World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Research Article
ISSN: 2583-6579
SJIF Impact Factor: 6.916
Year - 2026
Volume: 5; Issue: 2
Page: 547-554

MORPHOLOGICAL RESTORATION OF NEURAL ARCHITECTURE BY *CRASSULA OVATA*: A CONTROLLED HISTOPATHOLOGY STUDY IN RATS

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Article Received: 1 January 2026 | | ***Article Revised: 22 January 2026*** | | ***Article Accepted: 11 February 2026***

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DOI: https://doi.org/10.5281/zenodo.18639490

How to cite this Article: Satheeshkumar N., Dr. S. Kannan, Dr. B. Sangameswaran (2026) MORPHOLOGICAL RESTORATION OF NEURAL ARCHITECTURE BY *CRASSULA OVATA*: A CONTROLLED HISTOPATHOLOGY STUDY IN RATS. World Journal of Pharmaceutical Science and Research, 5(2), 547-554. https://doi.org/10.5281/zenodo.18639490

ABSTRACT

Aims: This study investigated whether *Crassula ovata* leaf extract could protect brain tissue from haloperidol-induced structural damage in rats, as assessed by histopathological evaluation. **Methodology:** Thirty rats were allocated to five treatment groups (n = 6). Neurotoxic changes were induced using haloperidol (10 mg/kg, i.p.). The standard group received imipramine (25 mg/kg), while test groups were treated with *C. ovata* extract at 200 mg/kg or 400 mg/kg. Brain samples were fixed, processed, sectioned, and stained with haematoxylin and eosin (H&E) to investigate morphological alterations. **Results:** Haloperidol exposure produced marked neuronal injury, including cell shrinkage, vacuolation, nuclear condensation, and disturbance of cortical organisation. Both doses of *C. ovata* mitigated these abnormalities, with the 400 mg/kg group demonstrating near-normal histoarchitecture resembling the control and standard groups. **Conclusion:** *Crassula ovata* extract markedly attenuates haloperidol-induced structural deterioration in the brain, supporting its potential role as a natural neuroprotective agent.

KEYWORDS: *Crassula ovata*, histopathology, neuroprotection, haloperidol, neuronal degeneration, H&E staining.

1. INTRODUCTION

Haloperidol, a classical antipsychotic medication, is widely recognised for producing extrapyramidal complications and oxidative disturbances that can culminate in neuronal degeneration when administered repeatedly. These changes can be visualised microscopically through characteristic alterations such as cytoplasmic vacuolation, nuclear pyknosis, and disorganisation of neural layers.

Medicinal plants are being increasingly studied for their potential to counteract drug-induced neurotoxicity. *Crassula ovata*, a succulent species from the Crassulaceae family, contains various phytochemicals—including alkaloids, steroids, and resinous substances—that are reported to possess antioxidant and protective activity. Although its antioxidant potential is documented in in-vitro models, only limited data are available describing its influence on neuronal morphology under toxic conditions.

Given this background, the present work was designed to provide histological evidence regarding the neuroprotective efficacy of *C. ovata* against haloperidol-induced brain damage in rats.

2. MATERIALS AND METHODS

2.1 Plant Material

Leaves of *Crassula ovata* were authenticated by ABS Botanical Garden, Salem (Ref No. AUT/SSMC/304).

2.2 Experimental Animals

Albino rats (150–200 g) were maintained under standard laboratory conditions throughout the study.

Ethical approval: IAEC Reg. No. 2255/PO/Re/S/23/CPCSEA; Proposal No. SSMCOP/IAEC/M.Pharm/05/06/2025.

2.3 Extract Preparation

Shade-dried leaves were powdered and subjected to ethanolic Soxhlet extraction. The concentrate obtained was stored airtight until further use.

