RESEARCH PAPER

EVALUATION OF THE ANTIPSYCHOTIC ACTIVITY OF *FICUS CARICA* FRUIT EXTRACT IN WISTAR RATS

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ABSTRACT

Stereotypical behaviours, delusions, and hallucinations are some of the characteristics that characterize psychotic disorders. People are searching for safer, plant-based alternatives to current antipsychotic medications because they often have unfavourable side effects. The current study aimed to evaluate the antipsychotic activity of Ficus carica fruit extract at 200 and 400 mg/kg in Wistar rats using a ketamine-induced model of psychosis. The rats were divided into five groups: a standard group (olanzapine 5 mg/kg, i.p.), a ketamine control (50 mg/kg, i.p.), and two test groups that were given Ficus carica fruit extract orally for 21 days at 200 and 400 mg/kg. On day seven, locomotor activity was measured using an actophotometer to assess the effects of ketamine-induced hyperactivity. On day 10, we measured stereotypical behaviours such as turning, falling, and head bobbing. After 21 days, the cataleptic effect was assessed. The results showed that *Ficus carica* fruit extract significantly reduced both locomotor hyperactivity and stereotyped behaviors in a dose-dependent manner. The effects of the 400 mg/kg dose were comparable to those of olanzapine, suggesting that it might have antipsychotic properties. These results, which also confirm the traditional use of Ficus carica and show potential as a natural therapeutic agent for psychotic illnesses, call for more pharmacological and mechanistic investigation.

Keywords: Schizophrenia, Psychosis, stereotypic behaviour, locomotor activity.

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1. INTRODUCTION

For centuries, people around the world have utilized crude extracts obtained from natural sources for their medicinal properties. Traditional systems of medicine continue to be widely practiced, particularly in developing countries, for the treatment of various ailments. With advancements in pharmaceutical and medical sciences, the active molecular constituents of these crude drugs, known as lead compounds, can now be isolated, identified, and studied for their therapeutic potential. Herbal medicines continue to be used extensively in many countries because of their traditional acceptance, accessibility, and perceived lower incidence of adverse effects.[1].

Mental, behavioural, and social health problems account for an increasing portion of health problems globally. They are the third most incapacitating condition in the world (after dementia and quadriplegia, but before blindness and paraplegia), and they result in significant suffering for individuals as well as monetary losses. Psychosis is a group of mental symptoms that make a person lose their sense of reality. It usually refers to a clinical construct of specific symptoms, particularly delusions, hallucinations, and abnormal thinking; however, the term itself is not consistently defined and may vary among sources. Psychosis is a feature of many medical, neurological, psychiatric, neurologic, and neurodevelopmental illnesses [2].

Herbs and plants have been used for thousands of years to enhance human well-being. Among them are a few well-known medicinal plants. Figs (Ficus carica L.), which belong to the Moraceae (mulberry) family, are deciduous trees or shrubs that are native to the Middle East and Southwest Asia. Fruits and leaves have been widely used as both prized food and traditional medicine due to their therapeutic qualities The various parts of the plant are traditionally used by rural communities as a mild laxative, expectorant, and anti-inflammatory agent, as well as a deobstruent for managing liver and spleen disorders. Pharmacological studies have also reported several biological activities of the plant, including hypoglycemic, antispasmodic, antioxidant, hepatoprotective, antitumorigenic, and antiplatelet effects.[3].

Phytochemical studies have been conducted on the fruits, leaves, roots, and latex of this plant [4].

Carotenoids and polyphenols are the two primary categories of phytochemicals found in figs. The primary polyphenol groups present in figs include phenolic acids, flavones, flavanones, flavanols, anthocyanins, and proanthocyanidins. Quercetin-3-O-rutinoside (rutin), (-)-Epicatechin, (+)-catechin, cyanidin-3-O-rutinoside, bergapten, myricetin, and kaempferol are some of the main phenolic compounds identified and measured in the figures/parts along with other phenolic acids. However, reports state that the primary phenolic acids are gallic and ellagic acids [3].

2. MATERIALS AND METHODS

2.1 Plant Material

The fruit powder of *Ficus carica* L. was procured in February 2025 from Neutroxia Food and Infotech LLP. The material was used for the preparation of the ethanolic fruit extract.

2.2 Preparation of Ethanolic Extract of *Ficus carica* Fruit

The ethanolic fruit extract of *Ficus carica* (EEFC) was prepared by Soxhlet extraction using 90% ethanol as the extraction solvent. Briefly, 100 g of dried Ficus carica fruit powder was packed into a Soxhlet extraction thimble and subjected to continuous extraction with 90% ethanol. The extraction was continued until the solvent in the siphon tube became nearly colourless, indicating exhaustive extraction of the soluble constituents. The resulting extract was collected and concentrated to remove the solvent. The concentrated extract was subsequently preserved under suitable conditions until further phytochemical and pharmacological investigation [5].

2.3 Preliminary phytochemical screening:

The prepared EEFC was subjected to preliminary phytochemical screening to determine the presence of major classes of secondary metabolites. The extract was qualitatively screened for alkaloids, glycosides, phytosterols, phenolic compounds, terpenoids, flavonoids, and saponins using standard qualitative chemical tests [8].

