

Investigating the behavioral and antioxidative effects of ethanolic extract from *Schumannia phyton magnificum* (K. Schum) in ketamine-induced mice.

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Abstract

This work presents an investigation on the behavioral and antioxidative effects of ethanolic extract from *Schumanniohyton magnificum* (K. Schum) in mice. Psychosis has several detrimental effects on health, as a result, a therapeutic strategy for managing psychosis is crucial to maintaining the global community's health because when mental illness comes up in the human brain it's reflected through different display of behavior like slow reasoning ability, depression, memory loss and isolating of oneself from others. However, it is not known whether *Schumanniohyton magnificum* leaves could cure or prevent psychosis because no study has ever cover the aspect of this plant nor any ethnobotanical study done on its activity in managing psychosis, this further emphasizes the urgency for innovative treatment approaches. The plant was administered through oral route to group of ketamine induced mice at a dosages of 100, 200 and 400 mg/kg; compared with controls group of mice for 14 days. The behavioral assessment was demonstrated using the Open Field Test for assessing the ketamine-induced hyperlocomotion, Y-Maze test was used for assessing the behavior, learning and memory (cognition) and novel object recognition test to evaluate the willingness of the mice to explore new environment or object in animal models of the central nervous disorders. Thereafter, some biochemical assay were conducted. This research shows that after 14 days of administration, the animals were sacrificed and antioxidant bioassay was carried out on the brain. *Schumanniohyton magnificum* treatment significantly ($P < 0.05$) reduced hyper-locomotion induced by ketamine, which is a predictor of positive symptoms. *Schumanniohyton magnificum* treatment (100 and 400 mg/kg) significantly enhanced spatial memory formation preventing cognitive deficits by ketamine. *Schumanniohyton magnificum* treatments significantly increased the SOD & CAT activities, as well as decreased MDA levels, this is suggesting that the antipsychotic-like action of *Schumanniohyton magnificum* maybe through inhibition of oxidative crises induced by ketamine. This study could potentially pave new way for cost-effective interventions that address both the health and socioeconomic burdens associated with psychosis.

Key point

envenoming, cognition, mechanism of identification, medicinal plants.

Introduction

The study of psychopharmacology gives rise to understanding the interplay between pharmacological and their effects on brain circuits and behavior. This work presents an investigation on the behavioral and antioxidative effects of ethanolic extract from *Schumanniohyton magnificum* (K. Schum) in mice. The way it's contends with different medications which may enhance certain cognitive functions, they do not necessarily cure the underlying mental disorders. Their analysis reveals that the enhancements in communication and thinking facilitated by medication may lead to significant psychological changes that extend beyond mere biological explanations [1, 2]. This perspective challenges the prevailing notion that mental disorders can be fully understood through a purely neurobiological lens, suggesting that psychological processes are intricately linked to the complexities of brain function [1]. This prompt a re-

evaluation of the relationship between pharmacological interventions and the psychological dimensions of mental illness, paving the way for future research that bridges the gap between neuroscience and psychopharmacology through behavioral studies.

Psychosis has several detrimental effects on health, as a result, a therapeutic strategy for preventing or managing psychosis is crucial to maintaining the global community's health because when mental illness comes up in the human brain it's reflected through different display of behavior like slow reasoning ability, depression, memory loss and isolating of oneself. However, it is not known whether *Schumanniphyton magnificum* leaves could cure or prevent psychosis because no study has ever cover the aspect of this plant nor any ethnobotanical study carried out on its activity in managing psychosis, which further emphasizes the urgency for this work. The study of *Schumanniphyton magnificum* ethanolic extract emerges as a potential avenue for therapeutic intervention. The investigation into its neuro-behavioural profile in mice is particularly relevant, as it aligns with the overarching goal of enhancing health outcomes and independence for individuals affected by psychosis by focusing on the effectiveness of this plant, the research aims to contribute to the broader discourse surrounding psychosis treatment, offering insights that may inform future therapeutic strategies [1; 2]. This study could potentially pave new way for cost-effective interventions that address both the health and socioeconomic burdens associated with psychosis.