2.4 Experimental Design

Animals were assigned to five groups:

Group	Treatment Description	Dose & Route
Group I	Normal control	—
Group II	Haloperidol control	10 mg/kg, i.p.
Group III	Haloperidol + Imipramine	25 mg/kg
Group IV	Haloperidol + *C. ovata* extract	200 mg/kg
Group V	Haloperidol + *C. ovata* extract	400 mg/kg

2.5 Histopathology Procedure

At the end of the study, rats were sacrificed, and brain tissues were carefully excised. The tissues were:

- Fixed in 10% buffered formalin
- Processed through graded alcohol
- Embedded in paraffin
- Sectioned at 4–5 µm thickness
- Stained using haematoxylin and eosin (H&E)

Slides were examined under light microscopy to evaluate:

- Neuronal integrity
- Cytoplasmic and nuclear changes
- Evidence of degeneration
- Preservation or disturbance of cortical layers

3. RESULTS

3.1 Group I — Normal Control

Sections exhibited healthy neurons, clear cellular outlines, and uniform staining. No degenerative features were noted.

3.2 Group II — Haloperidol Control

This group displayed pronounced neurotoxic alterations, including:

- Cytoplasmic vacuoles
- Contracted and darkly stained (pyknotic) nuclei
- Loss of organised cortical layering
- Disrupted neuropil

These findings are typical indicators of haloperidol-induced neuronal injury.

3.3 Group III — Imipramine Standard

Imipramine treatment markedly reduced the severity of neuronal damage. Most cells retained normal morphology, and degenerative changes were minimal.

3.4 Group IV — *C. ovata* (200 mg/kg)

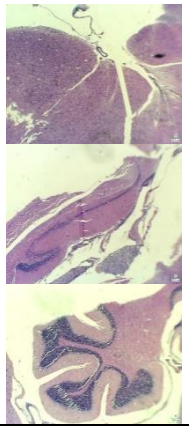
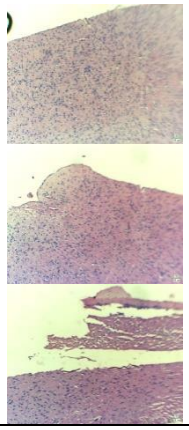
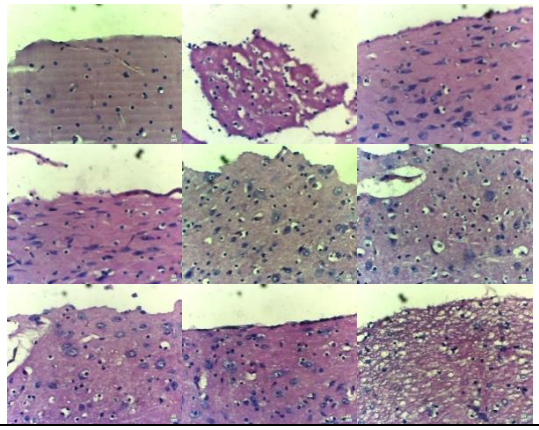
Moderate protective effects were observed. Vacuolation was reduced, and cortical organisation appeared partially restored compared with the haloperidol control

