicine has described *D. stramonium* as a valuable therapy for numerous human illnesses such as wounds, ulcers, rheumatism, fever, inflammation, asthma, and toothache. A leaf extract taken orally can treat asthma along with sinus infection, and stripped bark can heal burns, swellings, and ulcers when applied externally to the affected area. However, in the modern system of medicine, the therapeutic potentials

of *D. stramonium* are dominated by its toxic effects. The intake of large doses of *D. stramonium* disturbs the central nervous system and produces symptoms like confusion, hallucinations and amnesia, and bizarre behavior. In addition, the signs and symptoms of acute *D. stramonium* poisoning include dryness of the lips and the epidermis, pupil dilation, urinary retention, impaired vision, and fast heartbeat.

Table 6. Taxonomic classification of *Datura stramonium* (Thorn Apple).

Taxonomic Rank	Taxon
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Solanales
Family	Solanaceae
Genus	<i>Datura</i>
Species	<i>stramonium</i>
Common name	Thorn Apple



Figure 7. *Datura stramonium* (Thorn Apple).

(Tesseromatis, 2019) reviewed about a food poisoning case which occurred at Greece. According to the Athens Greek newspaper Kathimerini of 18/5/2006 seven people in Greece were hospitalized (some of them in ICU) after having consumed a salad of *Amaranthus blitum*. The Greeks call the *Amaranthus blitum* var. *silvestre*, *vlita* (Modern Greek: βλίτα), and eat the leaves and the tender shoots cooked in steam or boiled and then served with olive oil, lemon and salt. The authorities discovered the toxic plant *Datura stramonium* harvested among the normally cultivated blitum in a field, in Megara region west to Athens and sold in supermarkets. The patients recovered due to prompt medical treatment. preserve this knowledge. Furthermore, most ethnobotanical studies are focused on professional traditional practitioners and ignore the knowledge of ordinary people in the locality. All parts of *Datura* plants contain dangerous levels of the tropane alkaloids atropine, hyoscyamine, and scopolamine, which are classified as delirants, or anticholinergics. It has been abused worldwide for hundreds of years because of its hallucinogenic properties. The risk of fatal overdose is high among uninformed users, and many hospitalizations occur. The amount of toxins varies widely from plant to plant and a given plant's toxicity depends on its age, and the local weather conditions. Additionally, within a given plant, toxin concentration varies by part and even from leaf to leaf. When the plant is younger, the ratio of scopolamine to atropine is about 3:1; after flowering, this ratio is reversed, with the amount of scopolamine continuing to decrease as the plant gets older. The approximate fatal dose for adult humans is >10 mg atropine or >2–4 mg scopolamine. (Meenakshi Sharma, 2021) reviewed that In addition to a number of beneficial health outcomes, the presence of anticholinergic alkaloids such as tropane renders the *Datura* species toxic to the nervous system, and the symptoms of toxicity include fever, dry skin, dry mouth, headache, hallucinations, convulsions, rapid and weak pulse, acute confusion, delirium, tachycardia, coma, and death. However, *D. fastuosa* was rendered safe up to a 2000 mg/kg body-weight dosage since it produced no sign of toxicity or mortality. Histological studies demonstrated the reduced weight of the organs, necrotic modifications in the liver accompanied by elevation of serum alkaline phosphatase, serum glutamic-oxaloacetic transaminase, and glutamyl pyruvic transaminase. Moreover, due to its toxicity, *D. stramonium* should

not be used in case of glaucoma, pyloric stenosis, paralytic ileus, tachycardia arrhythmias, enlarged prostate, and acute pulmonary edema. The seed extracts at a concentration greater than 0.5% induced adverse physiological modifications. In fact, all the parts of *Datura* have severe anticholinergic effects due to suppression of central and peripheral cholinergic neurotransmission, ultimately leading to death in humans. Intoxication with *Datura* extracts leads to adverse impact on the central nervous system, disorientation, memory loss, inability to process information, impaired vision due to mydriasis, myoclonic jerking, hyperpyrexia, and respiratory and cardiovascular problems. *Datura*, in general, constitutes significant amounts of carbohydrates, fats, protein, moisture, ash content, and crude fiber. Besides, major phytochemicals found in *Datura* include alkaloids, phenolic compounds, tannins, flavonoids, and cardiac glycosides. In addition, many amino acids such as alanine, phenylalanine, glutamate, and tyrosine have also been isolated from the seeds. *Datura* species are particularly rich in tropane alkaloids.

In 2007, Diker et al. reported two patients in coma intoxication following *Datura* seed tea ingestion. The CPK levels of one of them reached 6694 U/L and he developed fatal metabolic acidosis. In 2008 Wiebe et al. reported that delirium developed in four patients due to *Datura stramonium* poisoning. Rhabdomyolysis occurred in two of them but they recovered with suitable treatment. J. Russel et al. reported 2010 six members of the same family, who ate homemade stew containing *Datura*, with anticholinergic toxidrome (confused, laughing, vomiting, dizzy, thirsty and hallucinated). Approximately 1 hour later, another relative arrived at the home discovered them, called emergency medical services, and all six were transported to the hospital by ambulance. All patients fully recovered. Krenzelok 2010 refers to *Datura* “gardeners eye” and “cornpickers eye,” syndrome. When the sap or dried plant material enters the eye directly, mydriasis, most commonly unilateral and cycloplegia are sudden in onset and often profound frightening to the victim and to the clinician, suggestive of significant cerebral pathology due to the high concentrations of belladonna alkaloids in the entire plant. Bouziri A. et al. reported in 2011 an unusual case of *Datura* intoxication occurring in a geophagous young child in Tunisia after accidental ingestion of the plant due to the underlying geophagia facilitating the occurrence of poisoning. In a 2012 study with 19 patients in Iran, where the plant’s name is *Tatoore*, children were poisoned more commonly than teenagers and poisoning in adults was rare. All of the children ingested the plant accidentally. The most presenting symptom was irritability and the most common sign was sinus tachycardia. Most of the symptoms were controlled by parenteral benzodiazepines. The many reports concerning *Datura stramonium* toxicity show that the potential of such an incident is not so rare. Younger persons, who consume the plant for recreational purposes know that it leads to the desired delirium, but they have not realized the health risks associated to this abuse. Other age groups, who accidentally ingest parts of the plant as a food ingredient, can’t imagine the danger to be poisoned and this is especially important for children who are a particularly sensitive case. The difficulties for prompt diagnosis are associated with the altered mental status and the variable presentations of affected persons.

