RESEARCH PAPER

# Evaluation of the Neuroprotective Effect of Ethanolic Extract of *Coccinia grandis* (L.) Voigt in Haloperidol-Induced Parkinsonism in Wistar Rats

**Vinita V. Alman[1*], Vikas R. Dhole[1*], Sanganna C. Burli[1], Prashant S. Kumbhar[1]**

*[1*]Department of Pharmacology, Ashokrao Mane College of Pharmacy,*
*Pethvadgaon, Maharashtra, India.*
*Email: Vinitaalman@gmail.com, vikasdhole48@yahoo.com*

**ABSTRACT**

**Background:** Motor and non-motor deficits are brought on by the gradual degradation of dopaminergic neurones in the substantia nigra in Parkinson's disease (PD), a neurodegenerative condition. There are long-term risks and decreasing efficacy with the current pharmaceutical treatments, which mostly alleviate symptoms. Neuroprotective compounds originating from plants are thus a topic of great interest. The medicinal plant coccinia grandis has anti-inflammatory and antioxidant characteristics due to its abundance of flavonoids and phenolic compounds, among other bioactive components.

**Objective:** The purpose of this study was to determine whether an ethanolic extract of Coccinia grandis had any protective effects on neurones or anti-Parkinsonian effects in a rat model of Parkinson's disease produced by haloperidol.

**Materials and Methods:** A preliminary phytochemical screening was conducted on the aerial portions of Coccinia grandis after they were extracted using ethanol. Haloperidol (1 mg/kg) administered intraperitoneally produced Parkinsonism. The experiment included five groups of animals: healthy controls, disease controls, conventional therapy (Levodopa + Carbidopa), low-dose extract, and high-dose extract. There was also a normal control group. Various behavioural indicators were assessed, such as catalepsy, locomotor activity, rotarod performance, grid-hang test, and parallel bar test. Neuronal protection was assessed through histological analysis of brain tissue.

**Result**: Phytochemical analysis revealed the presence of several compounds, including glycosides, tannins, phenols, steroids, alkaloids, and saponins. Coccinia grandis significantly enhanced locomotor activity, motor coordination, strength of muscles and balance while minimizing cataleptic behavior in treatment groups compared to disease control groups. Histopathological analysis indicated less neuronal degeneration and maintained normal architecture of the brain in extract treated groups. The higher dose group had more neuroprotective activity than the lower dose group.Conclusion: ethanolic extract of Coccinia grandis exhibited potent anti-Parkinsonian activity in haloperidol-induced Parkinsonism with potential as a promising complementary medicine agent for management of Parkinson's disease.

**Keywords:** *Coccinia grandis*, Parkinsonism, Haloperidol, Neuroprotection, Motor coordination, Wistar rats.

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## 1. INTRODUCTION

The neurodegenerative disorder known as Parkinson's disease (PD) progresses over time and is second only in frequency to Alzheimer's disease. It is a worldwide public health concern that affects about 1% to 2% of the elderly population. One defining feature of the disease is the progressive depletion of dopaminergic neurones in the substantia nigra pars compacta and the striatum. Resting tremor, muscular rigidity, bradykinesia, postural instability, and gait abnormalities are the hallmark motor symptoms of Parkinson's disease, and they are all caused by this deficit. In addition to movement issues, patients frequently experience non-motor aspects that significantly diminish quality of life. These include cognitive deficiencies, depression, sleep problems, autonomic dysfunctions, and olfactory dysfunction.[1]

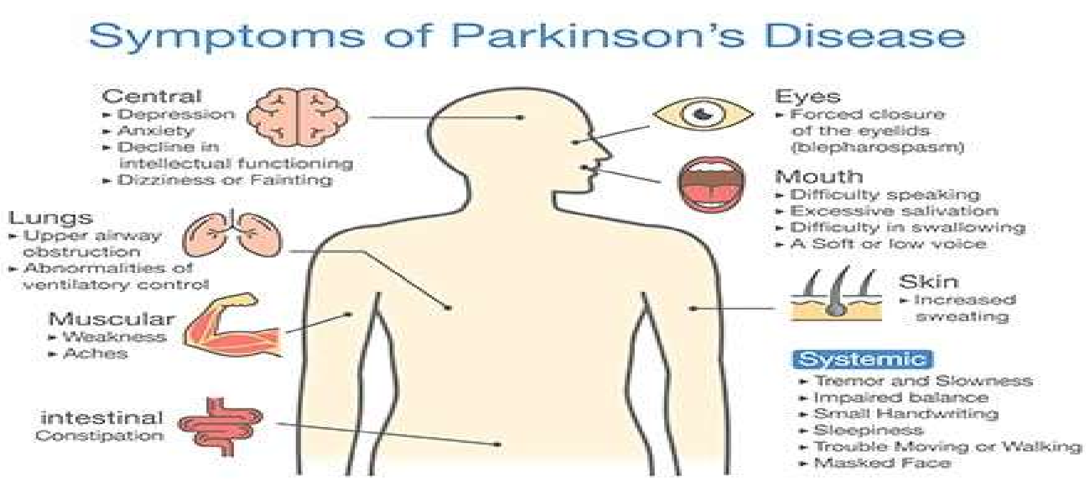


**Fig.No. 1: Symptoms of Parkinson's disease**

Multiple variables, including both hereditary predisposition and environmental triggers, contribute to the complicated pathophysiology of Parkinson's disease. Several harmful processes that have been suggested to have a role in the development of diseases include oxidative stress, mitochondrial malfunction, neuroinflammation, excitotoxicity, protein degradation pathway failure, and the formation of Lewy bodies containing α-synuclein. The breakdown of dopaminergic neurones is largely caused by oxidative stress. The production of reactive oxygen species (ROS) during dopamine metabolism has the potential to cause lipid peroxidation, protein oxidation, DNA damage, and ultimately, the death of neurones. Additionally, neurodegenerative processes are worsened by mitochondrial failure and chronic neuroinflammation, which generate greater oxidative damage.

