

AMELIORATIVE EFFECT OF *LENTINULA EDODES* ON HALOPERIDOL INDUCED CATALEPSY AND VACUOUS CHEWING MOVEMENTS IN WISTAR RATS

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Abstract

Background: *Lentinula edodes* is the most consumed mushroom in the world and has been well known for its therapeutic potential as an edible and medicinal candidate, it contains dietary fibers, vitamins, proteins, minerals, and carbohydrates. *Lentinula edodes* exhibits significant antioxidant and free radical scavenging activity, which could help protect neurons from oxidative damage. In this study, the effect of *Lentinula edodes* on haloperidol induced catalepsy and vacuous chewing movements was studied in rats.

Material and method: Wistar rats were selected to study the protective effect of *Lentinula edodes*. Haloperidol induced catalepsy and vacuous chewing movements were assessed to note the effect of the mushroom. the readings were noted on the 28th day of the study.

Result: The results of the analysis reveal that *Lentinula edodes* possesses significant neuroprotective activity in rodents. when compared with the saline-treated group. The haloperidol induced catalepsy and vacuous chewing movements were significantly decreased in treatment groups when compared with the saline group.

Conclusion: The findings of our investigation clearly indicate that *Lentinula edodes* possesses significant ameliorative effect on haloperidol induced catalepsy and vacuous chewing movements in the rats. This observed effect may be attributed to the rich phytochemical composition of the mushroom. *Lentinula edodes*, have strong antioxidant qualities because of their high phenolic content, flavonoids, and polysaccharides.

Keywords:

Lentinula edodes, Neuroprotective activity, Catalepsy, Vacuous chewing movements.

Introduction:

Lentinula edodes is the most consumed mushroom in the world and has been well known for its therapeutic potential as an edible and medicinal candidate, it contains dietary fibers, vitamins, proteins, minerals, and carbohydrates. (Ejaz, 2024).

Due to its delicious flavor, nutritional advantages, and medicinal value, *Lentinula edodes*, which makes up 17% of the world's edible fungus supply, is currently the second most popular edible mushroom on the market (Huang, Qian, Jiang, & Zheng, 2019). *Lentinula edodes* has been shown to have a number of positive effects in contemporary chemical and pharmacological research, such as anti-tumor (Ziaja-Soñtys et al., 2020), anti-bacterial (Hatvani, 2001), anti-oxidant (Jiang, Luo, & Ying, 2015), anti-inflammation (Han et al., 2017), Reno protective effects (Song, Ren, Wang, Jia, & Zhang, 2020), and immunomodulatory activity (Nagashima et al., 2017).

According to reports, *L. edodes* is a high-protein, low-fat food that contains a number of classes of bioactive compounds, including carbohydrates (58 ~ 60%), proteins (20 ~ 23%), fiber (9 ~ 10%), lipids (3 ~ 4%), ash (4 ~ 5%), vitamins, folates, niacin, and minerals (Hu et al., 2020; Morales et al., 2019; Xu, Yan, Tang, Chen, & Zhang, 2014). Polysaccharides are the main component and the most significant active bioactive compounds in *L. edodes*. This edible fungus has been reported to have a variety of nutritional values and pharmacological activities in recent years, particularly in the last 20 years (Gaitán-Hernández, López-Peña, Esqueda, & Gutiérrez, 2019).

Shiitake mushrooms, or *Lentinula edodes*, have strong antioxidant qualities because of their high phenolic content, flavonoids, and polysaccharides. Strong anti-inflammatory and free radical scavenging properties (DPPH, ABTS) are demonstrated by methanolic and aqueous extracts, which successfully lower oxidative stress and prevent lipid peroxidation, especially in the fruiting body and mycelium. Studies demonstrate that antioxidants plants reduce free radicals and protects neurons. Haloperidol induces catalepsy through oxidative stress in the brain and dopamine D2 receptor blockade, which can be mitigated by substances with antioxidant activities. *Lentinula edodes* exhibits significant antioxidant and free radical scavenging activity, which could help protect neurons from oxidative damage (Xu X, 2011; Jiang T, 2015). In this study, the effect of *Lentinula edodes* on haloperidol induced catalepsy and vacuous chewing movements was studied in rats.

Materials and Methods:**Drug and Extract:**

The pre-filled capsules containing *Lentinula edodes* powder were acquired from Gluckspilze Austria. Haloperidol (serenace) was purchased from Searle Pakistan.

Animals:

For this investigation, Wistar rats weighing 180–210 g was acquired. To remove sex-related differences in medication impact, the trial was limited to male rats. All the animals were kept in a noiseless room with a temperature of (25-30°C) with 12h light/12h dark period and 66% relative humidity. The rodents were given a standard rodent diet and unlimited access to water. Rats were given drugs for consecutive 28 days through oral gavage and intraperitoneal (IP) injection.

Grouping of animals

Group I: Normal control, given normal saline 10 mL/kg, *p.o.*

Group II: Treatment group, *Lentinula edodes* 250 mg/kg group (LEE 250 mg/kg), *p.o.*; + haloperidol 1 mg/kg *i.p.*

Group III: Treatment group, given *Lentinula edodes* 500 mg/kg group (LEE 500 mg/kg), *p.o.*

Group IV: Positive control, haloperidol 1 mg/kg *i.p.*

Behavioural Assessment:

Following behavioural tests were performed on the 28th day of the study:

Determination of Catalepsy – (Bar/Block Test)

In this assessment, the rat's rear paw was lowered till it reached the ground in this assessment, while the front paw was placed on a 4 cm block. The rat's tail was held gently until it securely grabbed the block. If the rat did not change its position within 20 seconds, it was noted. However, the deadline was five minutes. The evaluation was repeated at 60, 90, 120, 150, 180, and 210 minutes prior to returning the animal to its cage (Bhangale, 2016).

