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Assessment of Mitigatory Potentials of Rutin Hydrate on 5-Fluorouracil-induced Toxicity in the Prefrontal Cortex of Adult Wistar Rats

Adeola Boluwatife Adeniji[1*], Ponle Bamidele Fakunle[2], Joshua Anjola Ajao[3], David Temidayo Ovioke[4], Testimony Deborah Evans[5]

[1, 3, 4, 5] Department of Human Anatomy, Faculty of Basic Medical and Health Sciences, Lead City University, Ibadan, Oyo State, Nigeria.

[2] Department of Anatomy, Faculty of Basic Medical Sciences, Obafemi Awolowo College of Health Sciences, Olabisi Onabanjo University, Sagamu Campus, Ogun State, Nigeria.

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***Corresponding author:** Adeola Boluwatife Adeniji

Abstract

Background: *5-Fluorouracil is an important chemotherapeutic agent whose use has been associated with neurological complications, including oxidative imbalance, neuronal injury, and neuroinflammation. The prefrontal cortex is involved in important cognitive and behavioural functions and may be vulnerable to chemotherapy-associated toxicity. Rutin hydrate is a flavonoid with reported antioxidant and neuroprotective properties.*

Aim: *This study assessed the mitigating potential of rutin hydrate on 5-Fluorouracil-induced toxicity in the prefrontal cortex of adult Wistar rats.*

Methodology: *Thirty-six adult Wistar rats weighing 170–220 g were randomly assigned into six groups of six animals each: control, 5-FU toxicant, preventive, therapeutic, rutin-only, and prophylactic groups. Rutin hydrate was administered orally at 100 mg/kg, while 5-Fluorouracil was administered intraperitoneally at 15 mg/kg according to the respective treatment schedules. Body and brain weights were assessed. Prefrontal cortical tissues were evaluated histologically using haematoxylin and eosin and Cresyl Violet staining. Superoxide dismutase (SOD), malondialdehyde (MDA), and succinate dehydrogenase (SDH) were assessed as indicators of oxidative stress and mitochondrial function. Data were analysed using one-way analysis of variance followed by Tukey's multiple-comparison test, with significance set at $p < 0.05$.*

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Results: *The 5-Fluorouracil-only group showed a reduction in body weight and significantly lower relative brain weight compared with the control group. Absolute brain weight did not differ significantly among groups ($p = 0.3137$), whereas relative brain weight showed a significant overall difference ($p = 0.0492$). The 5-FU-only group demonstrated the lowest SOD (Superoxide dismutase) and SDH (Succinate dehydrogenase) activities and the highest MDA (malondialdehyde) concentration; however, differences among groups were not statistically significant for SOD ($p = 0.3476$), MDA ($p = 0.3451$), or SDH ($p = 0.3400$). Histologically, 5-FU exposure was associated with marked cortical disruption, extensive vacuolation, reduced preservation of healthy neurons, reduced Cresyl Violet staining, and chromatolytic changes. Rutin-treated groups demonstrated comparatively better preservation of neuronal morphology, cortical organization, and Nissl substance.*

Conclusion: *Rutin hydrate demonstrated potential mitigatory activity against 5-FU-associated prefrontal cortical toxicity, with the clearest evidence observed in the qualitative histological findings. The biochemical findings showed favourable directional trends but were not statistically significant. Further studies using quantitative histomorphometry, broader molecular and biochemical markers, and behavioural assessments are warranted.*

Keywords: *5-fluorouracil, oxidative stress, prefrontal cortex, rutin hydrate, Wistar rats.*

1. Introduction

5-Fluorouracil (5-FU) is a widely used antimetabolite chemotherapeutic agent employed in the management of several solid malignancies. Although its therapeutic activity depends largely on interference with nucleic acid synthesis and cellular proliferation, its systemic effects may extend beyond malignant tissues. Increasing evidence indicates that chemotherapy can produce neurological complications involving oxidative stress, neuroinflammation, altered neurogenesis, and structural or functional changes within the central nervous system (Subramaniam et al., 2022; Zhou et al., 2023).

Chemotherapy-associated neurotoxicity is particularly relevant because neurological complications may persist beyond the period of drug administration and contribute to cognitive and behavioural disturbances. Experimental studies have demonstrated that 5-FU exposure can alter neurogenesis and promote persistent neuroinflammatory responses, providing evidence that the effects of the drug are not restricted to peripheral tissues (Subramaniam et al., 2022). Changes in oxidative balance have also been implicated in 5-FU-associated neural injury, with increased lipid peroxidation and impaired antioxidant defence reported in experimental models (Suwannakot et al., 2021; Zhou et al., 2023).

The prefrontal cortex (PFC) is an important cortical region involved in executive functions, behavioural regulation, decision-making, working memory, and other higher-order processes (Chafee & Heilbronner, 2022; Hathaway & Newton, 2023). Its high metabolic requirements and extensive neuronal connectivity may contribute to its vulnerability to pathological processes capable of disrupting neuronal homeostasis. Consequently, structural changes within the PFC may have functional implications even when gross brain morphology remains relatively preserved.

Oxidative stress is one proposed mechanism underlying chemotherapy-induced neural injury. Excessive generation of reactive oxygen species relative to endogenous antioxidant capacity may promote lipid, protein, and nucleic acid damage. Superoxide dismutase (SOD) constitutes an important component of enzymatic antioxidant defence, while malondialdehyde (MDA), a product of lipid peroxidation, can serve as an indicator of oxidative membrane damage. Succinate dehydrogenase (SDH), a mitochondrial enzyme involved in cellular energy metabolism, provides an additional indication of mitochondrial functional status. Alterations in these parameters may therefore provide biochemical evidence of cellular stress and impaired metabolic function.

