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Review article

Phytochemical composition and neuroprotective potential of *Mirabilis jalapa*: a review

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ABSTRACT

Four-o'clock plant, scientifically named as *Mirabilis jalapa*, has gained significant attention for both its ornamental beauty and its medicinal properties, widely utilized as folk remedies. It is a plant grown in the warm climate as a species and showed different pharmacological effects in various therapeutic sectors such as neuroprotective and anxiolytic. Using PubMed, Web of Science Semantic Scholar and Google Scholar and the search terms *Mirabilis jalapa* phytochemicals; neuroprotection; anxiolytic effect; traditional medicine; flavonoids; alkaloids and neurological disorders literature supporting the medicinal role of *Mirabilis jalapa* were sourced.



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The members of *Mirabilis jalapa* contain flavonoids, alkaloids, triterpenes leaves and saponin through which it provides possibility for the neuroprotection feature. According to research, extracts of the plant can help prevent oxidative stress, a major factor in illnesses including Alzheimer's and Parkinson's. Animal studies reveal that components from *M. jalapa* interfere with Aluminum cytotoxicity by increasing antioxidant enzyme levels, as well as decreasing oxidative damage biomolecules. In addition, the flavonoid constituent has anxiolytic effects because its extract interferes with GABAergic transmission, whereas its effectiveness is comparable to diazepam. Furthermore, the plant has exhibited anticonvulsant effect possibly due to interaction with Ca channel and Glu transmission. Thus, these studies show directions in which the plant works, indicating that it may possess valuable means to treating neurological disorders, although further clinical trials are needed to understand the exact effects of the plant in human organisms. *Mirabilis jalapa* therefore Discovered to be of great potential as natural antioxidant and neuroprotective compound as well as anxiolytic remedies.

Keywords: *Mirabilis jalapa*, phytochemicals, neuroprotection, anxiolytic, traditional medicine, flavonoids, alkaloids, therapeutic potential, neurological disorders.

INTRODUCTION

Mirabilis jalapa belongs to the Nyctaginaceae family which contains about 30 genera and 400 species of the Four-o-clock plant, also known as the Marvel of Peru. It is widely grown for the aesthetic and therapeutic purposes throughout the warm areas of America, India and some parts of Africa [1-4]. The common name of this plant is Four-o-clock, derived from the fact that its tubular, trumpet-shaped flowers bloom only at four o'clock in the afternoon and remain open all night. These flowers can be found in white, red, pink, yellow, and bi coloured with a sweet smell to attract humming birds and butterflies [5-6]. It is also cultivated to obtain large black carrot lhummingbirdsike enlarged fleshy taproot part which may weigh up to 18 kg in the required environmental conditions [7]. In folk medicine, Mirabilis jalapa was used to treat kidney infection, diuretic and tonic, purgative, and emetic [8-12]. The pharmacological activities of the plant include antimicrobial [13-15], anti-inflammatory [16-17], antidiabetic [8] and anticancer^[18], antiprotozoal, anti-dermatologic. It shows the presence of tannins, alkaloids and flavonoids, glycosides terpenes saponins steroids and emodin due to which it possesses a number of medicinal activities. These bioactive compounds are the subject of current pharmaceutical investigation, where literature works describes the plant for its pharmacokinetics and immunomodulatory pharmacodynamics, and antispasmodic properties ^[21]. This makes Mirabilis jalapa a suitable candidate for natural compounds for formulation of new drug molecules for different therapeutic uses.

Neurological Disorders

Neurological disorders are a diverse group of conditions affecting the nervous system, including the brain, spinal cord, and peripheral nerves, with common types including Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, migraine, cerebral palsy, and Guillain-Barré syndrome. These disorders can arise from various causes, such as genetic factors, environmental exposures, autoimmune reactions, degenerative processes, and metabolic disorders. Symptoms can vary widely, encompassing cognitive impairments (like memory loss), motor dysfunction (such as tremors and weakness), sensory changes (including numbness or tingling), and seizures. The diagnosis often involves a combination of medical history, physical examinations, imaging studies (like MRI and CT scans), and electrodiagnostic tests. Treatment approaches may include medications (such as anticonvulsants and immunomodulatory therapies), physical therapy, occupational therapy, and sometimes surgery, depending on the specific condition and its severity ^[22].

