

# An Overview of Medicinal Plants that Have Central Nervous Activity

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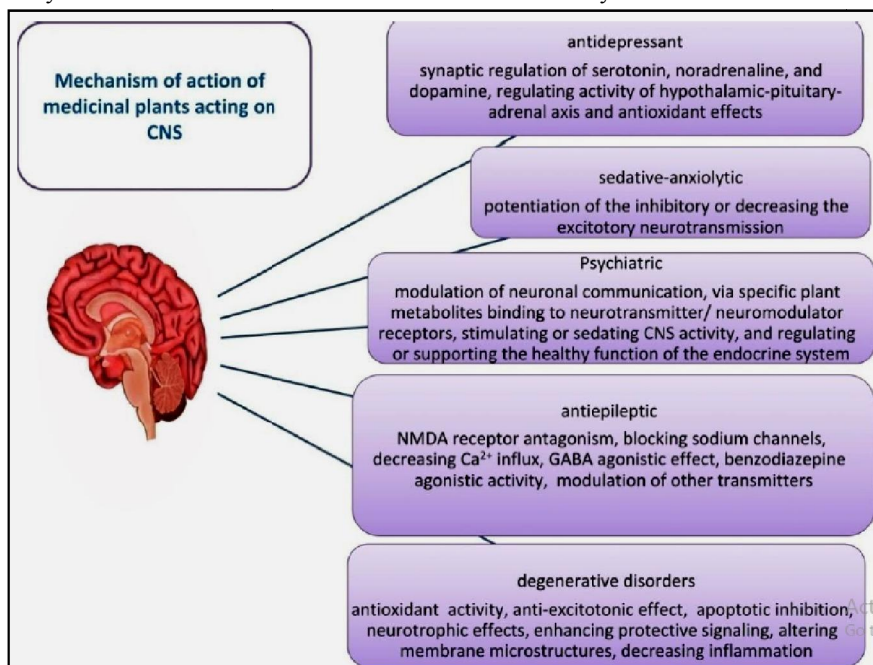
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**Abstract:** According to current research, a wide range of plants have pharmacological effects on the central nervous system, including sedative, anticonvulsant, depressive, antipsychotic, anxiolytic, anti-Parkinson, memory-enhancing, locomotor, and neuroprotective properties. The effects of medicinal plants on the central nervous system are covered in the present review, with an emphasis on the mechanisms involved.

**Keywords:** Antidepressant, Antiparkinson, Antipsychotic.

## I. INTRODUCTION

Many secondary metabolites from plants cure and prevent sickness. Many medical plants are anticonvulsant, antidepressant, antianxiety, sedative, locomotor, and memory-enhancing. Parkinson's, Alzheimer's, dementia, stress, and fatigue were alleviated. Herbal remedies for depression controlled serotonin, noradrenaline, and dopamine synaptically, regulated the hypothalamic-pituitary-adrenal axis, and had antioxidant effects [1]. Increasing inhibitory or decreasing excitatory neurotransmission rendered them sedative and anxiolytic.



**Fig : The mechanism of central nervous effects of medicinal plants**

Most medicinal herbs used to treat mental diseases bound to neurotransmitter/neuromodulator receptors, stimulated or slowed CNS activity, and supported endocrine system function [2-3]. Medical plant antiepileptic effect was mediated by NMDA receptor antagonism, sodium channel blockage, Ca<sup>2+</sup> influx decrease, GABA agonistic impact, benzodiazepine agonistic activity, dopamine output reduction, and transmitter interaction and regulation [4]. For

neurodegenerative disorders, medicinal plants had antioxidant activity, anti-excitotoxic effects, apoptotic inhibition, neurotrophic effects, enhanced protective signaling, altered membrane microstructures, decreased inflammation, and prevented polyubiquitinated protein aggregates in critical brain regions. Our review will focus on medicinal plant central nervous effects.

**Plants with anticonvulsant effect:****Bacopa monniera**

Bacosides and crude *Bacopa monnieri* plant extract are also anticonvulsants. It protected against glutamate-mediated excitotoxicity during seizures and cognitive impairment from pilocarpine-induced epilepsy [98]. Pentylentetrazol, maximal electroshock, strychnine, hypoxic stress, and lithium–pilocarpine-induced status epilepticus were used to test the anticonvulsant activity of the ethanolic *Bacopa monniera* extract. *Bacopa monniera* ethanolic extract was given orally to rats and mice at 50 and 55 mg/kg 2 and 4 hours before convulsive shocks. All models showed strong anticonvulsant efficacy from the ethanolic leaf extract, which works like benzodiazepines (GABA agonists) [7].

**Benincasa hispida**

Alcoholic *Benincasa hispida* extract was tested for anticonvulsant effects in mice given maximum electroshock test (MEST), pentylentetrazole, and strychnine. *Benincasa hispida* alcoholic extract protected animals against maximum electroshock-induced convulsion and shortened recovery time. It also prevented pentylentetrazole-induced convulsions and strychnine-induced convulsions in mice [8].

