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ANTIDEPRESSANT-LIKE ACTIVITY OF *LENTINULA EDODES* MUSHROOM IN MICE

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Abstract

Background: Depression is considered as the most common health issue, because of its high level of occurrence worldwide. It is considered as one of the major cause of mental disability. Mushrooms have emerged as promising candidates due to their neuroactive compounds.

Objective: This study was conducted to evaluate the antidepressant-like effects of *Lentinula edodes* (shiitake mushroom) extract in mice using two doses: 250 mg/kg and 500 mg/kg per oral.

Material and Method: Behavioral assessments were conducted using the Forced Swimming Test (FST) and Tail Suspension Test (TST) to measure depressive-like behaviors, while the Home Cage Test was used to evaluate locomotor activity and rule out nonspecific motor stimulation.

Result: The dose 500 mg/kg significantly reduced immobility time in both FST and TST compared to the control group, indicating a strong antidepressant-like effect. No significant changes in locomotor activity were observed in the Home Cage Test, suggesting that the observed behavioral effects were not due to increased general activity.

Conclusion: These findings suggest that *Lentinula edodes* possesses dose-dependent antidepressant-like properties and may serve as a potential natural therapeutic candidate for the treatment of depression.

Keywords:
Lentinula edodes, depression, tail suspension test, forced swim test, home-cage test.

Introduction:

Depression is considered as the most common health issue, because of its high level of occurrence worldwide. It is considered as one of the major cause of mental disability [1]. In a report of 2017 by World Health Organization, it has been reported that globally depression is largest contributor to disability in which 322 million people lived with this disability [2].

Depression may greatly affect human mental as well as physical health. The symptoms of depression include sadness, anxiety, fatigue, insomnia or digestive disorders [3]. The most commonly used antidepressant drug include amitryptyline which belongs to the class tricyclic antidepressants, among serotonin class, drugs used are sertraline, fluoxetine and citalopram [4]. Report based on world health organization, it was reported that 25% increased rate have been in depression patient due to COVID-19 pandemic [5].

Fungi like primary basidiomycetes and mushrooms are one of the significant edible foods. They are very important because of their low calories, high- minerals, amino acids, fibers and vitamins containment [6]. These mushrooms are pharmacologically invaluable because of their ability to produce some ingredients of high medicinal value and potential effects. Such mushrooms are called medicinal mushrooms [7]. One of the medicinal mushrooms, known as Lentinula edodes, is recognized with different names in different countries. In the Chinese language, it is called Xianggu while in the Japanese, it is Shiitake. Shiitake mushroom was first discovered in between 1000 and 1100 AD in China [8].

Figure 1. *Lentinula edodes* (Shiitake mushroom)

Shiitake consists of different chemical compounds which have various medicinal effects on the human body. These compounds include alkaloids, sterols, phenols, proteins, and carbohydrate complexes [9]. Phenolic compounds and ecothionine that are present in shiitake have tendency to induce antioxidant effect [10]. This study was planned to explore the antidepressant-like activity of *Lentinula edodes* mushroom in mice.

Material and Method:

Drug and Extract:

The pre-filled capsules containing *Lentinula edodes* powder were acquired from Gluckspilze Austria. Fluoxetine was purchased from Hilton Pharmaceuticals Pakistan, and from Sigma Aldrich, USA other used chemicals were purchased and research was performed.

Selection and Housing of Animals:

For the assessment of antidepressant-like activity, male Swiss albino mice were employed in this research study. These mice were obtained from Karachi University and were bred and housed at the Department of Pharmacology's animal facility at the University of Sindh, Jamshoro. The mice had a weight range of 20-25 grams and were approximately 3 months old at the time of the experiment. Mice were housed under controlled conditions, maintaining a temperature of 25-30°C and a 12/12 hours light-dark cycle. The animals were provided with standard diet and water ad libitum throughout the study. The drug was administered orally for duration of 60 days. The care and handling of the animals adhered to the guidelines outlined in the "Guide for the Care and Use of Laboratory Animals" by the US National Research Council

Animal Grouping:

The animals were categorized into four groups: the control group (treated with distilled water), the *Lentinula edodes* 250mg/kg group (LEE 250 mg/kg), the *Lentinula edodes* 500mg/kg group (LEE 500mg/kg), and the fluoxetine 20mg/kg group. Each group consisted of 6 male mice.