Mechanism of Action of Neurological Agents

Neuroprotective agents have the characteristic of protecting neurons from toxic insult or cellular injury, including an action or process that is directed towards the prevention or slowing of neuronal dysfunction and death. These mechanisms for the most part involve; reducing oxidant stress through the neutralization of free radicals by antioxidants, minimizing excitotoxicity by antagonizing the effects of excessive glutamate at NMDA receptors as found in memantines and finally moderation of inflammation through restraining cytokines that promote brain inflammation. Moreover, neuroprotective molecules can increase mitochondrial activity for cell energy production besides inhibiting apoptosis or stimulate the neurotrophic factors that favoured neuronal growth and recovery. Through a direct modulation of these pathways drugs target to either delay or halt neurodegeneration involved in Alzheimer's disease, Parkinson's and stroke and other conditions ^[23-25].

Anxiolytic Drugs

The general MOA of anxiolytic drugs primarily involves the modulation of neurotransmitter systems in the brain, particularly focusing on gamma-aminobutyric acid (GABA), serotonin, and norepinephrine. Most anxiolytic medications enhance GABAergic activity by binding to GABA-A receptors, increasing the frequency of chloride ion channel openings when GABA binds, leading to hyperpolarization of neurons. This hyperpolarization reduces neuronal excitability, producing a calming effect and alleviating anxiety symptoms. Additionally, some anxiolytics, particularly selective serotonin reuptake inhibitors (SSRIs) work by increasing serotonin levels in the brain by inhibiting its reuptake into presynaptic neurons, which enhances serotonergic transmission and

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can improve mood. Serotonin norepinephrine reuptake inhibitors (SNRIs) further modulate anxiety by increasing both serotonin and norepinephrine levels. Some anxiolytics, primarily act as partial agonists at 5-HT1A serotonin receptors, balancing serotonin levels without the sedative effects Collectively, these mechanisms help alleviate anxiety symptoms by restoring balance in neurotransmitter activity in the brain^[27-29].

Alzheimer's Treatment

Alzheimer's disease treatments primarily focus on improving symptoms and slowing cognitive decline by targeting key neurotransmitter systems. Cholinesterase inhibitors work by inhibiting the enzyme that breaks down acetylcholine, increases its levels in the brain to enhance memory and learning, particularly in early to moderate stages. Memantine is an NMDA receptor antagonist that affects glutamate in a way to reduce neuronal damage related to moderate to severe forms of the condition. Emerging therapies like aducanumab target beta-amyloid plaques, attempting to clear these abnormal protein deposits to slow disease progression. This multi-faceted approach aims to manage symptoms, protect neurons, and slow Alzheimer's disease progression, though it cannot cure the condition ^[30-32].

Anticonvulsants

Also known as antiepileptic drugs (AEDs), primarily work to prevent and control seizures by modulating neuronal excitability and neurotransmitter systems in the brain. They utilize several key mechanisms of action: sodium channel inhibitors block voltage-gated sodium channels, stabilizing neuronal membranes and reducing seizure activity; calcium channel inhibitors inhibit T-type calcium channels, decreasing excitatory neurotransmitter release; GABAergic drugs enhance the effects of gamma-aminobutyric acid (GABA), the primary inhibitory neurotransmitter, thereby increasing inhibitory signaling; and glutamate inhibitors reduce the action of glutamate, an excitatory neurotransmitter, by blocking its receptors. Collectively, these mechanisms help to stabilize neuronal activity and effectively manage seizures in individuals with epilepsy ^[33, 34].

This review aims at reviewing the studies on the therapeutic efficacy of *Mirabilis jalapa* especially concerned with the effects of the extract on neurological diseases based on neuroprotection and anxiolytic effects. The plant has been used as traditional medicine in the management of several diseases and it's have active ingredients like flavones, flavonoids, alkaloids and other active compounds with some antioxidant, anti-inflammatory and neuroprotective activities. The current article synthesizes literature from PubMed, Google Scholar & Web of Science to reveal the prospect of *Mirabilis jalapa* in managing neuropathological disorders such as Alzheimer's and Parkinson's diseases besides its anxiolytic potency.

