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EVALUATION OF ANTIPARKINSONS AND MONOAMINE OXIDASE-MAO-B INHIBITORY PROPERTIES OF SENNA OCCIDENTALIS IN RATS

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Abstract :

Parkinson's disease is a progressive neurodegenerative disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra, leading to motor and non-motor dysfunction. The present study was designed to evaluate the antiparkinsonian and monoamine oxidase-B (MAO-B) inhibitory activity of Senna occidentalis in MPTP-induced Parkinsonian rats. Parkinsonism was induced by administration of MPTP (25 mg/kg, i.p.), and animals were divided into five groups: vehicle control, MPTP control, standard drug (Levodopa 12 mg/kg + Benserazide 3 mg/kg), and Senna occidentalis extract at doses of 200 mg/kg and 400 mg/kg (p.o.).

Behavioral assessments including rotarod, open field, hole board, forced swimming, and tail suspension tests were performed to evaluate motor coordination, locomotor activity, and behavioral despair. Biochemical parameters such as dopamine levels, MAO-B activity, malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), glutathione peroxidase (GPx), and nitric oxide (NO) were estimated in brain tissue. MPTP administration produced significant motor impairment, increased oxidative stress, elevated MAO-B activity, and reduced dopamine levels.

Treatment with Senna occidentalis significantly improved behavioral performance and biochemical parameters in a dose-dependent manner. The higher dose (400 mg/kg) showed more pronounced neuroprotective effects, comparable to the standard drug. The protective effect may be attributed to the presence of phytoconstituents such as flavonoids, phenolics, alkaloids, and terpenoids, which exert antioxidant and MAO-B inhibitory actions.

In conclusion, Senna occidentalis exhibits significant antiparkinsonian activity through modulation of oxidative stress, inhibition of MAO-B enzyme, and restoration of dopaminergic function, suggesting its potential as a neuroprotective agent in Parkinson's disease.

Keywords: *Parkinson's disease, MPTP, Senna occidentalis, MAO-B inhibition, oxidative stress, dopamine, neuroprotection, antioxidant activity.*

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INTRODUCTION:

The term parkinsonism refers to the characteristic motor features seen in Parkinson's disease (PD), including bradykinesia, akinesia, resting tremor, rigidity, and disturbances in gait and postural stability. These manifestations are primarily attributed to the progressive loss of dopaminergic neurons in the substantia nigra pars compacta (SNc). As a result, most discussions on the pathophysiology of parkinsonism focus on the circuit-level consequences of dopamine depletion within the basal ganglia and its interconnected brain networks. A foundational understanding of basal ganglia anatomy is essential to appreciate these mechanisms. Experimental studies in parkinsonian animal models and observations in patients with PD—particularly nonhuman primates—have significantly contributed to current knowledge of these circuit dysfunctions [1–2].

Clinically, parkinsonism presents with a combination of rigidity, bradykinesia, tremor, and postural instability. While it may arise from various causes, idiopathic Parkinson's disease remains the most common form. As the disease progresses, many patients also develop cognitive impairment. In addition, a wide range of non-motor symptoms has gained increasing recognition, including anxiety, depression, personality changes, autonomic dysfunction (such as bladder, sexual, and cardiovascular abnormalities), sleep disturbances, and sensory symptoms like pain. PD is typically a progressive neurodegenerative disorder that leads to increasing disability in the absence of effective disease-modifying therapy.

The pathogenesis of Parkinsonism is multifactorial and involves impaired protein degradation, intracellular protein misfolding and aggregation, oxidative stress, mitochondrial dysfunction, neuroinflammation, and apoptotic cell death. Genetic studies, particularly in younger-onset cases, highlight the importance of hereditary factors. Approximately 10–15% of cases are linked to identifiable genetic mutations. Mutations in the α-synuclein (SNCA) gene, including gene duplication and triplication, are strongly associated with PD, which is now classified as a synucleinopathy. Other genetic contributors include mutations in LRRK2, UCHL1, and parkin (PARK2), the latter being commonly associated with early-onset autosomal recessive Parkinsonism. Additional genetic loci continue to be identified in familial and sporadic forms of the disease [3-4].

Environmental and endogenous factors also play an important role in disease development. Epidemiological studies suggest that cigarette smoking, caffeine consumption, nonsteroidal anti-inflammatory drug use, and higher serum uric acid levels may have protective effects. In contrast, increased risk has been associated with occupational exposure to pesticides, heavy metals such as lead and manganese, certain professions (e.g., farming and healthcare work), and vitamin D deficiency. The presence of Lewy bodies—intracellular inclusions rich in α-synuclein—within dopaminergic neurons supports the concept of PD as a progressive protein misfolding disorder. Braak staging proposes a predictable spread of pathology, beginning in the olfactory structures and lower brainstem (stages 1–2), progressing to the substantia nigra (stage 3), then to limbic and thalamic regions (stage 4), and finally involving the neocortex (stage 5), with motor symptoms typically emerging at stage 3.

Dopamine depletion within the basal ganglia disrupts the balance between dopaminergic and cholinergic signaling, leading to increased inhibitory output from basal ganglia circuits and impaired movement initiation. Pharmacological treatments aim to restore dopaminergic function using agents such as levodopa and dopamine agonists, while antimuscarinic drugs help rebalance cholinergic activity. Drug-induced parkinsonism can occur due to dopamine receptor blockade (e.g., antipsychotics) or neurotoxic injury (e.g., MPTP exposure), further highlighting dopamine's central role in motor control.

Parkinson's disease has a long historical background, with early descriptions of tremor and movement disorders found in ancient Indian Ayurvedic texts ("Kampavata") as well as references in Chinese and Greek medical writings. However, the first formal clinical description was provided by James Parkinson in 1817 in An Essay on the Shaking Palsy, where he characterized the cardinal motor features of the disorder. Later, Jean-Martin Charcot recognized it as a distinct neurological disease and named it Parkinson's disease, expanding its clinical profile to include non-motor features .

In the early 20th century, Konstantin Tretiakoff identified degeneration of the substantia nigra as a key pathological hallmark. The discovery of dopamine as a neurotransmitter by Arvid Carlsson in the 1950s and the subsequent recognition of dopamine deficiency in the striatum in the 1960s revolutionized understanding of the disease and led to the development of levodopa therapy, which remains the gold standard treatment. Over time, additional pharmacological classes such as dopamine agonists, MAO-B inhibitors, and COMT inhibitors were introduced. The development of deep brain stimulation (DBS) in the late 20th century further transformed the management of advanced PD.

More recently, research has focused on genetic susceptibility, α-synuclein aggregation, and neurodegenerative mechanisms, driving interest in disease-modifying strategies such as gene therapy, neuroprotective agents, and stem cell–based approaches. Despite significant advances, Parkinson's disease remains incurable, and ongoing research continues to aim at earlier diagnosis, slowed progression, and improved quality of life for affected individuals [5–6].