Histological assessment provides complementary structural information. Haematoxylin and eosin (H&E) staining permits evaluation of general cortical cytoarchitecture and neuronal morphology, whereas Cresyl Violet staining demonstrates Nissl substance and can provide information about neuronal integrity and chromatolytic changes. Combining these approaches with biochemical assessment may provide a broader assessment of toxicant-associated neural alterations.

Rutin hydrate is a naturally occurring flavonoid that has attracted attention because of its antioxidant and neuroprotective properties. Experimental studies have reported beneficial effects of rutin in models of neurological injury, including preservation of neuronal structure and modulation of pathways associated with oxidative stress and neuronal survival (Nicola et al., 2024; Sreelatha et al., 2024). Evidence from other experimental models also suggests that rutin may attenuate tissue injury associated with oxidative and inflammatory processes.

Despite increasing interest in the neurological effects of chemotherapy and the potential protective properties of flavonoids, evidence specifically examining the effects of rutin hydrate on 5-FU-associated toxicity in the prefrontal cortex remains limited. The present study therefore assessed the mitigatory potentials of rutin hydrate against 5-FU-induced toxicity in the PFC of adult Wistar rats using body and brain weight measurements, biochemical markers of oxidative and mitochondrial function, and histological assessment.

2. Materials and Methods

2.1 Study Design and Experimental Animals

This study employed an experimental laboratory-based design. Thirty-six healthy adult Wistar rats weighing between 170 and 220 g were used. The animals were obtained from a certified breeding facility and transported to the Animal House of the Department of Human Anatomy, Lead City University, Ibadan, Nigeria. Only healthy and active animals without visible signs of illness or injury were included.

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The rats were housed in clean, well-ventilated wire-mesh cages under standard laboratory conditions at approximately 22–28°C, with a 12-hour light/12-hour dark cycle. Standard laboratory rat chow and clean drinking water were provided ad libitum. Animals were allowed to acclimatize for two weeks before commencement of treatment.

2.2 Ethical Considerations

Ethical clearance was obtained from the Department of Human Anatomy, Faculty of Basic Medical and Health Sciences, Lead City University, Ibadan, Nigeria (Ethical Clearance No. LCU/FBMHS/ANA/REC/2026/049), dated 24 August 2026. The research protocol was reviewed and authorized by the Head of the Department for ethical and academic purposes. All procedures involving the experimental animals were conducted in accordance with applicable institutional research-ethics requirements and the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Measures were taken to minimize pain and stress during the experimental procedures.

2.3 Experimental Design and Treatment Groups

The 36 rats were randomly allocated into six groups of six animals each:

- **Control group (C):** Normal saline, 10 mL/kg orally for 3 days.
- **Toxicant group (T1):** 5-FU, 15 mg/kg intraperitoneally for three consecutive days.
- **Preventive group (T2):** 5-FU, 15 mg/kg intraperitoneally, with rutin hydrate, 100 mg/kg orally, administered concurrently for three days.
- **Therapeutic group (T3):** 5-FU, 15 mg/kg intraperitoneally for three days, followed by rutin hydrate, 100 mg/kg orally, for three days.
- **Rutin-only group (T4):** Rutin hydrate, 100 mg/kg orally for three days.
- **Prophylactic group (T5):** Rutin hydrate, 100 mg/kg orally for three days, followed by 5-FU, 15 mg/kg intraperitoneally, for three days.

2.4 Drug Preparation

Commercial 5-FU injection containing 500 mg/10 mL (50 mg/mL) was used. The required dose for each animal was calculated according to body weight.

Rutin hydrate powder was procured from Winlab Stores, University Teaching Hospital, Lagos, Nigeria. A daily suspension was prepared in 0.5% carboxymethyl cellulose (CMC) at a concentration of 20 mg/mL.

2.5 Drug Administration

5-FU was administered intraperitoneally, whereas rutin hydrate was administered orally using an appropriate stainless-steel/orogastric cannula. Body weights were measured before drug administration to determine individual doses.

2.6 Sample Collection and Prefrontal Cortex Isolation

At the end of the respective treatment periods, animals were euthanized under light chloroform anaesthesia followed by cervical dislocation. The brains were carefully excised and rinsed in cold physiological saline. Absolute brain weight was recorded, and relative brain weight was calculated as:

Relative brain weight (%) = (Absolute brain weight / Final body weight) × 100.

The skull was opened and the meninges removed. The prefrontal cortex was identified using the stereotaxic coordinates described by Paxinos and Watson (2006), with the medial PFC comprising the prelimbic, infralimbic, and anterior cingulate regions. Three animals per group were used for biochemical analysis and three for histological assessment.

2.7 Histological Analysis

For histological analysis, prefrontal cortical tissues were fixed in 10% formocalcium for at least 48 hours and processed using standard paraffin-embedding procedures. Sections of approximately 5 µm thickness were obtained and stained with H&E and Cresyl Violet.

H&E staining was used to assess general cortical cytoarchitecture, neuronal morphology, vacuolation, nuclear changes, and neuronal preservation. Cresyl Violet staining was used to assess Nissl substance and neuronal morphology, including evidence of chromatolysis, neuronal shrinkage, and degeneration. Sections were examined under a light microscope at ×40 and ×400 magnifications, and representative photomicrographs were obtained using a digital microscope camera.

2.8 Biochemical Analysis

Prefrontal cortical tissues designated for biochemical assessment were homogenized in ice-cold phosphate-buffered saline using a glass-Teflon homogenizer. The homogenates were centrifuged at 10,000 rpm for 15 minutes at 4°C, and the resulting supernatants were used for biochemical assays.