2) *Aconitum ferox*

Aconitum, commonly known as monkshood or wolf’s bane, is a genus of perennial plants belonging to the family Ranunculaceae. The genus *Aconitum* contains over 300 species and is distributed widely throughout the Northern Hemisphere, including Asia, Europe, and North America. *Aconitum* species are known for their attractive flowers, which range in colour from white to purple and blue. However, from centuries they are known for their efficacy as a potent medicine as well as for their poisonous alkaloids hence, it is known as the “queen of poisons”. The morphology of aconite is striking and distinctive, making it easily recognizable. They are herbaceous with large, deeply lobed leaves that are often palmate or divided into three to five leaflets. The stem of an aconite plant is erect, branched, and can grow up to 2 meters tall which is typically green or purplish in colour. The flowers are distinctive, with a hooded shape that resembles a monk’s cowl. They are typically blue or purple, although some species may have white or yellow flowers. The flowers are generally arranged in long spikes or clusters. They produce dry, elongated fruits that split open to release their seeds. The roots of an aconite plant are fleshy, tuberous, and often spindle-shaped. They are used in traditional medicine but can be toxic if ingested. The plants contain a variety of alkaloids, including aconitine, mesaconitine, and hypaconitine, which can cause severe cardiotoxicity, neurotoxicity and cytotoxicity. Vatsanabha botanically identified as *Aconitum Ferox* is native to the Himalayas and is found in regions such as Nepal, Bhutan, and Tibet. It is a perennial plant that can grow up to 2 meters in height. The leaves are large and palmate, with deeply cut lobes. They are dark green in colour and can reach up to 30 cm in diameter. The flowers of *Aconitum Ferox* are blue to violet in color and are arranged in a dense, elongated cluster at the top of the stem. Each flower has 5 petals, 2 of which are large and helmet-shaped, while the other 3 are smaller and narrow. The flowers bloom in the late summer and early autumn. The roots of *Aconitum ferox* are thick and fleshy, with a cylindrical shape. They are dark brown to black in colour and can grow up to 1 meter in length which contain toxic alkaloids. Overall, the morphology of *Aconitum ferox* is typical of plants in the Ranunculaceae family, with large, deeply cut leaves and showy, helmet-shaped flowers. (Sahana V. M. Vats, 2024)

Table 7. Taxonomic classification of *Aconitum ferox* (Vatsanabha).

Taxonomic Rank	Taxon
Kingdom	Plantae
Division	Tracheophyta
Class	Magnoliopsida
Order	Ranunculales
Family	Ranunculaceae
Genus	<i>Aconitum</i>

Taxonomic Rank	Taxon
Species	<i>ferox</i>
Common name	Vatsanabha



Figure 8. *Aconitum ferox* (Vatsanabha).

Aconitum ferox is a highly toxic with the estimated fatal dose of 1g of root powder with a fatal period of 6 hours which contains a potent cardiotoxin and neurotoxin known as Aconitine. Ingesting even a small amount of the plant can result in severe symptoms and even death. Symptoms of *Aconitum ferox* poisoning can occur within minutes to hours after ingestion and may include, Numbness and tingling in the mouth and throat, Severe gastrointestinal symptoms, such as nausea, vomiting, and diarrhoea, Irregular heartbeat, heart palpitations, and chest pain, Muscle weakness, paralysis, and respiratory failure, Confusion, dizziness, and loss of consciousness. About 54 species of *Aconitum* have been chemically investigated (Rana 2006). *Aconitum* species are the rich sources of diterpene alkaloids and flavonoids. Chinese group have reviewed the structure of diterpenoid alkaloids from *Aconitum* species (Pan and Chen 1993). It also consists of free fatty acids, polysaccharides and different classes of alkaloids. A Hand book of natural products data, diterpenoid and steroidal alkaloids, covers spectral data of 400 diterpenoid alkaloids reported before the end of 1988 (Atta-ur-Rahman 1993).

(S.L. Deore, 2013) evaluated toxicity of *Aconitum* by developing a chemical lab-scale method and to compared it with the traditional Ayurvedic Shodhana process. Shodhana eliminates harmful matter, modifies or converts undesirable properties to desirable, enhanced therapeutic actions. By Shodhana, only toxic constituents from plants are either removed or made less toxic before their use in the formulation. For this they used two methods :- one is the ayurvedic Shodhana method, in this the roots of *A. ferox* were cut into small pea-sized pieces and kept in earthen pot containing cow urine for 8 days, and on each day, cow urine was changed for 7 days. On the 8th day, cow urine was not changed. The earthen pot was kept in sunlight. Then, it was washed with cold water, the upper layer was taken out, and was again washed with warm water. The pieces of drug were dried immediately by exposing them to sunlight. The dried pieces were grinded to get the powder form. And the other method they used was Shodhana by modified chemical method for this they made chemical composition of lab-prepared cow urine by mixing Water e 95%; urea e 2.5%; minerals (nitrogen, sulfur, phosphate, sodium, manganese, carbolic acid, iron, chlorine, magnesium) and hormones (corticosteroids) e 1%; salts (malic, citric, tartaric, succinic, hippuric acids, calcium salts) and enzymes (urokinase) 1.5%; vitamin A, B, C, D, E, lactose, and creatinine e 0.5%. Then the crude powdered plant material obtained from both techniques was defatted with petroleum ether and then subjected to soxhlet extraction to complete 20 cycles with chloroform. The chloroform extract thus obtained was filtered and concentrated on a water bath to obtain a thick paste. For toxicity study, a total of five animals were taken for each group. The test substance was administered using a stomach tube. From the sighting study, the dose of 5 mg/kg was selected for Before Shodhana Extract and Lab Scale-Treated Extract. This dose of 5 mg/kg of Before Shodhana Extract and Lab Scale-Treated Extract showed evident toxicity while 300 mg/kg for Cow Urine-Treated Extract showed no toxicity till the 14th day. After the 14th day, the blood was withdrawn from the retro-orbital plexus of rats and pathological laboratory tests were performed that might be affected by the drug.