Symptoms of Parkinson's Disease [7-8]

1. Motor Symptoms

- Bradykinesia (slowness of movement)
- Resting tremor (pill-rolling tremor)
- Muscle rigidity (stiff muscles)
- Postural instability (poor balance, falls)
- Shuffling gait (small, dragging steps)
- Reduced arm swing while walking
- Freezing of gait (sudden inability to move)
- Hypomimia (masked facial expression)
- Hypophonia (soft speech)
- Micrographia (small handwriting)

2. Non-Motor Symptoms

A. Neuropsychiatric

- Depression
- Anxiety
- Apathy
- Cognitive impairment
- Dementia (advanced stage)
- Hallucinations (late stage or drug-induced)

B. Autonomic

- Constipation
- Urinary urgency or incontinence
- Orthostatic hypotension
- Excessive sweating
- Sexual dysfunction

C. Sleep-related

- Insomnia
- REM sleep behavior disorder
- Excessive daytime sleepiness

D. Sensory

- Loss of smell (anosmia)
- Pain or abnormal sensations

3. Early/Prodromal Symptoms

- Reduced smell
- Constipation
- Sleep disturbances (especially REM behavior disorder)
- Mild mood changes
- Subtle loss of fine motor skills

MECHANISM OF ACTION

he mechanism of Parkinson's disease is primarily related to the progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta, resulting in a marked reduction of dopamine levels in the striatum. This dopamine deficiency disrupts the normal balance between the direct and indirect pathways of the basal ganglia, leading to overactivity of the inhibitory output from the globus pallidus interna and reduced stimulation of the thalamus to the motor cortex. As a consequence, voluntary motor activity becomes impaired, producing the characteristic features of bradykinesia, rigidity, tremor, and postural instability. In addition, there is a relative increase in cholinergic activity due to dopamine depletion, further contributing to motor dysfunction. The overall result is impaired initiation and smooth execution of movements due to basal ganglia circuit dysfunction [9-10].

PATHOPHYSIOLOGY OF PARKINSON'S

The pathophysiology of Parkinson's disease is primarily characterized by the progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta, leading to a significant reduction in dopamine levels within the striatum. This dopamine deficiency disrupts the normal functioning of the basal ganglia motor circuits, resulting in an imbalance between the direct (facilitatory) and indirect (inhibitory) pathways. The reduced activation of the direct pathway and increased activity of the indirect pathway cause excessive inhibitory output from the globus pallidus interna to the thalamus, thereby decreasing excitatory stimulation of the motor cortex. This ultimately leads to impaired initiation and execution of voluntary movements, manifesting as bradykinesia, rigidity, tremor, and postural instability. In addition to dopaminergic loss, pathological accumulation of misfolded α-synuclein protein forms Lewy bodies, which contribute to neuronal dysfunction and cell death. Oxidative stress, mitochondrial dysfunction, impaired protein degradation, neuroinflammation, and apoptotic mechanisms further accelerate neuronal degeneration. As the disease progresses, these pathological changes extend beyond the substantia nigra to involve multiple brain regions, contributing to both motor and non-motor symptoms of the disease [11-12].

ETIOLOGY OF PARKINSON'S DISEASE

The etiology of Parkinson's disease is multifactorial, involving a complex interaction of genetic susceptibility, environmental exposures, and age-related neurodegenerative processes. In most cases, the disease is idiopathic, but genetic factors contribute in a significant minority of patients, particularly in early-onset forms. Mutations in genes such as SNCA (α-synuclein), LRRK2, PARK2 (parkin), PINK1, and DJ-1 are associated with familial Parkinsonism, affecting protein handling, mitochondrial function, and

neuronal survival. Environmental factors also play an important role, with increased risk linked to exposure to pesticides, herbicides, heavy metals such as manganese and lead, and rural or agricultural occupations, while factors like smoking, caffeine intake, and higher uric acid levels have been associated with a reduced risk. Age is the strongest risk factor, as the incidence of Parkinson's disease increases significantly with advancing age due to cumulative oxidative stress, mitochondrial dysfunction, and impaired cellular repair mechanisms. Together, these genetic and environmental influences lead to progressive degeneration of dopaminergic neurons in the substantia nigra, resulting in dopamine deficiency and the characteristic motor and non-motor features of the disease [13].

PARKINSON ON HERBAL PLANTS

Several medicinal plants have shown potential benefits in the management of Parkinson's disease due to their neuroprotective, antioxidant, and anti-inflammatory properties. Among them, *Mucuna pruriens* is the most significant as it naturally contains L-DOPA, which helps increase dopamine levels and improves motor symptoms. *Withania somnifera* (Ashwagandha) exhibits strong antioxidant activity and protects neurons from oxidative stress-induced damage. *Bacopa monnieri* (Brahmi) supports cognitive function and enhances neuronal signaling, while *Curcuma longa* (Turmeric), rich in curcumin, reduces neuroinflammation and may inhibit α-synuclein aggregation. *Ginkgo biloba* improves cerebral blood flow and provides antioxidant protection, and *Camellia sinensis* (green tea) contains polyphenols that help prevent neuronal degeneration. Additionally, *Zingiber officinale* (ginger) contributes anti-inflammatory and antioxidant effects. Overall, these herbal plants do not cure Parkinson's disease but may help in reducing oxidative stress, protecting dopaminergic neurons, and alleviating some motor and non-motor symptoms [14].

TREATMENT OF PARKINSON'S DISEASE

The treatment of Parkinson's disease is mainly symptomatic and aims to restore the balance of dopamine in the brain and improve motor function. The cornerstone of therapy is levodopa combined with carbidopa, where levodopa is converted into dopamine in the brain while carbidopa prevents its peripheral breakdown, thereby increasing its availability in the central nervous system. Dopamine agonists such as pramipexole and ropinirole directly stimulate dopamine receptors and are often used in early stages or as adjunct therapy. MAO-B inhibitors (selegiline, rasagiline) and COMT inhibitors (entacapone) reduce dopamine degradation and prolong the action of levodopa. Anticholinergic drugs like trihexyphenidyl are useful in controlling tremor by reducing cholinergic overactivity in the striatum. In advanced cases, deep brain stimulation (DBS) of structures such as the subthalamic nucleus or globus pallidus interna may be performed to improve motor symptoms. Along with pharmacological and surgical approaches, physiotherapy, occupational therapy, speech therapy, and lifestyle modifications play an important role in improving mobility, independence, and overall quality of life [15].

5. MATERIALS AND METHODS:

COLLECTION AND AUTHENTICATION OF PLANT

senna occidentalis were obtained collected from Thirupathi, Andhra Pradesh, India, and authenticated by Dr Madhava Chetty, Professor and Head, Department of Botany, S.V. University, Thirupathi, Andhra Pradesh.

EXTRACTION OF PLANT MATERIAL

Coarsely powdered senna occidentalis were extracted with ethanol for 6-8 hours at room temperature. After extraction, the extracts were evaporated by using a rotary evaporator and dried at room temperature. The obtained crude extracts were weighed and stored at 4^{o}C for further analysis by adding few drops of chloroform as a preservative.