Rather than altering the condition, the pharmaceutical treatment for Parkinson's disease primarily addresses symptoms. Combinations of levodopa and peripheral decarboxylase inhibitors, such as carbidopa, constitute the standard of care. In addition to amantadine, other therapy alternatives include dopamine agonists, catechol-O-methyltransferase inhibitors, monoamine oxidase-B (MAO-B) inhibitors, and anticholinergic drugs. While these medications do alleviate motor symptoms, they are not without their side effects, which include dyskinesia, motor fluctuations, psychotic alterations, hallucinations, and diminished therapeutic efficacy. Furthermore, the ongoing degeneration of dopaminergic neurones cannot be halted or reversed by any of the current therapeutic options. Consequently, there is a growing demand for the discovery of more effective and safer therapeutic drugs that can offer neuroprotection and delay the disease's course.

Because of their excellent safety level and abundance of bioactive phytoconstituents, medicinal plants are a hotspot for research into neuroprotective chemicals. For a very long time, herbal therapy has been an integral component of traditional medicine systems like Ayurveda, which focuses on the treatment of neurological problems. Neurodegenerative diseases may be amenable to the antioxidant, anti-inflammatory, anti-apoptotic, and neuroprotective characteristics exhibited by several phytochemicals. Many people think that herbal medications work because they include a cocktail of phytochemicals that target multiple pathologies simultaneously.

The ivy gourd, or Coccinia grandis (L.) Voigt, is endemic to tropical areas like India and is a member of the Cucurbitaceae family. A wide variety of liver disorders, including diabetes mellitus, inflammation, ulcers, fever, and others, have traditionally been treated with various portions of the plant. Coccinia grandis phytochemical research has uncovered several bioactive chemicals, including steroids, glycosides, tannins, triterpenoids, alkaloids, phenolic compounds, and saponins. There is evidence that some of these phytochemicals have potent impacts on inflammation, infection, diabetes, liver health, and immune regulation.

Two phytoconstituents that stand out for their capacity to protect neuronal cells from oxidative injury are flavonoids and phenolic compounds. By reducing oxidative stress, decreasing inflammatory reactions, keeping mitochondrial function appropriate, and preventing neuronal death, natural antioxidants can alleviate neurodegeneration, according to experimental investigations. Consequently, there is promising evidence that plants with high quantities of these chemicals may hold therapeutic agent potential for the treatment of Parkinson's disease.

For the purpose of testing anti-Parkinsonian medicines, the medication haloperidol is commonly used to produce a well-established laboratory model of Parkinsonism. Haloperidol has extrapyramidal side effects comparable to those seen in Parkinson's disease because it blocks the dopamine $D_2$ receptor. Catalepsy, motor impairment, muscle rigidity, decreased locomotor activity, and neuronal damage generated by oxidative stress are side effects of chronic haloperidol administration. Therefore, new treatment compounds for neuroprotection and anti-Parkinsonian effects can be studied efficiently using this paradigm.

Coccinia grandis has a broad range of pharmacological

actions, but nothing is known about its effectiveness in treating Parkinson's disease. A neuroprotective effect against haloperidol-induced neuronal injury and motor dysfunction was hypothesised for the ethanolic extract of Coccinia grandis due to its high phytochemical content, putative antioxidant and anti-inflammatory actions.
We set out to determine whether Ethanolic Extract of Coccinia grandis had any effect on Haloperidol-induced Parkinsonism in Wistar Rats by doing this investigation. The purpose of this study was to determine its neuroprotective potential by examining its effects on histological examination of brain tissue and behavioural characteristics such as catalepsy, locomotor activity, motor coordination, muscle strength, and balance. The study's findings will provide experimental proof that Coccinia grandis may be useful as an adjunctive treatment for Parkinson's disease.

## 2. MATERIALS AND METHODS

### 2.1 Plant Material

Coccinia grandis (L.) fresh shoots and foliage In January of 2025, the Voigt were collected from the village of Herle in the Kolhapur district of Maharashtra, India. For future reference, a voucher specimen was stored at the Department of Pharmacognosy, Ashokrao Mane College of Pharmacy, Peth Vadgaon, Kolhapur, Maharashtra, India, after a certified taxonomist recognised the plant material. [9]

**Fig.no.2: *Coccinia grandis* plant**

After collecting the plant materials, they were thoroughly rinsed with distilled water to remove any dust or other contaminants. After being left to dry in the shade for approximately two weeks at room temperature, the plant parts that were growing above ground were mechanically pulverised into a coarse powder. The powdered substance was subsequently preserved for future use in an airtight container.

### 2.2 Preparation of Extract

The Coccinia grandis aerial parts were dried and powdered before being extracted using ethanol. In order to facilitate the extraction of phytoconstituents, about 500 g of powdered plant material was soaked in an adequate amount of ethanol and left to stand for 72 hours with occasional shaking.[10]


**Fig.no.3: Extraction of *Coccinia grandis***

The maceration process was terminated when the extract was filtered using muslin cloth and then Whatman No. 1 filter paper. A semisolid mass was obtained by further drying the filtrate and then concentrating it at reduced pressure with a rotary vacuum evaporator. The % yield was determined by weighing the dried extract, which was then stored in a refrigerator at 4°C until needed. The following formula was used to compute the percentage yield:

Percentage Yield (%) = (Weight of Dried Extract / Weight of Plant Material) × 100

### 2.3 Qualitative Phytochemical Analysis

Preliminary phytochemical screening of the ethanolic extract of *Coccinia grandis* was carried out using standard qualitative chemical tests to identify the presence of various classes of secondary metabolites.

### 2.4 Experimental Animals

An animal facility that is certified by CPCSEA provided the healthy adult Wistar albino rats, which range in weight from 150 to 250 g and can be of either sex. The animals were kept in cages made of polypropylene in a controlled environment with a temperature of 25 ± 2°C, relative humidity of 55 ± 5%, and a light/dark cycle of 12 hours.

During the duration of the study, the animals were given water at will and a regular pellet meal. The animals were given a week to get used to the lab environment before they were tested.

Following CPCSEA protocols for the handling of laboratory animals, the Ashokrao Mane College of Pharmacy's Institutional Animal Ethics Committee (IAEC) at Peth Vadgaon, Kolhapur, examined and authorised the study's experimental procedure.

