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Protective Effect of Hirsutidin against Rotenone-Induced Parkinsonism via Inhibition of Caspase-3/Interleukins-6 and 1β

Muhammad Shahid Nadeem, Jalaluddin Azam Khan, Fahad A. Al-Abbasi, Shareefa A. AlGhamdi, Amira M. Alghamdi, Nadeem Sayyed,* Gaurav Gupta, and Imran Kazmi*

Cite This: *ACS Omega* 2023, 8, 13016−13025

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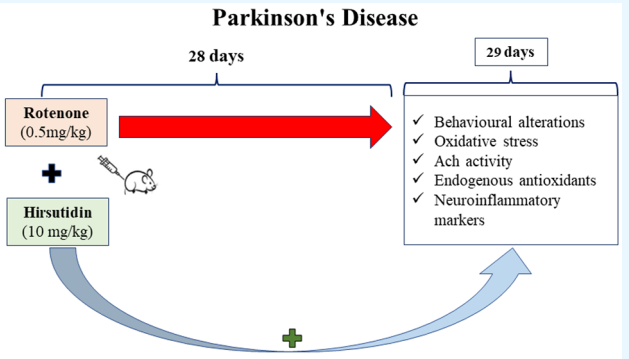
ABSTRACT: A participant of the chemical family recognized as anthocyanins, hirsutidin is an *O*-methylated anthocyanidin. It is a natural substance, i.e., existing in *Catharanthus roseus* (Madagascar periwinkle), the predominant component in petals, as well as callus cultures. The literature review indicated a lack of scientifically verified findings on hirsutidin's biological activities, particularly its anti-Parkinson's capabilities. Using the information from the previous section as a reference, a present study has been assessed to evaluate the anti-Parkinson properties of hirsutidin against rotenone-activated Parkinson's in experimental animals. For 28 days, rats received hirsutidin at a dose of 10 mg/kg and rotenone at a dose of 0.5 mg/kg s.c. to test the neuroprotective effects. The hirsutidin was given 1 h before the rotenone. Behavioral tests, including the rotarod test, catalepsy, Kondziela's inverted screen activity, and open-field analysis, were performed. The levels of neurotransmitters (5-HT, DOPAC, 5-HIAA, dopamine, and HVA), neuroinflammatory markers (TNF-α, IL-6, IL-1β, caspase-3), an endogenous antioxidant, nitrite content, and acetylcholine were measured in all the rats on the 29th day. Hirsutidin exhibited substantial behavioral improvement in the rotarod test, catalepsy, Kondziela's inverted screen activity, and open-field test. Furthermore, hirsutidin restored neuroinflammatory markers, cholinergic function, nitrite content, neurotransmitters, and endogenous antioxidant levels. According to the study, hirsutidin has anti-inflammatory and antioxidant characteristics. As a result, it implies that hirsutidin may have anti-Parkinsonian effects in rats.



1. INTRODUCTION

Parkinson's disease (PD) symptoms include central nervous system disturbances that are chronic, severe, delayed-onset, degenerative disorders. The major factor causing this condition is neurodegeneration of the dopaminergic system, which results in the downregulation of dopamine (DA) and an imbalance between the concentrations of acetylcholine and dopamine.[1] Numerous current therapy modalities reveal a failed recovery in Parkinson's patients as a result of the disease's incredibly complex nature.[2] PD is characterized by long-lasting euro-progressive cardinal indications, such as bradykinesia, tremors, postural disproportion, and muscular stiffness, as well as secondary symptoms like a disturbance in gait, poor walking, and difficulties speaking. The treatments that are currently available greatly reduce the motor symptoms of early stage PD but eventually lose their effectiveness.[3] As more individuals approach the middling age for the beginning of PD and the illness affects 12 million people globally by 2040, the disease's prevalence will ideally increase in the ensuing decades. The utmost important features are genetics (PINK1, PARK1, Parkin genes), gender (men are more affected), and age, but the risk of PD also appears to be related to increased exposure to environmental adulteration (pesticides, metals, and solvents) as a result of the world's growing industrialization.[4,5] The primary pathogenic condition that occurs alongside mitochondrial failure is PD. Reactive oxygen species (ROS) were produced as an outcome of increased oxidative damage brought by dopaminergic loss. The ROS produced interferes with mitochondrial activity and leads to protein misfolding, which damages cells and induces apoptosis.[6,7]

Rotenone is a good validity paradigm, preventing the NADH complex-I of the electron transport chain from functioning affecting mitochondrial degradation.[8,9] Rotenone exposure for an extended period of time causes PD-like symptoms in

Received: January 11, 2023
Accepted: March 16, 2023
Published: March 29, 2023

https://doi.org/10.1021/acsomega.3c00201
ACS Omega 2023, 8, 13016−13025

humans. When administered to rats *in vivo*, rotenone causes neurological and behavioral changes that lead to PD. Numerous pathways, including altered calcium signaling, mitochondrial malfunction, oxidative damage, accumulation of α -synuclein, and cell death, are linked to rotenone. Rotenone, an inducer, caused motor impairments and neural symptoms that repeat in clinical PD.[10,11]

Currently, a wide range of medication alternatives is available for the treatment of PD, including catecholamine-*O*-methyltransferase inhibitors, anticholinergic drugs, dopamine agonists, L-dopa, and monoamine oxidase inhibitors. The actual therapy for PD symptoms is L-dopa, which is considered to be the gold standard.[12,13] L-Dopa, however, requires carbidopa to pass the blood−brain barrier (BBB) because it has adverse properties and peripheral degradation that prevent it from doing so on its own. There are currently more safe and effective options available because these medications would help PD sufferers with their symptoms.[14,15]