Schumanniphyton magnificum has been reported to be useful in managing many conditions such as epilepsy, snake bite envenoming, antiviral infections, anti-depressant, and sexual maturation and fertility. *Schumanniphyton magnificum* (K. Schum) arms belongs to the Rubiaceae family, it is commonly known as **magnificent shrub**, and 'mgba mmiri' in Ibo language of Nigeria [3]. This small tree can be found growing in West and Central Africa's tropical regions. The lowland rainforest regions of Ghana, Cameroon, Sierra Leone, and southeast Nigeria (Calabar and Igbogodo) are where it is prima. Therefore, this study was designed to investigate the behavioural profile of *Schumanniphyton magnificum* ethanolic extract in ketamine induced mice.

Methodology

Study area

Collection of plant samples

Fresh leaves of *Schumanniphyton magnificum* were collected from a private farm in Okitipupa, Ondo state and authenticated by Mrs. Olofinlade Jumoke, the herbarium curator with herbarium number UNIMED P.B.T.H Number 0075 in the Department of Biosciences and Biotechnology, University of Medical Sciences, Ondo state. Voucher specimen of each plant sample was thereafter deposited in the herbarium of the same Department.

Plant extraction

The leaves of *Schumanniphyton magnificum* were rinsed properly with water and air dried; the dried leaves were ground into a powdered form with a blender. 100g of the powdered leaves is soaked into a reagent bottle containing 1000ml of 100% ethanol for 48 hours [4]. The mixture was filtered using a mesh sieve cloth, a funnel and a clean container, the filtrate is then poured into a conical flask and then connected to the rotary evaporator to obtain a pure extract without the ethanol. 10 g of the extract was obtained and put in a sterile sample bottles. The plant's extraction was done at Department of Biosciences and Biotechnology, UNIMED.

Experimental Animals

Thirty-six (36) mice weighing between 18g -22g were procured from the Animal House of the University of Medical Sciences, Ondo State. The animals were maintained 12/12- hour light/dark cycle at room temperature ($25 \pm 1^{\circ}\text{C}$) at the same animal house. The animals had access to standard pellet diet and clean water at liberation. The experimental protocol has been approved by the Animal Ethics Committee of the University of Medical Sciences, Ondo. **(Attached with this work is the ethical approval certified to carry out this work by the ethics committee of the University).**

Drug Preparation and Treatment

Doses of *Schumanniphyton magnificum* extract (100 mg/kg, 200 mg/kg and 400 mg/kg) were chosen for this study based on the findings from preliminary studies of the toxicity test conducted.

Schumanniphyton magnificum extract and risperidone were dissolved in distilled water and administered orally, and ketamine was diluted with distilled water and administered intraperitoneally (i.p).

Experimental Design

According to earlier report by [5, 6] with a little modification, this experiment assessed the effect of ethanolic extract of *Schumanniphyton magnificum* on ketamine-induced schizophrenia-like behaviors and neurochemical alterations in mice. Mice were randomly sorted into 6 groups: test ($n = 6$). Group 1 was kept as Normal control (vehicle or d.H₂O), Group 2 was kept as negative control group (ketamine 10 mg/kg, i.p.), Group 3–5 were kept as treatment and were given ethanolic extract of *Schumanniphyton magnificum* (100, 200, and 400 mg/kg) together plus ketamine (10 mg/kg, i. p.) each, and Group 6 was kept as the positive control group (Risperidone 0.5 mg/kg) plus ketamine (10 mg/kg, i.p.) respectively for 14 days. After day 14th, each group were be assessed for behavioral test (hyperlocomotion, Y-maze and NORT) and biochemical assays.

Behavioral Assessment

Open Field Test (OFT): Open-field observation box (dimensions: 25 cm × 25 cm × 30 cm) made of transparent Perspex and behavioral events recorded using a camcorder and tracked with Behavior Tracker® software. The base of the maze had 16 squares (6.5 cm × 6.5 cm) demarcated with a non-toxic permanent marker. Thirty minutes after the treatments, the animals were placed individually into the open-field observational box and their behavior recorded for 5 min using a camcorder (Everio™ model, GZ-MG 130 U, JVC, Tokyo, Japan) suspended above the maze with the aid of a stand. Novelty-induced rearing was counted as the number of times the mouse stood on its hind limbs with its forelimbs against the wall of the observation cage (supported rearing) or in free air (unsupported rearing). The number of rearing (both supported and unsupported) was tracked for 5 min. Also, the number of line crossing was counted as a representation of locomotor activity. After each session, the observation chamber was cleaned with 70% ethanol to remove residual odor [7].