### 2.5 Experimental Design

Haloperidol (1 mg/kg, intraperitoneally) was administered for 21 days in a row to induce Parkinsonism.[10] A 21-day oral regimen of C.Grandis 200 mg/kg and 400 mg/kg, as well as the usual medication levodopa + carbidopa 100+25 mg/kg, was delivered.

There were a total of six animals used in the study, distributed evenly among five groups of three.

**Table no.:1 Experimental design**

| Group | Treatment | Dose | Duration |
|---|---|---|---|
| GROUP I | Normal vehicle | - | 21 days |
| GROUP II | Haloperidol | (1mg/kg i.p) | 21 days |
| GROUP III | Haloperidol+Levodopa+Carbidopa | (100 mg/kg+25 mg/kg p.o) | 21 days |
| GROUP IV | Haloperidol + *Coccinia grandis* | 200 mg/kg p.o. | 21 days |
| GROUP V | Haloperidol + *Coccinia grandis* | 400 mg/kg p.o | 21 days |

The treatment was continued for 21 days, and neurobehavioral assessments were performed at predetermined intervals on 7, 14, 21 th day.[11]

### 2.6 Neurobehavioral Studies

#### 2.6.1 Actophotometer Test

Locomotor activity of rats was assessed using a digital actophotometer. Each animal was individually placed in the activity cage, and the number of beam interruptions produced by spontaneous movement was recorded over a period of 5 min.[12]

Reduction in locomotor activity indicated motor impairment, whereas increased activity following treatment suggested improvement in motor function.[13]


**Fig.no.3 Actophotometer**

#### 2.6.2 Rotarod Test

Motor coordination and muscular endurance were evaluated using a rotarod apparatus. Rats were trained prior to experimentation to remain on a rotating rod.[14]

During the test, each rat was placed on the rotating rod operating at a constant speed, and the fall-off time was recorded. Increased retention time indicated improvement in motor coordination and neuromuscular function.[15]

**Fig.no.4 Rotarod test**

**2.6.3 Parallel Bar Test**

Motor balance and coordination were assessed using the parallel bar apparatus. Animals were placed on two horizontal parallel bars, and the time required to traverse the bars and maintain balance was observed.[16]

During the observation period, any instance of the animal turning upside down or losing balance was also noted carefully.Healthy rats generally remained on the bars for more than 5 seconds. Animals falling within 5 seconds were considered to exhibit impaired motor coordination or muscular weakness.The maximum cut-off time for the test was fixed at 120 seconds.

Enhancement of motor coordination and balance was reflected by improved performance on the parallel bar.

**Fig.no. 5: Parallel bar test**

**2.6.4 Grid-Hang Test**

The grid-hang test was used to assess muscular strength and grip endurance. Rats were positioned on a wire mesh grid and then the grid was turned upside down. The test's time limit was set at 120 seconds max. If the rat continued to hang for more than this period, then the trial was terminated and a time of 120 seconds was entered as the final value.

The duration of the time the animal was held till it fell was recorded. Better neuromuscular strength and coordination was suggested by the increase of hanging time. [17]

**Fig.no.: 6 Grid hang test**

**2.6.5 Catalepsy Test**

Catalepsy was measured with a standard bar test. Each rat's forepaws were allowed to rest on a horizontal wooden bar that was about 9 cm above the bench surface.

Time the animal took to maintain the posture without correcting it was recorded. The number of seconds that the rat spent with at least one forepaw on the bar or its posture corrected was recorded. The longer the duration was, the more rigid the muscles were and the cataleptic. The time of the test was capped at 120 seconds. An increase in catalepsy time was correlated with Parkinsonian symptoms while a decrease was correlated with anti-Parkinsonian activity.[18,19]

**Fig.no. 7: Catalepsy bar test**

**2.8 Histopathological Examination**

Animals were sacrificed under an aesthetic at the end of the experimental period; the brain tissues were carefully removed and fixed in 10% neutral buffered formalin.

The tissues were fixed in graded alcohols, cleared in xylene and embedded in paraffin wax. The sections were cut with a rotary microtome and stained with hematoxylin and eosin (H&E) (about 5 µm).

Histopathological changes such as neuronal degeneration and vacuolation, inflammatory cell infiltration and alterations in neuronal architecture were studied in the stained sections under light microscope. Photomicrographs were taken for documentation and comparison between various treatment groups. [20]

**2.9 Statistical Analysis**

Data from all the experiments were presented as Mean ± Standard Error of Mean (SEM). Data was analysed statistically using Graphpad prism software (Version 10.0). The data among different experimental groups were compared one by one by using one way Analysis of variance or ANOVA and Tukey's multiple comparison post hoc test. A value of less than $P < 0.05$ was deemed statistically significant.

**3. RESULTS**

**3.1 Percentage Yield of Ethanolic Extract**

The ethanolic extract of *Coccinia grandis* aerial parts was obtained as a dark green semisolid mass following maceration. The percentage yield of the extract was found to be **12% w/w**.

**Table 2. Percentage Yield of Ethanolic Extract of *Coccinia grandis***

| Plant material | Solvent | Percentage yield (% w/w) |
|---|---|---|
| Aerial parts of *Coccinia grandis* | Ethanol | 12 |

**3.2 Qualitative Phytochemical Analysis**

Preliminary phytochemical screening of the ethanolic extract of *Coccinia grandis* revealed the presence of several bioactive phytoconstituents, including alkaloids, flavonoids, glycosides, steroids, tannins, phenolic compounds, and saponins.

**Table 3. Qualitative Phytochemical Screening of Ethanolic Extract of *Coccinia grandis***

| Phytochemical constituent | Result |
|---|---|
| Alkaloids | + |
| Flavonoids | + |
| Glycosides | + |
| Steroids | + |
| Tannins | + |
| Phenolic compounds | + |
| Saponins | + |
| Proteins | – |
| Carbohydrates | ± |

(+): Present; (−): Absent

**3.3 Effect of Ethanolic Extract of *Coccinia grandis* on Locomotor Activity**

Haloperidol administration significantly reduced locomotor activity in the disease control group compared to the normal control group. Treatment with ethanolic extract of *Coccinia grandis* significantly increased locomotor activity in both dose groups. The high-dose extract-treated group exhibited greater improvement compared to the low-dose group and showed activity levels comparable to the standard-treated group.