(Shyaula, 2011) reviewed that the interest on *Aconitum* mainly based on diterpene alkaloids. Its flavonoid constituents are studied as the chemotaxonomic markers (Lim et al. 1999). The diterpenoid alkaloids can be divided into the following two broad categories on the basis of various substituents, which apparently affect both the chemical and pharmacological properties of these alkaloids. Alkaloids that possess a hexacyclic C19-skeleton and alkaloids bearing a C20-skeleton. C19-diterpenoid alkaloid groups comprise the toxic ester bases and can be further divided into four groups on the basis of the skeleton variations. Besides diterpenoid alkaloids, other various alkaloids like higenamine, coryneine, lipohypaconite, lipodeoxyaconitine, lipoaconitine and benzyl mesaconine are also reported from *Aconitum*. Four cases of aconite poisoning had been managed in Manipal teaching hospital (Paudel et al. 2008). Similarly, three cases of aconite poisoning in Nepalese family were managed in Hong Kong after analysis of residual herbs and urine samples (Chan et al. 2010). In the urine analysis, the alkaloids commonly detected in local aconite poisoning cases included bikhaaconitine, pseudoaconitine, indaconitine and yunaconitine. The tribesmen from Nepal usually spent their winter in cities and sell their herbs for earning. In above case, the herbs were brought from Nepal six month before the incident. It occurred mainly due to mistakenly taken of *Aconitum* instead of another plant 'Nirmasi' (*Delphinium denudatum*) which resembled to it. Management of aconite poisoning needs immediate attention to the vital functions and close monitoring of blood pressure and cardiac rhythm. Clinical judgments are far more important than the laboratory findings as there is a time-lag before laboratory confirmation. Activated charcoal is advisable if the patient presents within one hour.

3) *Strychnos nux-vomica*

Strychnos, created by Linnaeus in 1753, is a genus of trees and climbing shrubs of the gentian order. The genus is pan-tropical and comprises of 200 species of which about 75 species are found in Africa, 73 species in America and 44 species in Asia. Five species of genus *Strychnos* are endemic to South India and Andaman Islands (Hill, 1917). Species like *Strychnos colubrina*, *Strychnos nux-blanda*, *S. potatorum* are considered endangered. *Strychnos nux-vomica* is indigenous to India and South-East Asia. In India it is commonly observed in moist deciduous and semi evergreen forests of West Bengal, Bihar, Maharashtra, Odisha, Central and South India up to altitude of 500m amsl. In India most of the industrial seed requirement is collected from natural populations existing in forest and its fringes. Limited or no cultivation, shrinking of natural habitat and heavy demand by pharmaceutical industries creates an atmosphere of seed shortage. This encourages the tribal collectors to muster more for fetching maximum income. Often seeds are collected unscientifically by lopping its branches or cutting down the trees. Young saplings are cut for fire wood by local dwellers. Shortage of seeds in the forest floor, poor natural regeneration coupled with habitat loss compels this valuable wealth to restrict in few areas. Presently this species is sparsely observed in the forests and has been included in the list of rare endangered tree (RET) category in some states like Chhatisgarh (Chaubey and Krishnamurthy, 2015). Almost all part of this tree contains alkaloids of medicinal importance but seed is official in many pharmacopeia. It is rich in alkaloids, flavonoids, tannins and triterpenoids, glycosides, lignins and steroids (Walter et al., 2013). More than 90 chemical compounds have been isolated from different parts of nux vomica but strychnine and brucine are the principal toxic alkaloids. They occur not only in the seeds but also in roots, wood, bark, fruit pulp and hard fruit shells. Seeds contain 2.6 to 3.0% of total alkaloids, of which 1.25 to 2.5% is strychnine and 1.5 to 1.7% is brucine. The seeds additionally contain chlorogenic acid, a glycoside (loganin), and 3.0% of fixed oil. (Behera)

Table 8. Taxonomic classification of *Strychnos nux-vomica* (Poison nut).

Taxonomic Rank	Taxon
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Gentianales
Family	Loganiaceae
Genus	<i>Strychnos</i>
Species	<i>nux-vomica</i>
Common name	Poison nut



Figure 9. *Strychnos nux-vomica* (Poison nut).

Strychnine and brucine are the most important alkaloids of *Nux vomica*. Both of them are potent stimulants of the spinal cord. Thus, the most characteristic feature of *Nux vomica* is to render the reflex center in the central nervous system (CNS) more sensitive to afferent stimuli (McIntosh, 1940). In addition, strychnine and brucine increase the secretion of gastric juices and heighten sensory awareness. There are three important applications of *Nux vomica* and its alkaloids, which may be related to the nervous system. Firstly, *Nux vomica* is used as a stimulant drug in the digestive tract. Secondly, it is used in paralytic conditions arising from dysfunction of the motor nerves in particular. The poisonous properties of *Nux vomica* have been known for centuries, and in the Pharmacopoeia of the People's Republic of China, it is classified as a highly toxic medicine (Committee for the Pharmacopoeia of China,