Anthocyanins are reddish-blue plant flavonoids that are mostly found in higher plants' blooms and fruits. These polyphenols contribute to the pigments of fruits, vegetables, and flowers.[16] There are several anthocyanin flavonoid pigments in nature, and studies have demonstrated that they have antioxidant properties.[17] It is believed that this skill serves as a protection against variability of illnesses brought on by ROS.[17] According to studies, dietary foods high in anthocyanins have positive impacts on several health issues, including cardiovascular health,[18,19] diabetes,[20] obesity,[20,21] bacterial infection,[22] cancer,[23] eye health,[24] and neurotoxicity.[25]

A member of the chemical family known as anthocyanins, hirsutidin is an *O*-methylated anthocyanidin. It is a natural substance, i.e., existing in *Catharanthus roseus* (Madagascar periwinkle), the predominant component in petals, as well as callus cultures. The literature review indicated a lack of scientifically verified findings on hirsutidin's biological activities, particularly its anti-Parkinson's capabilities. Using the information from the previous section as a reference, a recent study has been assessed to evaluate the anti-Parkinson's properties of hirsutidin against rotenone-activated Parkinson's in experimental animals.

Another study showed the hepatoprotective properties of hirsutidin by attenuating alcohol-induced oxidative stress in rodents[26] and the antiulcer consequence of hirsutidin against ethanol-induced ulcers in rats via regulation of antioxidant mechanisms.[20] There is no clear mechanistic role of hirsutidin but due to its strong antioxidant property, it may be essentially used in treating the disorders. Current orthodox treatments for PD are inadequate, presenting some demerits, hence it is necessary to identify potential components from the natural origin for the treatment of neurodegenerative diseases, such as PD.

2. METHODS

2.1. Drugs and Reagents. Sigma-Aldrich, USA, provided the rotenone and other chemicals acquired from authenticate sources were of analytical quality. Hirsutidin was received as a gifted from SRL, India. Rat enzyme-linked immunosorbent assay (ELISA) kit analysis of tumor necrosis factor-α (TNF-α), interleukins-1β (IL-1β), IL-6, and caspase-3 (MyBioSource, USA) were used to quantity.

2.2. Animals. For testing, 180 ± 20 g male Wistar rats were purchased and housed in a standard lab environment at 24 °C and RH of 50−60%. All the rats received an unlimited supply of water and pellet food throughout the operation. The rats were housed in polypropylene cages that were 28 × 21 × 14 cm. Before the start of the trial, animals had a 10-day acclimation phase. The rats utilized in the study underwent no prior surgeries. Rats were randomized into 5 clusters (n = 6 each). The experimental plan kept the regular circadian cycle and its impact on the outcomes. Before conducting, the present study established support from the institutional animal ethics committee (IAEC/TRS/PT/022/018), and it followed the ARRIVE recommendations.

2.3. Experimental Protocol. There were 24 rats used and grouped in four cages (n = 6).

- **Group I** received normal saline.
- **Group II** received as a rotenone control for 28 days at a dose of 0.5 mg/kg s.c.[27,28]
- **Group III** received hirsutidin at 10 mg/kg/day respectively for 28 days 1 h prior to rotenone at 0.5 mg/kg s.c.
- **Group IV** received hirsutidin per se at 10 mg/kg/day respectively for 28 days.

On the 29th day, behavioral tests were conducted and animals were sacrificed for further neurochemical estimation.

2.4. Behavioral Parameters. *2.4.1. Rotarod Test.* The test was employed to assess posture, coordination, and motor skills. Each rat was trained individually by being placed on a hanging rod that rotated for 60 s at a speed of 5−20 rpm (25−30 rpm). After the medication was administered, the test was performed again on the treated rats. The animals were free to move around on the rod, and the moment each animal fell was recorded. A 180 s should be the absolute maximum for one animal on the rod.[29]

2.4.2. Catalepsy. The rat was subjected to a catalepsy test by having 1 forepaw on a parallel plank that was 9 cm overhead the ground and the other forepaw on a stage that was 3 cm high. Any movement's time of occurrence is noted. The test is scored according to the following three steps, which are performed in that order:

- **Step 1:** As the rat was positioned on a level table and moved normally, it received a score of 0, and when it moved slightly upon gentle contact or otherwise stayed still, it received a score of 0.5.
- **Step 2:** A score of 0.5 was awarded if the hind paw did not move within 10 s while it was kept on a 3 cm high box.
- **Step 3:** A 9 cm wooden plank was used to support only one of the hind paws while leaving the other unsupported. For a stiffness measurement that was completed in 10 s, a score of 1 was given. A score of 3.5 was given to the rat that had total catalepsy (stiffness). Rats were positioned with their front paws on the hardwood surface in a half-rearing place. It was scheduled how long the rats took to maintain their posture on the wooden bar using just their two hindlimbs. To assess the passing of time and compare each rat's performance, the sessions were videotaped. Each rat had a predetermined cutoff time of 3 min.[30−32]

2.4.3. Kondziela's Inverted Screen Activity. An animal's muscular strength was measured through the Kondziela test using its four limbs.[33] The rat was tested by positioning it in the center of an inverted screen for 120 s. It was noted when the rat dropped from the screen.