SOD activity was determined using a commercial assay kit according to the manufacturer's protocol and expressed as U/g tissue. Lipid peroxidation was assessed through MDA concentration using a commercial assay based on the thiobarbituric acid reactive substances method, with absorbance measured at 532 nm. Results were expressed in µM. SDH activity was determined using a commercial assay kit according to the manufacturer's protocol and expressed as µmol/min/g tissue.

2.9 Statistical Analysis

Data were expressed as mean ± standard error of the mean (SEM). Statistical analyses were performed using GraphPad Prism version 10. Differences among the six experimental groups were analysed using one-way analysis of variance (ANOVA), followed by Tukey's multiple-comparison test where appropriate. Primary comparisons included the control versus 5-FU-only groups, 5-FU-only versus the preventive, therapeutic, and prophylactic groups, and control versus rutin-only groups. A probability value of $p < 0.05$ was considered statistically significant.

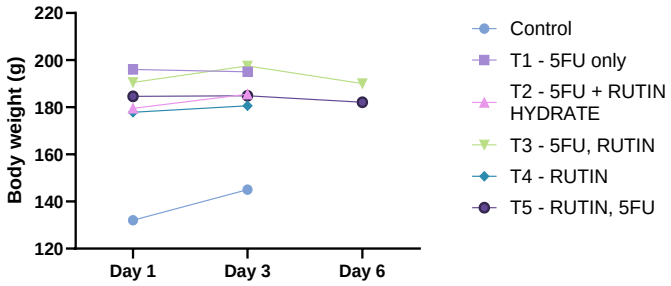
2.10 Source of Funding

The study was self-funded by the researcher.

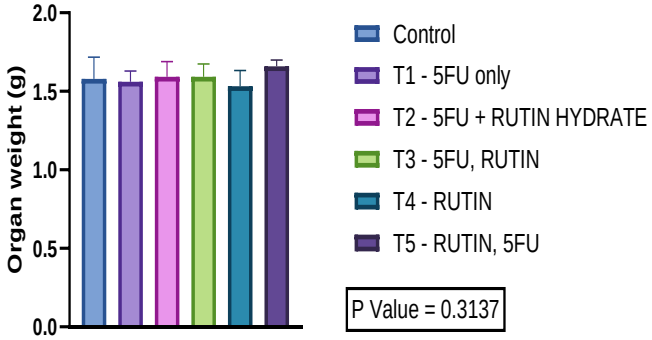
3. Results

3.1 Body Weight and Brain Weight

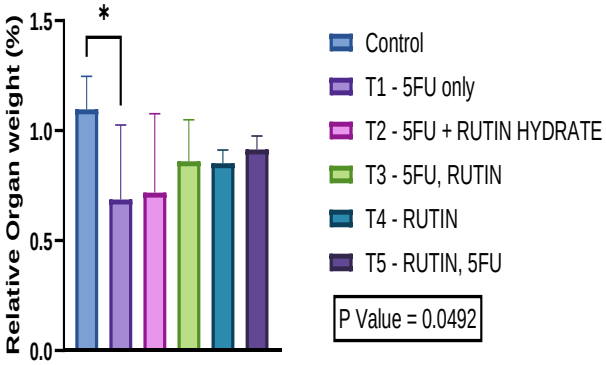
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Changes in body weight varied among the experimental groups. The control group showed an increase in body weight between Day 1 and Day 3, whereas the 5-FU-only group showed a slight reduction. The preventive group demonstrated an increase during the treatment period, while the rutin-only group showed a slight increase. The therapeutic group increased between Day 1 and Day 3 but subsequently decreased by Day 6. The prophylactic group remained relatively stable during the initial treatment period and showed a slight reduction by Day 6.

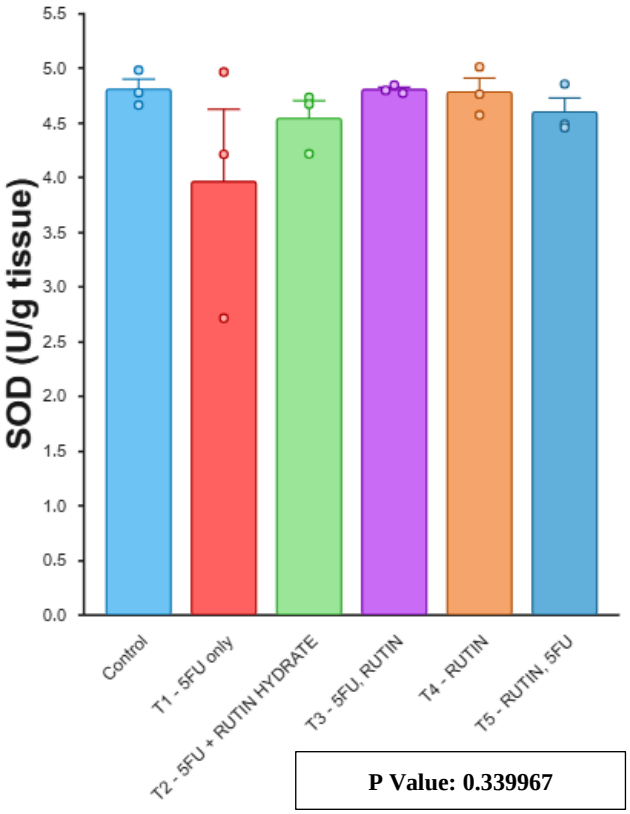


Absolute brain weight did not differ significantly among the experimental groups (p = 0.3137). The prophylactic group had the highest mean absolute brain weight, whereas the rutin-only group had the lowest mean value; however, these differences were not statistically significant.