Selection of animal for MPTP induced Parkinson evaluation

225-220 g body weight were offered by from our college animal house. All the rats were kept at room temperature and allowed to acclimate in standard conditions less than 12 hr light/ 12 hr dark cycle in the animal house. Animals are fed with commercial pellet diet and water ad libitum freely throughout the study. The experimental procedure was approved by IAEC (Institution of Animal Ethical Committee). The animals were divided into 5 groups each group of 6 animals.

Mptp Induced Preparation [16]

The MPTP-induced Parkinson's disease model is widely used to replicate dopaminergic neurodegeneration similar to human Parkinson's disease. In this method, MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is administered to experimental animals, most commonly mice, either via intraperitoneal or systemic routes depending on the study design. After administration, MPTP readily crosses the blood–brain barrier and is metabolized by monoamine oxidase-B (MAO-B) in astrocytes to form its active toxic metabolite MPP^{+} (1-methyl-4-phenylpyridinium). MPP^{+} is then selectively taken up by dopaminergic neurons through dopamine transporters (DAT), where it accumulates in

mitochondria and inhibits complex I of the electron transport chain. This leads to mitochondrial dysfunction, reduced ATP production, oxidative stress, and eventual degeneration of dopaminergic neurons in the substantia nigra pars compacta. The progressive loss of these neurons results in motor abnormalities such as bradykinesia, rigidity, and tremor, thereby closely mimicking Parkinsonian features. This model is extensively used for evaluating neuroprotective agents and studying disease pathophysiology.

Preparation of Levodopa and Benzerazide

12mg/kg of levodopa and 3 mg/kg of Benzerazide was dissolved in distilled water. Levodopa and benzerazide was freshly prepared daily and given via i.p to the standard group.

Preparation of sample

200 mg/kg and 400 mg/kg were dissolved in distilled water and it was prepared freshly and given via oral route to group IV& V respectively for 7 days.

Group Treatment

Group I Vehicle control (normal saline, i.p.)
Group II MPTP only (25 mg/kg, i.p.)
Group III MPTP (25 mg/kg, i.p.) + Standard drug: Levodopa (12 mg/kg) + Benserazide (3 mg/kg, i.p.)
Group IV MPTP (25 mg/kg, i.p.) + Senna occidentalis 200 mg/kg, p.o.
Group V MPTP (25 mg/kg, i.p.) + Senna occidentalis 400 mg/kg, p.o.

EVALUATION PARAMETERS

Motor Co-Ordination Test (Rota Rod Test)

Principle

The rota rod performance test is carried out on a rotating rod that provides forced motor activity in animals. The animals were placed on a rotating rod which is placed horizontally, suspended above a cage floor, which is high enough to induce avoidance of fall. Animals naturally try to stay on the rotating rod avoid falling to the ground. The length of time (duration) the animal stay on the rod without falling, gives a measure of their coordination, balance, physical condition and motor-planning [46]

Procedure

Motor Co-ordination test was conducted using rota rod apparatus. Animal was placed individually on the rotating rod and trained for 3 min trail at 25 rpm on the day before the first day of testing. A cut off time of 180s was fixed and each animal performed 3 separate trials at 5 min interval. After each trial, 5 min rest period was given to alleviate stress and fatigue. Motor coordination can be tested by comparing the latency to fall on the very first trial between treatment groups. The time taken by animals to fall from the rotating rod was noted [17].

Locomotor Activity

Principle

The locomotor activity (horizontal activity) can be easily measured using an actophotometer which operates on photoelectric cells which are connected in circuit with a counter. When the beam of light falling on the photocell is cut off by the animal, a count is recorded. An actophotometer could have either circular or square area in which the animal moves [48].

Procedure

The spontaneous locomotor activity of each animal was recorded individually, using Actophotometer. The apparatus was placed in a sound attenuated and ventilated room during the testing period. All the animals were placed individually in the activity cage for 3 min to habituate them before starting actual locomotor activity task for the next 3 min. the basal activity score was noted. The units of the activity counts were arbitrary and based on the beam breaks by movement of the animal. Counts/3 min is used as an index of locomotor activity [18].

Forced Swimming Test

Principle

Forced swimming test Is a behavioural despair test. This test is most widely used to assess alterations in depression-like behaviour in animals. The time spent by the animal as immobile in water represents the depression-like behaviour [19].

Procedure

The test was performed according to the method described by Porsolt et al., 1977, with slight modifications. Animals were forced to swim in a glass cylinder (20 cm height, 14 cm diameter) containing 10 cm depth of water at 25^{o} c. After the initial 2 min acclimatization period, the total duration of immobility was measured during final 4 min of the 6 min test session. Animal were considered to be immobile, when they made no further attempts to escape except the movements necessary to kept their heads above the water. After 6 min, the animals were removed from water, allowed to dry, and returned back to their home cage [20].

Hole Board Test

Principle

When a animal is placed on the hole board apparatus, which is elevated to 25 cm from the base, shows anxiety as it is exposed to a new environment, thus showing characteristics head poking behaviour. Decrease in anxiety shows increased exploration of the holes. Whereas increased anxiety shows lower number of head poking [21].

Procedure

The hole board apparatus consist of a wooden board (40*40cm) placed 25 cm above the ground. It consists of 16 holes which is about 3 cm in diameter, spaced symmetrically in a diamond pattern. Animals were placed on the corner of the apparatus and were

observed for the next 5 min for the number of head dipping. A head dipping is counted when the animal introduces its head into any hole of the box up to the level of the ears. The apparatus was thoroughly cleaned between each subject [22].

Tail Suspension Test

Principle

The tail-suspension test (TST) is a widely used assay for screening potential antidepressant drugs. The test is based on the principle that animal subjected to the short-term, inescapable stress of being suspended by their tail, will develop an immobile posture [23].

Procedure

The tail suspension test is another well characterized test for assessing depression-like and anti-depressant like activity. In this test animal were individually suspended by the tail to a horizontal ring –stand bar (distance from floor = 30cm) using adhesive tape (distance from tip of tail = 2cm). Typically animal demonstrated several escape-orientated behaviours interspersed with temporally increasing bouts of immobility. A 6-mins test session was employed, which was videotaped. The parameter recorded was the number of seconds spent immobile [24].

Biochemical Procedures [25-26]

The biochemical estimations were carried out using standard protocols on brain tissue homogenates prepared from each experimental group. After the completion of behavioral studies, the animals were sacrificed, and the brains were quickly removed, washed with ice-cold saline, and homogenized in appropriate buffer solutions (usually phosphate buffer, pH 7.4). The homogenates were centrifuged, and the supernatant was used for biochemical analysis.

Dopamine levels in the brain were estimated using standard spectrofluorometric or HPLC methods, where the neurotransmitter was extracted from the tissue homogenate and quantified by comparing with standard calibration curves. MAO-B enzyme activity was measured in brain tissue using specific substrates such as benzylamine, and the rate of product formation was determined spectrophotometrically to assess enzyme inhibition.

