

Behavioural and biochemical studies of *Schumanniophyton magnificum* (K.schum) leaves in mice.

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Abstract

Current evidences indicate that efforts to develop novel antipsychotic agents with multipronged mechanisms of action have been limited. The study evaluated the behavioural activities of ethanolic extract of *Schumanniohyton magnificum* leaves in mice. It investigated the neuro-behavioral and antioxidant properties of the ethanolic extract of *Schumanniohyton magnificum* leaves administered through the oral route of mice at different doses 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. 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 (100, 200, and 400 mg/kg) 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. Additionally, *Schumanniohyton magnificum* treatment (100, 200, and 400 mg/kg) 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. Therefore this plant might be one of the plants to watch out for the treatment of psychosis.

Introduction

Neuro-psychopharmacology is the study of how drugs alter brain circuits to modify behavior. This multidisciplinary area of study, which examines how drugs affect the mind, is linked to basic neuroscience and psychopharmacology (Hague, 2022). It includes studies on the various ways that psychoactive substances work. This includes behavioral impacts on test animals, biochemical and molecular characterization, and therapeutic use (Gerrits & Ree, n.d.). Neuro-psychopharmacology performs better than psychopharmacology in terms of "how" and "why," and it also addresses other facets of brain activity. Consequently, the clinical portion of the field includes pharmacology-based neurologic (non-psychoactive) and psychiatric (psychoactive) treatment (Ardila, 2007). Developments in neuropsychopharmacology may have an impact on eating and sleeping patterns, anxiety disorders, affective disorders, psychotic disorders, degenerative illnesses, and sleep disorders (Aminoff et al., 2012).

Psychosis has several detrimental effects on health status and independence. It is also regarded as a high-cost condition from a socioeconomic standpoint from a cost-effectiveness standpoint. As a result, a therapeutic strategy for preventing or treating psychosis is crucial to maintaining and even improving the global community's health. However, it is not known whether *Schumanniohyton magnificum* leaf could cure or prevent psychosis. Therefore, this study was designed to investigate the Neuropsychopharmacology profile of *Schumanniohyton magnificum* ethanolic extract in mice.

Schumanniophyton magnificum has been reported to be useful in managing many conditions such as epilepsy, snake bite envenoming, antiviral infections, antidepressant, and sexual maturation and fertility. *Schumanniophyton magnificum* (K. Schum) arms belongs to the Rubiaceae family, it is commonly known as magnificent shrub, and 'mgba mmiri' in Ibo language of Nigeria (Joshua et al., 2020). 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 primarily found (Iwu, 2014). The plant reaches a height of approximately 15 feet, with soft-wooded stems, and bears enormous, opposite-leaf flowers in a dense cluster that is subtended by broad bracts. The flowers can be either white or yellow. African ethnomedicine treats a wide range of illnesses, including fever and malaria, with *Schumanniophyton magnificum*. However, there are few to no studies that have been elucidated on the neuropsychological role of the ethanolic extract of *Schumanniophyton magnificum* plant hence this study. The aim of this study was to investigate the neurobehavioral, and antioxidative effects of the ethanolic extract of *Schumanniophyton magnificum* through oral route in mice.

Materials and Method

Study area

Collection of plant samples

Fresh leaves of *Schumanniophyton 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 *Schumanniophyton 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 (Shahamat et al., 2016). 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. 10g 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 *Schumanniophyton magnificum* extract (100 mg/kg, 200 mg/kg and 400mg/kg) were chosen for this study based on the findings from preliminary studies. *Schumanniophyton 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 Chatterjee et al., (2011) with a little modification, this experiment assessed the effect of ethanolic extract of *Schumanniophyton 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 *Schumanniophyton 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), biochemical assays and histological examination.

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.

Y-Maze Test

The effect of ethanolic extract of *Schumanniophyton magnificum* on ketamine-induced cognitive impairment, as an index for the spatial cognitive dysfunction associated with schizophrenia was

evaluated by Chatterjee et al., (2011) with a little modification, this experiment assessed the effect of ethanolic extract of *Schumanniphyton magnificum* on ketamine-induced spatial working memory deficits. 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 120°. 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)(Monte et al., 2013). 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 Chatterjee et al., (2011). Basically, in the NORT there are no positive or negative reinforcers 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) (Ennaceur, 2010)(Gaskin et al., 2010; Hammond et al., 2004). 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 (Hammond et al., 2004). 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 (Mumby et al., 2002).

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 10,000g for 10 minutes at 4°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 Marklund and Marklund 1974. 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 Jollow *et al.*, (1974). 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 °C. 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 Claiborne (1985). 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 Battenberg et al. (1962) 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 K₂HPO₄ and 1 ml of DTNB at 412 nm.