Y-Maze Test

Individual mice were gently placed in a Y-maze apparatus comprised of three arms labeled A, B, and C that is, all the same length = 21 cm, breadth = 7 cm, and height = 15.5 cm, and each arm symmetrically separated from the other by one hundred and twenty degree. Each mouse spent 8 min in the apparatus, and its exploration was automatically recorded and saved on a computer by a camera set above the apparatus. By allowing the mouse to explore all three arms of the labyrinth, spontaneous alternation (which is a predictor of spatial working memory) was measured using Y-maze software and this parameter is driven by mice's intrinsic desire to explore previously unexplored arms. Based on the software settings, spontaneous alternation was calculated as the total number of correct alternations (ABC, BCA, or CAB but not ABA or BAB) / (total arm entries – 2) [7, 8]. To remove the bias caused by the previous mouse's odor cues, the apparatus was cleaned properly with 70% ethanol and allowed to dry.

NORT (Novel object recognition test)

The effect of ethanolic extract of *Schumanniphyton magnificum* on ketamine-induced cognitive impairment, as an index for the spatial cognitive dysfunction associated with schizophrenia was evaluated by [7]. Basically, in the NORT there are no positive or negative re-enforcers and this methodology assesses the natural preference for novel object displayed by rodents. The task consists of three phases. The habituation phase in which the animal is allowed freely exploring the field arena in the absence of object, familiarization phase, a single animal is placed in the open field arena containing two identical sample object (A + A), for a few minutes. The experimental context is not drastically different during the familiarization and the test phase. After a retention interval during the test phase, the animal is returned to the open field arena with two objects, one is identical to the sample and the other is novel (A + B) [8]. During both familiarization and test phase, objects are located in opposite and symmetrical corners of the arena and location of novel versus familiar object is counterbalanced [8]. Normal mice spend more time exploring the novel object during the first few minutes of the test phase, and when this bias is observed, the animal could remember the sample object and can discriminate the sample from a novel object after delays of several minutes [9].

Biochemical Assays

Immediately after the behavioral tests, the animals were sacrificed by cervical dislocation and the brains were immediately removed and kept in the refrigerator with ice block for 20 minutes. Thereafter, the whole brain was weighed and homogenized with 5 ml of 10% w/v phosphate buffer (0.1M, PH 7.4). Each brain tissue homogenates were centrifuged at 10,000 g for 10 minutes at 40°C, the pellet was discarded and the supernatant was immediately separated into various portions for the different biochemical assays.

Antioxidant enzymes assay

Estimation of Superoxide dismutase activity

SOD activity was measured by the method of [10]. The reaction mixture consists of 2.875 ml Tris-HCL buffer (50 mM, pH 8.5), pyrogallol (24 mM in 10 mM Hcl) and 100µl PMS in a total volume of 3ml. The enzyme activity was measured at 420 nm and was expressed as Units/mg protein. One unit of enzyme is defined as the enzyme activity that inhibits auto-oxidation of pyrogallol by 50%.

Estimation of reduced glutathione (GSH) level

GSH content of the tissue will be determined by the method of [10]. Briefly 1 ml of PMS (10%) is mixed with 1.0 ml of sulphosalicylic acid (4%). The samples incubated at 4°C for 1 h and then centrifuge at 1200 Xg for 15 min at 4 oC. The assay mixture (3ml) consists of 0.4 ml supernatant, 2.2 ml phosphate buffer (0.1 M, pH 7.4) and 0.4 ml DTNB (4 mg /1 ml). The yellow color developed read immediately at 412 nm. The GSH concentration was calculated as nmol DTNB conjugate formed/gm tissue.

Estimation of catalase activity

Catalase activity was assayed by the method of [10]. Briefly the reaction mixture consists of 1.95 ml phosphate buffer (0.1M, pH 7.4), 1.0 ml hydrogen peroxide (0.019M) and 0.05 ml PMS in a final volume of 3 ml. Changes in absorbance was recorded at 240 nm every minute for 5 minutes. Catalase activity was calculated as nmol H₂O₂ consumed/min/mg protein.