Antidepressant Activity:

Forced Swim Test

In the test procedure, the mice were placed in a tank filled with water, the dimensions of which were specified at 40 cm in height and 18 cm in diameter. The tank contained sufficient depth, approximately 15 cm of water, allowing the mice to reach the tank's bottom and assume a floating-like posture. Mice were actively participating in escape-directed behaviors, swimming and climbing, before the test. But as time progressed they found themselves usually assuming a peculiar stationary attitude, and shows immobility. The immobility time of each animals was noted for 6 minutes [11].

Tail Suspension Test

The tail suspension test is a valuable method for assessing the behaviour of mice to gauge the effectiveness of antidepressants. Each animal is individually suspended by its tail at a height of 50 cm above the base, using adhesive tape to ensure that the tail is suspended approximately 1 cm from its tip. The immobility time, recorded using a stopwatch over duration of 6 minutes, serves as a crucial indicator. This test aids in understanding mouse behaviour; initially, mice attempt to escape the situation, but under stressful conditions, they exhibit immobility [12].

Locomotor Activity:

Home Cage Test

The Home Cage Test (HCT) is employed as a phenotype test to assess learning, memory, and depression by evaluating locomotor activity. The movement of each mouse is monitored hourly, with activity recorded and plotted. Distinct variations in behaviour and movement are typically observed during the light and dark phases of the test. To facilitate the observation of home cage activity, specially designed cages equipped with video tracking systems are used. Each cage is equipped with a top-notch high-definition video recorder featuring infrared-sensitive lighting. This infrared lighting prevents the illumination of the room during the test, ensuring accurate monitoring [13].

Results:

Forced Swim Test

Forced swim test was conducted four times over the course of the 60-day study, specifically on days 7, 15, 30, and the final assessment on day 60. The study results demonstrate a noteworthy reduction in immobility time within the *Lentinula edodes* groups when comparing each group's outcomes to their respective distilled water control group (as depicted in figure 2). Furthermore, the administration of Fluoxetine (20 mg/kg, p.o.) led to a significant decrease in the immobility time of the mice when compared to the distilled water group (Figure 2).