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ACS Omega 2023, 8, 13016−13025

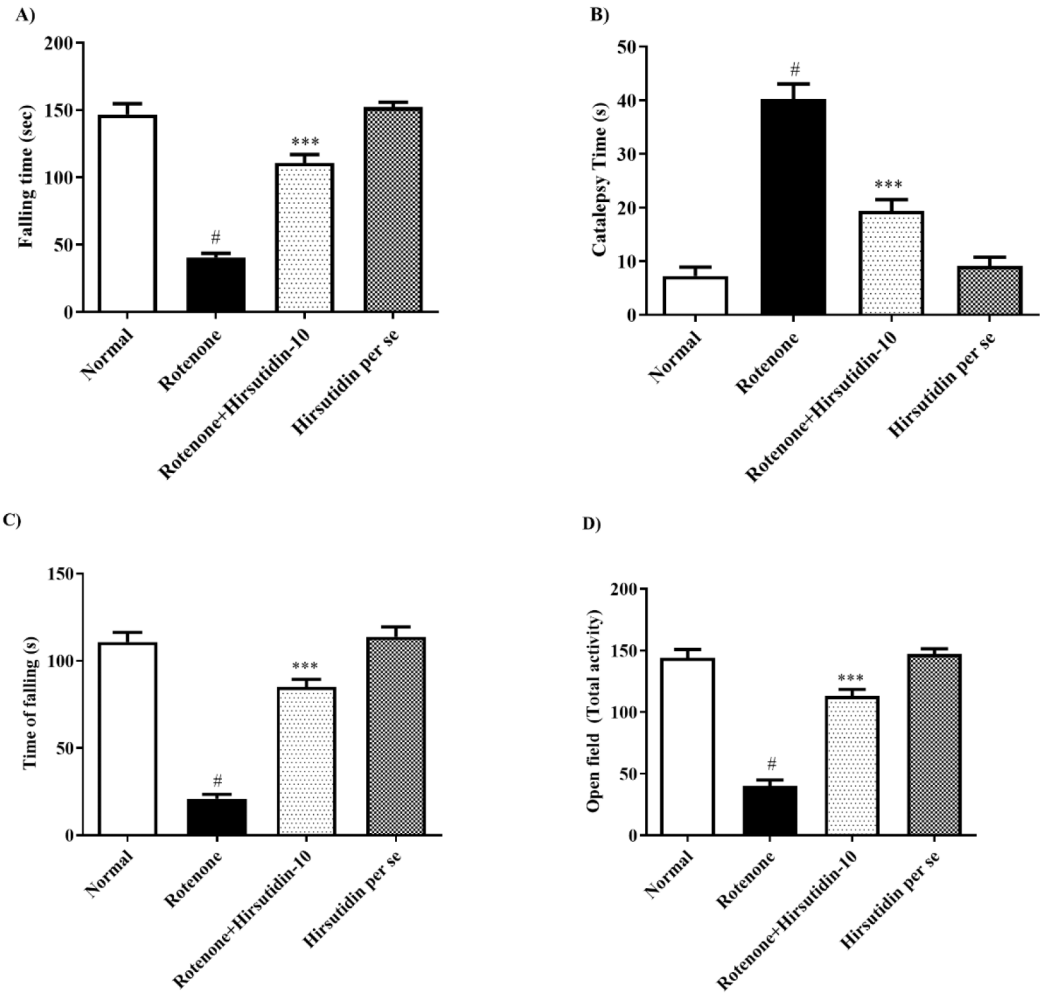

Figure 1. (A–D) Effects of hirsutidin in rotenone-injected rats on (A) Rotarod test, (B) Catalepsy, (C) Kondziela's inverted screen test, (D) Open-field test. Mean ± SEM (n = 6). #p < 0.05 vs normal, ***p < 0.0001 vs rotenone control. One-way ANOVA was followed by Tukey's test.

2.4.4. Open-Field Analysis. There were 25 squares (20 × 20 cm) on a rectangular open field with a cloth-covered floor. A locomotor activity study was conducted on rats kept in the middle square. The rat was allowed to measure a distance, no rearing was done, time was recorded by starting location, and the numeral of admissions was counted in the center square. Total movement was calculated.[34]

2.5. Neurochemical Analysis. *2.5.1. Homogenization of Brain Tissue.* On the 29th day, immediately following a behavioral analysis, the rats were alienated to estimate the levels of neurochemicals, neurotransmitters, and neuroinflammatory indicators.

2.5.2. Acetylcholine (ACh) Activity. The technique defined by Batool et al. was used to evaluate the amount of ACh in the brain. An enzyme in the tissue model was inactivated by boiling it, releasing the bound ACh, which then interacts with ferric chloride. The brown color that resulted from this reaction was measured at 540 nm in comparison to the reagent blank. The amount of ACh present was measured as μmol/g of tissue.[35]

2.5.3. Malondialdehyde (MDA) Determination. To conduct the test, trichloroacetic acid, and TBARS solution are added to the isolated supernatant after which it is boiled for 90 min and chilled in ice-cold water. After centrifuging the mixture at 1500 × g for at least 15 min, the combination was measured spectrophotometrically at 532 nm. As μmol of MDA/g of the brain, the amount of MDA generated was indicated.[36]

2.5.4. Reduced Glutathione Assay (GSH). To determine the levels of GSH in the brain, an equivalent volume of brain homogenate is precipitated with 1 mL of trichloroacetic acid. Phosphate buffer solution (PBS) and the DTNB reagent (5–5′-dithio-bis(2-nitro-benzoic acid)) were added to the supernatant. A UV spectrophotometer was used to detect the absorbance at 412 nm. Plotting a standard curve allowed for the determination of the GSH concentration. The outcomes were shown as mg GSH/g of brain.[37]

