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Original Article

Antipsychotic-like Effects of Jobelyn® in Ketamine-induced Psychosis in Mice

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Abstract:

Background: Jobelyn® (JB) is a polyherbal formulation with proven benefits on psychosis, a psychiatric disorder, validated in dopamine-agonist models. However, its effect in ketamine, a glutamate antagonist, is linked to schizophrenia's pathology due to N-methyl-D-aspartate (NMDA) receptor hypofunction, which remains largely unknown. Hence, this study investigates the antipsychotic effectsof JB in ketamine-induced mouse models.

Methods: Antipsychotic activity of Jobelyn®(JB) (5, 10, and 50 mg/kg, p.o.) was assessed based on the inhibition of stereotyped behaviour induced by ketamine and ketamine-induced hyperactivity in mice. Ketamine-enhanced immobility in forced swim test (FST) and drug-induced ptosis and catalepsy in mice were also used to further evaluate JB's antipsychotic properties and its potential to cause extrapyramidal side effects.

Results: JB (5, 10, and 50 mg/kg, p.o.) significantly ($p<0.05$) inhibited stereotypy induced by apomorphine (1 mg/kg, i.p.) or ketamine (10 mg/kg, i.p.) and ketamine-induced hyperactivity. Furthermore, JB significantly ($p<0.05$) reduced the ketamine-induced enhancementofimmobility (30 mg/kg, i.p.) in mice, suggesting antipsychotic activity. JB also dose-independently depleted the monoamine as indexed by the ptosis paradigm. However, JB (5, 10, and 50 mg/kg, p.o.) did not cause cataleptic behaviour, as it failed to alter the duration of stay of the animals on the inclined plane.

Conclusion: This study provides valuable evidence that JB contains biologically active constituent with antipsychotic properties. The behavioural findings suggest possible modulation of dopaminergic and glutamatergic pathways, thus justifying its ethnomedicinal claims in the management of psychotic disorders.

Keywords: *Psychosis, Schizophrenia, NMDA receptor, Antipsychotics, Jobelyn®*

1. Introduction

Schizophrenia is one of the most severe and persistent psychiatric disorders, affecting approximately 1% of the global population, with relatively similar prevalence across sexes, cultures, and geographic regions [1]. It is a complex neuropsychiatric disorder characterized by positive symptoms, negative symptoms, and cognitive impairments. Positive symptoms include conceptual disorganization, delusions, hallucinations, hyperactivity, and stereotypic behaviour, while negative symptoms are characterized by social withdrawal, anhedonia, reduced emotional expression, and diminished motivation [2]. Cognitive dysfunctions, including impaired executive function, learning deficits, poor working memory, reduced attention span, and impaired information processing, are also common features of schizophrenia [2]. Notably, negative and cognitive symptoms predominate in nearly one-third of patients and are associated with poor long-term outcomes and limited responsiveness to conventional pharmacological treatment [3].

Antipsychotic medications used in the treatment of schizophrenia are broadly classified into typical and atypical agents [4]. Typical antipsychotics, such as haloperidol, are effective in managing positive symptoms but show limited efficacy against primary negative symptoms and are frequently associated with extrapyramidal side effects [4]. In contrast, atypical antipsychotics, such as clozapine, demonstrate modest benefits against negative symptoms [5,6]. However, their long-term use is often associated with serious adverse effects, including metabolic disorders such as diabetes mellitus and hematological complications such as agranulocytosis [7]. Despite decades of research, progress in developing novel antipsychotic drugs with combined efficacy against positive, negative, and cognitive symptoms remains limited. One major challenge is the scarcity of appropriate animal models capable of replicating the complex symptom profile of schizophrenia and facilitating effective drug screening [8].

Although the precise pathophysiological mechanisms underlying schizophrenia remain incompletely understood, the dopamine hypothesis has dominated scientific explanations of the disorder for over five decades and has contributed significantly to the development of conventional antipsychotic agents such as haloperidol [9,10]. However, an exclusive focus on dopaminergic dysfunction has provided only limited progress in understanding schizophrenia and in the development of innovative therapies, largely because the disorder involves multiple neurotransmitter systems and receptor targets [6].

Increasing evidence from pharmacological, post-mortem, and clinical studies implicates glutamatergic dysfunction, particularly involving the N-methyl-D-aspartate (NMDA) receptor, in the pathophysiology of schizophrenia [11]. NMDA receptor antagonists such as phencyclidine (PCP) and ketamine have been shown to induce psychosis-like symptoms in healthy individuals [12] and exacerbate psychotic symptoms in patients with schizophrenia [13]. Importantly, ketamine disrupts cognitive function in both humans and animal models [14], producing deficits that resemble those observed in schizophrenia. Consequently, ketamine-induced psychosis models are increasingly recognized as valuable translational tools for investigating the neurobiology of schizophrenia and evaluating the antipsychotic potential of therapeutic agents, including natural products [15].