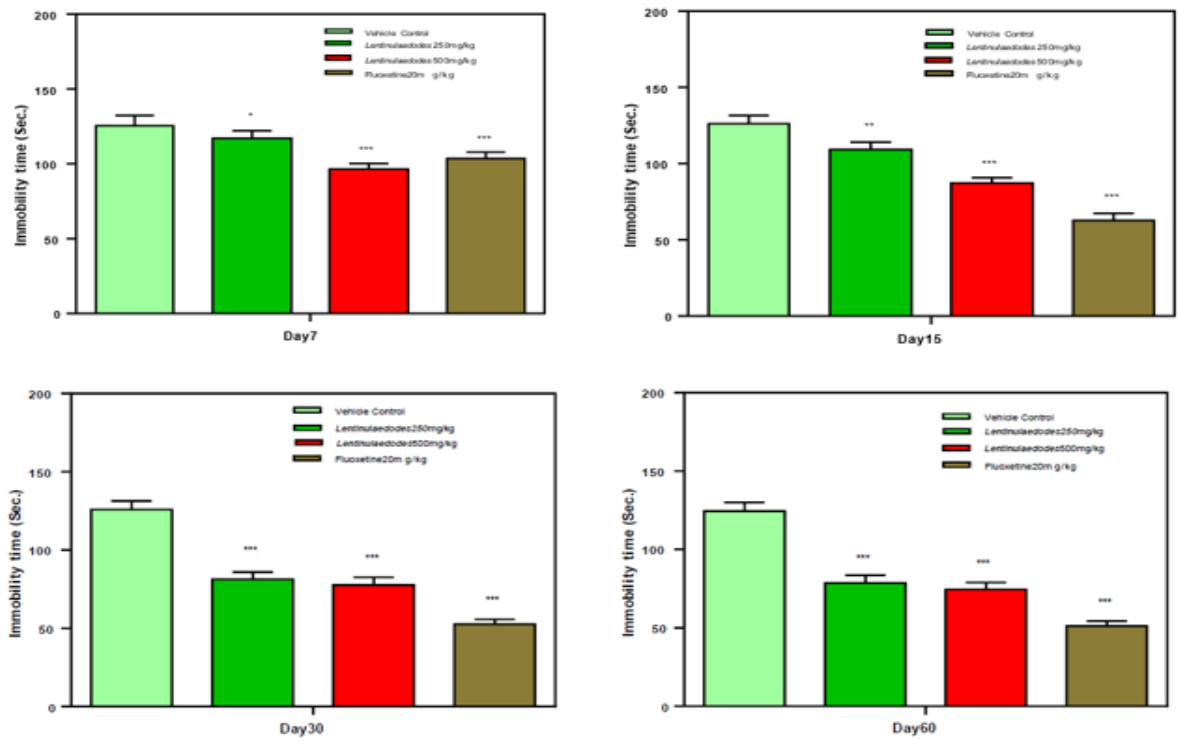

Figure 2: Impact of *Lentinula edodes* on immobility time as assessed through the forced swim test on day 7th, 15th, 30th and 60th.

Each group comprises 6 mice (n = 6). The findings are depicted as mean values with their associated standard errors (mean ± S.E.M.), and statistical significance is indicated as ***P<0.001, **P<0.01, *P<0.05, following the ANOVA, along with Tukey's post-hoc test for comparison.

Tail Suspension Test:

In this test marked reduction in the immobility time of mice within the *Lentinula edodes* groups when comparing the results of each group to their respective distilled water control group. Additionally, following the administration of Fluoxetine (20 mg/kg, p.o.), there was a significant decrease in immobility time observed in the mice when compared to the distilled water control group (as illustrated in Figures 3).