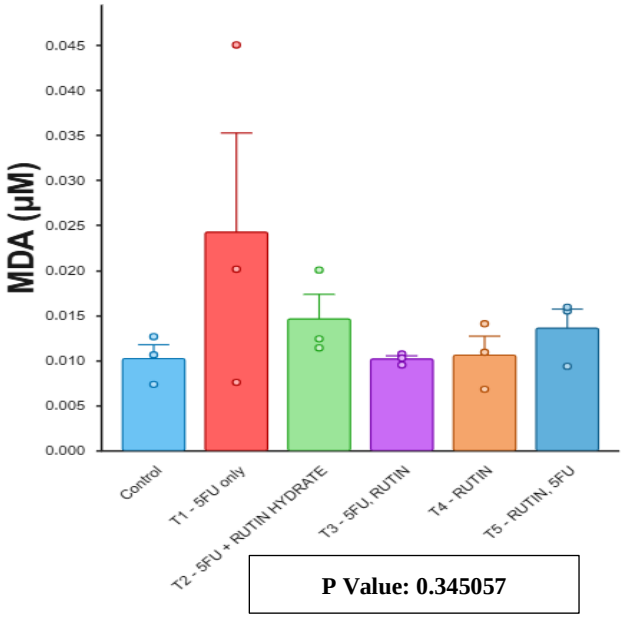
Relative brain weight differed significantly among the experimental groups (p = 0.0492). Tukey's multiple-comparison analysis showed that the 5-FU-only group had a significantly lower relative brain weight than the control group ($p < 0.05$). The preventive, therapeutic, rutin-only, and prophylactic groups showed higher relative brain weights than the 5-FU-only group, although these pairwise differences were not statistically significant.

3.2 Biochemical Markers



3.2.1Succinate Dehydrogenase

The 5-FU-only group exhibited the lowest mean SDH activity. The preventive, therapeutic, rutin-only, and prophylactic groups showed higher SDH activities than the 5-FU-only group, with values generally comparable with the control group. However, the overall difference among groups was not statistically significant (p = 0.3400).

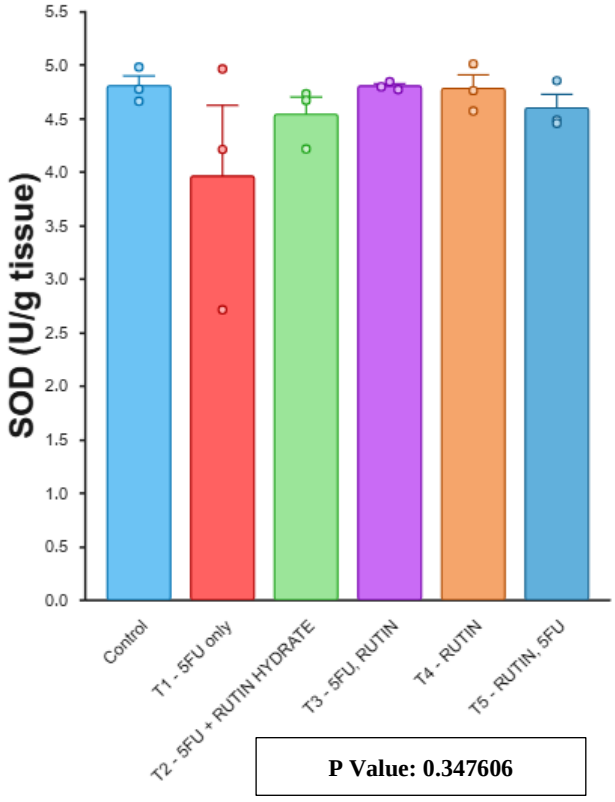


3.2.2Malondialdehyde

The 5-FU-only group demonstrated the highest mean MDA concentration. The preventive, therapeutic, rutin-only, and

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prophylactic groups exhibited comparatively lower MDA concentrations, with the therapeutic group recording a value closest to that of the control group. These differences were not statistically significant (p = 0.3451).



3.2.3Superoxide Dismutase

The 5-FU-only group showed the lowest mean SOD activity. The preventive, therapeutic, rutin-only, and prophylactic groups demonstrated relatively higher SOD activities, with values comparable with the control group. The observed differences were not statistically significant (p = 0.3476).

3.3 Histological Findings

*3.3.1*Haematoxylin and Eosin

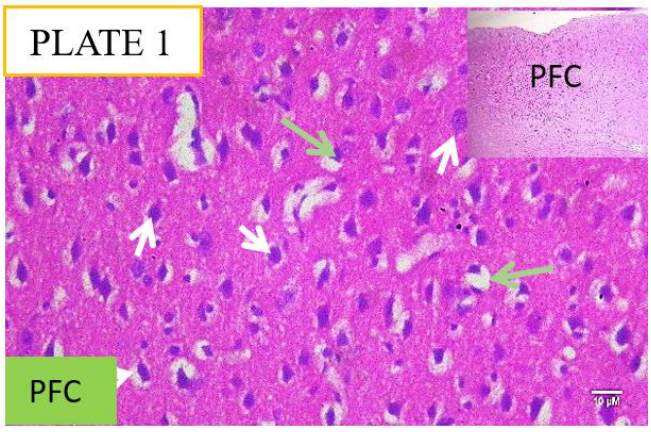


Plate 1 (Control Group):

The control group demonstrated preserved prefrontal cortical architecture with little or no vacuolation and healthy-appearing pyramidal (green arrows) and stellate neurons (white arrows). No obvious axonal degeneration or gliotic changes were observed.