Natural products possess high chemical diversity, biochemical specificity, and diverse pharmacological activities, making them promising candidates for the development of novel therapeutic agents for neurological and psychiatric disorders [16]. Jobelyn® (JB), a unique polyherbal formulation with recognized antianaemic, immunomodulatory, and energizing properties, is widely used in Western Nigeria for managing neurological disorders, particularly epilepsy in children [17–19]. It has also been reported to enhance stamina, concentration, healing, stress resistance, vigilance, and work efficiency in healthy individuals, while improving overall well-being in degenerative and age-related conditions [18].

Phytochemical analyses have shown that Jobelyn® is rich in bioactive compounds, including proanthocyanidins, anthocyanidins, apigenidins, proapigenidins, apigenins, luteolins, naringenins, flavonoids, and polyphenols, many of which are derived from *Sorghum bicolor* [20,21]. These phytochemicals have demonstrated a wide range of biological activities, including antioxidant, anti-inflammatory, and neuroprotective effects [20,22]. Jobelyn® also contains bioactive constituents obtained from *Parquetina nigrescens* (Periplocaceae) and *Harungana madagascariensis* (Clusiaceae). Specifically, compounds such as apigenin, luteolin, and naringenin have been reported to exert neuroprotective effects and attenuate neuroinflammation, suggesting their therapeutic potential in central nervous system (CNS) disorders [20,22].

Although Jobelyn® has previously demonstrated antidopaminergic activity in dopamine-based psychosis models [23], its effects in glutamatergic models of schizophrenia remain poorly understood. To the best of our knowledge, this study is among the first to investigate the antipsychotic-like effects of Jobelyn® in a ketamine-induced model of psychosis, thereby extending previous findings from dopamine-based models [23] to glutamatergic dysfunction relevant to schizophrenia [24].

2. Materials & Methods

2.1. Animals

A total of 140 adult male Swiss albino mice (*Mus musculus*) weighing 18–22 g were used for this study, considering the sex-dimorphic vulnerability associated with schizophrenia [23]. The animals were obtained from the Central Animal House, Faculty of Basic Medical Sciences, Delta State University, Abraka, Nigeria. The mice were housed in groups of five per plastic cage (42 × 30 × 27 cm) under standard laboratory conditions at 25 ± 1°C, with a 12:12 h light/dark cycle. Standard rodent pellet feed and water were provided *ad libitum* throughout the study period. The animals were acclimatized for at least one week before commencement of the experiments. For each behavioural paradigm, animals were assigned to treatment groups of n = 5 per group. All experimental procedures were approved by the University of Ibadan Animal Care and Use Research Ethics Committee (UI-ACUREC/App/12/2016/01) and conducted in accordance with the *National Institutes of Health Guide for the Care and Use of Laboratory Animals* (Publication No. 85–23, revised 1985).

2.2. Drugs

The following drugs were used in this study: Ketamine hydrochloride (KET) (Sigma-Aldrich, St. Louis, MO, USA), diluted in distilled water and administered intraperitoneally (i.p.). Risperidone (RIS) (Sigma-Aldrich, St. Louis, MO, USA), dissolved in distilled water and administered orally (p.o.). Jobelyn® (JB) (Health Forever Products Ltd., Lagos, Nigeria). Jobelyn® was commercially obtained from a licensed community pharmacy. The formulation consists primarily of *Sorghum bicolor* leaf sheath extract and other herbal constituents as previously characterized [20,23]. Batch number JX301020® 3X was used throughout the study. JB was dissolved in distilled water prior to administration. The doses of JB (5, 10, and 50 mg/kg) used in this study were selected based on findings from a preliminary study by Omogbiya et al. [23]. Appropriate vehicle groups received distilled water (10 mL/kg, p.o.) simultaneously. Risperidone was used as the standard antipsychotic because ketamine-induced psychosis models have been shown to respond preferentially to atypical antipsychotics [30].