**Brassica nigra**

Methanolic extract of *Brassica nigra* seeds was tested for antiepileptic action in mice with maximum electroshock, pentylene tetrazole, picrotoxin, and biccuculine-induced seizures. In PTZ, PIC, and biccuculine-induced seizure models, the extract (200 and 400 mg/kg, orally) prolonged the onset of tonic seizures and reduced their duration, while in MES model, it abolished tonic hind limb extensions by inhibiting voltage-dependent Na<sup>+</sup> channels or blocking glutamergic excitation mediated by the NMDA receptor [9]. In mice with pentylentetrazole (PTZ)-induced kindling, the methanolic extract of *Brassica nigra* seeds (75, 150, and 300 mg/Kg; ip) was tested for anti-epileptic properties. Methanolic *Brassica nigra* seed extract decreased seizure intensity and duration. In brain tissues, *Brassica nigra* extract enhanced SOD and NO and lowered MDA [10].

**Coriandrum sativum**

The CNS activity spectrum of *Clitoria ternatea* (CT) methanolic extract was determined. The CT was tested on cognitive behavior, anxiety, sadness, stress, and convulsions caused by PTZ and maximal electroshock. CT was further tested on DA, noradrenaline, serotonin, and acetylcholine-mediated behavior to explain these effects. The extract lowered transfer latency (TL) in the elevated plus maze (EPM) and raised object recognition discrimination index, suggesting nootropic action. The extract was more active in object recognition than EPM. The extract enhanced occupancy in the open arm of EPM by 160% and in the illuminated box of the light/dark exploration test by 157%, showing anxiolytic action. It reduced stress-induced ulcers, tail suspension test immobility, and PTZ and MES convulsions, indicating antidepressant potential. Serotonin and acetylcholine-mediated behavior reduction was seen in the extract. No substantial influence on DA- and noradrenaline-mediated behavior. The extract has nootropic, anxiolytic, depressive, anticonvulsant, and antistress properties [20].

**Cuminum cyminum**

The effect of the fruit essential oil of *Cuminum cyminum* on the epileptiform activity induced by pentylentetrazol (PTZ) was evaluated using intracellular technique. The results demonstrated that extracellular application of the essential oil of *Cuminum cyminum* (1% and 3%) dramatically decreased the frequency of spontaneous activity induced by PTZ in a time and concentration dependent manner. In addition it showed protection against pentylentetrazol-induced epileptic activity by increasing the duration, decreasing the amplitude of after hyperpolarization potential (AHP) following the action potential, the peak of action potential, and inhibition of the firing rate.

**Cuscuta planiflora**

In mice with pentylentetrazole-induced seizures, 80% plant methanol extract was tested for anticonvulsant properties. Seizures were delayed by different dosages of extracts ( $p < 0.01$ ), but their length did not alter appreciably. Pretreatment

with extracts substantially reduced death rates ( $p < 0.01$ ) and increased seizure protection compared to the control group ( $p < 0.05$ ). The optimal dosage was 50 mg/kg.

#### **Cynodon dactylon**

In mice, the ethanol extract of *Cynodon dactylon* aerial portions protected against chemo-induced convulsions. Extract-treated animals had higher catecholamine levels in their brains. After six weeks of therapy, mouse brains had considerably more GABA, which is thought to cause seizures. By changing catecholamine and brain amino acid levels in mice, the extract displayed anticonvulsive properties [27-28].

Pentylenetetrazole-induced convulsion was dose-dependently reduced by *Cynodon dactylon* aerial parts ethanol extract. The ethanolic extract of *Cynodon dactylon* was tested for its anticonvulsant properties against maximum electroshock and PTZ-induced convulsions in mice. Extract (200, 400, 600 mg/kg) decreased MES-induced hind limb tonic extensions and protected against PTZ-induced seizures.

#### **Equisetum arvense**

Hydroalcoholic extract (200 and 400 mg/kg) enhanced open-field activity, rota-rod falls, bar permanence, and barbiturate-induced sleeping duration (46% and 74%, respectively) in *Equisetum arvense* sedative and anticonvulsant tests. In pentylenetetrazole-seizure, it increased first convulsion delay, reduced severity, lowered rate (50% and 25%), and saved animals from mortality. 50, 100, and 150 mg/kg did not affect parameters in the raised plus maze.