Estimation of glutathione peroxidase activity

Glutathione peroxidase (GPX) activity was measured according to the procedure of [10] with some modifications. Briefly the reaction mixture consists of sodium azide (10mM), hydrogen peroxide (2.5mM), trichloroacetic acid (10%), reduced glutathione (4mM), dipotassium hydrogen orthophosphate (0.3M), Ellman's reagent (DTNB) and phosphate buffer (0.1M, pH 7.4). To 0.5 ml of phosphate buffer in a test tube was added 0.1 ml of NaN₃, 0.2 ml of GSH, 0.1 ml of H₂O₂ and 0.5 ml of sample (added last). The reaction mixture was incubated for 3 min at 37°C after which 0.5 ml of TCA was added and the final mixture centrifuged at 3000 rpm for 5 min. To 1 ml of the supernatants, 2 ml of K₂HPO₄ and 1 ml of

DTNB were added and the absorbance read against a reagent blank of 1 ml distilled water, 2 ml of K_2HPO_4 and 1 ml of DTNB at 412 nm.

Estimation of glutathione s-transferase (GST) activity

Glutathione S-transferase activity was determined. Briefly the reaction mixture consists of phosphate buffer (0.1M, pH 6.5), reduced glutathione (0.1M) and 1-Chloro-2,4-dinitrobenzene (20mM). The medium for the estimation was prepared by adding 150 μ l of CDNB in a test tube to which 30 μ l of reduced glutathione, 2.79 ml and 30 μ l of sample was added. The reaction was allowed to run for 3 min with readings taken every 60 seconds against the blank at 340 nm [10].

Estimation of Myeloperoxidase activity

Peroxidase activity with 3,3',5,5'- Tetramethylbenzidine (TMB, Sigma) was measured. Briefly, 10 μ l sample was combined with 80 μ l 0.75 nM H_2O_2 (sigma) and 110 μ l TMB solution (2.9 mM TMB in 14.5% DMSO (sigma) and 150 mM sodium phosphate buffer at pH 5.4), and the plate was incubated at 37 $^{\circ}$ C for 5 min. The reaction was stopped by adding 50 μ l 2 M H_2SO_4 (Sigma) and absorption was measured at 450 nm to estimate MPO activity [10].

STATISTICAL ANALYSIS

The data obtained were expressed as mean $\pm$ S.E.M. (standard error of mean). The data were analyzed using one-way analysis of variance (ANOVA) followed by post-hoc test (Student Newman-Keuls) for multiple comparisons where appropriate using Graph-pad Prism software version 7.0. A level of $P < 0.05$ was considered as statistically significant for all test.

RESULTS

Effect of Schumanniophyton magnificum on ketamine-induced hyper-locomotion:

The effect of ethanolic extract of *Schumanniophyton magnificum* on ketamine-induced hyper-locomotion in mice based on the total distance travelled in open-field test (OFT) is shown in Fig. 1a. The administration of ketamine (10 mg/kg, i.p.) significantly ($P < 0.05$) induced hyper locomotion compared with the group treated with vehicle (10mL/kg o.p), as shown by the increase in total distance travelled in the OFT compared with standard treatment. *Schumanniophyton magnificum* treatment across all groups show significant ($P < 0.05$) having decreased in the total distance travelled in the OFT compared with the standard treatment. Similarly, treatment with RIS (0.5 mg/kg, o.p) also significantly ($P < 0.05$) prevented the hyper-locomotion compared with the treated group.

Effect of Schumanniophyton magnificum on ketamine-induced spatial memory alteration in YMT:

Figure 1b shows the effects of *Schumanniophyton magnificum* on ketamine-induced spatial working memory deficit based on the percentage (%) alternations in the Y-maze test (YMT) in mice.

Administration of ketamine (10 mg/kg i.p) daily for 14 days, produced no significant ($P < 0.05$) % alternation behaviour of the animals in the YMT compared to control group, suggesting non spatial working memory impairment. *Schumanniohyton magnificum* treatments of (100 and 400 mg/kg o.p) with ketamine administration for 14 days produced a significant ($P < 0.05$) decreased in the (%) level of cognitive alternation performance of the animals when compared with the control group. Similarly, treatments with RIS (0.5 mg/kg, o.p) produced a significant ($P < 0.05$) decreased in the (%) level of cognitive alternation performance of the animals when compared with the control group.