2.3. Experimental Animal Models

2.3.1. Effect of JB on Ketamine-Induced Stereotypy

Ketamine-induced psychosis was used to evaluate the antipsychotic effect of JB according to the method described by Ben-Azu et al. [25]. Mice were randomly divided into six treatment groups (n = 5/group) based on previously validated behavioural paradigms [23,25]. Groups 1 and 2 received vehicle (10 mL/kg, p.o.), with Group 2 serving as the negative control. Groups 3–5 received JB (5, 10, and 50 mg/kg, p.o.), while Group 6 received risperidone (0.5 mg/kg, p.o.) as the positive control. Sixty minutes after pretreatment, animals in Groups 2–6 received a subanaesthetic dose of ketamine (10 mg/kg, i.p.). Each mouse was immediately placed in a transparent observation chamber (20 × 20 × 23 cm), and stereotypic behaviours were observed for 2 min at 10, 15, 20, 30, and 45 min post-ketamine administration. Stereotypic behaviour was scored according to previously described methods. The observation chamber was cleaned with 10% ethanol after each session to eliminate residual odour.

2.3.2. Effect of JB on Ketamine-Induced Hyperlocomotion

Ketamine-induced hyperlocomotion was evaluated according to the method of Ben-Azu et al. [25]. Mice were randomly assigned into six treatment groups (n = 5/group). Groups 1 and 2 received vehicle (10 mL/kg, p.o.), with Group 2 serving as the negative control. Groups 3–5 received JB (5, 10, and 50 mg/kg, p.o.), while Group 6 received risperidone (0.5 mg/kg, p.o.) as the positive control. Sixty minutes after pretreatment, Group 1 received no ketamine, whereas Groups 2–6 received ketamine (10 mg/kg, i.p.). Thereafter, mice were individually placed in the centre of an open-field chamber (35 × 30 × 23 cm). The duration of ambulation (s) and number of line crossings were recorded over 5 min using a stopwatch. Chambers were cleaned with 10% ethanol after each session.

2.3.3. Effect of JB on Ketamine-Enhanced Immobility in the Forced Swim Test

The forced swim test (FST) was used to evaluate ketamine-enhanced immobility, a behavioural correlate of negative symptoms of schizophrenia [25,26]. Mice were randomly assigned into six groups (n = 5/group). Group 1 received vehicle (10 mL/kg, p.o.) once daily for five days, while Groups 2–6 received ketamine (30 mg/kg, i.p.) once daily for five consecutive days. Twenty-four hours after the final treatment, Group 2 received no additional treatment and served as the negative control. Groups 3–5 were treated with JB (5, 10, and 50 mg/kg, p.o.), while Group 6 received risperidone (0.5 mg/kg, p.o.) as the positive control. Sixty minutes later, each mouse was placed individually in a transparent glass cylinder (height = 46 cm; diameter = 20 cm) containing water maintained at 25°C to a depth of 30 cm and forced to swim for 6 min. Immobility time was recorded during the final 5 min, excluding the first minute of active escape behaviour [26,27]. Reduced immobility time was considered indicative of improvement in ketamine-induced negative symptom-like behaviour. After each session, mice were immediately removed, dried with a towel, and kept in a warm open space until completely dry before returning to their cages.

2.3.4. Effect of JB on Ptosis Induction

Drug-induced ptosis was assessed as an index of monoaminergic depletion and a predictor of extra

pyramidal side effects associated with first-generation antipsychotic drugs such as haloperidol [17,23,25]. Mice were divided into five groups (n = 5/group). Group 1 received vehicle (10 mL/kg, p.o.), Groups 2–4 received JB (5, 10, and 50 mg/kg, p.o.), while Group 5 received haloperidol (HLP, 1 mg/kg, p.o.) as the positive control. Animals were placed individually in ptosis observation chambers immediately after treatment. Ptosis scores were assessed at 60, 90, and 120 min post-treatment using the following scale:

0 = eyes fully open
1 = eyes one-quarter closed
2 = eyes half closed
3 = eyes three-quarters closed
4 = eyes completely closed

2.3.5. Effect of JB on Catalepsy Test

The cataleptic effect of JB was evaluated according to a modified procedure described by Ben-Azu et al. [25] and Porsolt et al. [29]. Animals were divided into five treatment groups (n = 5/group). Group 1 received vehicle (10 mL/kg, p.o.), Groups 2–4 received JB (5, 10, and 50 mg/kg, p.o.), while Group 5 received haloperidol (1 mg/kg, p.o.) 60 min prior to catalepsy assessment. Catalepsy was assessed by gently placing the forelimbs of each mouse on a horizontal wooden bar (height = 6 cm; width = 4 cm; length = 16 cm). The duration of akinesia (time spent in an imposed posture before initiating movement) was recorded in seconds [29].