Lipid peroxidation was evaluated by estimating malondialdehyde (MDA) levels using the thiobarbituric acid reactive substances (TBARS) method, where the intensity of the colored complex formed was measured at a specific wavelength. Antioxidant enzymes including superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), and glutathione peroxidase (GPx) were estimated using standard colorimetric assays based on their ability to inhibit oxidation reactions or catalyze substrate conversion.

Nitric oxide levels were determined indirectly by measuring nitrite and nitrate concentrations using the Griess reagent method, which produces a chromophore measured spectrophotometrically. Mitochondrial complex I activity was assessed by monitoring NADH oxidation in the presence of specific electron acceptors, indicating mitochondrial respiratory chain function.

All biochemical estimations were performed according to established standard protocols, and results were expressed as mean ± SEM for statistical comparison between groups. These procedures collectively helped in evaluating the neuroprotective and MAO-B inhibitory potential of *Senna occidentalis* in MPTP-induced Parkinson's disease models.

Malondialdehyde (MDA)

Malondialdehyde (MDA) is a widely used biochemical marker for assessing lipid peroxidation and oxidative stress in experimental Parkinson's disease models. It is measured to evaluate the extent of free radical–induced damage to neuronal cell membranes, particularly in the brain regions such as the striatum and substantia nigra. In MPTP-induced Parkinsonian rats, MDA levels are significantly elevated due to excessive generation of reactive oxygen species (ROS), which leads to degeneration of dopaminergic neurons.

MDA estimation is commonly performed using the thiobarbituric acid reactive substances (TBARS) assay. In this method, MDA present in the brain tissue homogenate reacts with thiobarbituric acid (TBA) under acidic and high-temperature conditions to form a pink-colored MDA-TBA complex. The intensity of the color is measured spectrophotometrically at around 532 nm, and the concentration of MDA is calculated using a standard calibration curve. A reduction in MDA levels after treatment indicates the antioxidant and neuroprotective effect of the test drug by inhibiting lipid peroxidation and stabilizing neuronal membranes.

Superoxide Dismutase (SOD)

Superoxide dismutase (SOD) activity was estimated in brain tissue homogenate using a standard spectrophotometric method based on the enzyme's ability to inhibit the reduction of nitroblue tetrazolium (NBT). After sacrifice, the brain was removed and homogenized in cold phosphate buffer (pH 7.4), followed by centrifugation, and the supernatant was used for analysis. In this method, superoxide radicals generated from a reaction system reduce NBT to form a blue-colored formazan dye. The presence of SOD in the sample competes with NBT by dismutating superoxide radicals into hydrogen peroxide and oxygen, thereby inhibiting formazan formation. The reaction mixture was incubated under controlled conditions, and the absorbance was measured spectrophotometrically at around 560 nm. The degree of inhibition of NBT

reduction was used to calculate SOD activity, which was expressed as units per mg of protein. An increase in SOD activity after treatment indicates enhanced antioxidant defense and protection against MPTP-induced oxidative stress in Parkinson's disease models.

Catalase (CAT)

Catalase (CAT) activity was estimated in brain tissue homogenate to evaluate the antioxidant defense against hydrogen peroxide-induced oxidative stress. After the experimental period, the brain was excised, rinsed with ice-cold saline, and homogenized in phosphate buffer (pH 7.4). The homogenate was centrifuged, and the supernatant was used for analysis. CAT activity was measured spectrophotometrically by following the decomposition rate of hydrogen peroxide (H_2O_2). In this method, a known concentration of H_2O_2 was added to the tissue sample, and the decrease in absorbance was recorded at 240 nm over a fixed time interval. Catalase catalyzes the breakdown of hydrogen peroxide into water and oxygen, thereby reducing absorbance. The rate of decrease in absorbance was used to calculate CAT activity, expressed as units per mg of protein. An increase in catalase activity indicates improved antioxidant defense and reduced oxidative stress in MPTP-induced Parkinsonian rats.

Reduced Glutathione (GSH)

Reduced glutathione (GSH) levels were estimated in brain tissue homogenate to assess the intracellular antioxidant status in MPTP-induced Parkinsonian rats. After sacrifice, the brain was quickly removed, washed with ice-cold saline, and homogenized in appropriate buffer (commonly 0.1 M phosphate buffer, pH 7.4). The homogenate was centrifuged, and the supernatant was used for analysis. GSH estimation was performed using the Ellman's method, in which 5,5'-dithiobis-(2-nitrobenzoic acid) (DTNB) reacts with free sulfhydryl groups of GSH to produce a yellow-colored 5-thio-2-nitrobenzoic acid (TNB). The intensity of the yellow color was measured spectrophotometrically at 412 nm. The concentration of GSH was calculated using a standard curve and expressed as µmol/mg protein. A decrease in GSH levels indicates oxidative stress and depletion of cellular antioxidant defense, whereas restoration of GSH after treatment suggests neuroprotective and antioxidant activity of the test drug in Parkinson's disease models.

Rotarod Performance Results

The rotarod test was used to evaluate motor coordination, balance, and muscle grip strength in experimental animals. MPTP administration in Group II significantly reduced the fall-off time, indicating severe impairment of motor coordination compared to the vehicle control group. This confirms successful induction of Parkinsonian symptoms.

Treatment with the standard drug (Levodopa + Benserazide) in Group III significantly improved rotarod performance, as evidenced by increased latency to fall when compared to the MPTP control group. This indicates restoration of dopaminergic function and improved motor coordination.

Similarly, *Senna occidentalis* treatment showed a dose-dependent improvement in motor performance. Group IV (200 mg/kg) exhibited a moderate increase in fall-off time, while Group V (400 mg/kg) showed a more significant improvement, approaching the effect of the standard drug. This suggests that the extract enhances motor coordination and reduces bradykinesia in MPTP-induced Parkinsonian rats.

RESULTS

Percentage of yield

$$\text{Percentage of yield} = \frac{\text{Weight of crude extract}}{\text{Weight of dried material}} \times 100$$