**Table 4. Effect on Locomotor Activity**

| Sr no | Groups | Treatment Group | 7th Day | 14th Day | 21th Day |
|---|---|---|---|---|---|
| 1 | I | Normal vehicle | 223±1.42 | 228.2±1.32 | 227.7±1.45 |
| 2 | II | Haloperidol (1mg/kg i.p) 21 days | 105.2±1.17### | 90.67±1.05### | 73.67±1.26### |
| 3 | III | Haloperidol + Levodopa+ carbidopa (100 mg/kg+25 mg/kg i.p) 21days | 164.3±1.54*** | 174.7±1.76*** | 178.5±0.97** |
| 4 | IV | Haloperidol + *Coccinia grandis* (200 mg/kg) 21days | 134.3±1.54** | 144.3±1.42** | 157±1.57*** |
| 5 | V | Haloperidol + *Coccinia grandis* (400 mg/kg) 21days | 149.3±1.54** | 159.3±1.52*** | 172.2±1.55*** |

The data were expressed as Mean±SEM (n=6).Statistical comparisons were carried out using one-way analysis of variance(ANOVA),followed by Dunnett's post hoc test to evaluate differences between the treatment groups and the control group. Significance level were indicated as follows: ###p<0.001compared with normal and ***<0.001, **p<0.01,*p<0.05 when compared to Haloperidol control.

### 3.4 Effect on Rotarod Performance

Animals treated with haloperidol showed a significant decrease in retention time on the rotating rod. Administration of *Coccinia grandis* extract significantly increased retention time, indicating improvement in motor coordination and muscular endurance. The higher dose demonstrated superior efficacy.

**Table 5. Effect on Rotarod Performance**

| Sr no | Groups | Treatment Group | 7th Day | 14th Day | 21th Day |
|---|---|---|---|---|---|
| 1 | I | Normal vehicle | 178.3±1.52 | 179.8±1.01 | 180.5±0.76 |
| 2 | II | Haloperidol (1mg/kg i.p) 21 days | 90.5±0.99### | 78.5±0.76### | 66.5±0.68### |
| 3 | III | Haloperidol + Levodopa+ carbidopa (100 mg/kg+25 mg/kg i.p) 21days | 149.8±1.04*** | 166.5±0.66*** | 176.5±0.76** |
| 4 | IV | Haloperidol + *Coccinia grandis* (200 mg/kg) 21days | 119.8±1.01** | 131.5±0.76** | 141.5±0.87*** |
| 5 | V | Haloperidol + *Coccinia grandis* (400 mg/kg) 21days | 136.5±0.76** | 149±0.58*** | 161.5±0.74*** |

The data were expressed as Mean±SEM (n=6).Statistical comparisons were carried out using one-way analysis of variance(ANOVA),followed by Dunnett's post hoc test to evaluate differences between the treatment groups and the control group. Significance level were indicated as follows: ###p<0.001compared with normal and ***<0.001, **p<0.01,*p<0.05 when compared to Haloperidol control.

### 3.5 Effect on Parallel Bar Test

Haloperidol-induced Parkinsonian rats showed impaired balance and motor coordination. Treatment with *Coccinia grandis* significantly improved performance on the parallel bar apparatus. The high-dose extract produced a marked improvement compared to the disease control group.

**Table 6. Effect on Parallel Bar Performance**

| Sr no | Groups | Treatment Group | 7th Day | 14th Day | 21th Day |
|---|---|---|---|---|---|
| 1 | I | Normal vehicle | 49.5±0.56 | 61.33±0.66 | 87.83±0.79 |
| 2 | II | Haloperidol (1mg/kg i.p) 21 days | 82.17±0.65### | 102.8±0.84### | 122.5±0.95### |
| 3 | III | Haloperidol + Levodopa+ carbidopa (100 mg/kg+25 mg/kg i.p) 21days | 55.3±1.0.55*** | 68±0.68*** | 106±0.68** |
| 4 | IV | Haloperidol + *Coccinia grandis* (200 mg/kg) 21days | 61.67±0.49** | 74.67±0.83** | 91.83±0.79*** |
| 5 | V | Haloperidol + *Coccinia grandis* (400 mg/kg) 21days | 58.17±0.65** | 71.67±0.66*** | 97.83±0.79*** |

The data were expressed as Mean±SEM (n=6).Statistical comparisons were carried out using one-way analysis of variance(ANOVA),followed by Dunnett's post hoc test to evaluate differences between the treatment groups and the control group. Significance level were indicated as follows: ###p<0.001compared with normal and ***<0.001, **p<0.01,*p<0.05 when compared to Haloperidol control.

### 3.6 Effect on Grid-Hang Test

Haloperidol administration significantly reduced grip strength and hanging time. Treatment with ethanolic extract of *Coccinia grandis* improved neuromuscular strength and endurance in a dose-dependent manner.

**Table 7. Effect on Grid-Hang Test**

| Sr no | Groups | Treatment Group | 7th Day | 14th Day | 21th Day |
|---|---|---|---|---|---|
| 1 | I | Normal vehicle | 63.17±0.94 | 65.5±0.66 | 67.5±0.79 |
| 2 | II | Haloperidol (1mg/kg i.p) 21 days | 37±0.57### | 28±0.84### | 21±0.95### |
| 3 | III | Haloperidol + Levodopa+ carbidopa (100 mg/kg+25 mg/kg i.p) 21days | 51.5±0.76*** | 55.5±0.68*** | 60.5±0.68** |
| 4 | IV | Haloperidol + *Coccinia grandis* (200 mg/kg) 21days | 43.5±0.49** | 45.5±0.83** | 49.5±0.79*** |
| 5 | IV | Haloperidol + *Coccinia grandis* (400 mg/kg) 21days | 47.5±0.65** | 51.5±0.66*** | 55.6±0.79*** |

The data were expressed as Mean±SEM (n=6).Statistical comparisons were carried out using one-way analysis of variance(ANOVA),followed by Dunnett's post hoc test to evaluate differences between the treatment groups and the control group. Significance level were indicated as follows: ###p<0.001compared with normal and ***<0.001, **p<0.01,*p<0.05 when compared to Haloperidol control.