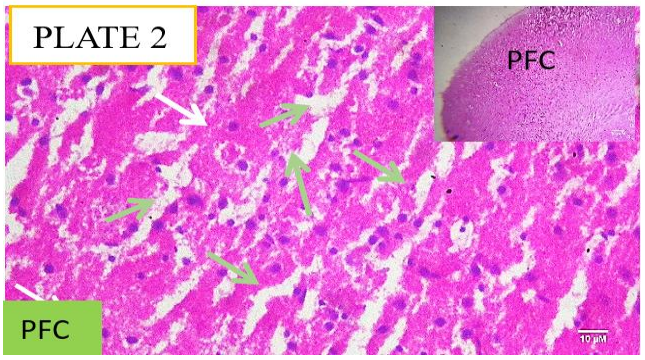


Plate 2 (Toxic Group):

The 5-FU-only group showed marked disruption of cortical architecture, extensive cytoplasmic vacuolation (green arrows), and reduced preservation of healthy neurons (white arrows).

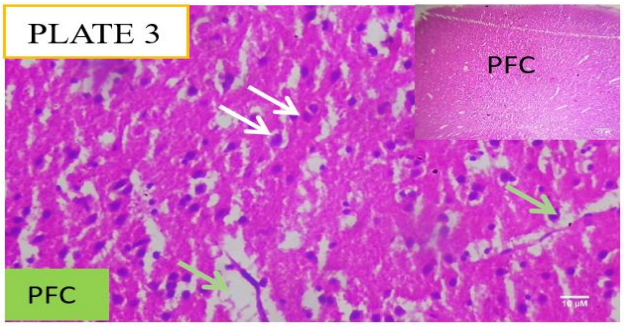


Plate 3 (Preventive Group):

The preventive group showed numerous healthy neurons with relatively preserved morphology (white arrows), although moderate vacuolation was observed (green arrows).

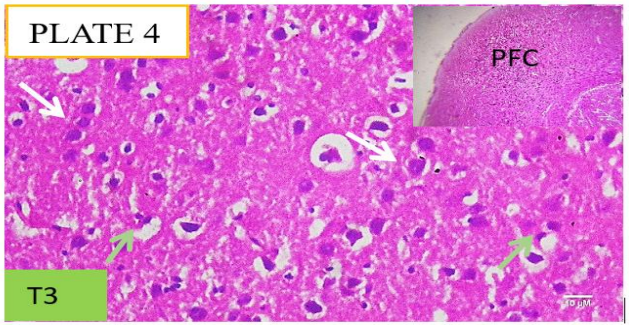


Plate 4 (Therapeutic Group):

The therapeutic group showed numerous healthy neurons (white arrows) and improved cortical organization, with mild-to-moderate vacuolation (green arrows) that appeared less extensive than in the 5-FU-only group.

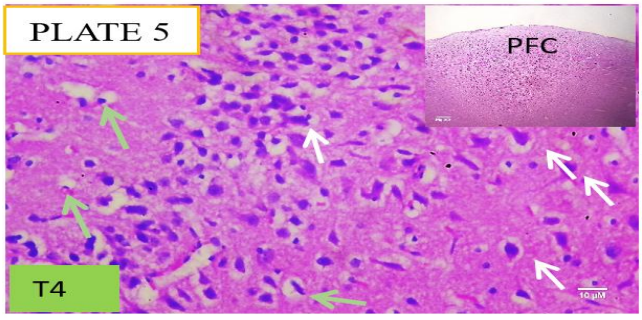


Plate 5 (Treatment Group):

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The rutin-only group showed numerous healthy neurons (white arrows), preserved neuronal morphology, and generally normal cortical architecture, with occasional vacuolation (green arrows) comparable to the control group.

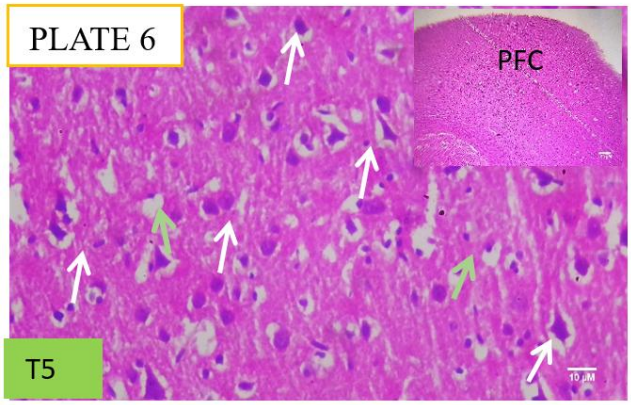


Plate 6 (Prophylactic Group):

The prophylactic group showed numerous healthy neurons (white arrows) and mild vacuolation (green arrows), with better preservation of cortical architecture than the 5-FU-only group.

3.3.2 **Cresyl Violet**

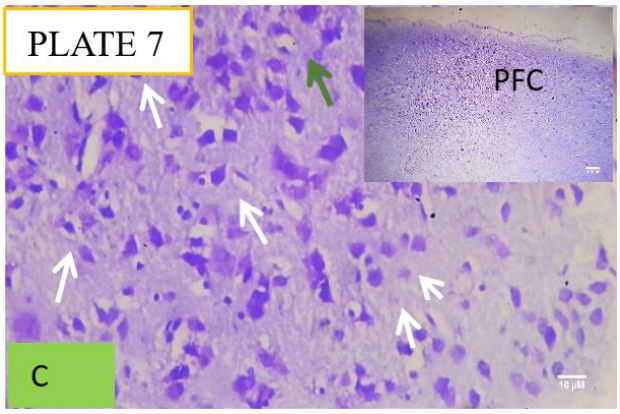


Plate 7 (Control Group):

The control group showed numerous healthy neurons (white arrows) with well-preserved morphology, intense staining, and abundant Nissl substance. Few scattered vacuolated areas (green arrows) were observed.