$$\text{Percentage of yield} = \frac{10g}{50g} \times 100 = 20\%$$

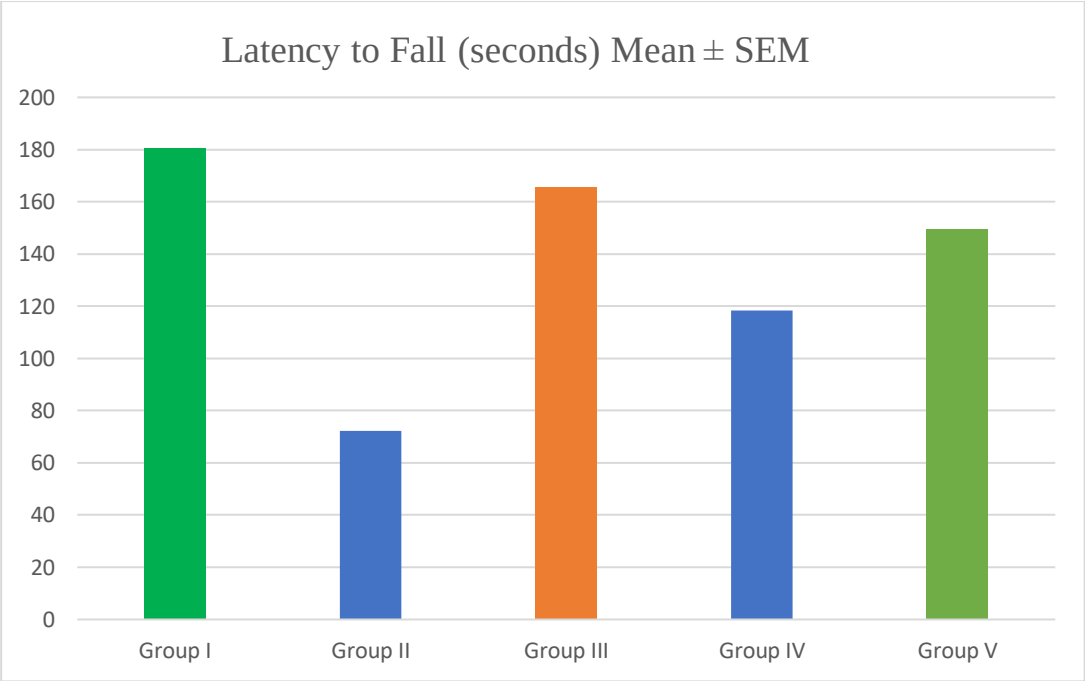
50gms of drug dissolved in 200ml of solvent in 1:4 Ratio

Phytochemical Test

Phytochemical Class	Result
Alkaloids	+ (Positive)
Flavonoids	+ (Positive)
Tannins	+ (Positive)
Saponins	+ (Positive)
Glycosides	+ (Positive)
Steroids	+ (Positive)
Terpenoids	+ (Positive)
Phenolic compounds	+ (Positive)
Proteins/Amino acids	− (Negative)
Carbohydrates	− (Negative)

Group	Treatment	Latency to Fall (seconds) Mean ± SEM
Group I	Vehicle control (normal saline, i.p.)	180.5 ± 5.2
Group II	MPTP only (25 mg/kg, i.p.)	72.3 ± 4.6
Group III	MPTP + Levodopa (12 mg/kg) + Benserazide (3 mg/kg, i.p.)	165.8 ± 6.1
Group IV	MPTP + Senna occidentalis 200 mg/kg (p.o.)	118.4 ± 5.7
Group V	MPTP + Senna occidentalis 400 mg/kg (p.o.)	149.6 ± 5.9

MPTP (Group II) significantly reduced rotarod performance, indicating severe motor impairment. Standard drug (Group III) restored motor coordination close to normal control levels. *Senna occidentalis* showed dose-dependent improvement, with 400 mg/kg producing better motor performance than 200 mg/kg. Results suggest significant antiparkinsonian and neuroprotective activity of the extract.



Locomotor Activity

Locomotor activity was assessed using the open field test to evaluate spontaneous movement, exploratory behavior, and overall motor function. MPTP administration in Group II produced a significant reduction in locomotor activity, indicating severe motor dysfunction and bradykinesia characteristic of Parkinson's disease.

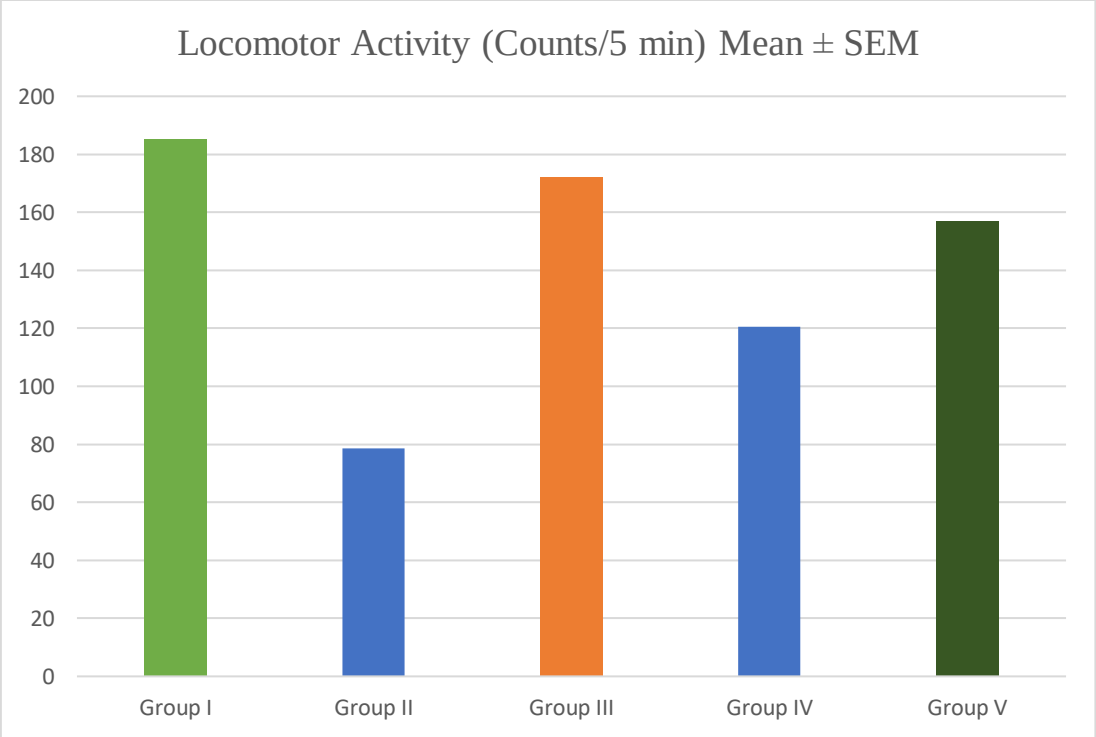
Treatment with the standard drug (Levodopa + Benserazide) in Group III significantly improved locomotor activity compared to the MPTP control group, demonstrating restoration of dopaminergic neurotransmission and motor function.

Senna occidentalis treatment showed a dose-dependent improvement in locomotor activity. Group IV (200 mg/kg) exhibited a moderate increase in movement scores, while Group V (400 mg/kg) showed a marked improvement, approaching near-normal activity levels. This suggests that the extract enhances exploratory behavior and motor coordination in MPTP-induced Parkinsonian rats.

Locomotor Activity

Group	Treatment	Locomotor Activity (Counts/5 min) Mean ± SEM
Group I	Vehicle control (normal saline, i.p.)	185.4 ± 6.3
Group II	MPTP only (25 mg/kg, i.p.)	78.6 ± 4.9
Group III	MPTP + Levodopa (12 mg/kg) + Benserazide (3 mg/kg, i.p.)	172.3 ± 5.8
Group IV	MPTP + Senna occidentalis 200 mg/kg (p.o.)	120.5 ± 5.2
Group V	MPTP + Senna occidentalis 400 mg/kg (p.o.)	156.9 ± 6.0

MPTP significantly reduced locomotor activity, confirming Parkinsonian motor deficit. Standard treatment restored near-normal movement. Senna occidentalis showed dose-dependent improvement in locomotor activity. Higher dose (400 mg/kg) exhibited stronger neuroprotective and behavioral recovery effects.