2.4. Statistical Analysis

Data were initially tested for normality using the Shapiro–Wilk test and expressed as mean ± standard error of the mean (SEM). Data from stereotypy and ptosis experiments, which were non-parametric, were analyzed using the Kruskal–Wallis test. Other datasets were analyzed using one-way analysis of variance (ANOVA) followed by the Newman–Keuls post hoc test for multiple comparisons where appropriate. Statistical analyses were performed using GraphPad InStat® Biostatistics software (GraphPad Software Inc., La Jolla, CA, USA; version 4.0). A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Effect of JB on ketamine-induced stereotypy

In mice, ketamine (10 mg/kg, i.p.) significantly ($P < 0.05$) induced stereotyped behaviours, including head movements, intermittent sniffing, chewing, and intense licking, compared with the vehicle-treated group (10 mL/kg, p.o.). Pretreatment with JB (5, 10, and 50 mg/kg, p.o.) significantly ($P < 0.05$) prevented these stereotyped behaviours. A similar effect was observed in animals treated with RIS (0.5 mg/kg, p.o.), a standard atypical antipsychotic, which significantly ($P < 0.05$) prevented the stereotyped behaviours induced by KET (10 mg/kg, i.p.) (Fig. 1).

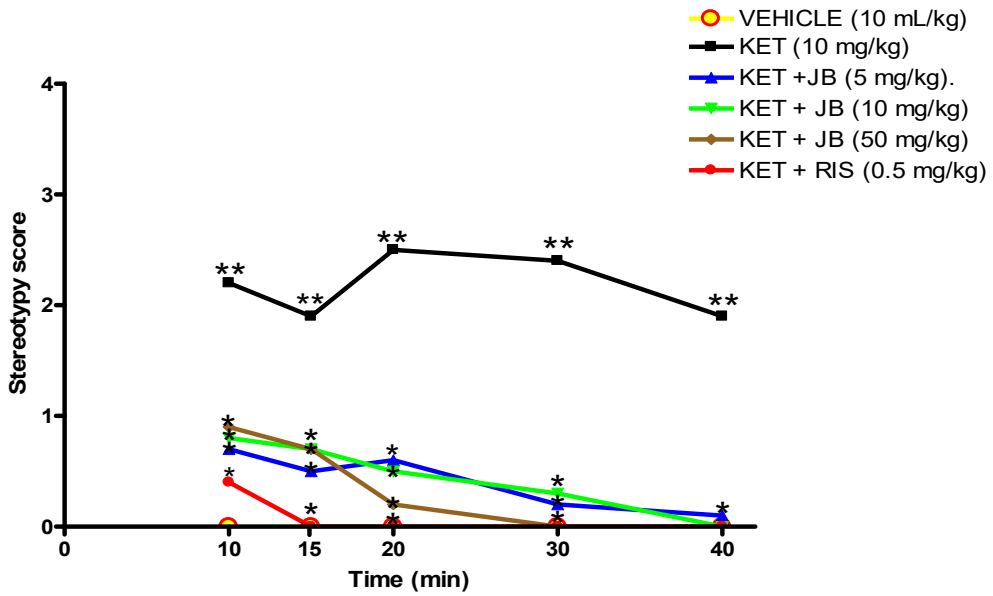

Fig. 1. JB reduces ketamine-induced stereotyped behaviours. Values represent the mean of 5 animals/group.

*** Denotes P< 0.05 compared to vehicle (Distilled water) and * Denotes P < 0.05 compared to KET (10 mg/kg, i.p.) (Kruskal-Wallis test; H = 19. 456). VEH = Vehicle, KET = Ketamine, RIS = Risperidone, JB = Jobelyn®*

3.2. Effect of JB on ketamine-induced hyperlocomotion

The effect of JB on ketamine-induced hyper-locomotion in mice, as assessed in the open-field test (OFT), is shown in Figs. 2 and 3. Administration of ketamine (10 mg/kg, i.p.) significantly ($P < 0.05$) induced hyper-locomotion compared with the vehicle-treated group (10 mL/kg, p.o.), as indexed by an increase in the number of line crossings and a reduction in ambulation time in the OFT. However, JB pretreatment (5, 10, and 50 mg/kg, p.o.) significantly ($P < 0.05$) prevented ketamine-induced hyper-locomotion, as indicated by a decrease in the number of line crossings and an increase in the duration of ambulation in the OFT. Similarly, pretreatment with RIS (0.5 mg/kg, p.o.) compared with the ketamine-treated group significantly ($P < 0.05$) prevented hyper-locomotion (Figs. 2 and 3).