2.5.5. Superoxide Dismutase (SOD) Activity. The obtained supernatant was combined with xanthine and xanthine oxidase before 30 min of incubation in potassium phosphate buffer. A blue formazan product was created by adding nitro blue tetrazolium to this mixture and mixing it thoroughly. This product's wavelength, 550 nm, was then measured spectrophotometrically. The amount of protein inhibiting 50% NBT reduction is used to compute one nitrite unit of SOD activity.[38]

2.5.6. Catalase Activity (CAT). A brain homogenate supernatant and phosphate buffer solution are included in the test combination (50 nM). Hydrogen peroxide (H_2O_2) was introduced to this combination, and the absorbance was

https://doi.org/10.1021/acsomega.3c00201
ACS Omega 2023, 8, 13016–13025

calculated spectrophotometrically at 240 nm once every 15 s. The activity was measured in micromoles per min/g of brain.[39]

2.5.7. Nitrite Content Assay. The amount of nitrite produced is a result of the oxidative stress the brain experiences. Using a UV spectrophotometer, an equal amount of brain homogenate and Griess reagent (a mixture of sulphanilamide, *N*-1-naphthyl ethylenediamine dihydrochloride, in phosphoric acid) were incubated for 10 to 15 min.[40,41]

2.5.8. Neurotransmitter Levels. HPLC was used to determine the concentrations of neurotransmitters, such as dopamine (DA), serotonin (5-HT), 5-hydroxy indole acetic acid (5-HIAA), and their corresponding metabolites, 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA).

2.5.9. Biological Markers of Inflammation. The levels of cytokines, such as IL-1β, IL-6, TNF-α, and caspase 3, were assessed using ELISA kit. The IL-1β, TNF-α, and IL-6 marker concentrations were expressed in pg/mL, and caspase 3 was detected in ng/mL.

2.6. Statistical Analysis. The outcomes of the ensuing techniques were calculated as mean ± SEM. An analysis of variance (ANOVA) was used in this study, and a normality test (Shapiro–Wilk test) was used to confirm its validity (Graph Pad Prism Software Version 8.0.1). For the analysis of the data, a one-way ANOVA followed by Tukey's *post hoc* test was conducted for comparisons of groups. A statistically significant was found at $P < 0.05$.

3. RESULTS

3.1. Behavioral Effects of Hirsutidin. *3.1.1. Rotarod Test.* When compared to the controls, the rotenone group significantly reduced ($p < 0.05$), the latency period. As compared with a group that had been exposed to rotenone, the hirsutidin (10 mg/kg dose) treated animals had a longer [$F(3, 20) = 81.08$; $P < 0.0001$] latency time (Figure 1A). Hirsutidin per se did not change significantly.

3.1.2. Catalepsy. When compared to the controls, the rotenone control group significantly increased ($p < 0.05$) the catalepsy period. As compared with the rotenone control group, the hirsutidin treated group lowered [$F(3, 20) = 51.24$; $P < 0.0001$] the catalepsy period (Figure 1B). There were no significant changes in hirsutidin per se.

3.1.3. Kondziela's Inverted Screen Activity. Rats were monitored using Kondziela's inverted screen test (Figure 1C). Based on one-way ANOVA analysis, treatment significantly affected muscular strength. In the rotenone control group, the time of falling meaningly downregulation was associated with the normal group ($p < 0.05$). When associated with the rotenone control group, hirsutidin-treated groups (10 mg/kg) had significantly longer times to fall [$F(3, 20) = 84.78$; $P < 0.0001$] than rotenone-treated groups. Hirsutidin per se did not show any significant changes.

3.1.4. Open-Field Test. To monitor locomotor activity, the open-field paradigm was used (Figure 1D). When compared to control rats, overall activity was considerably lower after rotenone administration ($p < 0.05$). Overall activity was markedly greater in the hirsutidin (10 mg/kg) -treated groups associated with the rotenone group [$F(3, 20) = 81.87$; $P < 0.0001$]. Not any noteworthy variations were detected in hirsutidin per se.

3.2. Analysis of Neurochemicals. *3.2.1. ACh Activity.* When compared to the controls, rotenone treatment significantly raises ($p < 0.05$) the ACh level. As associated with the rotenone cluster, hirsutidin treatment caused a substantial decrease [$F(3, 20) = 10.35$; $P < 0.0001$] in ACh activity (Figure 2). In the hirsutidin per se group, no significant changes were observed.

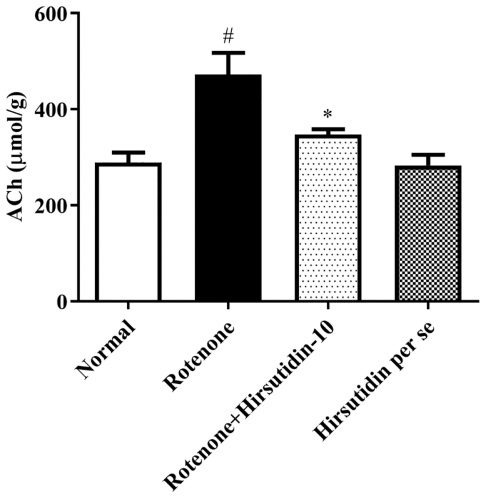

Figure 2. Inhibition of Ach by hirsutidin in rotenone-injected rats. Mean ± SEM ($n = 6$). #$p < 0.05$ vs normal, *$p < 0.05$ vs rotenone control. One-way ANOVA was followed by Tukey's test.

3.2.2. Endogenous Antioxidant Determination. While compared to controls, the rotenone control group significantly increased ($p < 0.05$) the MDA level. Comparing the hirsutidin-treated group to the rotenone control group, the hirsutidin at a dose of 10 mg/kg reduced [$F(3, 20) = 23.40$; $P < 0.0001$] the MDA level (Figure 3A).