2.4 Animals:

Wistar rats of either sex, weighing 150–200 g, were used for the present investigation. The animals were procured from Crystal Biological Solution, Pune, Maharashtra, India (Registration No. 2030/PO/RcBiBt/S/18/CCSEA). The animals were housed in the animal house facility of Dayanand College of Pharmacy, Latur, Maharashtra, India, under standard laboratory conditions.

Approximately six animals were housed per polypropylene cage and maintained under a 12 h light/12 h dark cycle, at a temperature of 22 ± 3°C and relative humidity of 30–70%. The animals had free access to drinking water and standard laboratory feed throughout the experimental period.

The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC), Dayanand College of Pharmacy, Latur, under Protocol No. DCOP/IAEC/2024–25/03. All experimental procedures were conducted in accordance with applicable ethical guidelines for the care and use of laboratory animals. Appropriate measures were taken to minimize animal discomfort, distress, and suffering during the experimental procedures.

2.5 Drugs and chemicals:

Olanzapine was obtained from Aurochem Pharmaceutical (India) Pvt. Ltd. Ketamine was used to induce psychotic-like behavioural alterations in the experimental animals. The doses of ketamine and olanzapine were selected based on previously reported experimental protocols.

2.6 Selection of doses:

Ketamine was administered at a dose of 50 mg/kg intraperitoneally (i.p.), whereas olanzapine was administered at a dose of 5 mg/kg i.p. EEFC was evaluated at doses of 200 and 400 mg/kg by the oral route (p.o.) [7].

2.7 Animal grouping:

2.7 Experimental Design and Animal Grouping

The animals were randomly divided into five experimental groups, with six animals in each group (n = 6). The treatment schedule was as follows:

- Group I (Vehicle control): Received distilled water (5 mL/kg, p.o.).
- Group II (Ketamine control): Received ketamine (50 mg/kg, i.p.).
- Group III (Standard): Received olanzapine (5 mg/kg, i.p.) as the standard antipsychotic treatment, followed by ketamine (50 mg/kg, i.p.).
- Group IV (EEFC 200 mg/kg): Received EEFC (200 mg/kg, p.o.), followed by ketamine (50 mg/kg, i.p.).
- Group V (EEFC 400 mg/kg): Received EEFC (400 mg/kg, p.o.), followed by ketamine (50 mg/kg, i.p.).

All treatments were administered once daily for 21 consecutive days. In Groups III–V, olanzapine or EEFC was administered 1 h before ketamine administration. Ketamine (50 mg/kg, i.p.) was administered once daily to Groups II–V, whereas Group I received the vehicle alone [7].

Behavioural assessments were performed at predetermined time points during the treatment period. Locomotor activity was assessed on day 7 using an actophotometer, while ketamine-induced stereotypic behaviours were evaluated on day 10. On day 21, cataleptic behaviour was assessed using the bar test to evaluate potential extrapyramidal motor effects associated with treatment.

2.8 Behavioral studies:

Previous research indicates that while ketamine administration (50 mg/kg, i.p.) causes hyperactivity and stereotyped behaviors during acute therapy,

long-term treatment results in negative and cognitive symptoms of psychosis. To induce psychotic symptoms in the rats used in this investigation, ketamine (50 mg/kg, i.p.) was administered. On the seventh day of therapy, locomotor activity was measured using an actophotometer. On the tenth day of treatment, 10 minutes were spent counting the number of falls, weaving, turnarounds, and head bobbing (stereotypical behaviors). The bar test was used to assess catalepsy test. On the twenty-first day, each animal was placed with its front paws nine centimeters above the ground on a horizontal bar. The duration until the animal removed either paw from the bar was noted at intervals of 30, 60, 90, and 120 minutes [7].

2.8.1 Assessment of locomotor activity:

The photoactometer (Orchid Scientific), was used to measure locomotor counts. On the seventh day of the experiment, the animal was put on the chamber floor and allowed to acclimate for five minutes. After that, locomotor activity was monitored for the following five minutes.

2.8.2 Assessment of stereotypic behaviours:

The total number of falls, rearings, turnarounds, and head bobbing (stereotypical behaviors) were recorded for ten minutes on the tenth day of the experiment.

2.8.3 Assessment of cataleptic behaviour:

The extrapyramidal side effect of EEFC, which is typically observed with conventional neurolyptics, was assessed using the bar test. On the twenty-first day, each animal was positioned with its front paws on a horizontal bar that was nine centimeters from the ground. At 30, 60, 90, and 120-minute intervals, the amount of time until the animal removed either paw from the bar was recorded.

2.9 Statistical analysis:

The mean ± SEM is used to express all results. The Tukey test was used to analyze behavioral assessments using one-way analysis of variance (ANOVA). A p-value of less than 0.05 was considered significant.