#### **Eschscholzia californica**

*E. californica* alkaloids' sedative effects were linked to chloride-current modulation, which was often manifested in inhibitory interneurons. Electrophysiological investigations on a recombinant  $\alpha 1 \beta 2 \gamma 2$  GABAA receptor found no impact from N-methylaureotetanine below 30  $\mu$ M. However, (*S*)-reticuline acted as a positive allosteric modulator at GABAA receptor  $\alpha 3$ ,  $\alpha 5$ , and  $\alpha 6$  isoforms. Depressant effects of *E. californica* aerial parts are attributed to chloride-current regulation by (*S*)-reticuline at  $\alpha \beta 2 \gamma 2$  and  $\alpha 5 \beta 2 \gamma 2$  GABAA receptors. Protopine, cryptopine, and allocryptopine increased 3H-GABA binding to rat brain synaptic membrane receptors. This may imply benzodiazepine-like action of these alkaloids.

#### **Gossypium species**

Aqueous extract of *Gossypium herbaceum* (AEGH) at 10, 30, and 100 mg/Kg, po was tested for antiepileptic efficacy by inducing convulsions in mice with maximal electroshock (MES), pentylenetetrazole (PTZ), and isoniazid. MES showed that *Gossypium herbaceum* aqueous extract prevented convulsions better than Diazepam. *Gossypium herbaceum* aqueous extract reduced convulsions better than phenobarbitone sodium in PTZ. The INH approach showed that *Gossypium herbaceum* aqueous extract delayed convulsions less than Diazepam.

#### **Hibiscus rosa-sinensis**

Ethanolic preparations of *Hibiscus rosa sinensis* flowers were anticonvulsant. The bioassay-guided fractionation showed that the acetone-soluble *H. rosa sinensis* floral ethanolic extract had anticonvulsant efficacy. The fraction protected mice against maximal electro shock, electrical kindling, and pentylenetetrazole-induced convulsions and reduced lithium-pilocarpine and electrical kindling convulsions. It reduced D-amphetamine's behavioral effects and increased pentobarbitone-induced sleep. It increased GABA and serotonin in the brain.

#### **Juglans regia**

Anticonvulsant effects of walnut kernel extract (WKE) on rats with pentylenetetrazole (PTZ; 2 mg/ml/min) seizures were evaluated. WKE administration significantly increased PTZ dose for initial myoclonic jerk ( $13.09 \pm 1.29$  vs.  $49.71 \pm 12.03$  mg/kg;  $p < 0.001$ ), decreased seizure severity, and achieved 0% fatality rate. Flumazenil (5 mg/kg ip) did not affect WKE's anticonvulsant effect. WKE and diazepam (DPZ; 0.5 mg/kg ip) produced a synergistic anticonvulsant effect, whereas ethosuximide (ESM) did not ( $p > 0.05$ ). The anticonvulsant effects were connected to  $\gamma$ -aminobutyric acid receptors, not benzodiazepine mechanisms.

#### **Plants with antidepressant activity:**

##### **Apium graveolens**

Methanolic extract of *Apium graveolens* seeds (AGM) (100, 200 mg/kg) demonstrated anti-depressant effects in mice and rats in forced swim and tail suspension tests, comparable to imipramine. Lower dosages of AGM had less anti-

depressant impact than 200 mg/kg. Mice showed mild sedation, protracted pentobarbital narcosis, and sleep following barbiturate treatment with celery oil constituents 3, n-butylphthalide, and sedanenolide.

**Avena sativa**

Methanolic extract of *Apium graveolens* seeds (AGM) (100, 200 mg/kg) showed anti-depressant effects in mice and rats in forced swim and tail suspension tests, equivalent to imipramine. Lower AGM doses demonstrated less antidepressant effect than 200 mg/kg. After barbiturate therapy with celery oil components 3, n-butylphthalide, and sedanenolide, mice demonstrated moderate sedation, persistent pentobarbital narcosis, and sleep.

**Bacopa monniera**

Bacosides A and B, bacosides I and II, bacosaponin C, and the extract of *Bacopa monniera* showed antidepressant efficacy in forced swimming and tail-suspension models in experimental mice, whereas bacoside VII did not.

**Benincasa hispida**

Methanolic extract (50, 100, and 200 mg/kg, orally for 14 days) was compared to traditional antidepressants (imipramine 15 mg/kg, fluoxetine 20 mg/kg, and phenelzine 20 mg/kg) in Swiss male albino mice. The methanolic extract of *B. hispida* exhibited antidepressant-like effect in rats, likely via MAO-A inhibition and interaction with dopaminergic,  $\alpha$ 1-adrenergic, serotonergic, and GABAergic systems.

**Clitoria ternatea**

*Clitoria ternatea* was evaluated for OCD treatment. *Clitoria ternatea* ethanolic extract affected mouse marble-burying. *Clitoria ternatea* ethanolic extract (100, 200, and 400mg/kg) reduced mouse marble burying. EECT may have reduced marble-burying behavior in mice owing to increased serotonergic activity and 5-HT reuptake.