### 3.7 Effect on Catalepsy

The disease control group exhibited a significant increase in cataleptic behavior compared to normal animals. Treatment with *Coccinia grandis* significantly reduced catalepsy scores. The high-dose extract showed greater reduction in cataleptic symptoms and was comparable to the standard treatment.

**Table 8. Effect on Catalepsy**

| Sr no | Groups | Treatment Group | 7th Day | 14th Day | 21th Day |
|---|---|---|---|---|---|
| 1 | I | Normal vehicle | 6.31±0.94 | 6.5±0.30 | 6.33±0.39 |
| 2 | II | Haloperidol (1mg/kg i.p) 21 days | 59.5±0.99### | 74.67±1.11### | 89.5±0.95### |
| 3 | III | Haloperidol + Levodopa+ carbidopa (100 mg/kg+25 mg/kg i.p) 21days | 21.83±0.76*** | 16.83±0.60*** | 11.83±0.63** |
| 4 | IV | Haloperidol + *Coccinia grandis* (200 mg/kg) 21days | 41±0.57** | 36.5±0.42** | 31.5±0.42*** |
| 5 | V | Haloperidol + *Coccinia grandis* (400 mg/kg) 21days | 29.83±0.65** | 23.68±0.60*** | 19.83±0.60*** |

The data were expressed as Mean±SEM (n=6).Statistical comparisons were carried out using one-way analysis of variance(ANOVA),followed by Dunnett's post hoc test to evaluate differences between the treatment groups and the control group. Significance level were indicated as follows: ###p<0.001compared with normal and ***<0.001, **p<0.01,*p<0.05 when compared to Haloperidol control.

### 3.11 Histopathological Evaluation

Histopathological examination of brain tissue from the normal control group revealed normal neuronal architecture with intact neuronal cells and absence of pathological alterations.

The disease control group showed marked neuronal degeneration, cytoplasmic vacuolation, inflammatory changes, and disruption of normal brain architecture, indicating haloperidol-induced neurotoxicity.

Animals treated with Levodopa–Carbidopa exhibited substantial restoration of neuronal morphology with minimal degenerative changes.

The ethanolic extract of Coccinia grandis showed significant neuroprotective effect. In the low-dose group, there were moderate improvements in neuronal architecture and reduction in degenerative changes, while in the high-dose group, the neuronal morphology was near normal with little cellular damage. Based on the findings, the extract has a dose-dependent neuroprotective effect against haloperidol-induced neuronal injuries.

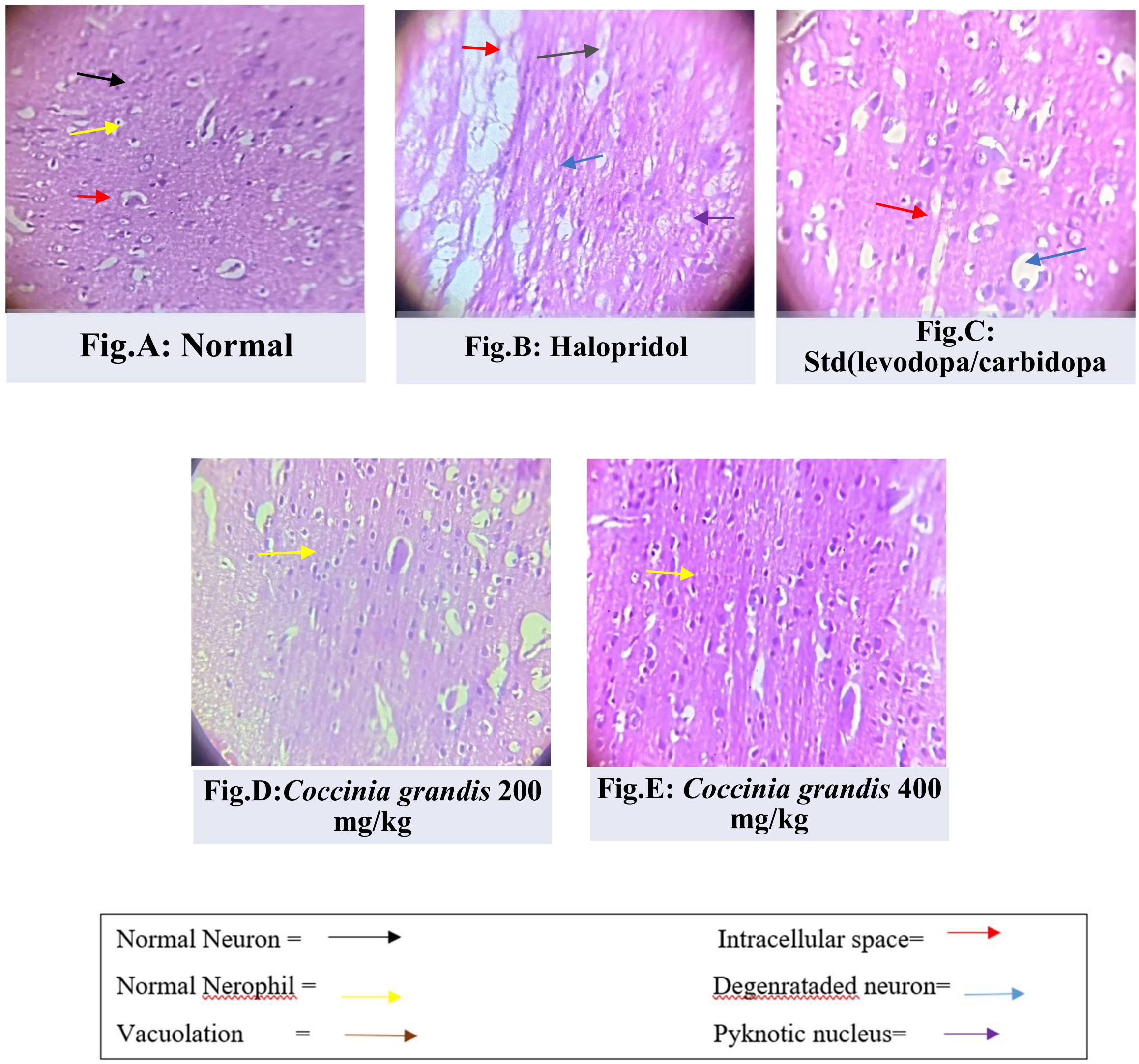


**Figure 8.** Histopathological images of brain sections from the experimental groups stained with hematoxylin and eosin (H&E) and assessed for protective effects of Coccinia grandis.