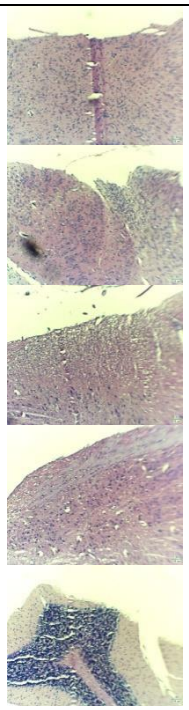
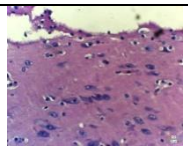
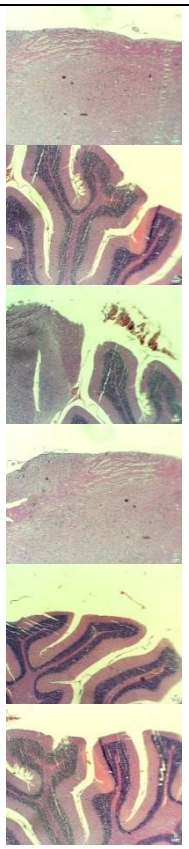
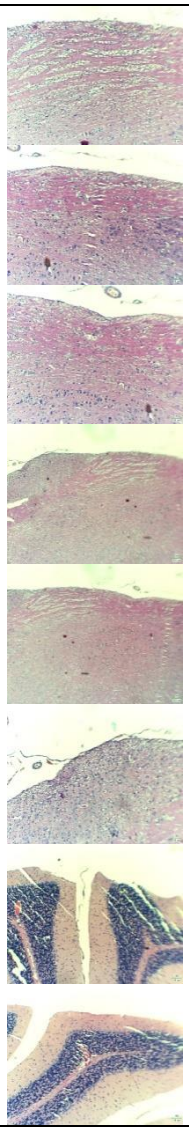
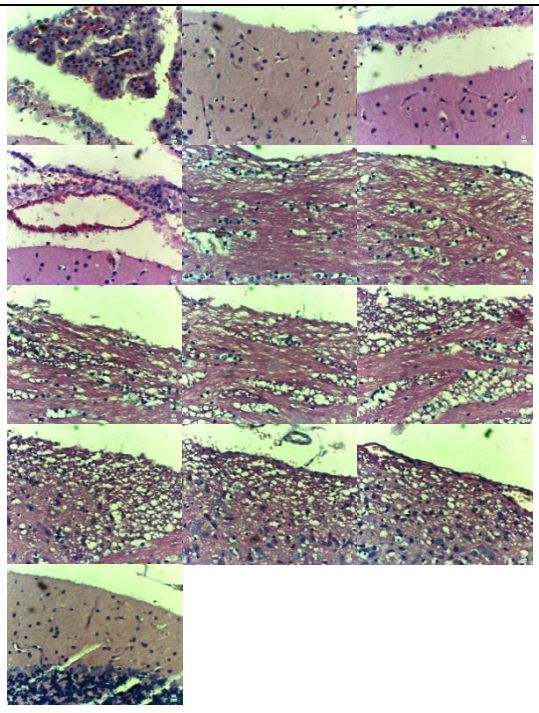
3.5 Group V — *C. ovata* (400 mg/kg)

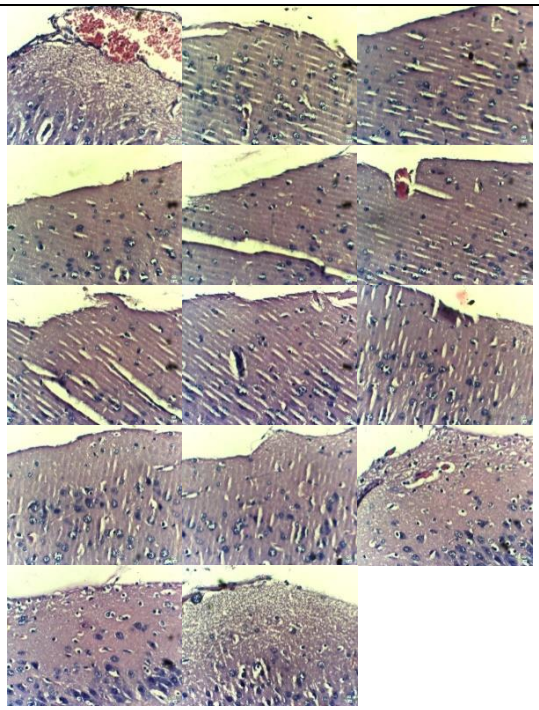
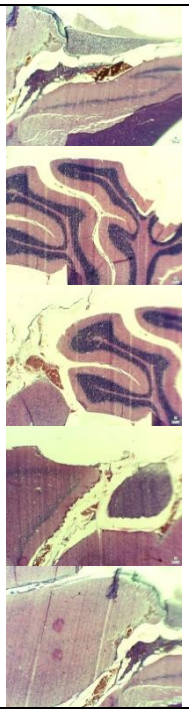
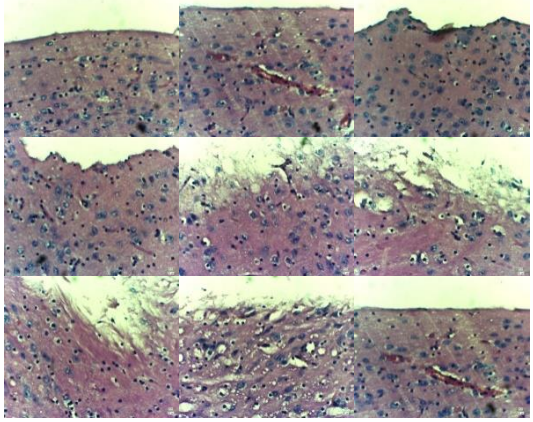
Marked preservation of neuronal structure was evident:

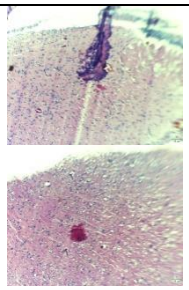
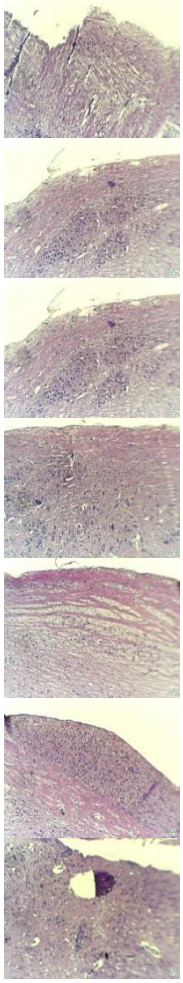
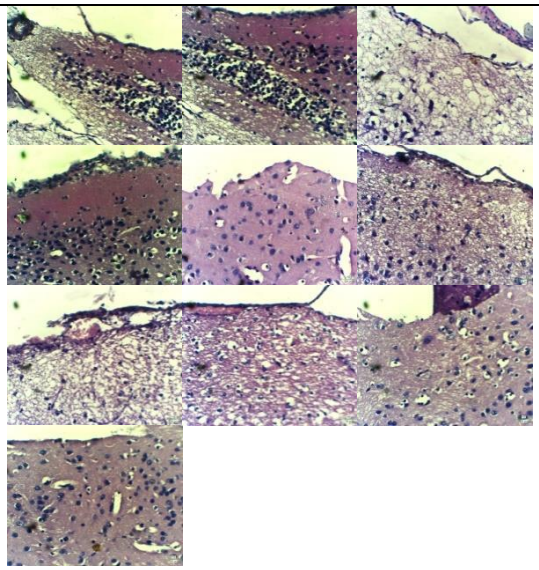
- Mostly normal cell bodies
- Minimal vacuolation
- Improved nuclear clarity
- Well-preserved cortical pattern

This group showed neuroprotection comparable to the standard drug.

Groups	4x	10x	40x
GI - Control			

			
GII - Haloperidol (10 mg/kg)			

GIII- Haloperidol (10 mg/kg)+ Imipramine(25mg/kg)			
GIV- Haloperidol (10 mg/kg)+ Test sample 200 mg/kg			

			
GV-Haloperidol (10 mg/kg)+ Test sample 400 mg/kg			

4. DISCUSSION

The histological findings reveal that haloperidol induces substantial damage to neuronal structures, consistent with oxidative and excitotoxic mechanisms reported in earlier studies. The improvements observed in the *C. ovata*-treated groups suggest the presence of constituents capable of counteracting these effects, likely through antioxidant or membrane-stabilising pathways.

The higher dose (400 mg/kg) demonstrated near-complete structural restoration, indicating a strong protective potential. This correlates with findings from in vivo behavioural and enzymatic studies showing enhanced SOD activity and improved locomotion. Together, these results support the hypothesis that *C. ovata* provides multi-level neuroprotection.

5. CONCLUSION

The extract of *Crassula ovata* significantly mitigates haloperidol-induced structural damage in rat brain tissue. The high dose (400 mg/kg) offered the greatest protection, demonstrating well-preserved neural architecture. These findings suggest the plant may serve as a promising natural neuroprotective agent.

Ethical Approval

Approved by IAEC (Reg. No. 2255/PO/Re/S/23/CPCSEA), Proposal No. SSMCOP/IAEC/M.Pharm/05/06/2025

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