Anti-Parkinsonian Activity of Ganoderma Lucidum in Experimentally Induced Parkinson’s Disease

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Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Parkinson's illness has been proclaimed as the second most neurodegenerative problem on the planet. Ganoderma lucidum is considered as a genuine restorative mushroom.

Aim: Our study was directed to assess the antiparkinsonian action of Ganoderma lucidum in rotenone-incited Parkinson’s disease in male Wistar rodents.

Methods: The impacts of Ganoderma lucidum were concentrated on catalepsy, muscle rigidity.

Results: Ganoderma lucidum fundamentally decreased the expanded length of catalepsy. Rotenone essentially initiated the disturbance of motor neurons as demonstrated by muscle rigidity of muscles and decreased locomotion. Ganoderma lucidum alleviated the disturbance of motor neurons by rotarod execution and locomotor action of the creatures. The exercises of cell reinforcement proteins catalase and superoxide dismutase, and the level of tripeptide glutathione were essentially diminished by rotenone. Besides, rotenone extended the level of lipid peroxidation thing malondialdehyde. Notwithstanding, Ganoderma lucidum supplementation to rotenone-infused rats essentially extended the degrees of superoxide dismutase, catalase, and glutathione, and diminished the level of malondialdehyde

Conclusion: Our study firmly supports the notion that Ganoderma lucidum has neuroprotective and antiparkinsonian action.

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1. INTRODUCTION

Parkinson's disease is pronounced as the second most normal neurodegenerative disorder on the planet. Loss of dopamine neurons in substantia nigra is thought to be the main cause of Parkinson's disease [1]. Realize that 7-10 million individuals are internationally influenced by the disease [2]. The etiology of the disease is still unclear [3]. The development of novel therapeutic or preventive strategies to fight Parkinson's disease is an ongoing process as causes of Parkinson's disease are largely unknown. Environmental and genetic both factors play important roles in making Parkinson's disease a multifactorial brain disorder. 10-15% cases of Parkinson's disease are inherited forms that are largely due to the genetic susceptibility or due to environmental exposures to toxins or different combination of both [4]. What triggers nerve degeneration and results in Parkinson's disease? It is needed to be researched extensively as the exact causes of Parkinson's disease are unclear. Rather than explaining the direct causes scientists can tell the contributing and risk factors involved in Parkinson's disease so far. Spinal or cerebral disorders caused by abnormal death of neurons along with motor, walking and cognitive abnormalities are categorized as neurodegenerative diseases. For these degenerative diseases oxygen free radicals are held responsible however for the control of these oxygen free radicals many research and growth into technologies are being conducted. Parkinson's disease, Alzheimer's disease and stroke are neurodegenerative diseases that are caused by lipid peroxidation, injury to DNA, cell membrane and protein and cell deformity and aging induced by oxidative stress. For the protection of neurons researchers are trying to develop therapeutic and preventive methods but facing limitation like side effects such as toxicity and less in vivo use. The job of oxidative stress has gotten the extraordinary significance in the pathology of Parkinson's disease [5]. Pesticides, genomic defects, brain microtrauma, drugs, focal cerebrovascular damage and environmental toxins are possible risk factors for Parkinson's disease [6]. Commonly used medications for motor symptoms relief are dopaminergic medication. For the management of Parkinson's disease, the standard medication includes dopamine precursors (L3,4 dihydroxy phenylalanine, levodopa, L-DOPA), MAO-B inhibitors (rasagiline, selegiline) and dopamine agonist (apomorphine and amantadine) that are used in combination or alone. The accessible drugs for this disease don't offer a cure all therapy [7].

Rotenone induces, in animals, neurotic characteristics like human Parkinson's disease, making it a promising creature model for Parkinson's disease with legitimized construction [8].

For thousands of years, mushrooms have been used for numerous diseases. To promote overall health and life longevity, use of mushroom was common in ancient Chinese and ancient Egyptians cultures. The use of mushroom for the treatment of diseases is also revealed from early reports of Materia Medica. Mushrooms are full of nutrients with low calories and no cholesterol. They are high in protein up to 44.93%. Essential health benefits that mushrooms provide includes anti-inflammatory, anti-diabetic, liver protective, anti-hypertensive, antimicrobial cholesterol lowering properties, antiviral, and antioxidant activities [9].