2015). Large doses of *Nux vomica* cause convulsions and death. There have been many reports of poisoning by *Nux vomica* and the severe toxicity caused by strychnine and brucine. Strychnine is highly toxic to humans, and it can be rapidly absorbed from the gastrointestinal tract to act upon the CNS, causing general CNS excitation (Marques et al., 2000). The absorption half-life of strychnine is approximately 15 min (Ellenhorn, 1997). Death by strychnine poisoning is usually caused by spasmodic fixation of the respiratory muscles or exhaustion of the CNS, particularly the respiratory center (McIntosh, 1940). *Nux vomica* and strychnine poisoning is characterized by violent convulsions. Regarding this, Dr. Christison stated that “Larger doses cause violent starting of the muscles, or even a tendency to lockjaw, which are succeeded by stiffness, weariness, pain or rending in the limbs”. In their highest degree these amount to violent tetanic spasm, occurring in frequent fits, with brief intervals of repose, acute sensibility and dreadful alarm. Convulsions are usually followed by intervals of complete relaxation of muscles, until the nervous system recovers from exhaustion, whereupon convulsions recur. Consciousness is retained during convulsions, and intense pain is felt from the violent contracting or stretching of muscles (McIntosh, 1940). In addition to convulsions, poisoning by *Nux vomica* and strychnine causes agitation and ataxia, slightly accelerated breathing, respiratory and cardiac arrest, a hard and fast pulse and strabismus, among other symptoms (Wood et al., 2002). Postmortem examination following *Nux vomica* or strychnine poisoning reveals evidence of severe muscle spasms and cardiac arrest, and the lungs, heart and mucous membrane of the stomach show congestion (Kasun et al., 2015). Furthermore, the abuse of *Nux vomica* (low doses over a long time period) can induce delirium tremens and excitable, cramp-type pains in the abdomen and legs. (Rixin Guo, 2018)

(Lesley Ponraj, 2017) investigated a rare case report of A 39-year-old man with no previous known comorbidities presented with acute onset myalgias and generalized body ache. He gave a history of consuming six leaves of the local “etti” plant after making it into a decoction with 100 ml of boiling water, with suicidal intent. Later, the plant was confirmed to be *Strychnine nux-vomica* by visualization. Following consumption, he had induced a few episodes of small volume nonbilious vomiting. On presentation to the Emergency Department, he was apprehensive and restless. His pulse rate was 60/min. His respiratory rate was 16 and blood pressure was 100/80 mmHg. The rest of the systemic examination was within normal limits except for moderate muscle tenderness over the calf and thighs. Within hours of consumption, he began to develop twitching movements of the arm and forearm muscles that were more pronounced in his sleep. His basic blood investigations revealed normal blood counts and metabolic panel including electrolytes (serum sodium of 140 mEq/L, serum potassium of 3.8 mEq/L, serum magnesium of 1.86 mg/dl, and corrected serum calcium of 8.46 mg/dl). While under observation, his heart rate dropped to 48 beats/min without any associated hypotension. The patient was put on cardiac monitor, and the vitals were closely monitored. He was kept on maintenance intravenous fluids, and urine output was closely monitored. The levels of serum potassium, magnesium and creatinine kinase were periodically monitored. He was started on tablet lorazepam 2 mg thrice daily for the muscle twitches and injection atropine 1.2 mg was administered as and when required for bradycardia <50 beats/min. He required 2 doses of injection atropine on day 1 of poisoning. The muscle twitches and hypervigilance reduced in severity and he was discharged on day 4.

4) *Lathyrus sativus*

Over consumption of seeds of *Lathyrus sativus* causes lathyrism, a paralytic disease of legs/hind limbs, in human and animals. Some of these amino acids and their amine derivatives are neurotoxic to both human and animals. Lathyrism, a paralytic disease is caused by the extensive use of seeds of *Lathyrus sativus*. A nonprotein amino acid, P-N-Oxalylamino-L-alanine (BOAA) present in these seeds is found to be responsible for this effect. The seeds of *Lathyrus* species had been in use as nutritious, tasty & inexpensive component of human diet among the poor in certain areas of Africa and Asia. Under adverse climatic conditions e.g. during flood and drought, when other crops are ruined, grass peas because of their hardy drought tolerant nature survive and become the survival food for human and cattle. Under such conditions when *Lathyrus sativus* seeds comprised up to two thirds of the diet, men and animals developed the paralytic neurotoxic disease, Lathyrism. (P. K. Manna, 1999) Grass pea is a food, feed and fodder crop belonging to the family Leguminosae (=Fabaceae), Subfamily Papilionoideae, tribe Viciae. The genus *Lathyrus* consists of about 160 annual and perennial species (Plitmann et al., 1995; Chtourou-Ghorbel et al., 2001), also reported as 187 species and subspecies by Allkin and coauthors (1986). The species are separated into 15 sections based on their morphological traits (Smartt et al., 1994). The plant has a very hardy and penetrating root system that supports growth on a wide range of soil types, including very poor soil and heavy clays. As a legume, it contributes to soil quality through the action of nitrogen-fixing symbiotic bacteria associated with the root system. Grass pea is extremely tolerant to environmental extremes, grows with as little as 250 mm of rain per year, and is typically the last plant standing in times of drought (Tekele-Haimanot et al., 1990; White et al., 2002). In short, *L. sativus* is a hardy plant suited to dry climates, producing good seed crops on poor soils in some of the world's most difficult farming areas. It is thus a good model for investigating the mechanism of drought resistance and seeking genes associated with drought resistance. The crop is not only tolerant to the extremely dry conditions found in Ethiopia but also withstands prolonged water logging as in Bangladesh (Smartt et al., 1994). The ability of grass pea to tolerate both drought and flood, the low cost required for its production, its high protein content, and its contribution to soil fertility through fixation of atmospheric nitrogen, have made this throughout history a highly desirable subsistence and insurance crop (Tadesse and Bekele, 2001a).

Table 9. Taxonomic classification of *Lathyrus sativus* (Grass pea).

Taxonomic Rank	Taxon
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Fabales

Taxonomic Rank	Taxon
Family	Fabaceae
Genus	<i>Lathyrus</i>
Species	<i>sativus</i>
Common name	Grass pea



Figure 10. *Lathyrus sativus* (Grass pea).