A Perment polyherbal Ayurvedic combination of equal parts *Clitoria ternatea*, *Withania somnifera* Dun., *Asparagus racemosus* Linn., and *Bacopa monniera* Linn. enhances mood clinically. The stress-induced depression model explored Perment's behavior and process. Chronic unexpected moderate stress (CUMS) depressed rats. Open field exploratory behavior, raised plus maze, social interaction, and behavioural despair evaluated behavior. Plasma noradrenaline, serotonin, corticosterone, and brain/adrenal corticosterone were tested to corroborate Perment's behavioral effects. After 21 days of CUMS, rats displayed anxiety and melancholy by decreasing locomotor activity in the open field exploratory behavior test and increasing immobility in the behavioural despair test. Perment fought depression better than anxiolytics. Perment elevated plasma noradrenaline and serotonin in stressed rats. Perment treatment did not alter brain corticosterone in stressed rats. The adrenal corticosterone level fell with Perment. Adrenergic and serotonergic system activation may explain the synergistic antidepressant and anxiolytic effects of Perment.

**Coriandrum sativum**

Diethyl ether extract of *Coriandrum sativum* seeds had a stronger antidepressant effect than aqueous extract due to its adrenergic, dopaminergic, and GABA-ergic effects.

**Cuscuta planiflora**

A randomized triple-blind controlled clinical experiment examined *Cuscuta planiflora* (500mg capsules) in serious depressive patients. Patients received 8 weeks of therapy. Beck depression assessment and Hamilton depression inventory examined depression before and after the trial. Treatment with *Cuscuta planiflora* resulted in a substantial reduction in mean Beck and Hamilton depression inventories ( $p < 0.01$ ) compared to control.

**Daucus carota**

The antidepressant efficacy of *Dacus carota* (DC) ethanol root extract was tested in several animal models, including the forced swim test (FST), tail suspension test (TST), apomorphine-induced hypothermia (AIH), reserpine-induced RIH, and 5-HTPPH in mice. In FST, TST, and HTPPH models, fluoxetine (25 mg/kg) was the usual medication, while in AIH and RIH models, desipramine (20 mg/kg). DC (400 mg/kg) has similar antidepressant effect to conventional drugs.

**Eschscholtzia californica**

The *Eschscholtzia californica* aqueous-alcoholic extract reduced catecholamine breakdown and adrenaline production. *Eschscholtzia californica* extracts inhibited dopamine beta-hydroxylase, monoamine oxidase (MAO-B), and diamine oxidases and drastically shortened the phenolase catalytic lag phase owing to their o-diphenol concentration. *Eschscholtzia californica* may be antidepressant and hypnotic due to these mechanisms.



Additionally, protopine inhibited serotonin and noradrenaline transporters in vitro. Protopine was tested for antidepressant effects in mice utilizing 5-hydroxy-DL-tryptophan (5-HTP)-induced head twitch response (HTR) and tail suspension tests with fluoxetine and desipramine as positive controls. In HTR test, protopine at 5, 10, 20 mg/kg dose-dependently increases 5-HTP-induced HTR. In the tail suspension test, protopine at 3.75, 7.5, and 30 mg/kg reduces immobility dose-dependently.

#### **Foeniculum vulgare**

*Vetiveria zizanioides* and *Foeniculum vulgare* were compared to fluoxetine for depressed behavior in albino rats. For antidepressant screening, forced swimming and tail suspension tests were performed. The immobility duration was measured for 6 minutes after administering the ethanolic extract of *Vetiveria zizanioides* (100mg/kg) and *Foeniculum vulgare* (200mg/kg), fluoxetine (10mg/kg), and saline 30 minutes before the testing. Both were compared to fluoxetine for antidepressant effects. *Vetiveria zizanioides* (100mg/kg) and *Foeniculum vulgare* (200mg/kg) reduced immobility time compared to control, causing antidepressant effects. However, collectively they are as efficacious as fluoxetine (10mg/kg).

Methanolic extract of *Foeniculum vulgare* fruits (MEFV) was tested for antidepressant effects utilizing force swim test in rats (FST), norepinephrine (NE) toxicity in mice, and haloperidol induce catalepsy (HIC) in mice. Oral *F. vulgare* extract (250 and 500 mg/kg) was given to FST rats, HIC rats, and mice with NE toxicity. The extract at 250mg/kg and 500mg/kg considerably ( $p < 0.001$ ) decreased immobility periods in rats, with 500mg/kg having a stronger impact than imipramine (30mg/kg). In NE toxicity model, MEFV dosage did not affect adrenergic system. A substantial ( $P < 0.001$ ) decrease in catalepsy duration was seen in MEFV and Fluoxetine groups compared to haloperidol group. In HIC, mice were slaughtered on day 7 to assess TBARS, glutathione, and nitrite. *Foeniculum vulgare*'s antidepressant-like effects may be due to its monoamine oxidase inhibitor and antioxidant properties.