Table 1: list of vernacular name

State	Common Name		
Telugu	Chandrakanta		
Assamese	Gophuligopal; Sarpamani;		
Bengal	Krishnakeli,		
English	Four o' clock, Marvel of		
Gujrati	Gubbaji		
Hindi	Gul-abbas		
Kannada	Sanjamalligie, Chandramalligie;		
Punjabi	Gulabbas;		
Tamil	Andhimalligai		
Sanskrit	Krishnakeli		
Oriya	Rangai		
Malayalam	Antmalari		
Marathi	Gulbas		
Persian	Gul-i-abbasa		

Taxonomy

Table 2: Taxonomy of Mirabilis jalapa			
Kingdom	Plantae		
Subkingdom	Viridiplantae		
Infrakingdom	Streptophyta		
Super division	Embryophyta		
Division	Tracheophyta		
Subdivision	Spermatophytina		
Class	Magnoliopsida		
Superorder	Caryophyllanae		
Order	Caryophyllales		
Family	Nyctaginaceae		
Genus	Mirabilis		
Species	Mirabilis jalapa		

Synonyms and Other Names

Jalapa congesta, Jalapa officinalis, Mirabilis ambigua, Mirabilis jalapa var. jalapa, Mirabilis jalapa subsp. lindheimeri, Mirabilis lindheimeri, Mirabilis jalapa var. lindheimeri, Mirabilis pedunculata, Mirabilis procera Bertol, Mirabilis planiflora, Mirabilis pubescens, Mirabilis suaveolens, Mirabilis xalapa and Nyctagojalapae Nyctago hortnesis Dum. Cours. Nyctago jalapa(L.) DC, Nyctago versicilor Salisb"

M. dichotoma Linn. (in Brazil), *M.* dichotoma Linn. *M.* lindheimeri Linn., and *M.* longiflora Linn. (in tropical America), and *M.* odorata Linn^[41-43].

Phytochemical Characteristics

Physico chemical evaluation of the ethanolic extracts of Mirabilis jalapa leaf revealed that the percent w/w of total ash was 15.15 % and Acid insoluble ash was 4.57 % while the Water soluble ash was fetched 3.75 % and water soluble extractive value was 26.22 % and alcohol soluble extractive value and ether soluble extractive value were 21.81 % & 24.94

The physicochemical parameter of the powder of the whole Mirabilis jalapa plant were: loss on drying $12.41\% \pm 0.005$, total ash $11.81\% \pm 0.001$, water soluble ash $5.06\% \pm 0.001$, acid insoluble ash $0.41\% \pm 0.001$, alcohol soluble extractive value $11.02\% \pm 0.007$, water soluble materials $18.63\% \pm 0.007$, and ether soluble materials $^{[46]}$.

The determined iodine value was 80 and the saponification value was 172.

A from seeds 3% of oil was obtained, and the oil has a density of 0.70 g/ml, surface tension 26.10 dynes/cm and viscosity

169.5 millipoise at 20.5 °C.

Table 3: The morphological features of Mirabilis Jalapa				
Parts	Images	Macroscopic features		
Plant		A herbaceous perennial plant that grows to a height of 30-75 cm with thick, fleshy stems.		
Leaf		Opposite leaves, 3.5-7.5 cm wide and 5-10 cm long, are unequal in shape, ranging from ovate to subcordate.		
Flower		Flowers are shortly stalked, funnel-shaped, and found in clusters, each subtended by an involucre of five ovate, connate bracts. The flowers may be striped or blotched fragrant colors, including white, yellow, purple, or red. The perianth is funnel-shaped with five lobes, while the stamens number between 3 and 6 and are exserted. The anthocarps are globose and turn black when ripened		
Seeds		The seeds are olive, brown or black and are about twice the size of a peppercorn.		
Tubers		The roots are thick, tuberous and swollen at the nods, and can be 10 cm or more in diameter.		

Chemical constituents Flowers

Many betaxanthins pigments (indicaxanthin, vulgaxanthin-I, miraxanthin-I, -II, -III, -IV, -V and -VI) were identified in the flowers by combining HPLC separation techniques to its fluorescence property of *Mirabilis jalapa*^[48-51].

Aerial parts: Triterpenes, flavonoids, Stigmasterol, Beta-sitosterol, ursolic acid, oleanolic acid and brassicasterolare present^[52].

Seeds

A fatty acid was identified as a minor constituent in the seed oil and was labelled as 8-cis-11, 14-hydroxy-octadeca-dienoic acid 1. Arginine, glycine, Histidine, threonine, tyrosine, asparatic acid and glutamic acid were found in seeds 2. The seeds cotyledons D-glucan reported as a polysaccharide containing 38 glycosyl units 2 of β -sitosterol, β -amyrin/ β -sitosterol-D-glucosid and/ β -amyrin-3-O- α -L-rhamnogycol- O/ β -D-glucoside 4,5were extracted from seeds two newly identified antimicrobial peptides also isolated from seeds and characterized including Mj-AMP-1 and Mj-AMP-2 ^[53-54].