Effect of Schumanniohyton magnificum on ketamine-induced spatial memory alteration in NORT:

Figure 1c shows the effect of *Schumanniohyton magnificum* on ketamine-induced spatial working memory deficit based on the discrimination index (NORT) in mice. Administration of ketamine (10 mg/kg i.p) daily for 14 days, produced a no significant ($P < 0.05$) decrease in discrimination index behaviour of the animals in the NORT compared to control group, suggesting of non-spatial working memory impairment. *Schumanniohyton magnificum* treatments of (100 and 400 mg/kg o.p) with ketamine administration for 14 days produced a significant ($P < 0.05$) decreased in the (%) level of cognitive alternation performance of the animals when compared with the control group. Similarly, treatments with RIS (0.5 mg/kg, o.p) produced a significant ($P < 0.05$) decreased in the (%) level of cognitive alternation performance of the animals when compared with the control group.

Effect of Schumanniohyton magnificum on Superoxide dismutase (SOD) activity in mice brain:

The effect of ketamine administered alone or in combination with *Schumanniohyton magnificum* on the activities of SOD in the brain of mice is shown in Fig. 1d. Administration of *Schumanniohyton magnificum* (100, 200 and 40 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) daily for 14 days significantly ($P < 0.05$) increased brain SOD activity compared with the group treated with the standard. Similarly, Risperidone (0.5 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) groups for 14 days produced a significantly ($P < 0.05$) increased brain SOD activity compared with the ketamine-treated group.

Effect of Schumanniohyton magnificum on Glutathione (GSH) concentration in mice brain:

The effect of ketamine administered alone or in combination with *Schumanniohyton magnificum* on the concentration of GSH in the brain of mice is shown in Fig. 1e. Administration of *Schumanniohyton magnificum* (100 and 400 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) daily for 14 days has no significantly ($P < 0.05$) increased in brain GSH concentration compared with the ketamine-treated group. Treatment with standard drugs risperidone (0.5 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) groups does not show any significant ($P < 0.05$) increase in GSH concentration compared with the ketamine-treated group.

Effect of Schumanniohyton magnificum on Catalase (CAT) activity in mice brain:

The effect of ketamine administered alone or in combination with *Schumanniohyton magnificum* on the activities of CAT in the brain of mice is shown in Fig. 1f. Administration of *Schumanniohyton*

magnificum (100, 200, and 400 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) daily for 14 days significantly ($P < 0.05$) increased brain CAT activity compared with the ketamine-treated group. Also (atypical antipsychotic drug) Risperidone (0.5 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) daily for 14 days significantly ($P < 0.05$) increased brain CAT activity compared with the ketamine-treated group.

Effect of *Schumanniphyton magnificum* on GPx concentration in mice brain:

The effect of ketamine administered alone or in combination with *Schumanniphyton magnificum* on the concentration of GPx in the brain of mice is shown in Fig. 1g. Administration of *Schumanniphyton magnificum* (100, 200 and 400mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) daily for 14 days has no significantly ($P < 0.05$) increased in brain GPx concentration compared with the ketamine-treated group. Treatment with standard drugs Risperidone (0.5 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) groups only show a significant ($P < 0.05$) increase in GPx concentration compared with the ketamine-treated group.

Effect of *Schumanniphyton magnificum* on GST concentration in mice brain:

The effect of ketamine administered alone or in combination with *Schumanniphyton magnificum* on the concentration of GST in the brain of mice is shown in Fig. 1h. Administration of *Schumanniphyton magnificum* (100mg/kg, o.p) with ketamine (10 mg/kg, i.p.) daily for 14 days only has significantly ($P < 0.05$) increased in brain GST concentration compared with the ketamine-treated group, while treatment of *Schumanniphyton magnificum* (200 and 400mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) daily for 14 days has no significantly ($P < 0.05$) increased in brain GST concentration compared with the ketamine-treated group. Also treatment with standard drugs Risperidone (0.5 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) groups with no significant ($P < 0.05$) increase in GST concentration compared with the ketamine-treated group.