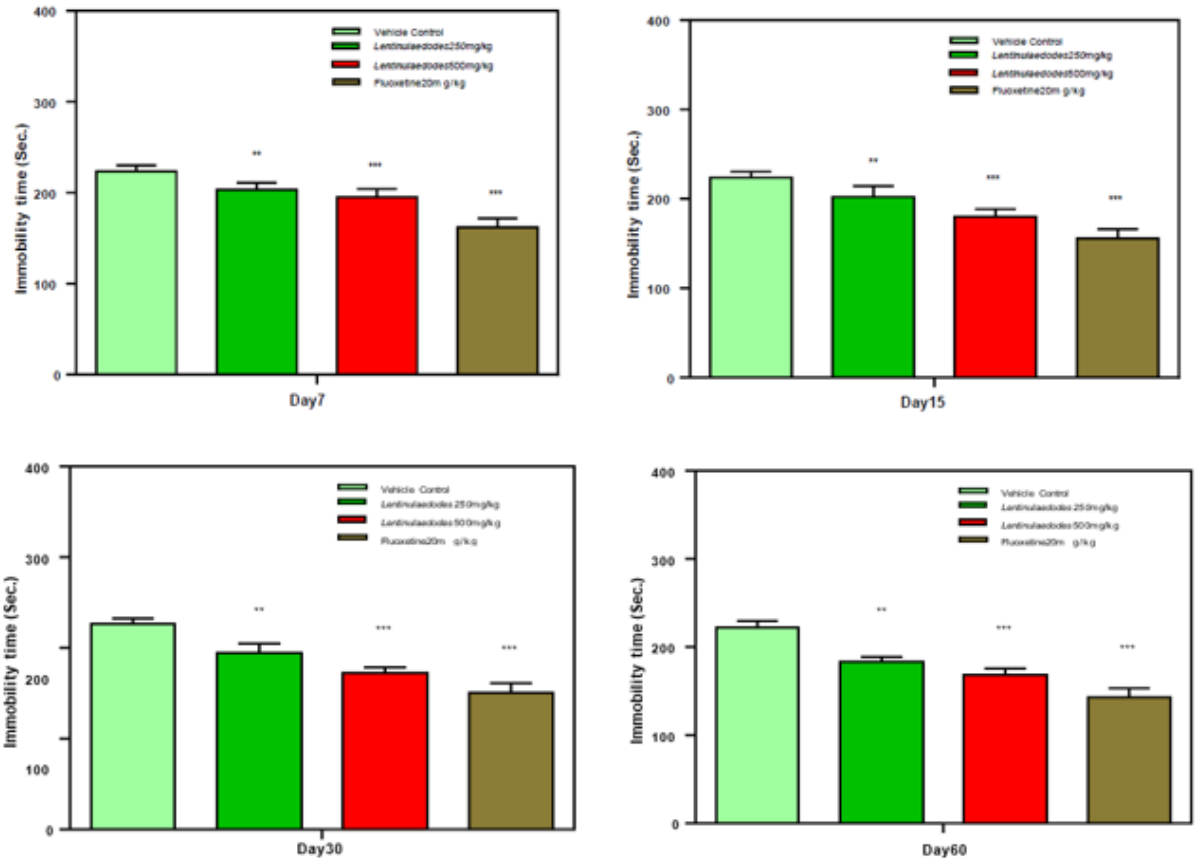

Figure 3: Impact of *Lentinula edodes* on immobility time as assessed through the tail suspension test on day 7th, 15th, 30th and 60th.

Each group comprises 6 mice (n = 6). The findings are depicted as mean values with their associated standard errors (mean ± S.E.M.), and statistical significance is indicated as ***P<0.001, **P<0.01, *P<0.05, following the ANOVA, along with Tukey's post-hoc test for comparison

Home Cage Test:

In this test there was no substantial alteration in the number of cage crossings by the mice within the *Lentinula edodes* groups when comparing each group results to their respective control group.

Furthermore, after administering the standard drug fluoxetine (20 mg/kg, p.o.), there was no significant decrease in the number of cage crossings observed in the mice when compared to the distilled water control group (as illustrated in Figures 4).