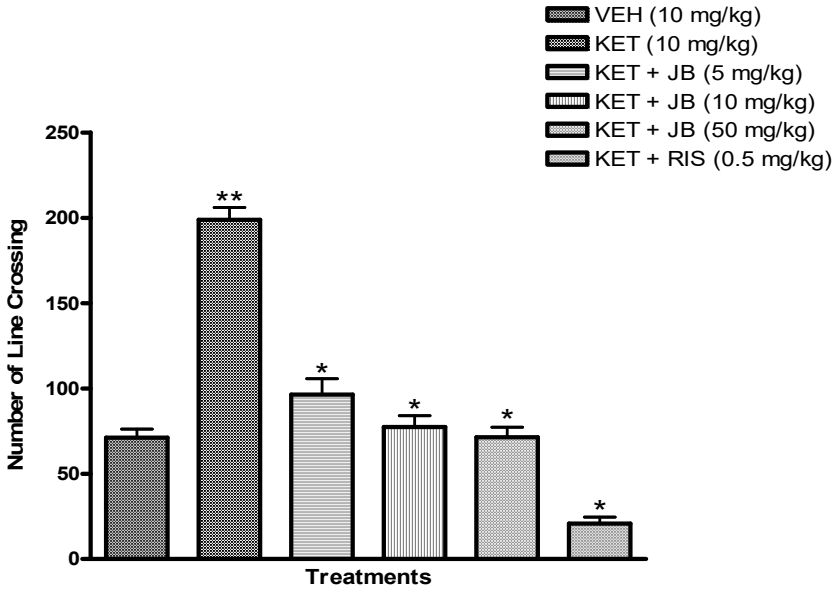

Fig.2. JB reduces ketamine-induced hyperlocomotion.

*Value represents the mean ± S.E.M of 5 animals per group. One-way ANOVA revealed that there is a significant [F (5, 24) = 81.94, P< 0.0001] difference between various treatment groups for the number of line crossing(s). ** Denotes P< 0.05 as compared to the vehicle group. * Denotes P< 0.05 as colmpared with the ketamine group. VEH = Vehicle, KET = Ketamine, RIS = Risperidone, JB = Jobelyn®*

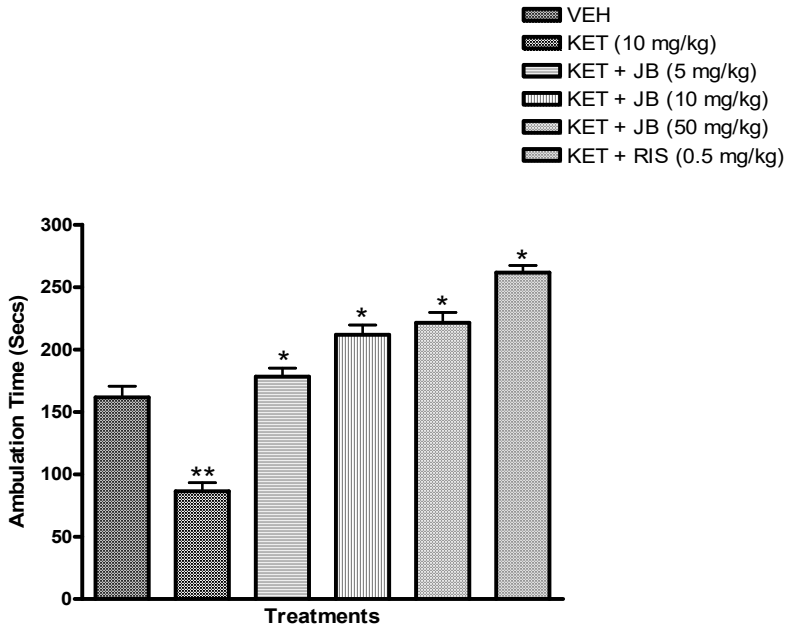

Fig.3. JB reverses ketamine-impaired ambulation time.

*Value represents the mean ± S.E.M of 5 animals per group. One-way ANOVA revealed a significant difference [F(5, 24) = 64.60, P< 0.0001] among treatment groups in ambulation time (seconds).** Denotes P< 0.05 as compared to vehicle group. * Denotes P< 0.05 as compared with the ketamine group. VEH = Vehicle, KET = Ketamine, RIS = Risperidone, JB = Jobelyn®*

3.3 Effect of JB on ketamine-enhanced immobility in forced swim test

Ketamine (30 mg/kg, i.p.) administration significantly ($P < 0.05$) increased immobility time compared with the vehicle-treated group, as measured by immobility duration in the FST in mice. JB (5, 10 and 50 mg/kg, p.o.) significantly ($P < 0.05$) decreased immobility time compared with the ketamine-treated group (30 mg/kg, i.p.) alone (negative control). Similarly, the group treated with RIS (0.5 mg/kg, p.o.) significantly ($P < 0.05$) reduced immobility time compared with the ketamine-treated group (Fig. 4).