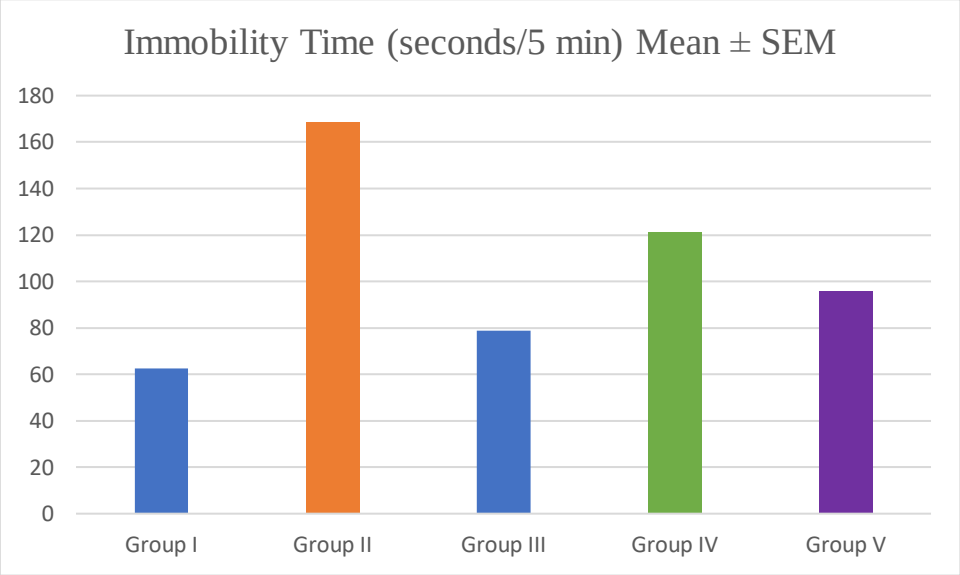
Forced Swimming Test Results

The forced swimming test was used to evaluate behavioral despair and motor activity in experimental animals by measuring immobility time. MPTP administration in Group II significantly increased immobility time, indicating reduced motivation, motor impairment, and depressive-like behavior associated with Parkinson's disease. Treatment with the standard drug (Levodopa + Benserazide) in Group III significantly reduced immobility time, suggesting improved dopaminergic neurotransmission and behavioral activity. This indicates partial reversal of MPTP-induced neurobehavioral deficits.

Senna occidentalis treatment showed a dose-dependent reduction in immobility time. Group IV (200 mg/kg) demonstrated moderate improvement, while Group V (400 mg/kg) showed a marked reduction in immobility time, approaching normal control values. This suggests enhanced motor activity, improved behavioral performance, and neuroprotective effects of the extract.

Group	Treatment	Immobility Time (seconds/5 min) Mean ± SEM
Group I	Vehicle control (normal saline, i.p.)	62.4 ± 3.8
Group II	MPTP only (25 mg/kg, i.p.)	168.7 ± 5.6
Group III	MPTP + Levodopa (12 mg/kg) + Benserazide (3 mg/kg, i.p.)	78.9 ± 4.1
Group IV	MPTP + Senna occidentalis 200 mg/kg (p.o.)	121.3 ± 5.0
Group V	MPTP + Senna occidentalis 400 mg/kg (p.o.)	95.6 ± 4.4

MPTP significantly increased immobility time, indicating behavioral despair and motor dysfunction. Standard drug markedly reduced immobility time. *Senna occidentalis* showed dose-dependent reduction in immobility time. High dose (400 mg/kg) showed strong antidepressant-like and neuroprotective activity.

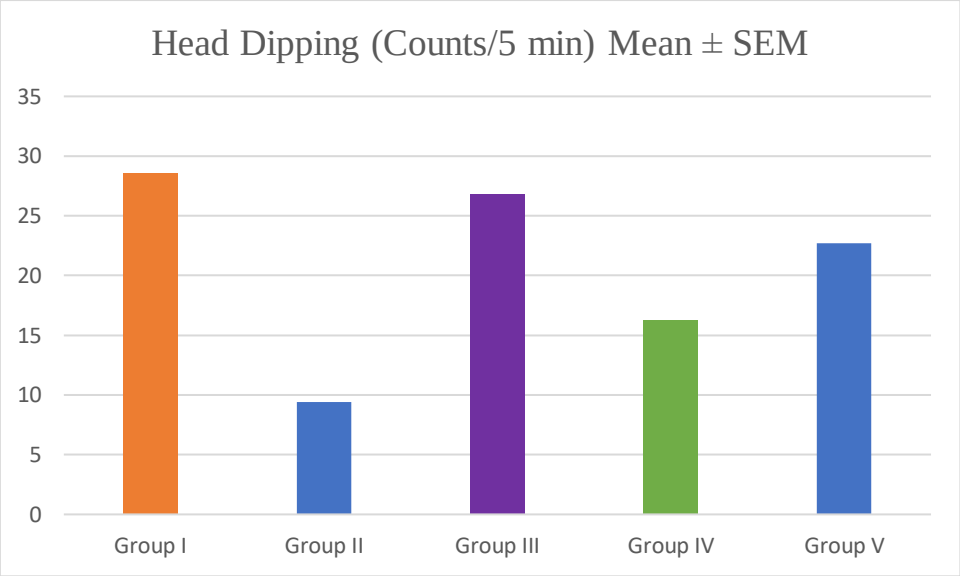


MPTP significantly increased immobility time, indicating behavioral despair and motor dysfunction. Standard drug markedly reduced immobility time. *Senna occidentalis* showed dose-dependent reduction in immobility time. High dose (400 mg/kg) showed strong antidepressant-like and neuroprotective activity.

Hole Board Test

The hole board test was used to evaluate exploratory behavior and anxiety-related locomotor activity in experimental animals. The number of head dips was recorded as an index of curiosity and central nervous system activity. MPTP administration in Group II significantly reduced the number of head dips, indicating reduced exploratory behavior and motor impairment due to dopaminergic neuronal loss. Treatment with the standard drug (Levodopa + Benserazide) in Group III significantly increased head dipping behavior compared to the MPTP control group, suggesting restoration of dopaminergic function and improved exploratory activity. *Senna occidentalis* treatment showed a dose-dependent improvement in exploratory behavior. Group IV (200 mg/kg) exhibited a moderate increase in head dips, while Group V (400 mg/kg) showed a marked improvement, approaching normal control values. This indicates enhanced CNS activity, reduced anxiety-like behavior, and improved motor coordination.