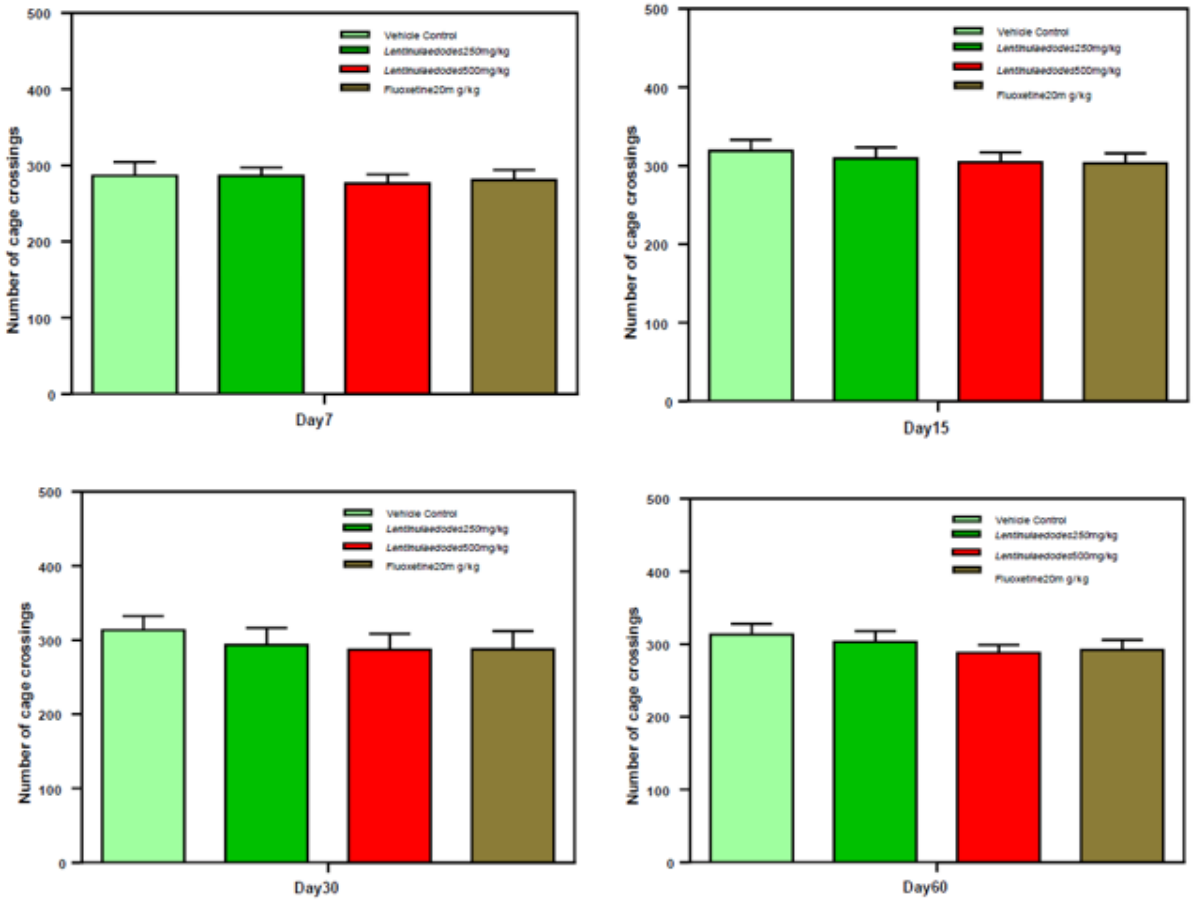

Figure 4: Impact of *Lentinula edodes* on immobility time as assessed through the home cage test on day 7th, 15th, 30th and 60th.

Each group comprises 6 mice (n = 6). The findings are depicted as mean values with their associated standard errors (mean ± S.E.M.), and statistical significance is indicated as ***P<0.001, **P<0.01, *P<0.05, following the ANOVA, along with Tukey's post-hoc test for comparison.

Discussion:

Depression, a psychiatric disorder affecting mood, behaviour, and thoughts, is commonly treated with pharmaceutical drugs. However, these drugs often come with side effects and the potential for interactions with other substances [3]. On the contrary, natural products are globally embraced due to their therapeutic benefits with minimal adverse effects [14].

Natural products have been used as a plentiful source of pharmacologically active compounds of which several have been valuable in the generation of modern therapeutic agents [15]. Among them mushrooms gain more attention over the last several years because they contain a variety of bioactive metabolites,

such as polysaccharides, terpenoids, phenolic compounds, and alkaloids which possess anti-inflammatory, antidepressant, neuroprotective effects [16].

In this study, two distinct doses of *Lentinula edodes* were administered to the mice. Among these doses, the higher dose of 500 mg/kg notably reduced immobility time to a highly significant degree in both FST and TST, demonstrating superior antidepressant-like effects in the mice. The lower dosage of 250 mg/kg also exhibited antidepressant-like activity in male mice (Figure 2 and 3). The behavioural assessments of mice exposed to *Lentinula edodes* demonstrated a notable reduction in behavioural activity over the course of the 60-day study, with outcomes similar to those of the standard drug fluoxetine. Research studies evidence that herbs rich in polyphenols can elicit antidepressant effects in animal models [17]. *Lentinula edodes*, in particular, contains a substantial quantity of polyphenols. The antidepressant-like activity exhibited by *Lentinula edodes* may be attributed to the presence of these polyphenols. However, further investigations are needed to elucidate the precise mechanism behind this antidepressant-like activity.

An interesting aspect to explore is that many established antidepressants are known to reduce locomotor activity [18]. To rule out the possibility of obtaining false positive results from the mushroom, a home cage test was conducted. An examination of locomotor activity, based on the number of home cage crossings, revealed insignificant decline in the mice's locomotor function (Figure 4). The objective of this test was to evaluate how *Lentinula edodes* affects spontaneous motor activity. The results from the home cage experiment revealed that the mushroom had a suppressive effect on the locomotor activity of mice, rather than stimulating their spontaneous motor activity. These combined findings indicate that the antidepressant impact of *Lentinula edodes* is not linked to the activation of skeletal muscles.