The amount of GSH in the rotenone-induced group was notably low ($p < 0.05$). When associated with the rotenone control group, treatment with hirsutidin knowingly increased [$F(3, 20) = 19.12$; $P < 0.0001$] the level of GSH (Figure 3B).

SOD levels in the rotenone-the group was extremely low ($p < 0.05$). In comparison to the rotenone group, therapy with hirsutidin significantly increased [F (3, 20) = 13.82; $P < 0.0001$] the level of SOD (Figure 3C).

CAT levels in the rotenone-induced group were exceptionally low ($p < 0.05$). When compared to the rotenone group, treatment with hirsutidin considerably raised [F (3, 20) = 5.629; $P < 0.0001$] the level of CAT (Figure 3D). The level of hirsutidin per se did not change significantly.

3.3. Inhibition of Nitrite Content by Hirsutidin. The amount of nitrite concentration was noticeably higher ($p < 0.05$) in the rotenone-induced group. When associated with the rotenone group, treatment with hirsutidin considerably restored [$F(3, 20) = 72.61$; $P < 0.0001$] the amount of nitrite content (Figure 4).

3.4. Hirsutidin Effect on Neurotransmitters. When compared to normal animals, the effects of rotenone treatment on dopamine, DOPAC, HVA, 5-HIAA, and 5-HT levels were noticeable ($p < 0.05$). When associated with the rotenone group, the hirsutidin-treated group markedly augmented the levels of dopamine [$F(3, 20) = 58.73$; $P < 0.0001$], DOPAC [$F(3, 20) = 23.07$; $P < 0.0001$], HVA [$F(3, 20) = 49.65$; $P < 0.0001$], 5-HIAA [$F(3, 20) = 20.28$; $P < 0.0001$], and 5-HT [$F(3, 20) = 59.49$; $P < 0.0001$] (Figure 5A–E).

3.5. Hirsutidin Affects Neuroinflammatory Markers. As associated with the control group, rotenone administration

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ACS Omega 2023, 8, 13016–13025

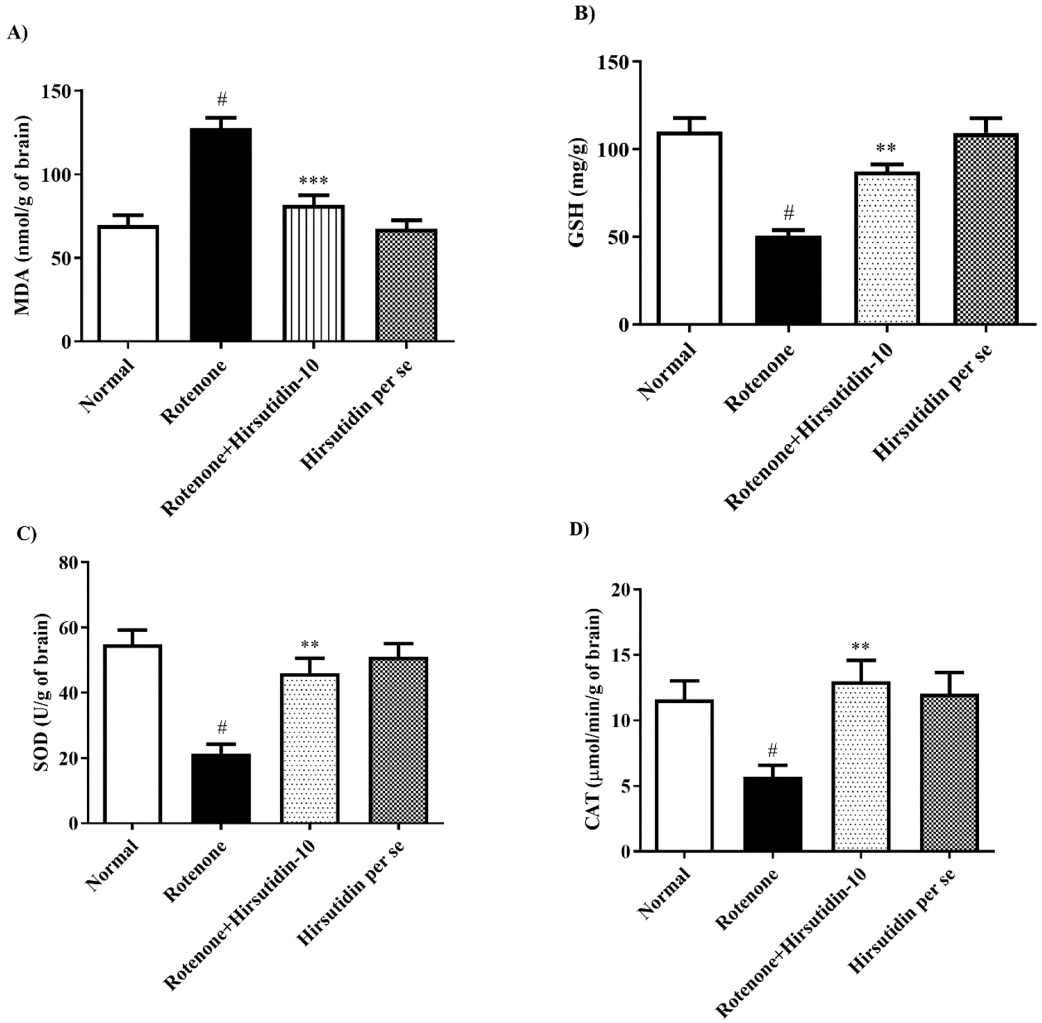

Figure 3. (A–D) Endogenous antioxidant following hirsutidin in rotenone-injected rats: (A) MDA, (B) GSH, (C) SOD, and (D) CAT. Mean ± SEM (n = 6). #p < 0.05 vs normal, *p < 0.05, **p < 0.001, ***p < 0.0001 vs rotenone control. One-way ANOVA was followed by Tukey's test.