Effect of *Schumanniphyton magnificum* on Malondialdehyde (MDA) concentration in mice brain:

The effect of *Schumanniphyton magnificum* of different doses (100, 200 and 400 mg/kg, o.p.), antipsychotic standard drugs with ketamine (10 mg/kg, i.p.) and ketamine alone on lipid peroxidase based on MDA content in the brain of mice is shown in Fig. 1. Administration of *Schumanniphyton magnificum* (400 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) daily for 14 days significantly ($P < 0.05$) decreased lipid peroxidation as evident in the MDA content compared with the ketamine-treated group. Treatment with (200 and 400 mg/kg, o.p.) and standard drugs Risperidone (0.5 mg/kg, o.p.) with ketamine (10 mg/kg, i.p.) groups for 14 days does not significantly ($P < 0.05$) decreased lipid peroxidation as evident in the MDA content compared with the ketamine-treated group.

Discussion

The exploration of cognitive impairments and behavioral despair induced by pharmacological agents has garnered significant attention in recent years, particularly in the context of ketamine's effects and potential therapeutic interventions [11]. This work delves into the intricate dynamics of cognitive

performance and behavioral responses in animal models, with a specific focus on the contrasting effects of ketamine and the potential mitigating influences of *Schumanniohyton magnificum* and risperidone.

The spontaneous alteration test is used to assess hippocampal damage, quantify the cognitive deficits in transgenic mice, and evaluate the effects of drugs on cognition. On the other hand, the recognition memory test is used to test memory functions in mice [7, 8, 12]. This is because mice cannot remember which arm it just visited and thus shows a decreased spontaneous alternation. Loss of memory is one of the signs of psychosis and when the condition progresses, other cognitive functions such as the ability to use tools are impaired. Many parts of the brain including the hippocampus, septum, basal forebrain and prefrontal cortex are involved in this task. The study conducted by Wolf et al.[12] presents a comprehensive behavioral test battery designed to evaluate multiple cognitive domains, including working memory, object discrimination, spatial memory, learning, and episodic-like memory in two dementia mouse models on a 129S6 background. The findings indicate that while the 129S6/Tg2576 mice exhibited notable impairments in spatial memory and episodic-like learning, they did not show significant deficits in the novel object recognition or the spontaneous alternation task. This suggests that the effectiveness of these behavioral assessments may be limited for the 129S6 background strain, raising questions about the applicability of certain tests in evaluating cognitive impairment across different mouse models [12]. The implications of these results are critical for the understanding of cognitive deficits associated with hippocampal damage, as they underscore the necessity for tailored testing approaches that accurately reflect the specific cognitive profiles of various transgenic mouse strains. By identifying the strengths and limitations of existing behavioral tests, researchers can better assess the cognitive impacts of pharmacological interventions and the progression of memory-related disorders, thereby enhancing the translational potential of animal models in the study of psychosis and other cognitive impairments [13].

The investigation into the behavioral and antioxidative effects of the ethanolic extract of *Schumanniohyton magnificum*, serves as a critical foundation for understanding its pharmacological properties. By focusing on the oral administration of the extract in mice, the study aims to elucidate the underlying mechanisms that contribute to its therapeutic potential. This approach not only highlights the importance of empirical research in validating traditional uses of the plant but also emphasizes the need for rigorous scientific inquiry into its phytochemical constituents and their respective biological activities.

Building on this foundation, the examination of *Schumanniohyton magnificum* reveals its potential efficacy in reversing the cognitive deficits associated with ketamine administration. The findings indicate that treatment with *Schumanniohyton magnificum*, at doses of 100 and 400 mg/kg, significantly ameliorates the cognitive impairments observed in the Y-maze tests, paralleling the effects seen with risperidone at a dose of 0.5 mg/kg. This comparative analysis underscores the promising role of *Schumanniohyton magnificum* as a therapeutic agent, akin to risperidone, in addressing the cognitive alterations induced by ketamine treatments. In synthesizing these insights, this work has evaluated the

interplay between ketamine, *Schumanniophyton magnificum*, and risperidone, investigating its neuro-behavioural approaches by which these substances influence cognitive performance and behavioral outcomes.