Mushroom extracted pharmaceutical compounds found to be effective in many diseases including neurodegenerative disorders, cancers and immunological diseases. In Asia Ganoderma lucidum has been used as traditional medicine for thousands of years. Ganoderma lucidum is the member of family polyporaceae of basidiomycota [10]. Mushrooms have acquired overall acknowledgment for their remedial and healthy benefits. Wellbeing conscious individuals need invulnerability boosters and cell security which increases the interest in mushrooms [11]. Ganoderma lucidum is well known for its medicinal effects. The exceptional medical advantages of Ganoderma lucidum "the mushroom of interminability" have been accounted for and it has in excess of 400 bioactive components [12].

Antioxidants to treat and control Parkinson's disease are important. The current study, therefore, attempted to assess the antiparkinsonian action of Ganoderma lucidum extricate in neurodegeneration induced by rotenone in rats.
2. METHODOLOGY

2.1 Animals

Animals were kept in propylene cages under normal research facility conditions. For analytical purposes, 30 male Wistar rats (200-220 g weight) were retained in propylene cages under normal research facility conditions [13]. Six rats were kept in one cage. The study was directed in the Pharmacology research lab of the Ziauddin University.

2.2 Drugs and chemicals

*Ganoderma lucidum* comprised of broke spores and fruiting bodies was purchased from Pharmanex Inc. All other chemicals were procured from Sigma Aldrich.

2.3 Study Design

Rotenone was administered at a dose of 2.5 mg/kg intraperitoneally (i.p.) when day by day for four weeks for the enlistment of Parkinson's disease [14].

Group I, Vehicle-injected control group (4ml/kg, i.p)
Group II, Rotenone-injected (2.5 mg/kg i.p) and vehicle-treated (4ml/kg, i.p)
Group III, Levodopa (6 mg/kg, p.o.) and rotenone (2.5mg/kg, i.p)
Group IV, Rotenone (2.5mg/kg, i.p) and extract (150 mg/kg, p.o.)
Group V, Rotenone (2.5mg/kg, i.p) and extract (300 mg/kg, p.o.)

2.4 Behavioral Procedures

2.4.1 Catalepsy test

Catalepsy is a social state where the creature can't right a remotely imposed posture, one technique from Costall and Naylor was used to measure catalepsy [15]. A 9 cm high bar was used, and each creature was placed on the level bar with the two forward legs in the half-rise position. We wrote down the time using a stopwatch. Catalepsy was incited by rotenone and analyzed for 210 minutes per 30-minute period.

2.4.2 Rotarod (Grip strength) test

A rotating rod instrument was used to verify the resistance to the restraint, on balance. The instrument is usually utilized to evaluate the "insignificant neurological shortage" such as coordination and motor work in rodents. Prior to starting the test, every animal was prepared to adapt to the apparatus. A pivoting pole of distance across 7 cm and speed 25 rpm was used, and every animal was set on it. The cutoff time was 300 sec. The normal results were recorded as fall of time [16].

2.5 Dissection and homogenization

Animals after treatment period were scarified by execution affected by gentle anesthesia. Brains were dissected out on the double; the cerebellum was discarded while the forebrain was separated for the assessment. A very cold isotonic saline solution was used to expel blood from the cerebrum. A phosphate substrate of 0.1 M (pH 7.4) was used to predict a 10% w/v. [14].

2.6 Biochemical Estimation

2.6.1 Malondialdehyde level

The identification pack of malondialdehyde was used to discover the lipid peroxidation sum adhering to maker's instructions. When thiobarbituric acid (250 µL) and acid reagent were present, samples (250 µL) were hatched and heavily vortexed. The samples were incubated at 60°C for one hour, then centrifuged to 10,000 g for 3 minutes. The reaction spectrum mixture was recorded at 532 nm. [14].

2.6.2 GSH level (reduced glutathione)

Assay pack, as per maker's instructions, was utilized for the assessment of diminished glutathione level. The absorbance of the samples was noted at 412 nm. [14].

2.6.3 Superoxide dismutase (SOD) level

The cell reinforcement protein superoxide dismutase movement was controlled by Cayman assay pack according to producer's instructions [14].

2.6.4 Catalase (CAT) level

The cancer prevention agent catalyst catalase movement was controlled by Cayman assay unit according to producer's instructions [14].