Valerie S. Palmer wrote about history of *Lathyrus* in a newsletter published in the year 2000 named “*Lathyrus Lathyrism Newsletter*” in which he described about first colloquium on *Lathyrus* which was commenced in the year 1985. Researchers from many isolated disciplines came together to develop a coordinated effort with a sense of purpose and urgency. The transforming moment was the airing of a videotape that he had recorded in northern India in 1983 while working on lathyrism with Peter Spencer. This showed the tragic clinical effects of continued consumption of the grass pea in the form of walking difficulties, inappropriate leg movements, and frank limb paralysis. These images galvanized the Pauconferees - most of whom were plant scientists - into action to develop low-toxin strains of the grass pea as a useful dryland crop and to prevent lathyrism in future generations. This scientific cooperation was known as INILSEL, the International Network for the Improvement of *Lathyrus sativus* and the Eradication of Lathyrism. Third World Medical Research Foundation (TWMRF), which led INILSEL for many years, carried out interdisciplinary research projects on the grass pea and lathyrism in Bangladesh and Ethiopia. The work in Bangladesh defined the neurophysiological deficits of lathyrism and pointed the way for bench research on cellular targets of the grass pea neurotoxin. TWMRF-sponsored research in Ethiopia, which was underwritten by the generosity of the British public through the funding of Band Aid, was an ambitious, multidisciplinary project that examined the prevalence of lathyrism and the relationship between grass pea consumption. Through cooperation with Clayton Campbell in Canada, low-toxin lines of grass pea were introduced into Ethiopia for adaptation to local conditions and eventual distribution of hybrids to farmers. *Lathyrus* researchers in Ethiopia, Bangladesh, India and throughout the world were kept abreast of the latest developments through the *Lathyrus* and *Lathyrism Newsletter*, edited by plant scientist Avtar Kaul, as well as the publications of the several symposia sponsored by TWMRF in coordination with other funding agencies, including IDRC. (Palmer, 2000)

(Ze-YiYana, 2006) reviewed that the seed of *L. sativus* provide a source of protein and carbohydrate that are able to sustain life during periods of famine when other food is unavailable (Spencer, 1989). The nutritive composition of *L. sativus* compares favorably with that of *Cicer arietinum*, field pea, faba bean and lupin. On the whole, protein values for grass pea are higher than contents for *C. arietinum* (18.0%), field pea (25.7%) and faba bean (26.9%), but lower than lupin (35.1%). The amino acid composition of *L. sativus* is similar to those of many grain legumes – rich in lysine but deficient in methionine, cysteine and tryptophan. However, *L. sativus* is not the only plant containing toxic b-1, besides being present in the seeds of 21 *Lathyrus* species (mainly *L. sativus*, *L. cicera* and *L. clymenum*), b-1 was also found in some other genera of leguminous plants including 17 species of *Acacia* and 13 species of *Crotalaria*. There have been several attempts to model neurolathyrism in primates, with limited success. Pyramidal dysfunction resembling the early reversible phase of human neurolathyrism was demonstrated in a carefully controlled study of well-nourished cynomolgus monkeys (*Macaca fascicularis*) fed a fortified diet of pure *L. sativus*. Animals additionally received by oral intubation a daily infusion of an alcoholic extract of grass pea, for a total daily intake of 1.1–1.4 g of ODAP/kg body weight. Other animals were given pure 1 with and without grass pea extract and fed fortified chickpea (*Cicer arietinum*) matched for protein, carbohydrate, fat, mineral and vitamin content. Animals developed comparable neurological signs after 2–4 weeks (300 mg/kg/day, increasing by 300 mg/kg/day after 15 days of synthetic 1 alone), 2–6 weeks (alcoholic extract plus synthetic 1), and 3–10 months (alcoholic extract plus grass pea diet). Affected monkeys showed a variable combination of fine tremor, periodic myoclonic-like jerks, mild-to-moderate increase in muscle tone of leg muscles, hindlimb extensor posturing, and a skater-like gait. Electrical stimulation of the motor cortex showed prolonged central motor conduction but neuropathological studies showed no convincing evidence of neuronal degeneration (Spencer et al., 1986, 1988).

(Rao, 2013) declared neurolathyrism is now a part of history in India by their review saying that Neurolathyrism is past history in India since *Lathyrus sativus* (khesari dal) is no longer used as a staple. A consensus has evolved that khesari dal is harmless as part of a normal diet. L-ODAP (β -N-oxalyl-L- α diamino propionic acid) the neurotoxic amino acid, from this pulse, is detoxified in humans but not in animals but still no laboratory animal is susceptible

to it under acceptable feeding regimens. L-ODAP is an activator of protein kinase C and consequential crucial downstream effects such as stabilization of hypoxia inducible factor-1 (HIF-1) could be extremely conducive to humans under a variety of situations. ODAP is gradually finding a place in several patents for this reason. Homoarginine the second amino acid from *L. sativus* can be a better substrate for endogenous generation of nitric oxide, a crucial signaling molecule associated with the cardiovascular and control of hypertension. These features could make *L. sativus* a prized commodity as a functional food for the general cardiovascular and overcome hypoxic events and is set to change the entire perception of this pulse and neuroathyrism. Several new concepts have emerged during the last three decades that will shape the future course for *L. sativus* and in a recent conference *L. sativus* had been rightly titled as the golden pulse of the future. Almost all recent research publications emphasize that there is no neuroathyrism when the pulse is consumed as part of a normal diet and this is very true in the Indian context. No legume other than *L. sativus* has in fact ever served as a staple food. Some of the recent findings and developments with *L. sativus* provide some strategic approaches in this direction and will be briefly reviewed. Conventional plant breeding techniques for the development of low ODAP seeds of *L. sativus* made sufficient progress in the last few years but for various reasons this approach has remained an unfulfilled promise.