Leaves

Flavonoids include quercetine and C- glycosyl flavonoid in leaves. Tricosan-12-one, n-hexacosanal, β -sitosterol was extracted out of the leaves and tetracosanoic acid out of the tartaric acid, citric acid, these molecules include leucuine, valine, tryptophan, and alanine and glycine were determined qualitatively using paper chromatography. D-pinitol, an o-methyl inositol. Succesively, fructanes as Fru 1, 6 bisphosphate (Fru 1, 6 P 2) in the range of 5001-2001 was cited as a major carbohydrate in leaves. Bioaasay solvent partitioning of the methanol extract of leaves and stems fixed was based on the isolation of an active polyphenolic amide N-transferuloyl-4'-O-methyldopamine.

Roots

The root is the largest source of biological content for searches by billions of users around the world. In Mirabilis jalapa Linn. The roots contain 3% resin, trigonelline the wealth of India: raw materials, 1998 carbohydrate which after hydrolysis produces galactose and arabinose. By using column chromatography and NMRspectroscopy and mass spectroscopy and astragaloside-II flazin among them are phytoconstituents are isolated from root Source of phytoconstituents many phytoconstituents are isolated from root Permission granted to use this image Phytochemicals come under various classes of natural products; alkaloids; flavonoids; phenols tannins and terpenoids. An anti-plant virus and also proposes a viral protein active against mechanical transmission of. Plant viruses was isolated and purified from roots using double precipitation with ammonium sulfate and exchange through an ion-exchanger Chromatography. Rotenoid mirabijalone A, B, C and D along with 9-O-methyl-4 hydroxyboeavinone -B 1.2.3.4and

tetrahydromethylisoquinoline-7,8-diol were isolated from the root of C. muconata. Boeavinone, urea, glycerin monoeicosate and betaethyl sitosterol were extracted from the 75% ethanol roots extract. According to the study the people should take in *Mirabilis jalapa* root may prevent the complication of high blood glucose caused by diabetes

Neurological Activity in *Mirabilis jalapa* Neuroprotective potential

This article focuses on the effects of administering Mirabilis jalapa flower extracts in addressing this problem of Aluminium induced neurotoxicity in Wistar rats. Neurotoxicity was induced with aluminium hydrochloride that damages the brain and has linkages to neurodegenerative diseases such as Alzheimer's. Various parts/ fractions of Mirabilis jalapa plant petroleum ether, acetone, methanol and aqueous fraction was tested at 250mg/kg and 500mg/kg. The results of the present work revealed that aluminium increased the serum level of ALT, AST, nitric oxide and TBARS and depressed the SOD and glutathione in rat. However, the extract of Mirabilis jalapa reduced the antioxidant enzymes significantly on these marker of oxidative stress and cellular damage. These outcomes suggest that the extracts can prevent the damage of brain cells and oxidative stress and enhance the antioxidant system, which could make Mirabilis jalapa a candidate for the treatment of neurodegenerative diseases related to aluminium toxicity.

Anti-anxiety

The work aims at investigating the stress alleviation effects of Mirabilisjalapa on Drosophila melanogaster (fruit fly) influenced from oxidative stress by MTX, a known stress agent. The research involved four groups of flies: The animals were divided into a control group, a group given MTX only, a group receiving both MTX and *M. jalapa* extract, and a group which received only the plant part of *M. jalapa*. Stress-induced flies had higher levels of oxidants; they had heightened CAT and SOD levels which indicate oxidants. Treatments using *M. jalapa* extract lowered the level of these enzymes which indicates that the extract helps in reversing the effects of stress through decreasing ROS. The phytochemical screening brought to light that the plant contained flavonoids, phenols, alkaloids, and tannins which assist the antioxidant property of the plant. They make a case that *M. jalapa* can be used as an anti-stress and call for more research on the plant for other related medicinal uses.