## DISCUSSION

Degeneration of dopaminergic neurones in the substantia nigra pars compacta causes a decrease in dopamine levels in the nigrostriatal pathway, a hallmark of the progressive neurodegenerative condition known as Parkinson's disease (PD). Motor dysfunctions as tremors, stiffness, bradykinesia, postural instability, and reduced locomotor activity are caused by an imbalance in neurotransmission. Although there are a number of medications on the market, there are presently only a handful of treatments that can alleviate symptoms rather than halt the neurodegenerative process in its tracks. Neuroprotection medications are still in need of improvement and safety concerns must be addressed.

This research looked at the effects of an ethanolic extract of the Coccinia grandis plant on a model of Parkinson's disease caused by haloperidol in Wistar rats. The extrapyramidal side effects of haloperidol, an antagonist of the dopamine $D_2$ receptor, are comparable to those of Parkinson's disease in people. Haloperidol is a good model for studying anti-Parkinsonian drugs since its long-term usage harms neurones, mitochondria, and the nervous system, leading to oxidative stress and motor deficits.

About 12% w/w ethanolic extract was obtained from the aerial part of Coccinia grandis, which is an efficient recovery of its phytoconstituents. The preliminary phytochemical screening showed that flavonoids, alkaloids, glycosides, tannins, phenolic compounds, steroids and saponins were present. These types of phytochemicals have been well documented as having antioxidant, anti-inflammatory and neuroprotective properties. The bioactive constituents present indicate that the pharmacological effects may be due to the synergic effect of several phytochemicals, not just one.

Motor activity and locomotor activity are sensitive indicators of dopaminergic functioning and motor performance. In the current study, haloperidol treatment caused significant decrease in locomotor activity in comparison with the normal animals. This decrease can be explained by blockade of dopamine receptors and by a dysfunction of the nigrostriatal neurotransmission. Ethanolic extract of Coccinia grandis showed significant improvement in locomotor activity, which was related to the restoration of motor function. The improvement was more significant in the higher dose group, indicating that the extract might have a dose-dependent effect. Improved locomotor performance could be associated with dopaminergic neuron survival and/or reduced oxidative damage in the basal ganglia.

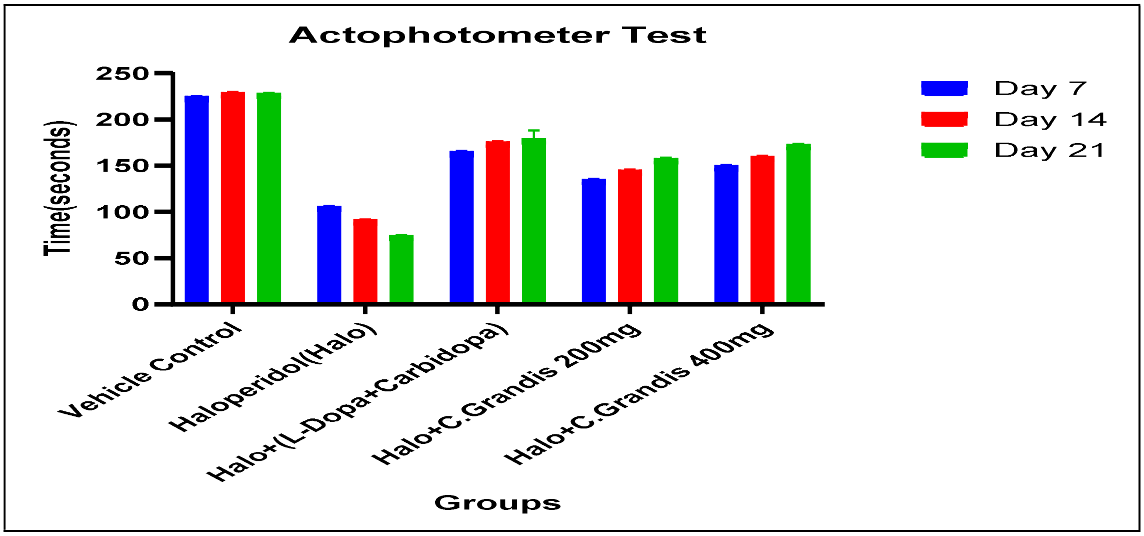


**Fig.no. :9 Actophotometer results graph**

Motor coordination and muscular endurance were assessed using the rotarod test. Haloperidol-treated animals exhibited significantly reduced retention time on the rotating rod, indicating impaired neuromuscular coordination and balance. Administration of *Coccinia grandis* extract significantly increased retention time compared with disease control animals. Improvement in rotarod performance suggests that the extract effectively protected neuronal pathways involved in motor coordination. Similar improvements have been reported with plant-derived antioxidants that reduce oxidative stress and improve neuronal survival in experimental Parkinsonism.