2. Neuroactive Phytochemicals and Cognitive/Psychological Functioning

Neuroactive phytochemicals are plant-derived bioactive compounds capable of influencing the structure and functioning of the nervous system through interactions with neurotransmitter systems, intracellular signalling pathways, oxidative processes, neuroinflammation and mechanisms associated with neuroplasticity. Their potential relevance to neuropsychological health is particularly evident in domains such as memory, attention, learning, emotional regulation, stress and anxiety. However, the psychological effects of these compounds are not uniform and may vary according to the phytochemical composition, dose, formulation, bioavailability, duration of exposure and characteristics of the individual. Among the plants considered in the present review, *Bacopa monnieri*, *Centella asiatica*, *Withania somnifera* and *Curcuma longa* provide examples of different ways in which plant-derived compounds may influence cognitive and psychological functioning.

The representative neuroactive plants discussed in this review are illustrated in Figures 3–6, with their taxonomic classifications presented in Tables 2–5.

Bacopa monnieri is particularly associated with cognitive functioning, especially memory. Evidence from human research suggests that its effects are more consistently observed in memory-related domains than in broader cognitive abilities. A recent systematic review and network meta-analysis of 29 randomized controlled trials involving 2,107 participants reported that higher-dose *B. monnieri* preparations produced significant improvements in working memory and short-term memory, while lower-dose preparations showed benefits for delayed memory. However, the effects were not consistently demonstrated across all cognitive domains, indicating that the cognitive effects of *B. monnieri* may be domain-specific rather than representing a generalized enhancement of cognitive performance. Earlier clinical evidence similarly suggested potential benefits for memory following sustained supplementation, although differences in extracts, dosage and study methodology limit direct comparison between studies. Thus, *B. monnieri* may be considered a promising neuroactive plant for memory-related functioning, while stronger standardized clinical evidence is still required before definitive conclusions can be drawn. (Luiz José Valotto Net, 2024)

Centella asiatica provides a more cautious example of the relationship between neuroactive phytochemicals and psychological functioning. Although traditionally regarded as a cognitive and neurological tonic, human evidence does not consistently demonstrate improvements across cognitive domains. A systematic review and meta-analysis of randomized controlled trials found no significant overall improvement in the major cognitive domains following *C. asiatica* administration. Nevertheless, some effects were observed in psychological states, including increased alertness and reduced anger shortly after administration. The authors also emphasized methodological limitations related to dosage, preparation, standardization and variation between products. Therefore, *C. asiatica* illustrates the importance of distinguishing traditional claims from outcomes supported by controlled human research. Its potential influence may extend beyond memory enhancement to aspects of mood and arousal, but further well-designed contemporary clinical trials are needed. (Panupong Puttarak, 2017)

In contrast to the predominantly cognitive focus of *Bacopa* and the limited cognitive evidence for *Centella*, ***Withania somnifera*** has attracted considerable research attention for its effects on stress and anxiety. A 2024 systematic review and meta-analysis involving nine randomized controlled trials and 558 participants found that *W. somnifera* preparations significantly reduced perceived stress, anxiety measured using the Hamilton Anxiety Scale and serum cortisol compared with placebo. A separate 2024 systematic review and meta-analysis involving five randomized controlled trials and 254 participants also reported significant reductions in anxiety and improvements in several sleep-related outcomes, although substantial heterogeneity was present between studies. More recent evidence from a 2026 systematic review and dose-response meta-analysis involving 22 randomized controlled trials further reported significant improvements in stress, anxiety and depressive symptoms. However, the authors emphasized the heterogeneity of existing trials and the need for higher-quality studies to establish optimal dosage and treatment duration. Collectively, these findings suggest that *W. somnifera* may have particular relevance to psychological functioning through modulation of stress- and anxiety-related symptoms rather than through cognitive enhancement alone. (Saleh A. Alsanie, 2026)

Curcuma longa, particularly its major polyphenolic constituent curcumin, represents another important neuroactive phytochemical with evidence extending across cognitive and psychological outcomes. A 2025 systematic review and meta-analysis of nine randomized controlled trials involving 501 participants found that curcumin supplementation significantly improved global cognitive function compared with placebo. The effect was more evident in studies lasting at least 24 weeks, in participants aged 60 years or older and in studies conducted among Asian populations, suggesting that duration, age and population characteristics may influence outcomes. A 2024 systematic review of human studies also reported evidence of improvements in

working memory across several adult populations, although variation in study populations and methodologies limits the generalizability of these findings. In relation to psychological functioning, a 2024 meta-analysis of eight randomized controlled trials involving 567 participants found a significant reduction in anxiety symptoms following curcumin supplementation; however, the very high statistical heterogeneity indicates that the findings should be interpreted cautiously. (Wenlong Wang, 2025)

Taken together, these findings indicate that neuroactive phytochemicals may influence different dimensions of neuropsychological functioning rather than producing a single generalized psychological effect. *Bacopa monnieri* shows comparatively stronger evidence for memory-related outcomes, *Centella asiatica* has more limited evidence with possible effects on alertness and mood, *Withania somnifera* is particularly associated with stress and anxiety reduction, while curcumin from *Curcuma longa* has demonstrated potential effects on cognition and anxiety. These differences may reflect variations in phytochemical composition, biological targets, dosage, duration and individual characteristics. Importantly, evidence from human trials remains variable, and findings from laboratory or animal studies should not automatically be interpreted as evidence of clinical psychological benefit.

The potential neuropsychological effects of these plants may involve several interconnected mechanisms, including modulation of neurotransmitter activity, regulation of oxidative stress and inflammatory processes, and effects on neuronal signalling and plasticity. Such mechanisms provide a biological basis for investigating phytochemicals as potential contributors to cognitive resilience and psychological well-being. Nevertheless, the translation of these findings into clinical practice requires standardized preparations, adequately powered randomized controlled trials, consistent outcome measures and greater attention to long-term safety. Consequently, neuroactive phytochemicals should be viewed as promising candidates for further investigation rather than established substitutes for evidence-based psychological or medical interventions.