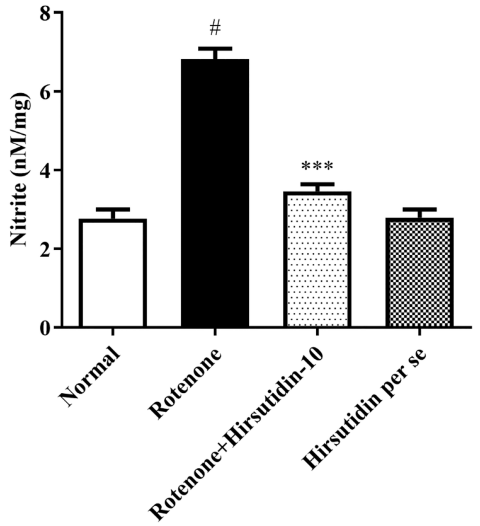

Figure 4. Hirsutidin inhibits nitrite content in rotenone-treated rats. Mean ± SEM (n = 6). #p < 0.05 vs normal, ***p < 0.0001 vs rotenone control. One-way ANOVA was followed by Tukey's test.

significantly raised the IL-1β, IL-6, TNF-α, and caspase-3 (p < 0.05). Comparing the hirsutidin-treated group to the rotenone-treated group, caspase-3 [F(3, 20) = 21.49; P < 0.0001], IL-1β [F (3, 20) = 57.92; P < 0.0001], IL-6 [F(3, 20) = 80.90; P < 0.0001], and TNF-α [F(3, 20) = 21.04; P < 0.0001] levels were considerably restored. (Figure 6A–D).

4. DISCUSSION

In this study, hirsutidin was evaluated for its ability to produce favorable effects on rotenone injections in rats by using behavioral and biochemical parameters, i.e., Ach activity, endogenous antioxidants, nitrites, neurotransmitters, and neuroinflammatory markers. A noncurable disorder, PD is characterized by a lack of neurotransmitters in SNPC.[42−44] PD is the slow progression to neuronal death, which is caused due to imbalance of dopamine and catecholamine in the nigrostriatal pathway.[44,45] Several rat paradigms have been developed for the evaluation of Parkinson's treatment. In rotenone-induced PD, behavioral patterns, antioxidant status, and neuroinflammatory markers deteriorated.[46,47] The prominent motor and nonmotor symptoms affect the multisystem, thus downregulating the functions of the nervous system.[48,49] The pathogenesis of PD is closely associated with oxidative stress generated ROS which led to neuroinflammation of

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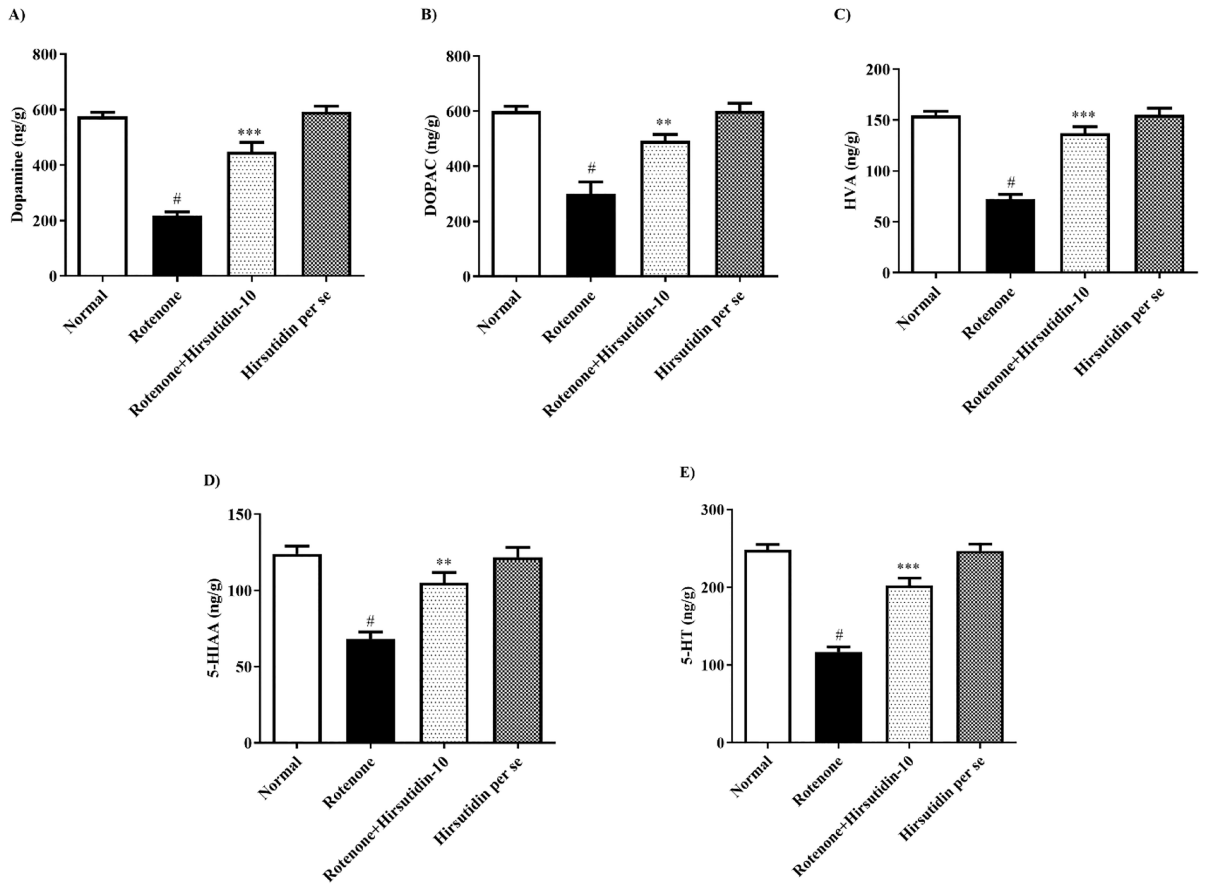