2.7 Statistical Analyses

A one-way analysis of variance (ANOVA) and Tukey's post hoc test were used to decide the
statistical significance between various groups. The standard for any statistically significant distinction was set as \( p < 0.05 \).

3. RESULTS

3.1 Ganoderma lucidum Reduces Rotenone Induced Catalepsy

The span of catalepsy was increased in vehicle + rotenone group when contrasted with vehicle group. Opposite, *Ganoderma lucidum* given preceding rotenone infusion significantly diminished the catalepsy when contrasted and the vehicle + rotenone group.

3.2 The Impact of *Ganoderma lucidum* on Rotarod

Time of fall was significantly decreased in vehicle + rotenone group when contrasted with vehicle bunch. Nonetheless, the persistent oral administration of *Ganoderma lucidum* before rotenone infusion significantly increased the hour of stay on the apparatus when contrasted and the vehicle + rotenone group.

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**Fig. 1.** Action of *Ganoderma lucidum* on catalepsy induced with rotenone  
###\( p < 0.001 \), ##\( p < 0.01 \), #\( p < 0.05 \) when compared with vehicle treated control  
***\( p < 0.001 \), **\( p < 0.01 \), *\( p < 0.05 \) when compared with vehicle + rotenone group

**Fig. 2.** Action of *Ganoderma lucidum* on rotarod  
###\( p < 0.001 \), ##\( p < 0.01 \), #\( p < 0.05 \) when compared with vehicle treated control  
***\( p < 0.001 \), **\( p < 0.01 \), *\( p < 0.05 \) when compared with vehicle + rotenone group
3.3 *Ganoderma lucidum* Reduces Rotenone Induced Increase in Malondialdehyde

Immensely increased degree of Malondialdehyde was observed in vehicle + rotenone groups of animals when contrasted and vehicle bunch. Notwithstanding, *Ganoderma lucidum* given before rotenone infusion remarkably decreased Malondialdehyde level when contrasted and vehicle + rotenone groups.

3.4 *Ganoderma lucidum* Inhibits Rotenone Induced Decrease in Glutathione

A remarkable decrease in glutathione level was observed in vehicle + rotenone treated group when contrasted and vehicle bunch, whereas *Ganoderma lucidum* given before rotenone infusion treated groups significantly increased glutathione level when contrasted and vehicle + rotenone group.

3.5 *Ganoderma lucidum* Inhibits Rotenone Induced Decrease in Superoxide Dismutase

The degree of cell reinforcement protein superoxide dismutase was also measured. There occurred remarkable reduction in superoxide dismutase level in vehicle + rotenone group when contrasted and vehicle control group. *Ganoderma lucidum* given preceding rotenone infusion significantly increased the movement of superoxide dismutase when contrasted and vehicle + rotenone treated group.

3.6 *Ganoderma lucidum* Inhibits Rotenone Induced Decrease in Catalase

The action of cell reinforcement catalyst catalase was also measured. The significant decrease in the action of catalase was observed in vehicle + rotenone group when contrasted and vehicle control group. *Ganoderma lucidum* given before rotenone infusion significantly increased the level of catalase when contrasted and vehicle + rotenone group.
Fig. 4. Action of *Ganoderma lucidum* on reduced glutathione (GSH) level

###p < 0.001, ##p < 0.01, #p < 0.05 when compared with vehicle treated control

***p < 0.001, **p < 0.01, *p < 0.05 when compared with vehicle + rotenone group

Fig. 5. Action of *Ganoderma lucidum* on superoxide dismutase

###p < 0.001, ##p < 0.01, #p < 0.05 when compared with vehicle treated control

***p < 0.001, **p < 0.01, *p < 0.05 when compared with vehicle + rotenone group
4. DISCUSSION

Perhaps the most well-known neurodegenerative disorders is Parkinson's disease. Parkinson's disease is an evolutionary disease with a complex pathogenesis. The need of disease-modifying therapy is crucial for Parkinson's disease patients as the number of patients with Parkinson's disease expected to be double in the next 20 years. A combination of different factors such as environmental, epigenetics and genetics are involved in the complex pathology of Parkinson's disease. According to epidemiological studies there is a link between increased Parkinson's disease risk and pesticide exposure. The association of risk for developing Parkinson's disease is more than 50% with the common pesticide exposure reported by a current meta-analysis. At present no disease modifying therapy is available. The mainstay treatment for the relief of motor symptoms is dopaminergic medications. Parkinson's disease progressively affects the quality of life by impairing the daily activities. Different subtypes of PD related to motor and nonmotor symptoms are identified by cluster analysis for the selection of therapeutic approach in accordance [10]. There is a need of neuroprotective drugs as a therapeutic approach for Parkinson's disease.