3. Neurobiological Mechanisms Underlying Neuroactive Effects

The neuropsychological effects associated with neuroactive phytochemicals appear to arise from the interaction of multiple biological pathways rather than from a single molecular target. Plant-derived compounds may influence neurotransmitter activity, oxidative balance, inflammatory signalling, neurotrophic factors and synaptic plasticity. These mechanisms are particularly relevant to cognitive and psychological functioning because alterations in neurotransmission, neuronal integrity and neuroplasticity can affect memory, attention, emotional regulation and stress responses. Evidence from *Bacopa monnieri*, *Centella asiatica*, *Withania somnifera* and *Curcuma longa* suggests that their potential neuroactive effects involve overlapping but distinct mechanisms. However, much of the mechanistic evidence remains derived from preclinical studies, and therefore biological plausibility should not be interpreted as definitive evidence of clinical efficacy.

Neurotransmitter modulation represents one important mechanism through which phytochemicals may influence psychological functioning. Neurotransmitters including acetylcholine, serotonin, dopamine, γ -aminobutyric acid (GABA) and glutamate play central roles in memory, attention, mood, anxiety and behavioural regulation. *Bacopa monnieri* has been investigated for its influence on cholinergic and other neurotransmitter-related pathways, providing a possible biological basis for its reported effects on learning and memory. Similarly, phytochemicals present in *Centella asiatica* have been investigated in relation to serotonergic, GABAergic and cholinergic signalling. *Withania somnifera* has also been associated with modulation of neurotransmission relevant to stress and anxiety. These mechanisms may help explain why different neuroactive plants can influence distinct psychological domains. Nevertheless, findings from experimental models cannot automatically establish equivalent neurotransmitter effects in humans, highlighting the need for controlled clinical investigation.

Oxidative stress and neuroinflammation constitute another interconnected mechanism relevant to neuropsychological health. The brain has high metabolic demands and is particularly vulnerable to oxidative damage. Excessive production of reactive oxygen species can disturb cellular membranes, mitochondrial function and neuronal signalling, while persistent neuroinflammation may further contribute to neuronal dysfunction. Several phytochemicals have demonstrated antioxidant and anti-inflammatory activity in experimental models. A 2024 systematic review of *Bacopa monnieri* identified evidence relating its potential neuroprotective effects to reductions in oxidative stress and inflammatory processes, as well as effects on mitochondrial dysfunction and apoptosis. Curcumin from *Curcuma longa* has similarly been extensively investigated for antioxidant and anti-inflammatory actions. A 2024 systematic review and meta-analysis found that curcumin reduced inflammatory mediators and oxidative-stress markers in experimental models of traumatic brain injury, while also increasing antioxidant-related factors. Importantly, these findings were based on animal studies, and therefore their relevance to human psychological health requires further clinical validation.

Neurotrophic signalling and synaptic plasticity provide another potential link between phytochemical activity and cognitive functioning. Brain-derived neurotrophic factor (BDNF) is an important regulator of neuronal survival, synaptic plasticity, learning and memory. Experimental evidence suggests that some neuroactive phytochemicals may influence BDNF-related signalling pathways. In particular, curcumin has been investigated for its effects on BDNF/TrkB and CREB-related signalling. The 2024 systematic review of curcumin in experimental traumatic brain injury reported increased BDNF and CREB together with changes in markers associated with neuronal survival and synaptic function. A broader review of curcumin's neurological effects has also described potential interactions with neuroinflammatory, oxidative-stress and neurotrophic pathways. These mechanisms provide a plausible explanation for potential effects on learning, memory and neuronal resilience, although mechanistic findings should be distinguished from demonstrated improvements in human cognitive performance.

Stress-related biological regulation is particularly relevant to the psychological effects reported for *Withania somnifera*. The hypothalamic–pituitary–adrenal (HPA) axis is a major physiological system involved in the regulation of stress responses. Persistent activation of the stress system and prolonged exposure to elevated glucocorticoids may influence emotional regulation, sleep and cognitive functioning. Clinical studies of *W. somnifera* have reported reductions in perceived stress, anxiety and cortisol concentrations, suggesting a possible relationship between its psychological effects and regulation of

stress-related physiological responses. A 2024 systematic review and meta-analysis involving nine randomized controlled trials and 558 participants reported reductions in perceived stress, anxiety and serum cortisol following *W. somnifera* supplementation. However, cortisol changes should not be interpreted as proof of direct HPA-axis normalization, and further mechanistic and clinical studies are necessary to establish the pathways involved.

Overall, the neuroactive potential of phytochemicals appears to arise from multitarget interactions involving neurotransmission, antioxidant defence, inflammatory regulation, neurotrophic signalling and stress-response pathways. Such interactions may contribute to the effects observed across cognitive and psychological domains. The multitarget nature of these compounds may be advantageous because cognitive and psychological functioning are themselves regulated by interconnected biological systems. At the same time, it creates challenges in determining which compounds, molecular pathways and doses are responsible for particular outcomes. Differences in extraction methods, phytochemical concentrations, bioavailability, treatment duration and individual characteristics may further contribute to variation between studies. Therefore, mechanistic evidence should be integrated with human clinical findings when evaluating the relevance of neuroactive phytochemicals to psychological health.

4. Neurotoxic Phytochemicals and Neuropsychological Disturbances

Although several plant-derived phytochemicals have demonstrated potential neuroprotective and neuroactive properties, certain phytochemicals can adversely affect the nervous system when exposure exceeds physiological tolerance or when inherently toxic compounds are consumed. Neurotoxicity may arise through disruption of neurotransmitter systems, excessive neuronal excitation, ion-channel dysfunction, oxidative stress, mitochondrial impairment or interference with normal neuronal signalling. The psychological and neuropsychological consequences can range from transient alterations in cognition and behaviour to severe neurological dysfunction. The neurotoxic effects of *Datura stramonium*, *Aconitum ferox*, *Strychnos nux-vomica* and *Lathyrus sativus* illustrate different mechanisms through which plant-derived compounds can adversely affect nervous-system functioning.

The neurotoxic plants discussed here are illustrated in Figures 7–10, with their taxonomic classifications presented in Tables 6–9.