Abnormal regulation of neurotransmitters such as serotonin, nor- adrenaline, and dopamine is widely considered a key factor in the development of depression. Selective serotonin reuptake inhibitors (SSRIs), a commonly prescribed class of antidepressant medications, increase the availability of extracellular serotonin, which is a highly significant factor in the onset of depression. Currently, we do not possess a precise mechanism to delineate how *Lentinula edodes* functions. Nevertheless, based on our findings, we can postulate that the antidepressant effect of *Lentinula edodes* might be linked to an augmentation in central noradrenergic and/or serotonergic neurotransmission.

Conclusion:

In light of the aforementioned observations, it can be inferred that the aqueous extract of *Lentinula edodes* demonstrates antidepressant-like properties and may serve as a potential natural therapeutic candidate for the treatment of depression.

Conflict of interest:

The authors declare that there is no conflict of interests regarding the publication of this paper.

References:

1. Agrawal, I., & Varga, C. (2024). Assessing and comparing disease prevention knowledge, attitudes, and 1. Moreno-Agostino, D., et al., Global trends in the prevalence and incidence of depression: a systematic review and meta-analysis. Journal of affective disorders, 2021. **281**: p. 235-243.
2. Friedrich, M.J., Depression is the leading cause of disability around the world. Jama, 2017. **317**(15): p. 1517-1517.
3. Kumar, K.S., et al., Depression-symptoms, causes, medications and therapies. The Pharma Innovation, 2012. **1**(3, Part A): p. 37.
4. Fasipe, O.J., Neuropharmacological classification of antidepressant agents based on their mechanisms of action. Archives of Medicine and Health Sciences, 2018. **6**(1): p. 81-94.
5. Kupcova, I., et al., Effects of the COVID-19 pandemic on mental health, anxiety, and depression. BMC psychology, 2023. **11**(1): p. 108.
6. Baars, J., Fungi as food. Fungi: Biology and applications, 2017: p. 147-168.
7. Łysakowska, P., A. Sobota, and A. Wirkijowska, Medicinal mushrooms: Their bioactive components, nutritional value and application in functional food production—A review. Molecules, 2023. **28**(14): p. 5393.
8. Wasser, S.P., Shiitake (Lentinus edodes). Encyclopedia of dietary supplements, 2005: p. 653-664.
9. Muszyńska, B., et al., *Lentinula edodes* (Shiitake)–biological activity. Medicina Internacia Revuo, 2017. **28**(108): p. 189-195.
10. Manik, A., et al., Phenolic Compounds and Antioxidant Potential in Mushrooms, in Mushroom Magic. CRC Press. p. 33-51.
11. Can, A., et al., The mouse forced swim test. Journal of visualized experiments: JoVE, 2012(59): p. 3638.
12. Can, A., et al., The tail suspension test. Journal of visualized experiments: JoVE, 2012(59): p. 3769.
13. Grieco, F., et al., Measuring behavior in the home cage: study design, applications, challenges, and perspectives. Frontiers in behavioral neuroscience, 2021. **15**: p. 735387.
14. Jamal, A., Embracing nature's therapeutic potential: Herbal medicine. International Journal of Multidisciplinary Sciences and Arts, 2023. **2**(3): p. 117-126.
15. Dzobo, K., The role of natural products as sources of therapeutic agents for innovative drug discovery. Comprehensive pharmacology, 2022: p. 408.
16. Yadav, S.K., et al., A mechanistic review on medicinal mushrooms-derived bioactive compounds: Potential mycotherapy candidates for alleviating neurological disorders. Planta Medica, 2020. **86**(16): p. 1161-1175.
17. Pathak, L., Y. Agrawal, and A. Dhir, Natural polyphenols in the management of major depression. Expert opinion on investigational drugs, 2013. **22**(7): p. 863-880.
18. Tucker, J. and S.E. File, The effects of tricyclic and ‘atypical’antidepressants on spontaneous locomotor activity in rodents. Neuroscience & Biobehavioral Reviews, 1986. **10**(2): p. 115-121.