#### **Glycyrrhiza glabra**

The forced swim test (FST) and tail suspension test (TST) were used to assess the effects of *Glycyrrhiza glabra* aqueous extract on depression in mice. Separate groups of male mice received oral *G. glabra* extract (75, 150, and 300 mg/kg) for 7 days. The 150 mg/kg extract dosage substantially decreased mice's FST and TST immobility durations without affecting locomotor activity. Extract was equally effective as imipramine (15 mg/kg ip) and fluoxetine (20 mg/kg ip). Liquorice extract reduced reserpine-induced mouse immobility in FST and TST. In TST, sulphiride (50 mg/kg ip, selective D2 receptor antagonist) and prazosin (62.5 µg/kg ip,  $\alpha_1$ -adrenoceptor antagonist) substantially reduced the extract-induced antidepressant-like effect. However, p-chlorophenylalanine (100 mg/kg ip, a serotonin production inhibitor) did not alter liquorice extract's antidepressant effect. Liquorice extract showed antidepressant effects via increasing brain norepinephrine and dopamine, but not serotonin.

#### **Gossypium species**

Adenyl cyclase-cAMP pathway activation in signal transduction system caused antidepressant-like action of detoxified *Gossypium herbaceum* seed aqueous extract. Adenyl cyclase activity was measured by radio-immunoassay after incubating aqueous extract of detoxified *Gossypium herbaceum* seeds 0.01, 0.03, 0.10, 0.30 mg/ml with rat cerebral cortex synaptic membranes. Antidepressant and anxiolytic effects of detoxified *Gossypium herbaceum* seed aqueous extract were induced by signal transduction system AC-cAMP pathway activation, shielding neurons from lesion.

#### **Haplophyllum species**

The oil has mild acetylcholinesterase (AChE) inhibition relative to normal drugs, but no BuChE inhibition. The inhibitory activity of acetyl cholinesterase was mostly concentrated in *H. tuberculatum* part extract chloroform and ethyl acetate fractions. The most effective fraction was stem ethyl acetate, with a 79% inhibitory efficacy and IC50 of 0.45 µg/ml. Other portions inhibited 70–77%.

#### **Hyoscyamus niger**

*Hyoscyamus niger* was tested for antidepressant effects in mice using the forced swim test (FST) and tail suspension test (TST). The mechanism of action was also examined. We also examined locomotor and anxiolytic activities. *Hyoscyamus niger* leaves ethanolic extract was given to mice orally at 25, 50, 100, 200, and 400 mg/kg for 14 days. *Hyoscyamus niger* ethanolic extract was also tested with standard antidepressants at sub-effective levels. The ethanolic extract greatly decreased FST and TST mouse immobility. The same dosages did not affect mouse motor activity. High

doses of extract were anxiolytic. Biogenic amine may be involved in antidepressant effect since interaction with conventional antidepressants lowered immobility count.

#### **Juglans regia**

*Juglans regia* fruit extract (100 and 150 mg/kg bw) was tested for antidepressant effects in depression animal models (forced swimming and tail suspension tests). In all depression models, both dosages greatly reduced immobility. Extract was less effective than fluoxetine. Antidepressant action may be due to omega-3 fatty acid in extract [80].

#### **Plants affected locomotion activity:**

##### **Alhagi maurorum**

*Alhagi maurorum* reduced animal movement and skeletal muscle relaxation. Exposed frogs' rectus abdominal muscle to 4 µg/ml bathing fluid extract for 5 minutes reduced ACh (3 µg/ml)-induced contraction by  $70 \pm 2.1\%$  (N = 4). Increasing ACh dosage to 8 µg/ml did not entirely reverse the blockage in the presence of extract. The greatest antagonism reversal was 27.7, demonstrating the extract inhibited ACh non-competitively. In conscious mice, 1.6 g/kg intraperitoneal ethanolic extract (EE) of *Alhagi maurorum* powdered roots caused moderate drowsiness. The extract reduced animal movement and skeletal muscle relaxation, indicating a neuromuscular junction effect.

#### **Bufotenidine isolated from *Arundo donax* showed neuromuscular blocking activity**

##### **Benincasa hispida**

Alcoholic extract of *B. hispida* was tested for anxiolytic effects in mice utilizing elevated plus maze, light-dark transition, and actophotometer-measured spontaneous motor activity. The extract was anxiolytic but did not affect actophotometer spontaneous motor activity [144]. However, *Benincasa hispida* fruit methanolic extract reduced spontaneous motor activity without muscle relaxant action [145].

##### **Caesalpinia crista**

The effects of *Caesalpinia crista* extract on gallamine-induced relaxation in rat tibial muscular contractility were measured in isometric-tension-anesthetized, 10-12-week-old male rats. IV *Caesalpinia crista* extract dose-dependently enhanced twitch contractions. The ED<sub>50</sub> was  $2.75 \times 10^{-4}$  g/kg bw. However, *Caesalpinia crista* extract or neostigmine reversed gallamine or puff adder venom relaxing. The scientists found that *Caesalpinia crista* extract activates the cholinergic pathway to contract muscles [146].