The findings from Adase et al. [14] pave the way for deeper investigations into the plant's pharmacological profile, thereby contributing to the broader discourse on the importance of ethnobotanical knowledge in contemporary therapeutic practices [13] present compelling evidence on the multifaceted potential of (R)-ketamine, highlighting its capacity to induce cognitive alterations and behavioral despair over a 14-day treatment period. The significant decline in cognitive alternation performance observed in the Y-maze tests, have been documented which serves as a critical measure of non-spatial working memory impairment [7, 8]. This foundational study establishes a baseline understanding of the adverse cognitive effects of ketamine, thereby framing the subsequent exploration of therapeutic interventions [15]. Overall, the literature surrounding *Schumanniophyton magnificum* provides a compelling narrative about its multifaceted roles in health management, while also calling for further research to unlock its full potential in modern medicine [3, 16].

Conclusion

In summary, this research reveals a compelling insights surrounding the neuroprotective properties of *Schumanniophyton magnificum*, particularly in relation to its ability to avert oxidative stress [15] and neuronal damage. The insights provided serve as a foundation for further exploration of this promising compound, suggesting that it may not only reduce the symptoms of psychosis but also enhance cognitive function in affected individuals. This emerging evidence positions *Schumanniophyton magnificum* as a significant area of interest for future research and therapeutic development.

Statement and Declaration

Author Contribution

AMA, and FO ---designed the manuscriptAO. OO and AS.....construct the experimentBOrevised the manuscript

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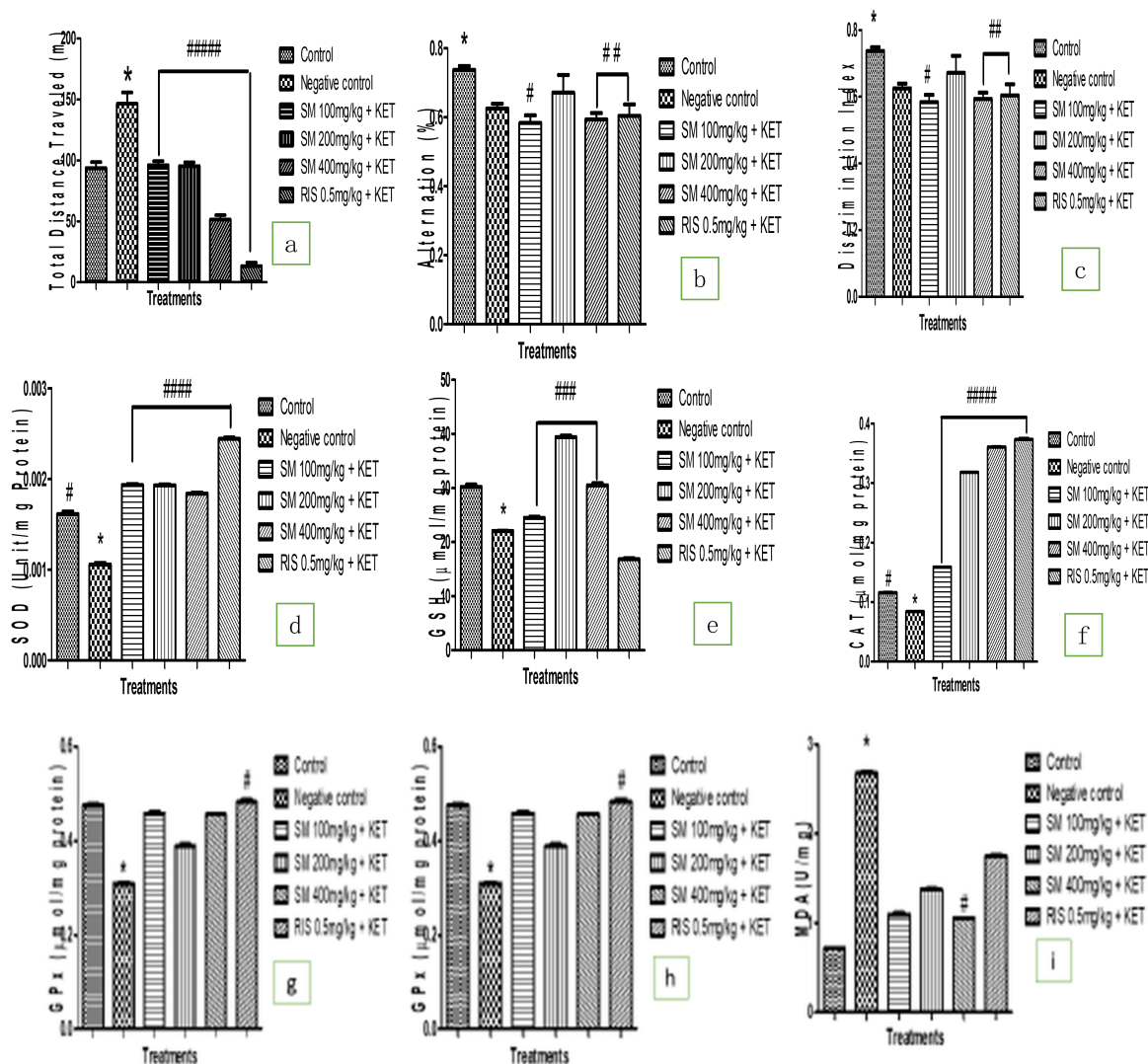
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Figures