Group	Treatment	Head Dipping (Counts/5 min) Mean ± SEM
Group I	Vehicle control (normal saline, i.p.)	28.6 ± 1.9
Group II	MPTP only (25 mg/kg, i.p.)	9.4 ± 1.2
Group III	MPTP + Levodopa (12 mg/kg) + Benserazide (3 mg/kg, i.p.)	26.8 ± 1.7
Group IV	MPTP + Senna occidentalis 200 mg/kg (p.o.)	16.3 ± 1.5
Group V	MPTP + Senna occidentalis 400 mg/kg (p.o.)	22.7 ± 1.6



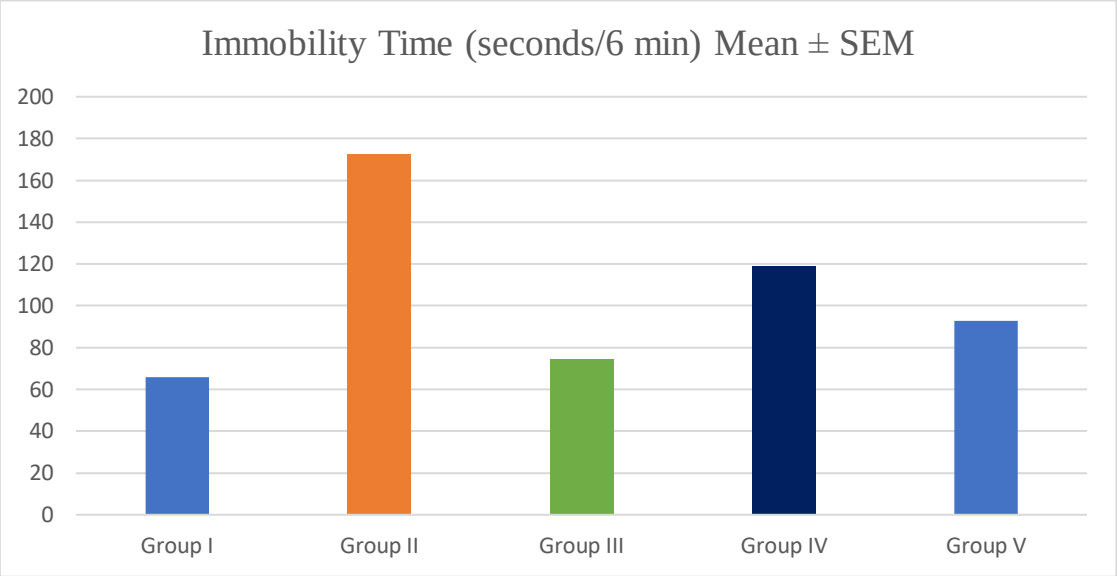
MPTP significantly reduced head dipping behavior, indicating reduced exploratory activity. Standard drug restored exploratory behavior close to normal levels. *Senna occidentalis* showed a dose-dependent increase in head dips. Higher dose (400 mg/kg) showed stronger neurobehavioral recovery.

Tail Suspension Test

The tail suspension test was used to evaluate depressive-like behavior and behavioral despair in experimental animals by measuring immobility time. MPTP administration in Group II significantly increased immobility time, indicating marked neurobehavioral impairment associated with dopaminergic dysfunction.Treatment with the standard drug (Levodopa + Benserazide) in Group III significantly reduced immobility time compared to the MPTP control group, suggesting improvement in dopaminergic transmission and behavioral activity.*Senna occidentalis* treatment showed a dose-dependent reduction in immobility time. Group IV (200 mg/kg) produced moderate improvement, while Group V (400 mg/kg) showed a significant reduction in immobility time, approaching normal control values. This indicates improved motivation, motor activity, and neuroprotective effects of the extract.

Group	Treatment	Immobility Time (seconds/6 min) Mean ± SEM
Group I	Vehicle control (normal saline, i.p.)	65.8 ± 3.5
Group II	MPTP only (25 mg/kg, i.p.)	172.4 ± 5.9
Group III	MPTP + Levodopa (12 mg/kg) + Benserazide (3 mg/kg, i.p.)	74.6 ± 4.2
Group IV	MPTP + Senna occidentalis 200 mg/kg (p.o.)	118.9 ± 5.1
Group V	MPTP + Senna occidentalis 400 mg/kg (p.o.)	92.7 ± 4.6

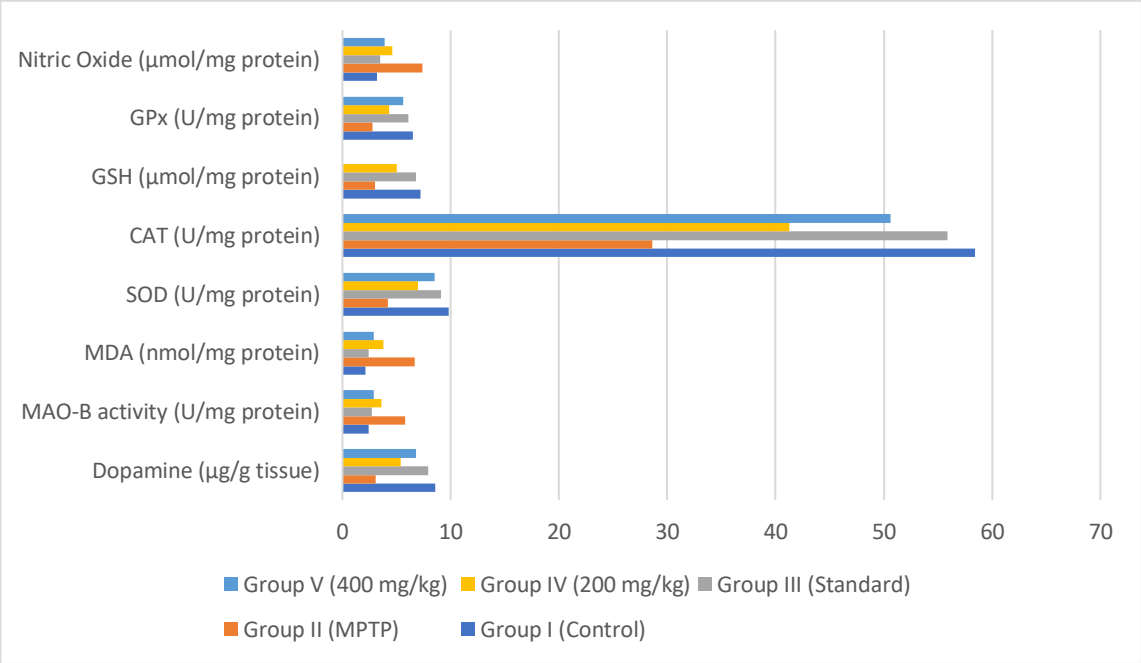
MPTP significantly increased immobility time, indicating depressive-like behavior and motor dysfunction. Standard drug markedly reduced immobility time. *Senna occidentalis* showed a dose-dependent reduction in immobility time. Higher dose (400 mg/kg) produced stronger behavioral recovery.