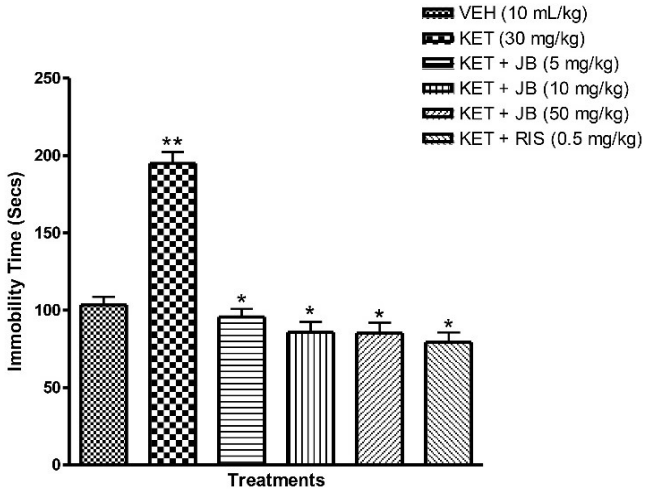

Fig. 4. JB reduces ketamine-enhanced immobility in FST.

*Value represents the mean ± S.E.M of 5 animals per group. One-way ANOVA revealed a significant difference [F(5, 24) = 38.88, P< 0.0001] among the treatment groups. ** Denotes P< 0.05 as compared to vehicle group. * Denotes P< 0.05 as compared with the ketamine group. VEH = Vehicle, KET = Ketamine, RIS = Risperidone, JB = Jobelyn®*

3.4. Effect of JB on Drug-induced Ptosis

Fig. 5 shows the results of drug-induced ptosis of JB and HLP. The effect of JB on ptosis induction at 60th, 90th, and 120th minutes (60 min after treatment) was evaluated using the ptosis scale. Pretreatment with JB (5, 10, and 50 mg/kg, p.o.) showed significant ($P< 0.05$) induction of ptosis compared to the vehicle (10 mL/kg, p.o.). Similarly, pretreatment with HLP (1 mg/kg, p.o.) was found to induce ptosis compared with the group treated with vehicle (10 mL/kg, p.o.).

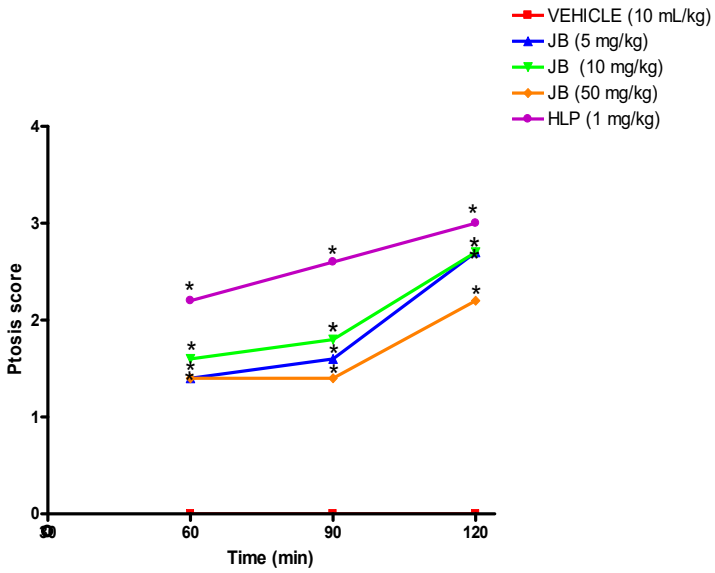

Fig.5. Effect of JB on Drug-induced Ptosis.

*Value represents the mean ± S.E.M of 5 animals per group. *Denotes P< 0.05 compared to vehicle group (ANOVA followed by Kruskal-Wallis test; H = 13.673). VEH = Vehicle, HLP = Haloperidol, JB = Jobelyn®.*

3.5. Effect of JB on Catalepsy Test:

Fig. 6 shows the results of the catalepsy test. JB (5, 10, and 50 mg/kg, p.o.) did not significantly ($P > 0.05$) prolong the duration of akinesia compared with the vehicle group (10 mL/kg, p.o.). However, HLP (1 mg/kg, p.o.) significantly ($P < 0.05$) prolonged the duration of akinesia compared with the vehicle group (10 mL/kg, p.o.).