The current study was coordinated to account for the antiparkinsonian activity of *Ganoderma lucidum* in Parkinson's models induced by rotenone.

The catalepsy actuated rotenone is usually used for Parkinson's disease [17,18]. In the present study, rotenone introduced significant catalepsy in rats when contrasted with the term vehicle control group. In any case, persistent oral administration of *Ganoderma lucidum* preceding rotenone infusion significantly decreased the term of catalepsy in rats when contrasted with the vehicle control group. This could show the neuroprotective capacity of *Ganoderma lucidum* in dopamine neurotransmission in striatum.

Furthermore, for the evaluation of the gripping force, the running test of the rotating rod was used. The rotenone group shows a significant decline in the fall schedule when contrasted with the vehicle control group. In contrast constant oral administration of *Ganoderma lucidum* preceding rotenone infusion significantly increased the hour of stay of rats on the apparatus when contrasted and vehicle control bunch. It can also be an indication of *Ganoderma lucidum's* neuroprotective ability against these driving symptoms [19].
Oxidative stress is an essential component of the pathogenesis of Parkinson's disease. The passage of the cells takes place due to the high free extreme discharge which occurs when there are defects in the electronic transport of the mitochondrial-I complex [20]. The brain of the patient with Parkinson's disease is believed to have increased oxidative damage to lipids, proteins and DNA [10]. Our study found an increase in malondialdehyde levels in both rotenone-treated and vehicle-treated rats. Nevertheless, pre-treatment with Ganoderma lucidum in rotenone-treated rats revealed a significant decrease in malondialdehyde concentration in the compared rats and in vehicle-treated rats.

Neuronal loss is tied to reduced glutathione depletion. The risk of lipid peroxidation and development of free extremist is increased when the availability of glutathione is reduced, which in turn disrupts the neuronal ability to detoxify hydrogen peroxide [21]. In our study, there was a decrease in glutathione levels in animals treated with rotenone as opposed to controls treated with vehicles. Be that as it may, pretreatment with Ganoderma lucidum in rotenone treated animals, significantly increased glutathione level when contrasted and vehicle treated rats. This evidence suggests an antioxidative effect of Ganoderma lucidum.

Superoxide dismutase a chemical that catalyzes the dismutation of superoxide into hydrogen peroxide and nonreactive oxygen species. At the point that cells are exposed to oxygen, Superoxide dismutase seems to be an antioxidant defense, which is available in almost every cell. Superoxide dismutase has a murderous effect on extreme free toxicity [22]. In brain tissue from rats treated with rotenone, a decrease in superoxide dismutase was observed, which revealed oxidative stress. In any case, pretreatment with Ganoderma lucidum showed a significant increase in Superoxide dismutase level when contrasted and vehicle treated rats.

An additional antioxidant that counteracts the harmful effects of hydrogen peroxide is catalase. Catalase converts hydrogen peroxide to non-reactive oxygen species and water and stops the collection of precursors that biosynthesize free radicals. the level of catalase is lessened by oxidative stress [23]. In our study, the rodents treated with rotenone showed a decrease in the level of catalase when compared with the controls treated with the vehicle. Be that as it may, pre-treatment with Ganoderma lucidum showed an increase in catalase levels in contrast and vehicle-treated rats.

In neurodegenerative diseases, calming drugs and cell-building activities are appropriate [24,25]. Consequently, our study suggests that Ganoderma lucidum, because of its strong cellular strengthening and attenuating action, could be responsible for neuroprotection in neurodegenerative diseases, including Parkinson's disease. Be that as it may, reishi should be kept away from by pregnant or breastfeeding mothers, individuals suffering from a blood disorder, going through surgery or sick with low pulse.

5. CONCLUSION

Based on the above facts, we conclude that Ganoderma lucidum successfully improves the neurodegeneration caused by rotenone due to its strong cellular strengthening and soothing motion. It proves that Ganoderma lucidum has an anti-parkinsonian effect.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Current study was examined and approved by the Ethics Committee of the Ziauddin University of Karachi.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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