Alzheimer's disease

Mirabilis jalapa used in the section on Ethnomedicine is known to possess memory-improving effects. The plant has been utilized in different traditional systems of medication in Africa, including the Nigerian, to cure senile dementia and neurodegenerative diseases including AD. Although it is not clarified how it operates, its position alongside the plant with pharmacologic effects involving anti-cholinesterase impact on cognitive function and

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memory consolidation endorses it. ALTOGETHER, similar to many other medicinal plants there is an urgent need to establish scientific evidence concerning the efficiency and the bioactive compounds present in the plant for the treatment of AD.

Table 3: Chemical structure of some active constituents in flower of Mirabilis jalapa











Table 6: Chemical structure of some active constituents in leaves of Mirabilis jalapa



Table 7: Chemical structure of some active constituents in Roots of Mirabilis Jalapa







Anxiolytic Activity-

This article focuses on the anxiolytic effect of Mirabilis jalapa through its methanolic extract with secondary metabolites including flavonoids, phenols, alkaloids, and tannins. wwwnaturaldatabase.com indicates that flavonoids isolated specifically quercetin interact with GAB receptors in the brain and dampen neuronal activity, even as do diazepam anxiolytics. Metho clinical evidence of experimental procedures such as Elevated Plus Maze and Open Field Test reveals that rats treated via the extract had manifested increased anxiety like behavior as suggested by the increased number of time taken to spend in the open arms and increased exploration, as compared to the normal rats. To this effect, the present study provides evidence showing that the ethanol extract of Mirabilis jalapa possesses anxiolytic effects, therefore proposing this plant as a possible replacement for pharmacological treatments for anxiety disorders in humans.

To measure the ability of Mirabilis jalapa as an anxiolytic agent, the authors used the Elevated Plus Maze (EPM) and Open Field Test (OFT). The ethanolic extracts, especially at the higher dose of 400mg/kg have raised the time spent in the open arms of EPM and improved the locomotor activity in the OFT, thereby suggesting anxiolytic effect similar to diazepam. These results propose the possibility that the plant's extract, which is rich in flavonoids, may have an anxiolytic effect or work through GABAergic mechanisms. In conclusion, Mirabilis jalapa has potential benefit for the treatment of anxiety and convulsive disorders, though additional research is necessary to determine the bioactive components and the pathways responsible for the clinical effects.

Anticonvulsant

Considering anticonvulsant activity, and further investigations in experimental models, Mirabilis jalapa can be looked forward for its naturality to manage neurological disorders. The anticonvulsant activity of ethanolic extracts of Mirabilis jalapa was tested using the Maximal Electroshock (MES) together with the Pentylenetetrazol (PTZ) seizure tests. Comparing both models, the extract at doses of 200mg/kg and 400mg/kg showed protection against seizures especially the 400mg/kg dose as it delays the onset of seizure and reduces the tonic hind limb extension. These effects are similar to the reference antiepileptic drug Phenytoin so that MJ might suppress seizures acting via various mechanisms, including inactivation of calcium channels or blockade of the NMDA receptordependent release of endogenous glutamate and facilitation of GABAergic neurotransmission. Possible reasons for such an effect are the content of flavonoids, phenolic compounds, and alkaloids in the plant extract.

The research work entitled "Anticonvulsant activity of aqueous extract of *Mirabilis jalapa Linn*. Roots in experimental animals" evaluates the antiepileptic effect of the root extract employing chemical convulsion models including; maximal electroshock (MES) and pentylenetetrazol (PTZ). The outcomes revealed a decrease in seizure length/symptoms similar to conventional medications such as phenytoin and diazepam, due to possible pointed alterations of neurotransmission by some bioactive ingredients within the plant extract including the alkaloids and flavonoids. This bears the modern scientific backing to its traditional function as an antiepileptic and general neurological condition remedy.

CONCLUSION

it was found that Mirabilis jalapa possess significant therapeutic importance in treating neurological disorders because of its multitude of phytochemical profile such as alkaloids, flavonoids, terpenoids and phenolic compounds. These bioactive constituents play a vital role for the therapeutic effects such as antioxidant, antiinflammatory, neuroprotector activity, anxiolitic and anticonvulsive activity, which are important for the management of neurodegenerative diseases like Alzheimer and Parkinson and anxiety, epilepsy, etc. Previous animal investigations have shown that plant has antioxidant, anti-neuro-inflammatory this and neuroprotective effects and ability to influence the levels of neurotransmission. Yet, to unlock its full therapeutic application, significant spell of pharmacology, including trials, have to be completed for the appropriate discovery of the usage and effectiveness on the human body, and safety profile before it makes its way into contemporary medicine.

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