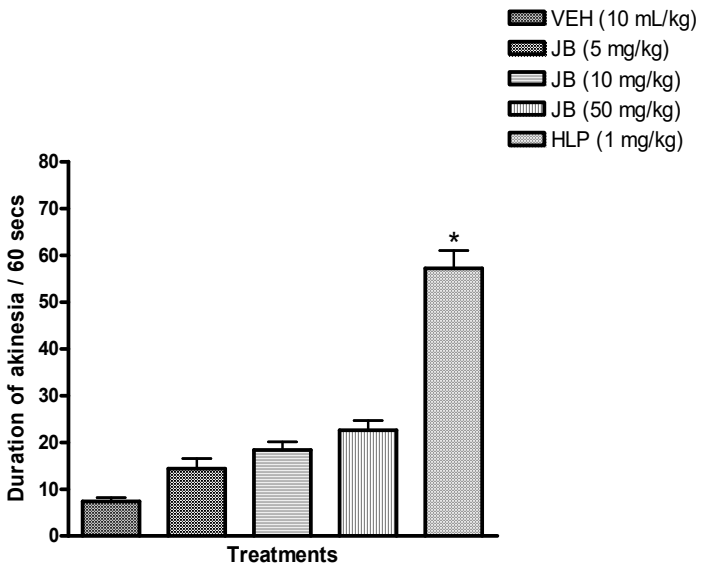

Fig. 6. Effect of JB on Catalepsy Test.

*Value represents the mean ± S.E.M of 5 animals per group. * Denotes P< 0.05 compared to vehicle group (ANOVA followed by Newman-Keuls post hoc test).VEH = Vehicle, JB = Jobelyn®, HLP = Haloperidol*

4. Discussion

Schizophrenia is a chronic and heterogeneous neuropsychiatric disorder characterized by profound behavioural, cognitive, and emotional disturbances. The present study evaluated the antipsychotic-like effects of Jobelyn® (JB), a polyherbal formulation with reported neuroactive properties, in ketamine-induced animal models of psychosis using behavioural phenotypes relevant to schizophrenia. Given the growing interest in plant-derived therapeutic agents with potentially fewer adverse effects than conventional psychotropic medications, herbal medicines continue to attract considerable attention as alternative or adjunctive interventions in neuropsychiatric disorders.

Pharmacological, post-mortem, and clinical evidence implicates glutamatergic dysfunction, particularly involving the NMDA receptor, in the pathophysiology of schizophrenia [11]. NMDA receptor antagonists such as ketamine induce psychosis-like symptoms in healthy individuals and exacerbate psychotic manifestations in patients with schizophrenia [12–15]. In the present study, JB significantly attenuated ketamine-induced stereotypy and hyperlocomotion across the tested dose range (5–50 mg/kg), suggesting potential antipsychotic-like activity.

Ketamine-induced hyperactivity and stereotyped behaviour are widely used behavioural paradigms for assessing compounds with potential antipsychotic effects [31]. Antipsychotic agents typically reduce spontaneous locomotor activity and reverse ketamine-induced behavioural disturbances [8,32]. Dopaminergic mechanisms play a critical role in locomotor activity, with ketamine known to alter dopamine transmission and receptor activation [33]. Hyperlocomotion in rodents has been associated with dopaminergic hyperactivation in the striatum [34], while glutamatergic modulation of dopaminergic transmission occurs through NMDA receptor-mediated regulation of GABAergic and dopaminergic pathways [35,36]. Blockade of NMDA receptors on inhibitory GABAergic interneurons has been linked to increased locomotion and repetitive behaviours in animal models [11,37].

The ability of JB to suppress ketamine-induced hyperactivity and stereotyped behaviour may therefore suggest modulation of dopaminergic neurotransmission secondary to glutamatergic dysfunction. This observation aligns with findings from our earlier study, in which JB attenuated behavioural alterations induced by both direct and indirect dopamine agonists, including apomorphine- and amphetamine-induced stereotypy and hyper locomotion [23]. Additionally, JB antagonized amphetamine-induced lethality in experimental animals

[23]. Collectively, these findings support the possibility of antidopaminergic activity contributing to the observed behavioural effects of JB. However, the precise receptor-level mechanisms remain to be established.

While conventional antipsychotics such as haloperidol are effective against positive symptoms of schizophrenia, their efficacy in managing negative symptoms remains limited [4,38,39]. In contrast, atypical antipsychotics such as risperidone and clozapine exhibit broader therapeutic benefits, partly due to combined dopaminergic and serotonergic receptor modulation [6,40]. In the present study, JB reduced ketamine-enhanced immobility in the forced swim test, producing effects comparable to risperidone. Ketamine-induced immobility has previously been used as a behavioural correlate of negative symptoms of schizophrenia, including social withdrawal, affective flattening, and anhedonia [25,26].