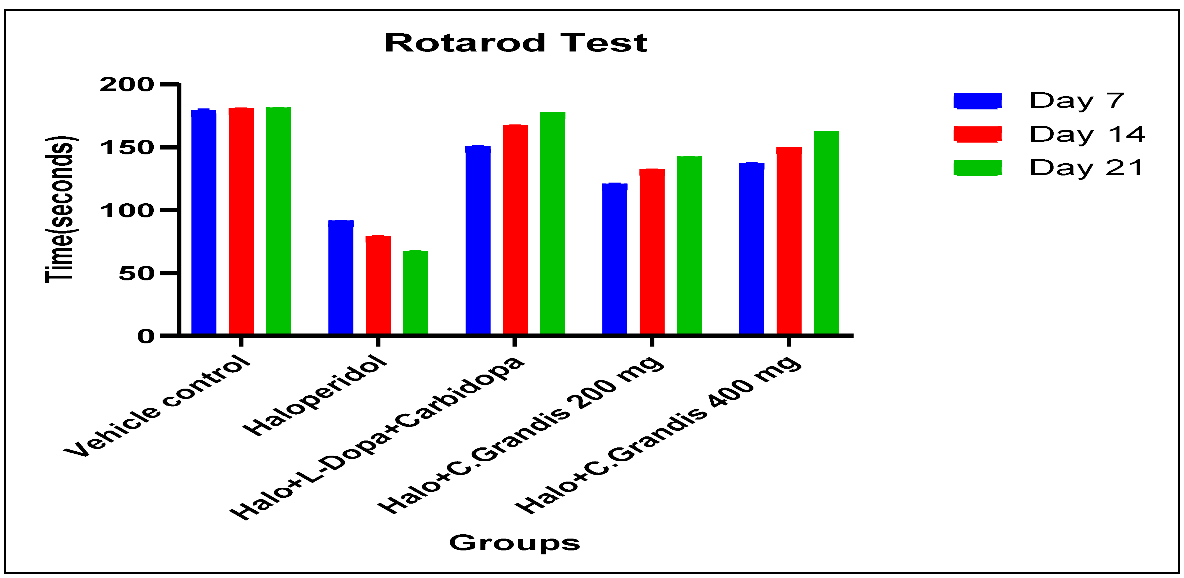


**Fig.no.:10 Rotarod test results graph**

The extracts also demonstrated beneficial effect on motor function and muscular strength with parallel bar test and grid hang test. Parkinsonian animals were found to have impaired balance and reduced grip strength, and a lack of neuromuscular coordination. Coccinia grandis had a substantial effect on improving performance in both tests. These results suggest that the extract could be used to potentially reduce the occurrence of neuromuscular dysfunction caused by haloperidol and to improve motor recovery. These effects might be associated with maintenance of the dopaminergic neurotransmission and decreased oxidative damage of the brain motor control regions.

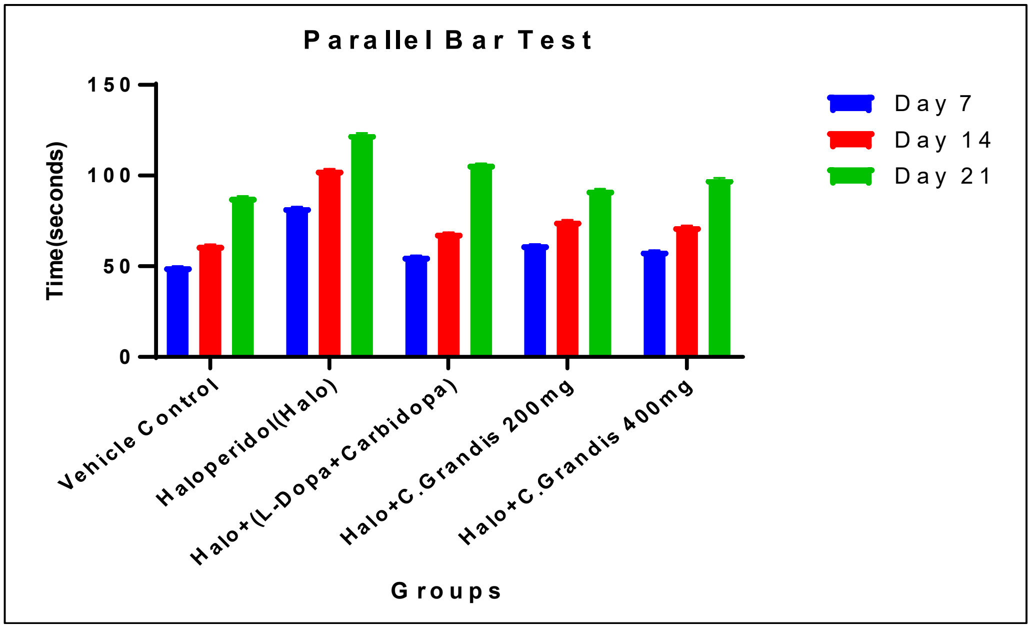


**Fig.no.:11 Parallel bar test results graph**

One of the most prevalent signs of Parkinson's disease, catalepsy has been extensively studied in animal models. Reduced motor control and the blocking of dopamine receptors create catalepsy, a condition that happens following haloperidol. While the catalepsy score was much higher in the control group, it was significantly lower in the Coccinia grandis-treated animals. Possible anti-Parkinsonian action and modification of dopaminergic signalling pathways are suggested by the reduction in catalepsy. Since the extract's efficacy in lowering cataleptic behaviour was dose-dependent, it follows that the therapeutic response is dose-dependent as well.

The grid-hang test was used to assess the neuromuscular coordination, muscular endurance, and forelimb muscle strength of the experimental animals. The current study demonstrated that rats given haloperidol had significantly shorter hanging times compared to control rats, indicating that the dopaminergic dysfunction was responsible for the impaired muscle strength and motor performance. Both groups of subjects benefited greatly from the ethanolic extract of Coccinia grandis, with the larger dose producing the most noticeable extension of the hanging duration. The grid-hang test showed that the extract increased muscular endurance and considerably decreased haloperidol-induced neuro-muscular impairments. The phytoconstituents in the extract may have an antioxidant and neuroprotective action, which would explain the findings by helping to keep neurones healthy and motor function intact. Results from several behavioural measures, including locomotor activity and rotarod performance, corroborate the beneficial impact of Coccinia grandis on motor impairments associated with Parkinson's disease.