Biochemical Parameters

The biochemical analysis of brain tissue revealed significant alterations in oxidative stress markers, neurotransmitter levels, and MAO-B enzyme activity following MPTP administration. Group II (MPTP only) showed a marked increase in lipid peroxidation (MDA levels) along with a significant reduction in endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), and glutathione peroxidase (GPx), indicating severe oxidative stress and neuronal damage. In addition, dopamine levels were significantly depleted, while MAO-B enzyme activity was significantly elevated in this group, confirming dopaminergic neurodegeneration.Treatment with the standard drug (Levodopa + Benserazide) in Group III significantly reversed these biochemical alterations by restoring dopamine levels, reducing MAO-B activity, decreasing MDA levels, and enhancing antioxidant enzyme activity. This indicates strong neuroprotective and antioxidative effects.*Senna occidentalis* treatment showed a dose-dependent improvement in all biochemical parameters. Group IV (200 mg/kg) produced moderate restoration of dopamine levels and antioxidant enzymes with a reduction in MDA and MAO-B activity. Group V (400 mg/kg) exhibited a highly significant protective effect, with near normalization of biochemical parameters, indicating strong antioxidant, neuroprotective, and MAO-B inhibitory activity.

Biochemical Parameter	Group I (Control)	Group II (MPTP)	Group III (Standard)	Group IV (200 mg/kg)	Group V (400 mg/kg)
Dopamine (µg/g tissue)	8.6 ± 0.4	3.1 ± 0.2	7.9 ± 0.3	5.4 ± 0.3	6.8 ± 0.3
MAO-B activity (U/mg protein)	2.4 ± 0.1	5.8 ± 0.2	2.7 ± 0.1	3.6 ± 0.2	2.9 ± 0.1
MDA (nmol/mg protein)	2.1 ± 0.1	6.7 ± 0.3	2.4 ± 0.1	3.8 ± 0.2	2.9 ± 0.1
SOD (U/mg protein)	9.8 ± 0.4	4.2 ± 0.2	9.1 ± 0.3	7.0 ± 0.3	8.5 ± 0.3
CAT (U/mg protein)	58.4 ± 2.1	28.6 ± 1.8	55.9 ± 2.0	41.3 ± 1.9	50.6 ± 2.0
GSH (µmol/mg protein)	7.2 ± 0.3	3.0 ± 0.2	6.8 ± 0.3	5.0 ± 0.2	6.1 ± 0.3
GPx (U/mg protein)	6.5 ± 0.3	2.8 ± 0.2	6.1 ± 0.2	4.3 ± 0.2	5.6 ± 0.3
Nitric Oxide (µmol/mg protein)	3.2 ± 0.2	7.4 ± 0.3	3.5 ± 0.2	4.6 ± 0.2	3.9 ± 0.2



DISCUSSION:

The present study was designed to evaluate the antiparkinsonian potential and monoamine oxidase-B (MAO-B) inhibitory activity of *Senna occidentalis* in MPTP-induced Parkinsonian rats. MPTP administration produced significant behavioral, biochemical, and neurochemical alterations consistent with Parkinson's disease pathology. These changes included marked reduction in locomotor activity, impaired motor coordination, increased immobility time in behavioral tests, depletion of dopamine levels, elevated MAO-B activity, and increased oxidative stress markers, confirming successful induction of Parkinsonism. The observed behavioral deficits in rotarod, open field, hole board, forced swimming, and tail suspension tests indicate severe impairment of motor function, exploratory behavior, and motivational activity due to dopaminergic neuronal loss in the substantia nigra. These findings are consistent with earlier reports that MPTP selectively destroys nigrostriatal dopaminergic neurons, leading to bradykinesia, rigidity, and behavioral despair. Biochemical analysis further supported these findings, showing a significant increase in lipid peroxidation (MDA), nitric oxide levels, and MAO-B activity, along with a decrease in endogenous antioxidant enzymes such as SOD, CAT, GSH, and GPx. The elevation of MAO-B activity contributes to excessive dopamine breakdown, while oxidative stress plays a crucial role in neuronal degeneration. These alterations collectively reflect mitochondrial dysfunction and free radical–mediated neurotoxicity induced by MPTP.

Treatment with *Senna occidentalis* significantly ameliorated these behavioral and biochemical abnormalities in a dose-dependent manner. The higher dose (400 mg/kg) exhibited more pronounced effects, nearly restoring normal motor and behavioral functions. This improvement was evidenced by enhanced performance in behavioral tests, increased dopamine levels, reduced MAO-B activity, and normalization of antioxidant status. The neuroprotective effect of *Senna occidentalis* may be attributed to its rich phytochemical composition, including flavonoids, phenolic compounds, alkaloids, and terpenoids. These constituents are known to possess strong antioxidant properties, free radical scavenging activity, and enzyme inhibitory potential. Flavonoids and phenolics may protect dopaminergic neurons by reducing oxidative stress and lipid peroxidation, while also stabilizing mitochondrial function. Additionally, the observed reduction in MAO-B activity suggests that the extract may inhibit dopamine degradation, thereby improving dopaminergic neurotransmission. The standard drug (Levodopa + Benserazide) produced significant reversal of MPTP-induced changes, validating the experimental model. The comparable effects observed with *Senna occidentalis*, particularly at higher doses, indicate its potential as a natural neuroprotective agent with MAO-B inhibitory properties. Overall, the results suggest that *Senna occidentalis* exerts significant antiparkinsonian activity through multiple mechanisms, including antioxidant defenses enhancement, inhibition of MAO-B enzyme, preservation of dopamine levels, and protection against mitochondrial dysfunction. These findings support its traditional medicinal use and highlight its potential for further development as a therapeutic agent in Parkinson's disease.

CONCLUSION:

The present study demonstrates that *Senna occidentalis* possesses significant antiparkinsonian and monoamine oxidase-B (MAO-B) inhibitory activity in MPTP-induced Parkinsonian rat models. MPTP administration produced marked behavioral deficits, neurochemical alterations, and oxidative stress, confirming successful induction of Parkinson-like symptoms. These changes were characterized by impaired motor coordination, reduced locomotor and exploratory activity, increased immobility behavior, depletion of dopamine levels, elevated MAO-B activity, and enhanced lipid peroxidation. Treatment with *Senna occidentalis* significantly reversed these alterations in a dose-dependent manner. The higher dose (400 mg/kg) showed greater neuroprotective efficacy compared to the lower dose (200 mg/kg), as evidenced by improved performance in behavioral tests, restoration of dopamine levels, reduction in MAO-B activity, and enhancement of endogenous antioxidant defenses.

The observed neuroprotective effects may be attributed to the presence of bioactive phytoconstituents such as flavonoids, phenolic compounds, alkaloids, and terpenoids, which exhibit strong antioxidant and free radical scavenging properties. These constituents likely protect dopaminergic neurons by reducing oxidative stress, inhibiting lipid peroxidation, and preserving mitochondrial function, thereby contributing to improved neuronal survival and function. In conclusion, *Senna occidentalis* exhibits promising antiparkinsonian potential through its antioxidant, neuroprotective, and MAO-B inhibitory mechanisms. The findings support its traditional medicinal use and suggest that it may serve as a potential natural therapeutic agent for the management of Parkinson's disease. Further detailed molecular studies and clinical investigations are recommended to confirm its efficacy and safety in humans.

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