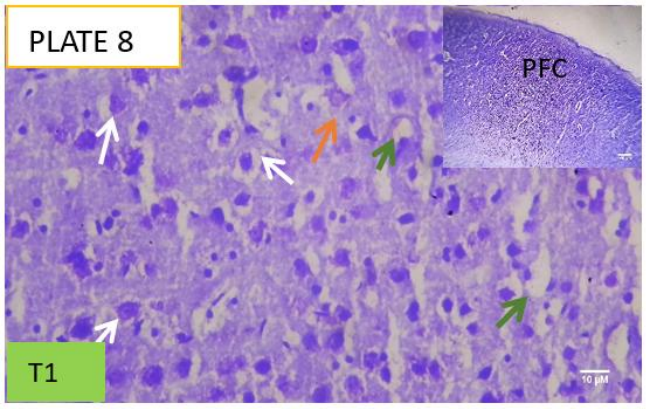


Plate 8 (Toxic Group):

The 5-FU-only group demonstrated reduced staining intensity, numerous vacuolated areas (green arrows), and chromatolytic (orange arrow) neuron associated with loss of Nissl substance.

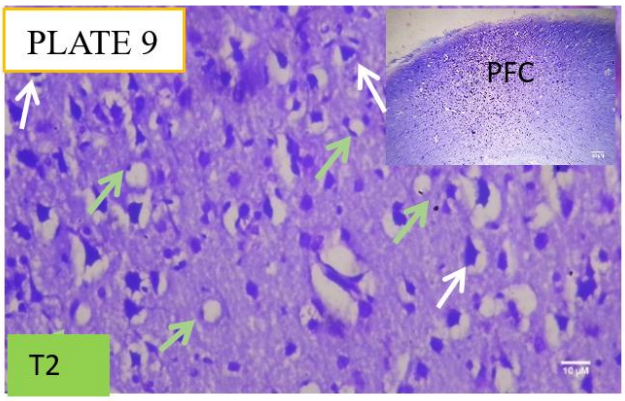


Plate 9 (Preventive Group):

The preventive group demonstrated numerous healthy neurons (white arrows) with relatively preserved Nissl substance and moderate vacuolation (green arrows), without obvious chromatolytic neurons.

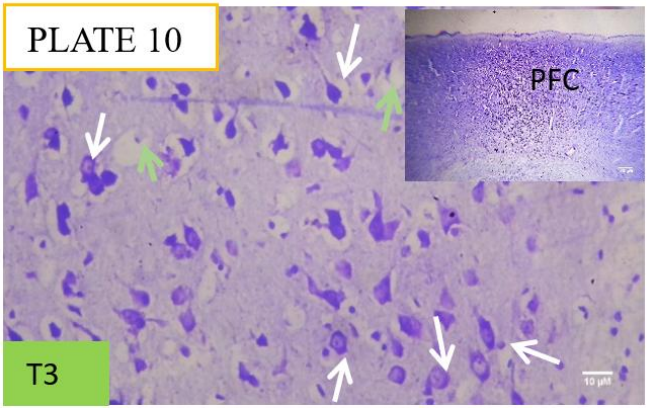


Plate 10 (Therapeutic Group):

The therapeutic group showed numerous healthy neurons (white arrows), improved staining, and better preservation of Nissl substance, with mild vacuolation (green arrows).

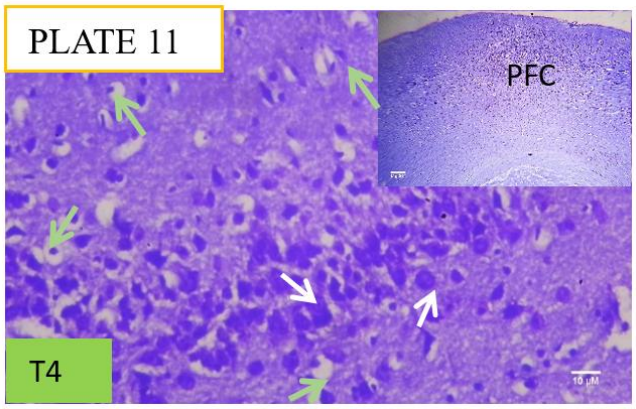


Plate 11 (Treatment Group):

The rutinonly group demonstrated well-preserved neurons (white arrows), intense staining, and normal distribution of Nissl substance, with occasional vacuolation (green arrows) comparable with the control group.

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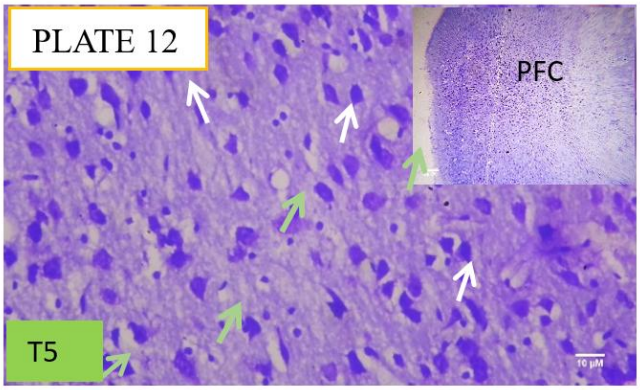


Plate 12 (Prophylactic Group):

The prophylactic group showed numerous healthy neurons (white arrows) and relatively preserved Nissl substance, with moderate vacuolation (green arrows) and no obvious chromatolytic neurons. H&E and Cresyl Violet photomicrographs were obtained at ×40 and ×400 magnifications.