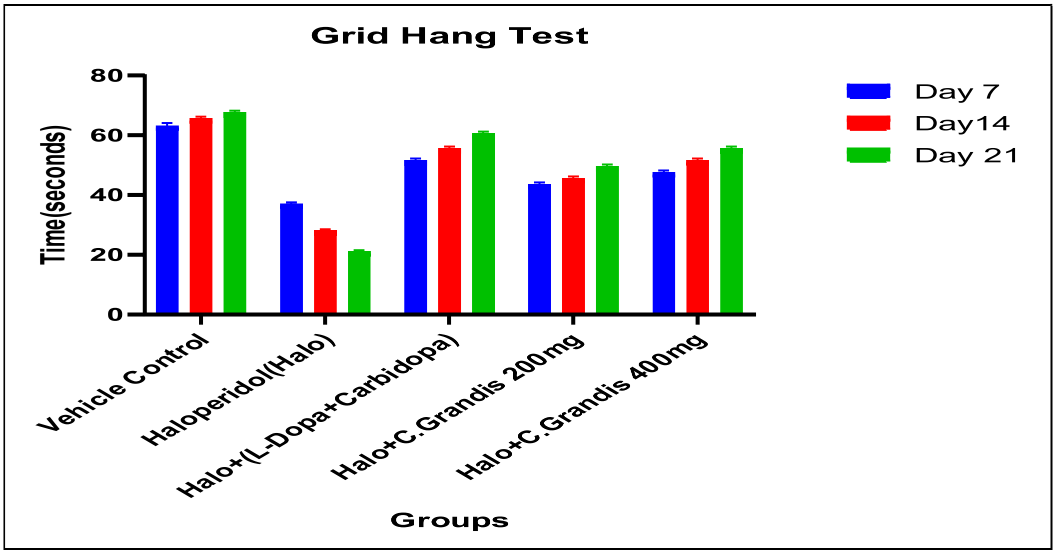


**Fig.no.:12 Grid hang test results graph**

The neuroprotective activity seen in this study could be due to the phytochemical constituents of Coccinia grandis. Flavonoids and phenols both are well known for their free radical scavenging and ability to inhibit lipid peroxidationThese substances control inflammatory and apoptotic signalling pathways, chelate metal ions, and manage reactive oxygen species levels. Another important role that flavonoids play in the development of Parkinson's disease is their purported ability to enhance mitochondrial function, reduce neuro-inflammatory responses, and increase neuronal survival.

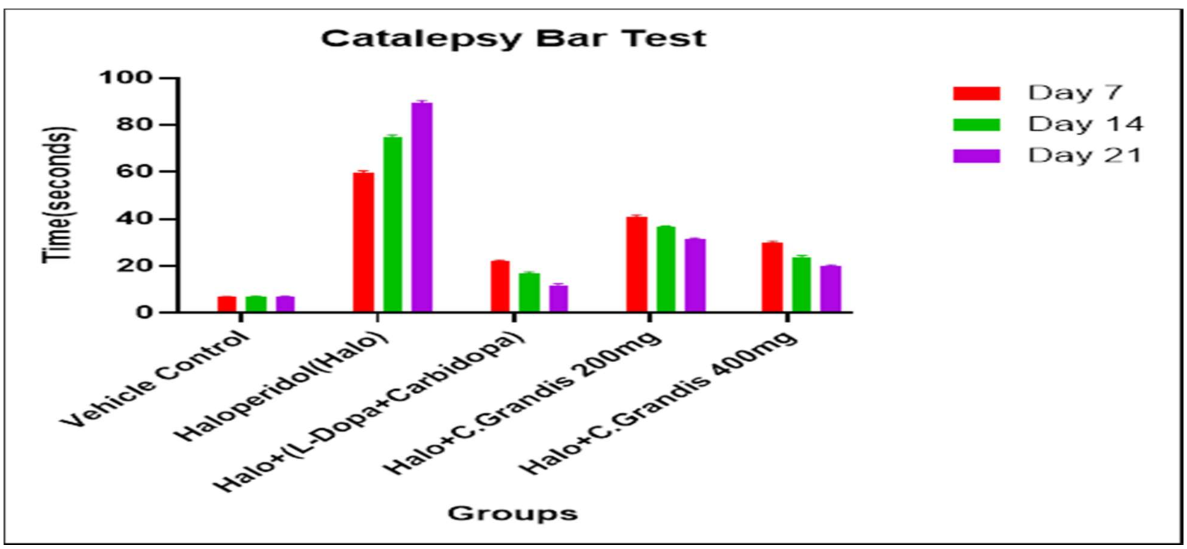


**Fig.no.:12 Catalepsy bar test results graph**

The extract was also shown to be neuroprotective by histopathological examination. Brain samples taken from control animals in the disease group revealed severe neurotoxicity with neuronal degeneration, vacuolation and abnormal tissue architecture. Animals treated with Coccinia grandis, on the other hand, exhibited significant preservation of the neuronal morphology and minimal pathological changes. The high dose group showed almost a normal histological appearance, having less of degeneration. These findings support and validate the behavioral and biochemical results and the effect of the extract in protecting the neurons from damage.

## CONCLUSION

The conclusion of the present study indicates that ethanolic extract of Coccinia grandis has a potent anti-Parkinsonian activity with several mechanisms. The observed behavioral improvement, restoration of the levels of antioxidant enzymes and preserving neuronal architecture are all indicative of the protective effects of the extract against haloperidol-induced damage to dopaminergic neurons. The antioxidant phytoconstituents found in the extract could help to reduce oxidative stress and strengthen the body's own defenses, which could help prevent neurodegeneration. While they do show some promise, some of the limitations should be noted. The study was carried out in one model of Parkinsonism and the exact molecular mechanisms responsible for the observed effects were not investigated. Future research should involve the identification of the bioactive compounds responsible for the neuroprotective activity, and the elucidation of their molecular targets. In addition, sophisticated biochemical, molecular and immunohistochemical studies can give greater insight into the mechanisms of action. Coccinia grandis has a therapeutic potential for Parkinson's disease that needs to be established through long-term studies and clinical evaluations. The overall results of the present study indicated that ethanolic extract of Coccinia grandis has strong neuroprotective and anti-Parkinsonian activities. The results offer scientific evidence for traditional medicinal applications of the plant and indicate its potential as a valuable natural therapeutic agent in the treatment of Parkinson's disease.

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