##### **Carthamus tinctorius**

The effects of *Caesalpinia crista* extract on gallamine-induced relaxation in rat tibial muscular contractility were measured in isometric-tension-anesthetized, 10-12-week-old male rats. IV *Caesalpinia crista* extract dose-dependently enhanced twitch contractions. The ED<sub>50</sub> was  $2.75 \times 10^{-4}$  g/kg bw. However, *Caesalpinia crista* extract or neostigmine reversed gallamine or puff adder venom relaxing. The scientists found that *Caesalpinia crista* extract activates the cholinergic pathway to contract muscles [146].

##### **Datura species**

The neuropsychopharmacological effects of *D. fastuosa* leaf and seed aqueous extracts were examined in rats and mice. The leaf and seed extracts at 400 and 800 mg/kg enhanced motor activity, decreased barbituric sleeping time, and counteracted haloperidol-induced catalepsy, ptosis, and forced swimming immobility. *D. fastuosa* also demonstrated antidepressant properties at low doses [148].

#### **Plant beneficial in Parkinson's disease:**

##### **Antirrhinum majus**

*Antirrhinum majus* synthesized auronones, flavonoids. Auronones and their extracts might prevent and cure phosphodiesterase (PDE)-dependent central nervous system diseases in animals and humans. Neurodegenerative disorders like Parkinson's, Alzheimer's, age-related dementia, dementia in general, neurological trauma like brain or central nervous system trauma, depression, anxiety, psychosis, cognitive dysfunction, mental dysfunction, learning and memory disorders, and central and peripheral nervous system ischemia should be treated prophylactically or therapeutically.

**Carthamus tinctorius**

The neuroprotective effects of astragali, ligusticum wallichii, angelica sinensis, and Carthamus tinctorius on brain infarction, global ischemia, and neurodegeneration after ischemia were examined. They enhanced cerebral blood circulation, which may reduce degenerative disorders including Alzheimer's and Parkinson's. The neuroprotective effects of hydroxysafflor yellow A (HSYA) on cerebral ischemia damage were studied in vivo and in vitro. Male Wistar-Kyoto (WKY) rats with middle cerebral artery occlusion (MCAO) were tested for neurological impairment scores before receiving a single dose of HSYA. In the brain slices, the infarction area was measured. To determine its neuroprotective impact, HSYA was evaluated in cultured fetal cortical cells exposed to glutamate and sodium cyanide (NaCN). In vivo, sublingual vein injection of HSYA at doses of 3.0 mg/kg and 6.0 mg/kg significantly reduced neurological deficit scores and infarct area in rats with focal cerebral ischemic injury compared to the saline group. HSYA at 6.0 mg/kg had similar potency to nimodipine at 0.2 mg/kg. Sublingual vein injection of 1.5 mg/kg HSYA indicated neuroprotection, although not significantly different from the saline group. In cultured fetal cortical cells, HSYA significantly inhibited neuron damage caused by glutamate and sodium cyanide (NaCN), but its neuroprotective effect on glutamate-mediated neuron injury was much greater than in NaCN-induced neuron damage.

**Cyperus rotundus**

In a Parkinson's disease model, a Cyperus rotundus rhizoma water extract was tested for neuroprotection against 6-OHDA-induced neuronal damage. At 50 and 100 microg/ml, Cyperus rotundus rhizoma water extract protected PC12 cells. 6-OHDA-induced reactive oxygen species, nitric oxide, mitochondrial membrane potential, and caspase-3 activity were reduced by Cyperus rotundus rhizoma water extract. Dopaminergic neurons in primary mesencephalic culture were likewise protected by Cyperus rotundus rhizoma water extract.

**Geum urbanum**

Lewy bodies and neurites are pathological hallmarks of Parkinson's disease and may contribute to disease progression. Lewy bodies and neurites are mostly made of fibrillated  $\alpha$ -Synuclein. The study examined the inhibitory effect of an ethanolic extract of Geum urbanum on  $\alpha$ -Synuclein fibrillation. Thioflavin T fibrillation assays and size exclusion chromatography monitored the plant extract's anti-fibrillation and anti-aggregation activities, while circular dichroism, Fourier transform infrared spectroscopy, intrinsic fluorescence, small angle X-ray scattering, and electron microscopy monitored structural changes. Geum urbanum reduced  $\alpha$ -Synuclein fibrillation and partially disintegrated preexisting fibrils in a concentration-dependent manner. Geum urbanum extract was found to delay  $\alpha$ -Synuclein fibrillation by reducing the fibrillation ability of aggregation-prone intermediates or directing the aggregation towards a non-fibrillar state.