4. Discussion

4.1 Effects of 5-Fluorouracil and Rutin Hydrate on Body Weight and Brain Weight

Body weight provides a useful general indicator of physiological status and systemic toxicity in experimental animals. In the present study, the 5-FU-only group showed a slight reduction in body weight, whereas the control group showed an increase during the corresponding treatment period. This pattern is consistent with reports that 5-FU administration can produce systemic effects capable of influencing nutritional status and body weight (Subramaniam et al., 2022; Suwannakot et al., 2021; Zhou et al., 2023). Similar alterations have also been described in experimental investigations of 5-FU-associated oxidative and neurological toxicity (Oresanya et al., 2025).

The rutin-treated groups generally demonstrated more favourable descriptive body-weight patterns than the 5-FU-only group. However, these observations should not be interpreted as evidence of a statistically confirmed effect because the present analysis did not establish significant treatment-related differences in body weight. The relatively stable pattern observed in the rutin-only group also provides no indication from the present study of an obvious adverse effect of the treatment on general body status.

Absolute brain weight did not differ significantly among the experimental groups ($p = 0.3137$). This suggests that the observed neural alterations were not accompanied by substantial changes in gross brain mass. In contrast, relative brain weight showed a significant overall difference ($p = 0.0492$), with the 5-FU-only group having a significantly lower value than the control group. Although the rutin-treated groups had higher relative brain weights than the 5-FU-only group, these pairwise differences were not statistically significant.

The difference between absolute and relative brain-weight findings highlights the importance of considering both measures when evaluating organ effects. Changes in relative organ weight may occur in the context of alterations in overall body mass without corresponding changes in absolute organ mass.

4.2 Effects of 5-Fluorouracil and Rutin Hydrate on Prefrontal Cortex Histology

The histological findings provided the clearest morphological evidence of differences between the experimental groups. The control group demonstrated preserved cortical architecture and healthy neuronal morphology, whereas the 5-FU-only group showed marked disruption, extensive vacuolation, and reduced preservation of healthy neurons.

These findings are consistent with experimental evidence that 5-FU can produce neural injury through processes involving oxidative stress, neuroinflammation, and neuronal dysfunction (Subramaniam et al., 2022; Zhou et al., 2023). The presence of cortical vacuolation and altered neuronal morphology in the present study indicates that structural alterations occurred following 5-FU exposure.

The rutin-treated groups generally demonstrated better preservation of neuronal morphology than the toxicant group. The preventive group showed moderate preservation, while the therapeutic group demonstrated improved cortical organization and less extensive vacuolation. The prophylactic group showed mild vacuolation and relatively preserved architecture. The rutin-only group displayed morphology broadly comparable to the control group.

Cresyl Violet staining provided additional evidence of neuronal preservation. The reduced staining intensity, loss of Nissl substance, and chromatolytic changes observed in the 5-FU-only group are compatible with neuronal injury. In contrast, the rutin-treated groups showed comparatively better preservation of Nissl substance and fewer obvious chromatolytic changes. These observations are broadly consistent with experimental reports of neuroprotective effects associated with rutin in other models of neurological injury (Nicola et al., 2024; Sreelatha et al., 2024).

Nevertheless, the histological assessment in the present study was qualitative rather than based on a standardized quantitative scoring system or morphometric analysis. Therefore, the observed morphological differences support an association with better structural preservation but should not be interpreted as a quantitative measure of the magnitude of neuroprotection.

4.3 Effects on Oxidative Stress and Mitochondrial Function

The biochemical findings showed consistent directional differences across the experimental groups. The 5-FU-only group had the lowest SOD activity, the highest MDA concentration, and the lowest SDH activity. The rutin-treated groups generally demonstrated higher SOD and SDH activities and lower MDA concentrations compared with the 5-FU-only group.

The lower SOD activity and higher MDA concentration observed after 5-FU exposure are directionally consistent with oxidative imbalance. Previous experimental studies have similarly implicated oxidative stress in 5-FU-associated neural injury (Suwannakot et al., 2021; Zhou et al., 2023). The higher MDA concentration in the toxicant group may therefore reflect increased lipid peroxidation, while the lower SOD activity may indicate reduced antioxidant defence.

Similarly, the lower SDH activity observed in the 5-FU-only group is directionally compatible with altered mitochondrial energy metabolism. Mitochondrial dysfunction is considered one of the

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mechanisms through which oxidative injury may contribute to neuronal damage.

Importantly, however, none of the differences in SOD ($p = 0.3476$), MDA ($p = 0.3451$), or SDH ($p = 0.3400$) reached statistical significance. These findings are directional trends rather than statistically demonstrated biochemical effects. Although the pattern is compatible with a possible beneficial influence of rutin hydrate on oxidative and mitochondrial parameters, the present study does not provide sufficient statistical evidence to establish this mechanism conclusively.

4.4 Relationship Between Histological and Biochemical Findings

The histological and biochemical findings showed broadly consistent patterns. The 5-FU-only group demonstrated the most pronounced structural abnormalities and also displayed the least favourable directional profile for SOD, MDA, and SDH. Conversely, the rutin-treated groups generally showed better morphological preservation accompanied by higher SOD and SDH activities and lower MDA concentrations than the toxicant group.