Datura stramonium is an important example of acute neuropsychiatric toxicity associated with plant-derived alkaloids. Its principal toxic constituents, including atropine, scopolamine and hyoscyamine, exert antimuscarinic effects that interfere with cholinergic neurotransmission. Because acetylcholine is essential for attention, memory, orientation and other cognitive processes, disruption of cholinergic signalling can produce prominent neuropsychological manifestations. Clinical reports of *Datura* poisoning have described agitation, confusion, disorientation, hallucinations, abnormal or disinhibited behaviour and delirium. A 2022 case series and literature review of *Datura* poisoning documented central anticholinergic manifestations including agitation, hallucinations, anxiety, confusion, disorientation and bizarre behaviour. These manifestations demonstrate that excessive exposure to a neuroactive plant compound can rapidly transform pharmacological activity into clinically significant neuropsychiatric toxicity. Thus, *Datura* provides a clear example of how disruption of neurotransmission can directly affect cognition, perception and behaviour. (Nillofar Khoshnam- Rad, 2022)

Aconitum ferox represents another form of plant-associated neurotoxicity, primarily related to aconitine and structurally related diterpenoid alkaloids. Aconitine interacts with voltage-gated sodium channels, altering their normal activation and inactivation and producing abnormal neuronal and muscular excitability. A 2021 clinical study examining aconitine intoxication reported deterioration of consciousness and neurological symptoms among affected patients, demonstrating that aconitine exposure can involve clinically relevant nervous-system disturbances. Reviews published in 2022 have further characterized aconitine as a compound with both pharmacological and toxic effects, emphasizing that excessive exposure may produce neurotoxicity in addition to its well-recognized cardiovascular toxicity. Therefore, the neuropsychological relevance of *Aconitum* lies primarily in altered consciousness, neurological dysfunction and abnormal neuronal excitability rather than in a specific psychiatric disorder. The severity of toxicity is also influenced by dose, preparation and administration method. (Pengyu Zhao, 2024)

Strychnos nux-vomica illustrates neurotoxicity through a different mechanism. The plant contains the highly toxic alkaloid strychnine, which acts primarily as a competitive antagonist of postsynaptic glycine receptors within the spinal cord and brainstem. Inhibition of glycinergic neurotransmission removes an important mechanism of neuronal inhibition, resulting in excessive motor-neuron activity and marked central nervous-system hyperexcitability. Contemporary clinical toxicology literature describes strychnine poisoning as producing severe muscular rigidity, spasms and convulsions while consciousness may remain relatively preserved during the early stages. From a neuropsychological perspective, the significance of *S. nux-vomica* therefore lies less in chronic changes in mood or cognition and more in the profound disruption of inhibitory neural control, which can rapidly impair normal behavioural and motor functioning. This distinction is important when interpreting the psychological consequences of neurotoxic plants because not all neurotoxicity manifests as a conventional psychiatric symptom. (Nux Vomica, 2012- updated 2023)

Lathyrus sativus provides an example of chronic neurotoxicity associated with prolonged exposure to a plant-derived excitatory amino acid. The principal neurotoxic compound, β -N-oxalyl-L- α , β -diaminopropionic acid (β -ODAP), has been associated with neurolathyrism, a neurological disorder characterized predominantly by irreversible motor impairment. Recent reviews continue to identify β -ODAP as the major factor limiting wider consumption of grass pea because of its association with neurolathyrism. Mechanistic research indicates that β -ODAP can activate ionotropic glutamate receptors and interfere with glutamate and cystine transport, contributing to excitotoxicity and oxidative stress. Excessive glutamatergic activity can promote calcium dysregulation, mitochondrial dysfunction and neuronal injury. Consequently, unlike the acute delirium associated with *Datura* or the intense neuronal hyperexcitability associated with strychnine, *L. sativus* illustrates how prolonged exposure to a neurotoxic phytochemical can contribute to progressive and potentially permanent neurological impairment. (Abraham Bekele-Alemu, 2024)

Together, these four plants demonstrate that neurotoxicity can affect the nervous system through substantially different biological pathways. *Datura stramonium* primarily disrupts cholinergic neurotransmission and may produce acute cognitive and behavioural disturbances; *Aconitum ferox* and its aconitine-related alkaloids can disturb neuronal excitability through ion-channel effects; *Strychnos nux-vomica* produces excessive neuronal activity through inhibition of glycinergic signalling; and *Lathyrus sativus* is associated with glutamate-related excitotoxicity and chronic motor-neuron injury. These differences highlight the importance of considering the specific molecular targets, dose and duration of exposure when evaluating the psychological and neurological consequences of plant-derived compounds. Importantly, evidence for these toxic effects comes from a combination of human poisoning reports, clinical observations and experimental research, and therefore the strength of evidence differs considerably among the four plants.

5. Neuroactive–Neurotoxic Continuum and Implications for Human Psychological Health

The neuropsychological effects of phytochemicals exist along a continuum ranging from potentially beneficial neuroactivity to significant neurotoxicity. Their effects depend on factors including dose, duration of exposure, bioavailability, preparation and individual susceptibility. The neuroactive plants discussed in this review demonstrate potential benefits in cognitive and psychological domains, whereas the neurotoxic plants illustrate how disruption of neurotransmission and neuronal function can result in adverse neurological and behavioural outcomes. Therefore, the presence of biological activity alone should not be interpreted as evidence of either therapeutic benefit or safety.

6. Conclusion

Overall, phytochemicals have considerable potential to influence cognitive and psychological functioning through multiple neurobiological pathways. Evidence from *Bacopa monnieri*, *Centella asiatica*, *Withania somnifera* and *Curcuma longa* suggests promising neuroactive effects, while *Datura stramonium*, *Aconitum ferox*, *Strychnos nux-vomica* and *Lathyrus sativus* demonstrate the potential for serious neurotoxicity. A balanced understanding of both benefits and risks, supported by well-designed human studies and appropriate safety evaluation, is essential for determining the role of phytochemicals in human neuropsychological health.

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