Determination of Vacuous Chewing Movements (VCMs)

The mouse counterpart of tardive dyskinesia, known as VCM, is typified by rapid jaw movements that are not directed toward any specific stimulus. During these movements, the lower jaw often swiftly deflects vertically. Rats were administered medicine on the 28th day and placed in individual cages zero times in order to quantify VCM. The VCM's were counted for ten minutes. If a VCM occurred within a grooming time, it was not counted. The activity was repeated at 30, 60, 90, and 120 minutes following the start of the initial experiment (Nade, 2015).

Statistical Analysis:

Data are shown as mean±standard error of mean (SEM). ANOVA following Tukey’s *post hoc* analysis was used for data analysis. The p-value of 0.05 or less is accepted as significant.

Results:

Determination of Catalepsy – (Bar/Block Test)

On 28th day, significant decrease in the cataleptic score was observed; more specifically at the dose of 500 mg/kg *Lentinula edodes* on 30, 60, 90, 120, 150, 180 and 210 minutes, when compared with the control group.

Table 1: Effect of *Lentinula edodes* on haloperidol induced catalepsy in rats

Drug treatment	60 min	90 min	120 min	150 min	180 min	210 min
Normal Saline	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Haloperidol (1mg/kg)	2.9 ± 0.0##	3.7 ± 0.312##	3.7 ± 0.244##	3.5 ± 0.11##	3.4 ± 0.07##	3.2 ± 0.044##
Haloperidol + LEE(250)	1.56 ± 0.4145*	2.663 ± 0.3751*	1.78 ± 0.4468*	1.661 ± 0.0832*	1.31 ± 0.5165*	0.74 ± 0.147**
Haloperidol + LEE(500)	1.12 ± 0.4632*	2.33 ± 0.3682*	1.512 ± 0.3023*	1.347 ± 0.3321**	1.268 ± 0.2562**	0.400 ± 0.442**

##p<0.001, *p<0.05 **p<0.01

Determination of vacuous chewing movements (VCM’s)

Administration of *Lentinula edodes* at a dose of 250 mg/kg and 500 mg/kg shows significant reduction in the rapid jaw movement in vacuous chewing test when compared with the control group.

Table 1: Effect of *Lentinula edodes* on haloperidol induced Vacuous Chewing Movements in rats

Drug treatment	0 min	30 min	60 min	90 min	120 min
Normal Saline	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
Haloperidol (1mg/kg)	20.9 ± 3.2##	19.7 ± 3.12##	23.7 ± 2.764##	17.5 ± 0.22##	18.4 ± 4.87##
Haloperidol + LEE(250)	14.67 ± 3.45*	12.77 ± 0.51*	13.67 ± 0.68*	14.15 ± 0.32*	11.31 ± 0.78*
Haloperidol + LEE(500)	11.34 ± 0.67*	12.66 ± 0.787*	11.78 ± 0.45*	11.56 ± 0.89**	11.89 ± 0.90**

##p<0.001, *p<0.05 **p<0.01

Discussion:

The most popular animal model of Parkinson's disease is vacuous chewing movements brought on by haloperidol (Turron, 2003).VCM is linked to certain surgical injuries in the brain as well as a decrease in neurotransmitters including dopamine and catecholamines (Salamone, 1998).

Lentinula edodes extracts contain significant levels of polyphenols and flavonoids that scavenge free radicals, with higher concentrations often found in fruiting bodies grown on logs. *L. edodes* crude polysaccharides, particularly in aqueous extracts, show high superoxide radical scavenging abilities. Key antioxidant compounds include tocopherols, ascorbic acid (vitamin C), and phenolic compounds. Studies have demonstrated significant DPPH radical scavenging and high antioxidant activity in methanol extract (Xu X, 2011).

These antioxidant properties make *Lentinula edodes* a valuable natural resource for combating free radicals and promoting overall health (Wasser, 2017). Haloperidol-induced VCM and catalepsy are often linked to oxidative damage and neurotoxicity in the basal ganglia. Studies indicate that the extract can reduce oxidative stress, which might mitigate the neurological side effects of chronic neuroleptic treatments like haloperidol (Jiang T, 2015; Nade, 2015).

In this study, rats were given a dose of 1 mg/kg body weight of haloperidol to induce parkinsonism. When compared to the control group (normal saline 10 mL/Kg), haloperidol prolonged the animals' stay on the bar in the catalepsy paradigm. However, at both doses—250 mg/kg and 500 mg/kg of *Lentinula edodes* — a notable decrease in the amount of time spent on the bar was noted. Numerous studies have shown that oxidative stress is the cause of Parkinson's disease symptoms. The ameliorative effect on catalepsy and VCM's were observed with both the doses of *Lentinula edodes* and this may be due to potential anti-oxidant effect of the mushroom.

In this study, VCMs were significantly reduced at both *Lentinula edodes* doses, with the 500 mg/kg dose showing a more substantial effect than the control group. In contrast to the control group, rats administered 1 mg/kg of haloperidol exhibited a highly significant increase in VCMs. *Lentinula edodes* had a powerful anti-Parkinson's impact, as evidenced by the considerable difference between the treated and negative control groups.

Conclusion:

The findings of our investigation clearly indicate that *Lentinula edodes* possesses significant ameliorative effect on haloperidol induced catalepsy and vacuous chewing movements in the rats. This observed effect may be attributed to the rich phytochemical composition of the mushroom. *Lentinula edodes*, have strong antioxidant qualities because of their high phenolic content, flavonoids, and polysaccharides.

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