**Hyoscyamus niger**

In a mouse MPTP model of Parkinson disease, petroleum ether and aqueous methanol extracts of Hyoscyamus niger seeds were tested for neuroprotection. Motor functions and striatal dopamine levels were measured in Parkinsonian mice treated twice daily with the extracts (125–500 mg/kg, po.) for two days. In MPTP-treated mice, aqueous methanol extract (0.03% w/w L-DOPA) decreased motor impairments (akinesia, catalepsy, and lower swim score) and striatal dopamine depletion more than petroleum ether extract. In isolated mitochondria, the extract significantly inhibited monoamine oxidase activity and reduced 1-methyl-4-phenyl pyridinium (MPP<sup>+</sup>)-induced hydroxyl radical (OH) formation. The methanolic extract of Hyoscyamus niger seeds protects mice against parkinsonism by inhibiting mitochondrial  $\bullet$ OH production.

**Juglans regia**

Walnut supplementation at 6% for 28 days was tested for neuroprotection in MPTP-induced neurodegeneration in a mouse model of Parkinson's disease (20 mg/kg bw/day, ip) for four days. MPTP injection reduced GSH, dopamine, metabolites, GPx, and mitochondrial complex I. MPTP increased TBARS, SOD, catalase, and MAO-B levels. The MPTP-induced neurotoxicity showed behavioral impairments and decreased TH expression. In PD mice, walnut supplementation reduced MPTP-induced impairment due to its MAO-B inhibitory, antioxidant, and mitochondrial protective effects.

**Juniperus communis**

In rats, methanolic Juniperus communis (MEJC) leaf extract was tested for reserpine-induced catalepsy. Reserpine (2.5 mg/kg, ip) caused catalepsy. The methanolic extract at 100 and 200 mg/kg, ip was tested for reserpine-induced

catalepsy in rats. MEJC extract substantially decreased catalepsy ( $p < 0.001$ ) in rats compared to reserpine treatment, with maximal reduction at 200 mg/kg. In reserpine-induced animal Parkinson's disease models, *J. Communis* was therapeutic.

Methanolic extract of *J. communis* (MEJC) was tested for neuroprotection in rats with chlorpromazine (CPZ)-induced Parkinson's disease (100 and 200mg/kg, ip). Neuroprotective action was assessed using behavioral criteria such as catalepsy (bar test), muscular stiffness (rot rod test), locomotor activity (actophotometer), and biochemical parameters (TBARS, GSH, nitrite, and total protein) in rats' brains. *J. communis* showed strong neuroprotective effects ( $P < 0.001$ ) against CPZ-induced Parkinson's-like symptoms.

#### **Memory enhancing effects:**

##### ***Anchusa italica***

Oral injection of Abnormal Savda Munsiq (ASMq) with *Anchusa italica* improved memory in chronically stressed mice produced by electric foot-shock. The stressed mice' step-through and Y-maze latency times increased and decreased, indicating memory enhancement. ASMq treatment significantly reduced blood levels of adrenocorticotrophic hormone, corticosterone,  $\beta$ -endorphin, and norepinephrine in the brain and body. By lowering brain and blood dopamine, 5-hydroxytryptamine, and 3,4-dihydroxyphenylalanine levels, ASMq dramatically reversed chronic stress.

#### **Plants with neuroprotective activity:**

##### ***Bellis perennis***

The impact of *Bellis perennis* on healthy neuronal cell viability was examined. Compared to the negative control (media), 90% alcohol reduced cell viability to 18%. Alcohol impact was negated by *Bellis perennis* at 2 $\mu$ l/ml, 4 $\mu$ l/ml, and 8 $\mu$ l/ml. It greatly enhanced cell viability.

##### ***Calendula officinalis***

In rats, *Calendula officinalis* Linn. floral extract (COE) protected against MSG-induced neurotoxicity. After 7 days of systemic MSG injection, adult Wistar rats received 100 and 200 mg/kg COE orally after 1h. After treatment, mice were killed for locomotion and brains were separated for LPO, GSH, CAT, TT, GST, Nitrite, and histopathological analysis. MSG impacted animal behavior, oxidative defense (LPO, nitrite, antioxidant depletion), and hippocampal neuronal histology. COE significantly decreased behavioral alterations, oxidative stress, and hippocampal damage in MSG-treated rats.

In mice, *Calendula officinalis* flower extract (COE) was investigated for neuroprotection against 3-NP-induced neurotoxicity by analyzing behavioral impairments, OS, and striatal damage. Adult female Wistar rats were pretreated with vehicle or COE (100 and 200 mg/kg) for 7 days, then cotreated with 3-NP (15 mg/kg intraperitoneally) for 7 days. Post-therapy rats were tested for sensory motor function and short-term memory. LPO, glutathione, total thiols, S-transferase, catalase, and nitrite were evaluated in killed animal brain homogenates. Striatal neuron damage was tested using brain slices. 3-NP elevated LPO and nitrite levels and depleted antioxidants, altering animal behavior and oxidative defense. It also lost striatal neurons. COE significantly decreased 3-NP-induced behavioral abnormalities, oxidative damage, and striatal neuronal death.