Estimation of glutathione s-transferase (GST) activity

Glutathione S-transferase activity was determined according to Jakoby (1974). 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 150µl of CDNB in a test tube to which 30µl of reduced glutathione, 2.79 ml and 30µl 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.

Estimation of Myeloperoxidase activity

Peroxidase activity with 3,3',5,5'- Tetramethylbenzidine (TMB, Sigma) was measured as described before (Rudolph et al, 2010). Briefly, 10 µl sample was combined with 80ul 0.75 nM H₂O₂ (sigma) and 110 µl 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^{0c} for 5 min. The reaction was stopped by adding 50 µl 2 M H₂SO₄ (Sigma) and absorption was measured at 450 nm to estimate MPO activity.

STATISTICAL ANALYSIS

The data obtained were expressed as mean ± 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 hyperlocomotion:

The effect of ethanolic extract of *Schumanniophyton magnificum* on ketamine-induced hyperlocomotion 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 hyperlocomotion 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 ketamine 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 ketamine treatment. Similarly, treatment with RIS (0.5 mg/kg, o.p) also significantly ($P < 0.05$) prevented the hyper-locomotion compared to ketamine treated group.

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

Figure 1b shows the effect 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. *Schumanniophyton 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 *Schumanniophyton 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 ketamine-treated group. 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 Schumanniohyton magnificum on GPx concentration in mice brain:

The effect of ketamine administered alone or in combination with *Schumanniohyton magnificum* on the concentration of GPx in the brain of mice is shown in Fig. 1g. Administration of *Schumanniohyton 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 *Schumanniophyton magnificum* on GST concentration in mice brain:

The effect of ketamine administered alone or in combination with *Schumanniophyton magnificum* on the concentration of GST in the brain of mice is shown in Fig. 1h. Administration of *Schumanniophyton 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 *Schumanniophyton 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 *Schumanniophyton magnificum* on Malondialdehyde (MDA) concentration in mice brain:

The effect of *Schumanniophyton 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 *Schumanniophyton 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 current study revealed the antipsychotic activity of *Schumanniophyton magnificum* against schizophrenia-like behaviors in experimental models of psychosis as evidenced by inhibiting the indicator of psychosis, as shown by decreased hyperactivity such as reduced in total distance travelled in the open field test. The Y-maze and novel object identification test are useful tools for assessing learning and memory behavior (cognition) in animals. In animal models of central neurological diseases, these tests can be used to gauge how willing mice are to investigate novel environments or objects. Learning, memory, attention, perception, language, intelligence, and reasoning are all components of the psychological process known as cognition. The Y-Maze model is used for assessment of short term memory (Simplice et al., 2011) and diminished percentage of alternation is an indicator of an impaired spatial working memory (Hritcu et al., 2012). On one hand, 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. 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

Schumanniphyton magnificum reversed the behavioural despair and cognitive impairment caused by ketamine treatment similarly to risperidone, as evidenced by decrease in the level of cognitive alteration performance in the Y-maze tests. The 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. However, *Schumanniphyton 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 which is similar to the treatments with RIS (0.5 mg/kg, o.p) which produced a significant ($P < 0.05$) decreased in the (%) level of cognitive alternation performance of the animals when also compared with the control group.

The brain continually goes through an oxidation/antioxidant process, which makes it prone to oxidative damage. The imbalance between hazardous reactive oxygen species (ROS) and antioxidants is what causes oxidative damage to the brain (Salvagno et al., 2024). Interestingly, it was revealed in this study that *Schumanniphyton magnificum* posses strong antioxidant effects.

Ketamine binds noncompetitively to the NMDA (N-Methyl-D-aspartic acid) receptor portions of the glutamatergic synapse to suppress glutamatergic neurotransmission (Coyle, 2006). Positive, negative, and cognitive symptoms of schizophrenia are induced by the indirect upregulation and downregulation of dopamine discharge in the meso-limbic and meso-cortical circuits, respectively, due to the hypofunction of the NMDA receptor in different regions of the brain (e.g., ventral tegmentum, striatum, prefrontal cortex, and hippocampus) (Nakazawa & Sapkota, 2020). The antipsychotic activity of *Schumanniphyton magnificum* increased the superoxide dismutase and catalase suggesting that the antipsychotic-like action of *Schumanniphyton magnificum* may be through inhibition of oxidative crises induced by ketamine (Giustarini et al., 2009). Moreover, *Schumanniphyton magnificum* significantly decreased the levels of malonaldehyde in contrast to the ketamine-treated group which shown a significant increase suggesting mitigated in lipid peroxidation caused by ketamine.