g. Effect of *Schumanniohyton magnificum* on (GPx) activity in mice brain

Effects of *Schumanniohyton magnificum* on oxidative stress markers in mice treated with ketamine-induced schizophrenia.

Value represents the mean $\pm$ S.E.M of 5 animals / group. # Denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test)

KET = Ketamine, SM = *Schumanniohyton magnificum*, RIS = Risperidone

h. Effect of *Schumanniohyton magnificum* on (GST) activity in mice brain

Effects of *Schumanniohyton magnificum* on oxidative stress markers in mice treated with ketamine-induced schizophrenia.

Value represents the mean $\pm$ S.E.M of 5 animals / group. # Denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test)

KET = Ketamine, SM = *Schumanniohyton magnificum*, RIS = Risperidone

i. Effect of *Schumanniohyton magnificum* on Malondialdehyde (MDA) concentration in mice brain

Effects of *Schumanniohyton magnificum* on oxidative stress markers in mice treated with ketamine-induced schizophrenia.

Value represents the mean $\pm$ S.E.M of 5 animals / group. # Denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test)

KET = Ketamine, SM = *Schumanniohyton magnificum*, RIS = Risperidone

Figure 1

a. Effect of *Schumanniophyton magnificum* ketamine-induced hyperlocomotion

Value represents the mean $\pm$ S.E.M of 5 animals / group. # denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test).

KET = Ketamine, SM = *Schumanniophyton magnificum*, RIS = Risperidone.

b. Effect of *Schumanniophyton magnificum* ketamine-induced spatial memory alteration in YMT

Value represents the mean $\pm$ S.E.M of 5 animals / group. # denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test).

KET = Ketamine, SM = *Schumanniophyton magnificum*, RIS = Risperidone

c. Effect of *Schumanniophyton magnificum* ketamine-induced spatial memory alteration in NORT

Value represents the mean $\pm$ S.E.M of 5 animals / group. # denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test).

KET = Ketamine, SM = *Schumanniophyton magnificum*, RIS = Risperidone

d. Effect of *Schumanniophyton magnificum* on Superoxide dismutase (SOD) activity in mice brain

Effects of *Schumanniophyton magnificum* on oxidative stress markers in mice treated with ketamine-induced schizophrenia.

Value represents the mean $\pm$ S.E.M of 5 animals / group. # denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test).

KET = Ketamine, SM = *Schumanniophyton magnificum*, RIS = Risperidone

e. Effect of *Schumanniophyton magnificum* on (GSH) activity in mice brain

Effects of *Schumanniophyton magnificum* on oxidative stress markers in mice treated with ketamine-induced schizophrenia.

Value represents the mean $\pm$ S.E.M of 5 animals / group. # denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test)

KET = Ketamine, SM = *Schumanniophyton magnificum*, RIS = Risperidone

f. Effect of *Schumanniophyton magnificum* on Catalase (CAT) activity in mice brain

Effects of *Schumanniophyton magnificum* on oxidative stress markers in mice treated with ketamine-induced schizophrenia.

Value represents the mean $\pm$ S.E.M of 5 animals / group. # denotes $P < 0.05$ as compared to Ketamine group (One way ANOVA followed by Newman Keuls test)

KET = Ketamine, SM = *Schumanniohyton magnificum*, RIS = Risperidone