Figure 5. (A–E) Effects of hirsutidin on neurotransmitter levels in rotenone-treated rats: (A) Dopamine, (B) DOPAC, (C) HVA, (D) 5-HIAA, (E) 5-HT. Mean ± SEM ($n = 6$). #$p < 0.05$ vs normal, **$p < 0.001$, ***$p < 0.0001$ vs rotenone control. One-way ANOVA was followed by Tukey's test.

brain.[50] The available medication options have adverse effects and do not therapeutically resolve the condition.

A strong lipophilic mitochondrial complex inhibitor, rotenone is an extensively utilized pesticide. Rotenone can simply penetrate the BBB and mimic neurological, behavioral, and neuropathological alterations of PD.[5,51,52] Earlier investigation revealed that rotenone induction causes dopaminergic damage in the substantia nigra leading to memory deficits in rats.[53−55] In accordance with previous investigations, the present study has shown a downfall in the behavioral pattern, antioxidant status, and neuroinflammatory markers when rotenone was administered in rats for 28 days.[46,56,57] The dopaminergic loss alters the behavior causing impaired motor and nonmotor performance.[58−60] But treatment with hirsutidin at a dose (10 mg/kg) improved all the behavioral parameters, such as rotarod test, catalepsy, Kondziela's inverted screen activity, and open field paradigm compared to rotenone-induced group.

Numerous studies have revealed that the cholinergic system is essential for controlling brain processes like memory, learning, motor skills, and sleep.[37,61,62] ACh is hydrolyzed into acetic acid and choline by the enzyme acetylcholinesterase, which is mostly found in postsynaptic synapses.[63−65] The current study's findings also show that rotenone treatment significantly raises ACh activity, which is consistent with past publications.[66,67] Concurrently declining ACh activity causes an increase in synaptic acetylcholine, which is necessary to influence cognitive function.[68,69] According to our research, hisutidin administration to rats reduced ACh activity, limiting acetylcholine hydrolysis and conversion such that an adequate quantity of ACh could be present in the synaptic cleft.

Mitochondria is the main powerhouse for ROS generation and its dysfunction increases ROS production causing oxidative damage to the tissues.[70−72] The present study showed that rotenone is directly responsible for oxidative injury, which hinders the mechanistic function of antioxidant enzymes as reported in earlier studies.[73,74] The study displayed that hirsutidin corrected all the antioxidant enzymes including an increase in SOD, GSH, CAT activity, and catalase levels while reducing MDA levels, which was different from the rotenone administration group.

Neurotransmitters, especially dopamine, which is crucial for regulating functional motions and signal transmission, are mostly depleted by oxidative damage.[75−77] The outcomes of the present investigation exhibited that rotenone dramatically reduced dopamine levels and changed the concentrations of its metabolites, which was consistent with earlier results.[78,79] Neurotransmitters, such as 5-HT, dopamine, and 5-HIAA levels were elevated during therapy with hirsutidin, whereas DOPAC and HVA levels decreased, representing enhancement in neuronal and behavioral functioning and the antioxidant activity of hirsutidin in PD.[76,80]

Another factor contributing to PD is neuroinflammation. Neuronal inflammation is caused due to overexpression of the

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ACS Omega 2023, 8, 13016−13025