The observed reduction in immobility time following JB treatment may indicate a protective effect against ketamine-induced negative symptom-like behaviours. Although risperidone's efficacy has been linked to serotonin 5-HT_2A receptor antagonism, the present findings do not permit definitive conclusions regarding serotonergic involvement in JB's mechanism of action. Nonetheless, the similarity in behavioural outcomes suggests that further mechanistic studies investigating serotonergic and glutamatergic receptor interactions may be warranted.

The present findings are further supported by the ptosis model, which has been used as an indirect behavioural index of monoamine depletion and antipsychotic activity [17,23,24]. Drug-induced ptosis has also been employed experimentally to evaluate the likelihood of extrapyramidal side effects associated with first-generation antipsychotics [41]. In this study, JB produced dose-independent ptosis across different observation periods, suggesting possible monoaminergic involvement. However, while ptosis may indicate central monoaminergic activity, caution is warranted in interpreting this response as definitive evidence of antipsychotic efficacy or extrapyramidal liability.

Importantly, JB did not induce catalepsy or impair sensorimotor performance compared with vehicle-treated animals. The catalepsy test is a well-established rodent paradigm for assessing extrapyramidal side effects, particularly those associated with dopamine D_2 receptor blockade by typical antipsychotics such as haloperidol and chlorpromazine [42]. Reduced propensity for catalepsy is often considered indicative of atypical antipsychotic properties and lower extrapyramidal risk [29]. Although first-generation or typical antipsychotics such as haloperidol inhibit apomorphine-induced stereotypy, atypical counterparts such as clozapine and risperidone are known to be less effective against stereotypy [43]. These observations in animals treated with RIS further support the notion that atypical antipsychotics preferentially act on D2 receptors in the limbic system [43]. The absence of cataleptic behaviour in JB-treated animals, despite its ability to attenuate hyperlocomotion and stereotypy, suggests a potentially favourable motor side-effect profile.

The observed behavioural effects of JB may be attributable to its phytochemical constituents, many of which have demonstrated neuroactive and neuroprotective properties. Previous studies have shown that JB contains several bioactive compounds—including luteolins, apigenidins, apigenins, and naringenins—that possess anti-inflammatory, antioxidant, neuroprotective, and neuro modulatory properties and are capable of crossing the blood–brain barrier [21,44–46]. These compounds may collectively contribute to the behavioural effects observed in the present study. However, the specific phytochemical components responsible for JB's antipsychotic-like activity remain unclear and warrant further investigation.

This study has several limitations that should be acknowledged. First, the relatively small sample size per experimental group may limit statistical power. Second, although behavioural paradigms provide useful translational insight, no receptor-binding studies, neuro chemical analyses, or histopathological assessments were performed to elucidate the precise mechanisms underlying JB's effects. Third, repeated behavioural observations were analyzed using conventional statistical approaches, which may not fully account for within-subject temporal effects. Future studies employing larger sample sizes, repeated-measures analytical models, and mechanistic investigations involving neurotransmitter pathways, receptor assays, and molecular biomarkers are recommended to strengthen the translational relevance of these findings.

5. Conclusion

The present findings demonstrate that Jobelyn® exhibits antipsychotic-like effects in ketamine-induced animal models of psychosis. JB attenuated behavioural alterations associated with positive and negative symptom-like phenotypes, including hyperlocomotion, stereotypy, and enhanced immobility, without inducing catalepsy. These findings suggest possible modulation of dopaminergic and glutamatergic pathways and provide preliminary scientific support for its ethnomedicinal use in the management of psychotic disorders. However, further mechanistic, toxicological, and clinical investigations are required to clarify its therapeutic potential and safety profile.

Declarations

Consent for publication: All authors approved the publication of this manuscript.
Data availability statement: Due to privacy and ethical restrictions, the supporting data validating the findings of this study are not publicly available. However, these can be provided by the corresponding author upon reasonable request.
Competing Interests: The authors declare that they have no conflicts of interest.
Authors' Contributions: All authors contributed adequately to the different phases of the study: IAO and BB conceptualized the study. IAO, BB, MO, OO, BO, and PB participated in the experimental bench work organization and execution; BB analyzed the results. MO, OO, AOJ, EOO, JOK and EPA were involved in the final text proof-reading and organization. IAO and BB interpreted the results and fine-tuned the final draft of the manuscript.
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