Conclusion

In experimental models of psychosis using ketamine, *Schumanniphyton magnificun* has been demonstrated to exhibit positive behavioral action. *Schumanniphyton magnificum* exhibits this effect that may be related to its capacity to avert oxidative stress and neuronal damage in the brain, hence reducing both positive and negative symptoms and enhancing animal cognitive functions. All things considered, the research suggest that *Schumanniphyton magnificum* is a viable therapy candidate that should be on lookout for, for further investigation in neurological conditions like psychosis

Declarations

Conflict of interest: Authors declared no conflict of interest.

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Figures

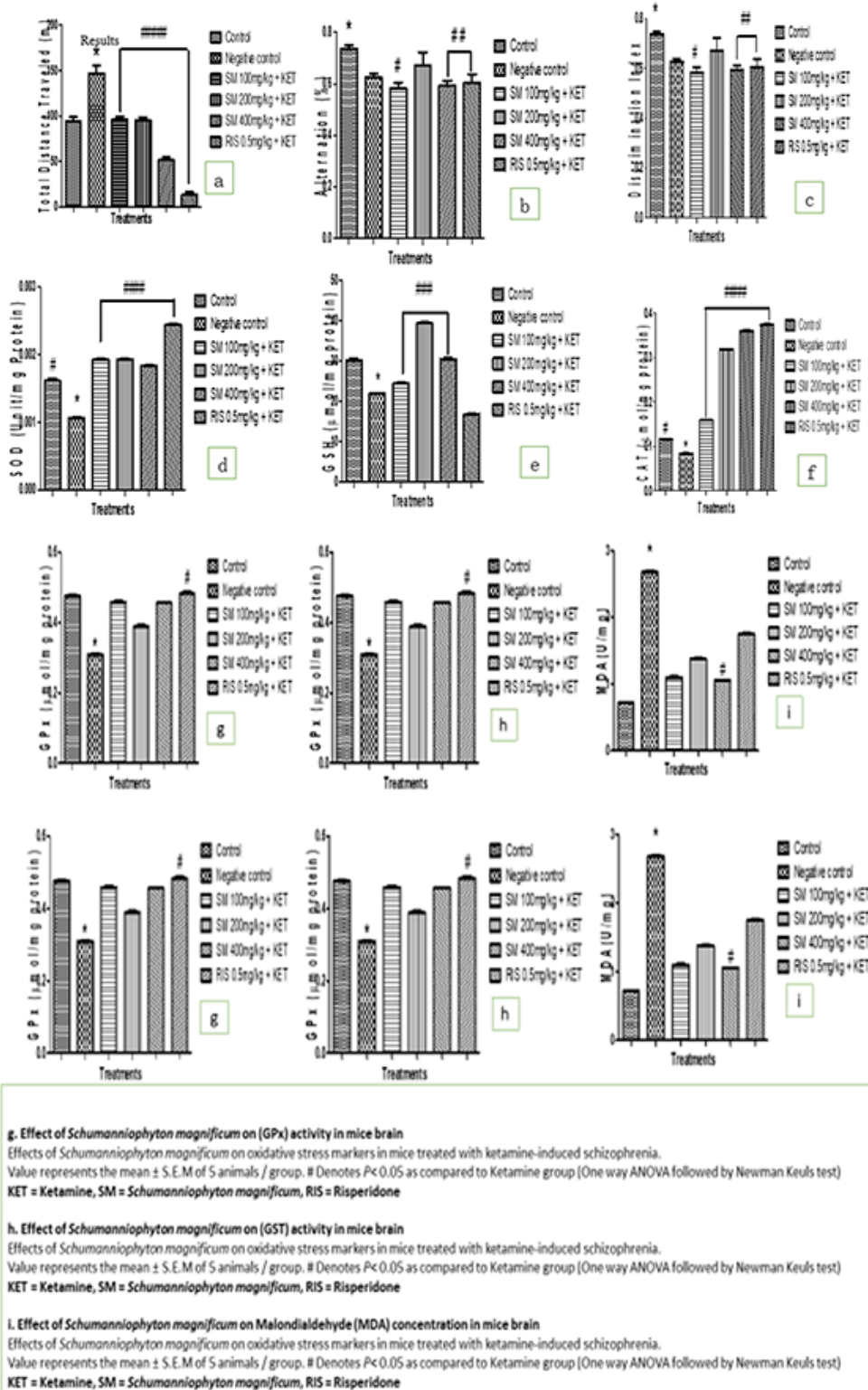


Figure 1

a. Effect of *Schumanniophyton magnificum* on 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* on 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* on 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 = *Schumanniophyton magnificum*, RIS = Risperidone