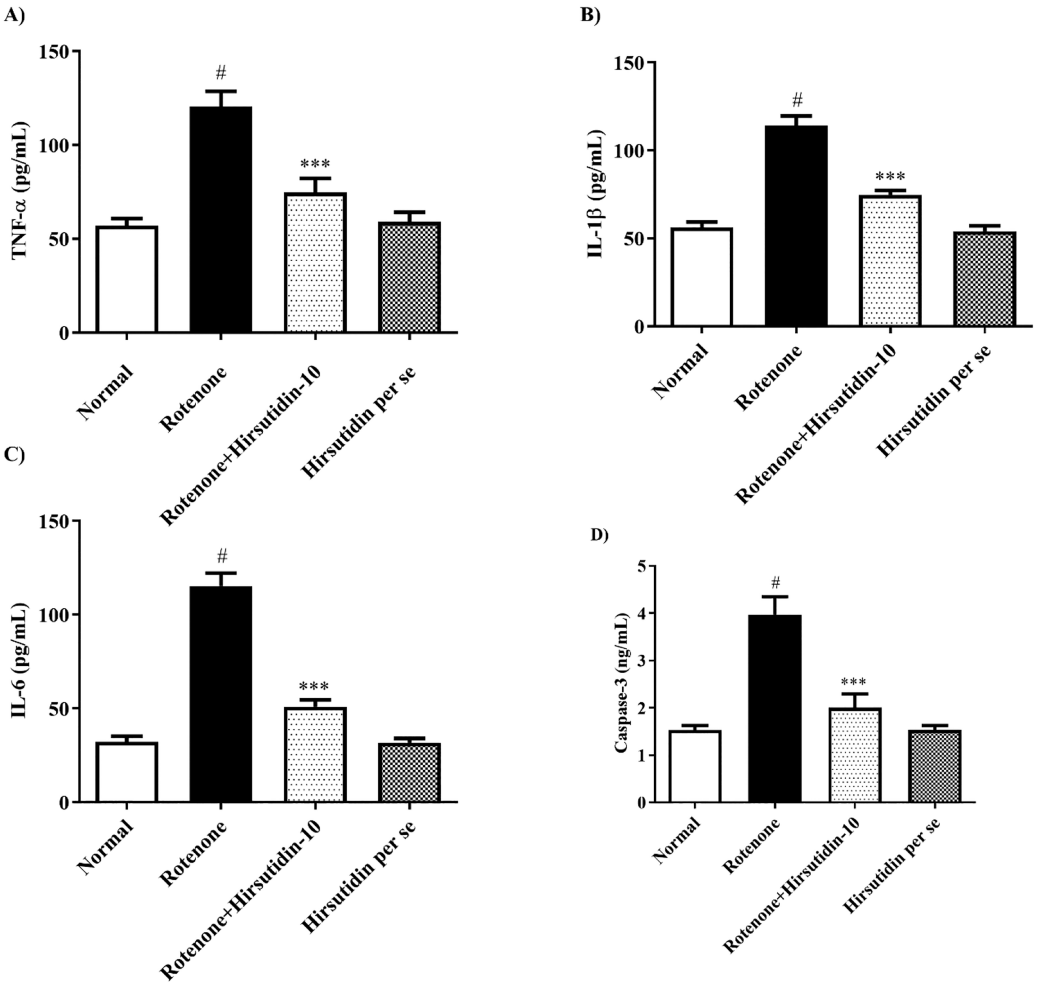

Figure 6. (A–D) Neuroinflammatory markers following hirsutidin in rotenone-injected rats: (A) TNF-α, (B) IL-1β, (C) IL-6, and (D) Caspase-3. Mean ± SEM (n = 6). #p < 0.05 vs normal, ***p < 0.0001 vs rotenone control. One-way ANOVA was followed by Tukey's test.

inflammatory cytokines, which activates the degenerative pathway leading to neuronal damage.[81,82] As mentioned in previous studies, rotenone showed upregulation in the cytokine levels and stimulation of caspase-3 as rotenone administration mains to neuronal inflammation.[83−85] The results indicated that hirsutidin at doses (10 mg/kg) attenuated rotenone-induced alterations by decreasing the cytokine levels including IL-6, IL-1ß, TNF-α, and caspase 3, which indicates its anti-inflammatory action.

These conclude that hirsutidin may also contribute to neuroprotective effects on rotenone-activated PD in a rodent paradigm by reducing oxidative stress and restoring neurotransmitter levels, as well as neuroinflammatory cytokines, due to its naturally occurring isoflavone with strong antioxidant activity. Restrictions of this study are the short duration and the fewer number of animals used. Future studies, along with more mechanistic cellular and antioxidant genes is used to better understand and confirm the mechanism of hirsutidin. Furthermore, research on the effect of higher doses of hirsutidin on Parkinson could be considered an option in preclinical and clinical research.

5. CONCLUSION

The current experiment indicated that hirsutidin improved the motor symptoms in rat-rotenone-induced Parkinson paradigm. Moreover, hirsutidin showed neuroprotective activity via decreasing overall oxidative stress and inflammatory cytokines.

AUTHOR INFORMATION

Corresponding Authors

Nadeem Sayyed − *School of Pharmacy, Glocal University, Saharanpur 247121, India;* orcid.org/0000-0003-0517-4934; Email: snadeem.pharma@gmail.com

Imran Kazmi − *Department of Biochemistry, Faculty of Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia*; Phone: +966543970731; Email: ikazmi@kau.edu.sa

Authors

Muhammad Shahid Nadeem − *Department of Biochemistry, Faculty of Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia*

Jalaluddin Azam Khan − *Department of Biochemistry, Faculty of Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia*

Fahad A. Al-Abbasi − *Department of Biochemistry, Faculty of Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia*

Shareefa A. AlGhamdi − *Department of Biochemistry, Faculty of Sciences, King Abdulaziz University, Jeddah 21589, Saudi*

https://doi.org/10.1021/acsomega.3c00201
ACS Omega 2023, 8, 13016−13025

Arabia; Experimental Biochemistry Unit, King Fahd Medical Research Center, King Abdulaziz University, Jeddah 21589, Saudi Arabia

Amira M. Alghamdi − *Department of Biochemistry, Faculty of Sciences, King Abdulaziz University, Jeddah 21589, Saudi Arabia*

Gaurav Gupta − *School of Pharmacy, Suresh Gyan Vihar University, Jagatpura, Jaipur 302017, India; Department of Pharmacology, Saveetha Dental College, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai 602105, India; Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University, Dehradun 248007, India;* orcid.org/0000-0001-7941-0229

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.3c00201

Author Contributions

Conceptualization and fund acquisition: Muhammad Shahid Nadeem and Imran Kazmi; Methodology and first draft of manuscript: Nadeem Sayyed; Critical Revision of manuscript: Jalaluddin Azam Khan, Fahad A. Al-Abbasi, Shareefa A. AlGhamdi, Amira M. Alghamdi, Nadeem Sayyed, and Gaurav Gupta.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The Deanship of Scientific Research (DSR) at King Abdulaziz University, Jeddah, Saudi Arabia, has funded this project under grant no. (KEP-22-130-42). The authors, therefore, acknowledge DSR for technical and financial support.

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