This convergence suggests that oxidative and mitochondrial disturbances may be associated with the structural changes observed in the prefrontal cortex. However, the absence of statistically significant differences in the biochemical measures means that a causal relationship cannot be established from the present data.

The findings also demonstrate the value of combining structural and biochemical assessments. Gross brain weight measurements did not show significant differences in absolute brain mass, whereas histological examination revealed clear differences in neuronal morphology. Thus, microscopic assessment may detect tissue alterations that are not reflected in gross organ measurements.

4.5 Implications, Limitations, and Future Directions

The findings provide preliminary evidence that rutin hydrate may have mitigatory potential against 5-FU-associated prefrontal cortical injury. The strongest evidence in the present study was morphological, based on the comparatively better preservation of cortical architecture and neuronal integrity in rutin-treated groups.

Several limitations should, however, be considered. The histological assessment was qualitative, and the biochemical evaluation was restricted to SOD, MDA, and SDH. In addition, inflammatory, apoptotic, molecular, and behavioural parameters were not assessed. These limitations restrict the extent to which the mechanisms and functional significance of the observed effects can be established.

Future studies should incorporate quantitative histomorphometry, a broader panel of oxidative stress and inflammatory biomarkers, assessment of apoptotic and neuroplasticity-related pathways, and behavioural or cognitive testing. Investigations comparing different doses and treatment schedules, together with longer follow-up periods, may also clarify the most effective timing of rutin administration.

5. Conclusion

The present study demonstrates that 5-fluorouracil administration was associated with alterations in the prefrontal cortex of adult Wistar rats, characterized by changes in body weight, reduced relative brain weight, marked neuronal vacuolation, reduced preservation of healthy neurons, and alterations in Nissl substance. The 5-FU-only group also showed directional reductions in superoxide dismutase and succinate dehydrogenase activities and an increase in malondialdehyde concentration, although these biochemical differences were not statistically significant.

Administration of rutin hydrate before, during, or after 5-FU exposure was associated with better preservation of prefrontal cortical morphology and more favourable directional changes in the assessed biochemical markers compared with 5-FU alone. Overall, the findings indicate that rutin hydrate has potential mitigatory activity against 5-FU-associated prefrontal cortical toxicity in adult Wistar rats. Further studies incorporating quantitative histomorphometry, additional molecular and biochemical markers, and behavioural assessments are required to clarify the mechanisms involved and determine whether the observed structural preservation translates into functional neuroprotection.

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Bibliography

1. Casale, J., & Patel, P. (2024). Fluorouracil. In *StatPearls*. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK549808/
2. Chafee, M. V., & Heilbronner, S. R. (2022). Prefrontal cortex. *Current Biology*, *32*(8), R346–R351. https://doi.org/10.1016/j.cub.2022.02.071
3. Hathaway, W. R., & Newton, B. W. (2023). Neuroanatomy, prefrontal cortex. In *StatPearls*. StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK499919/
4. Nicola, M. A., Attaai, A. H., Abdel-Raheem, M. H., Mohammed, A. F., & Abu-Elhassan, Y. F. (2024). Neuroprotective effects of rutin against cuprizone-induced multiple sclerosis in mice. *Inflammopharmacology*, *32*, 1295–1315. https://doi.org/10.1007/s10787-024-01442-x
5. Oresanya, M. E., Ehiremen, S. E., Alabi, A. O., Adejinmi, S. O., Abdusalam, M. K., Adelakin, L. A., Taiwo-Ola, D. O., Banjo, T. A., Amballi, A. A., Shallie, P. D., & Fakunle, P. B. (2025). *Nigella sativa* oil attenuates 5-fluorouracil-induced oxidative stress and anxiety-like behaviors in rats. *Asian Journal of Research and Reports in Neurology*, *8*(1), 187–197. https://doi.org/10.9734/ajorrin/2025/v8i1136
6. Paxinos, G., & Watson, C. (2006). *The rat brain in stereotaxic coordinates* (6th ed.). Academic Press.
7. Sreelatha, I., Choi, G.-Y., Lee, I.-S., Inturu, O., Lee, H.-S., Park, Y.-N., Lee, C.-W., Yang, I., Maeng, S., & Park, J.-H. (2024). Neuroprotective properties of rutin hydrate against scopolamine-induced deficits in BDNF/TrkB/ERK/CREB/Bcl2 pathways. *Neurology*

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International, *16*(5), 1094–1111. https://doi.org/10.3390/neurolint16050082

8. Subramaniam, C. B., Wardill, H., Davies, M. R., Heng, V., Gladman, M., & Bowen, J. (2022). 5-Fluorouracil induces an acute reduction in neurogenesis and persistent neuroinflammation in a mouse model of the neuropsychological complications of chemotherapy. *Molecular Neurobiology*, *60*, 1408–1424. https://doi.org/10.1007/s12035-022-03136-3
9. Suwannakot, K., Sritawan, N., Prajit, R., Aranarochana, A., Sirichoat, A., Pannangrong, W., Wigmore, P., & Welbat, J. U. (2021). Melatonin protects against the side-effects of 5-fluorouracil on hippocampal neurogenesis and ameliorates antioxidant activity in an adult rat hippocampus and prefrontal cortex. *Antioxidants*, *10*(4), 615. https://doi.org/10.3390/antiox10040615
10. Zhou, P., Wang, Z., Chen, C., Famurewa, A. C., & Olatunji, O. J. (2023). Naringin ameliorates 5-fluorouracil-elicited neurotoxicity by curtailing oxidative stress and iNOS/NF-κB/caspase-3 pathway. *Open Chemistry*, *21*(1), 20230126. https://doi.org/10.1515/chem-2023-0126

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