#### **ATP levels and the respiratory control ratio**

##### ***Cassia occidentalis***

Ethanollic and aqueous *Cassia occidentalis* leaf extracts (500 mg/kg, orally) were investigated for antidepressant and anti-anxiety effects in mice. In elevated plus maze paradigm, rats were exposed to new aversion and measured for anti-anxiety activity using actophotometer. Oral ethanollic and aqueous *Cassia occidentalis* leaf extracts at 500 mg/kg increased raised plus-maze open arm entries and time. *Cassia occidentalis* ethanollic and aqueous extracts 500 mg/kg orally reduced anxiety as well as diazepam 5 mg/kg ip. Oral ethanollic and aqueous *Cassia occidentalis* leaf extracts 500 mg/kg effectively decreased locomotor activity after 30 and 60 min. Despair swim and tail suspension tests measured antidepressants. In despair swim test apparatus, 500 mg/kg oral *Cassia occidentalis* leaf ethanollic and aqueous extracts significantly decreased immobility time. Ethanollic and aqueous *Cassia occidentalis* leaf extracts at 500 mg/kg orally were as antidepressant as fluoxetine 10 mg/kg ip. Oral *Cassia occidentalis* leaf ethanollic and aqueous extracts at 500 mg/kg decreased tail suspension immobility time significantly. Ethanollic and aqueous *Cassia occidentalis* leaves at 500



mg/kg orally were as antidepressant as fluoxetine 10 mg/kg ip. *Cassia occidentalis* leaf ethanolic extract is more antidepressant than aqueous.

Indian elderly plant-based tonic Geriforte contains *Cassia occidentalis*. Stressing animals investigated this compound for anti-stress (adaptogenic) activity. Geriforte doses helped swimming mice survive. Adrenal stress (5-hour swimming)-induced weight gain, ascorbic acid, and cortisol reductions were mitigated by the Geriforte 100 mg/kg prevented chemical ulcers and constraint. Geriforte suppressed milk-induced leucocytosis and carbon tetrachloride-induced liver weight and volume growth. Drug-treated rats gained weight gradually. Neither body temperature nor spontaneous motor activity changed. It lowers hexobarbital sleep time, suggesting CNS stimulation. Acute toxicity experiments on mice showed a 5-6 g/kg oral LD50.

### **Coriandrum sativum**

Brain ischemic-reperfusion neuroprotection was evaluated using *Coriandrum sativum*. In albino rats, blocking common carotid arteries for 30 minutes and reperfusion for 45 minutes induced extensive brain ischemia. After reperfusion, histological changes, lipid peroxidation, SOD, catalase, glutathion, calcium, and total protein were measured. Bilateral common carotid artery blockage increased lipid peroxidation, calcium, infarct size, and lowered glutathion, SOD, and catalase. Methanolic *Coriandrum sativum* leaf extract (200 mg/kg, po) pretreatment for 15 days increased endogenous superoxide dismutase, glutathion, catalase, and total protein and reduced brain infarct size, lipid peroxidation, and calcium. Brain histology showed less gliosis, lymphocytic infiltration, and cellular edema. Thus, *Coriandrum sativum* prevented ischemic-reperfusion and cerebrovascular insufficiency.

The neuroprotective efficacy of *Coriandrum sativum* against glucose/serum deprivation (GSD)-induced cytotoxicity was tested in vitro. PC12 cells were cultured for 24 h in standard media (high-glucose DMEM containing Fetal Bovine Serum) or 6 h in GSD (glucose-free DMEM, without serum) with or without 0.1, 0.2, 0.4, 0.8, and 1.6 mg/ml of *Coriandrum sativum* HAE, WF, EAF, or NBF. MTT assessed post-treatment cell viability. Under normal settings, HAE and its fractions were non-cytotoxic except for 1.6 mg/ml EAF or NBF, which decreased cell survival. GSD reduced cell viability 52%. Thus, HAE, EAF, and NBF increased toxicity and lowered cell viability. However, WF at 0.4, 0.8, and 1.6 mg/ml significantly decreased GSD-induced cell death. Under stress like hypoglycemia, water-soluble *Coriandrum sativum* chemicals may be neuroprotective and cytotoxic.

## **II. CONCLUSION**

Due to their safety and efficacy, medicinal plants that impact the central nervous system as sedatives, anticonvulsants, antidepressants, antipsychotics, anxiolytics, anti-Parkinson, memory enhancers, locomotors, and neuroprotectives were reviewed in the review.

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