3. RESULTS

3.1 Phytochemical investigation *Ficus carica* Extract

Sr. no	Phytochemicals	Test	Result
1	Alkaloid	Dragendroff's reagent test	+ve
2	Glycoside	Keller killani test	+ve
3	Phytosterol	Salkowski reaction	-ve
4	Phenolic compounds	Ferric chloride test	+ve
5	Terpenoid	-	-ve
6	Flavonoid	Shinoda test	+ve
7	Saponin	Foam test	+ve

Table 1. Phytochemical screening of *Ficus carica* Extract for the detection of major secondary metabolites.

The preliminary phytochemical screening of EEFC demonstrated the presence of alkaloids, glycosides, phenolic compounds, flavonoids, and saponins, while phytosterols and terpenoids were absent. These phytoconstituents may contribute to the pharmacological effects observed with EEFC.

3.2 FTIR analysis

Graph 1: IR Spectrum of *Ficus carica extract*

The results revealed characteristic absorption bands indicating the presence of functional groups such as hydroxyl, carbonyl, and aromatic compounds. The strong absorption peak observed at 1707.1 cm^{-1} is indicative of the presence of carbonyl (C=O) functional groups, suggesting aldehydes, ketones, carboxylic acids, or esters and the broad absorption around 1606.48261 $cm^{-1}$is characteristic of (C=C) groups, which could be associated with aromatic amines. Furthermore, the peaks in the 3302.42132 cm^{-1} region strongly suggest the presence of (O-H) functional groups.

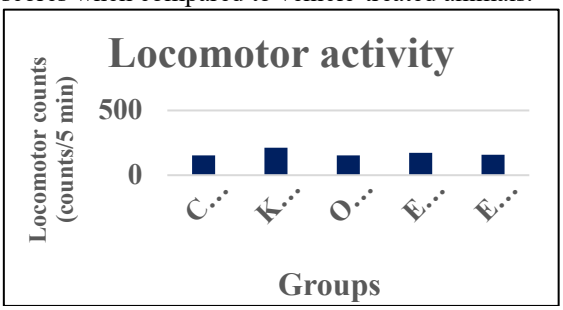
Sr.no	Wavenumber (cm^{-1})	Functional groups
1	1707.1	C=O

2	1606.48	C=C
3	3302.42	O-H

Table no 2: Interpretation of IR of *Ficus carica*

3.3 Effect of EEFC on locomotor activity:

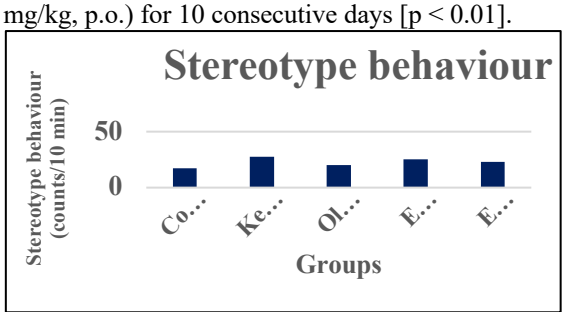
While EEFC therapy (200 and 400 mg/kg, p.o.) for 7 consecutive days considerably decreased [$p < 0.001$, respectively] total locomotor ratings compared to the ketamine group, ketamine (50 mg/kg, i.p.) significantly raised total locomotor scores when compared to vehicle-treated animals.



Graph 2: Effect of ethanolic fruit extract of *Ficus carica* on locomotor activity by using an actophotometer

3.4 Effect of EEFC on stereotypic behaviours:

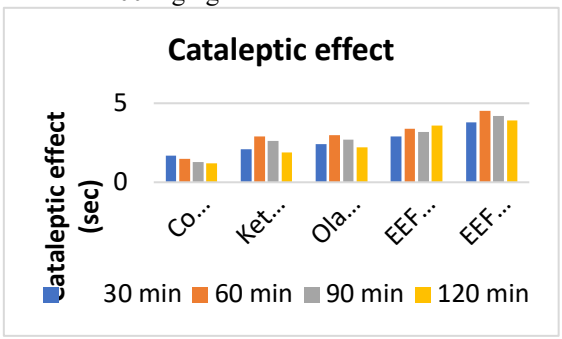
In comparison to the vehicle-treated group, ketamine (50 mg/kg, i.p.) significantly caused stereotypical behaviors. These behaviors were reversed by administering EEFC (200 mg/kg, 400 mg/kg, p.o.) for 10 consecutive days [$p < 0.01$].



Graph 3: Effect of ethanolic fruit extract of *Ficus carica* on stereotype behaviour

3.5 Effect of EEFC on catalepsy:

The findings show that whereas treatment with EEFC for 21 consecutive days at a dose of 200 mg/kg did not cause a cataleptic effect, the bar test showed a significant [$p < 0.01$] cataleptic impact at a dose of 400 mg/kg.



Graph 4: Effect of ethanolic fruit extract of *Ficus carica* on cataleptic effect

4. DISCUSSION

The present study was designed to investigate the antipsychotic-like activity of *Ficus carica* fruit extract in Wistar rats using ketamine-induced behavioral models, with particular emphasis on stereotyped behavior and catalepsy. The major finding of the present investigation was that oral administration of *Ficus carica* fruit extract attenuated ketamine-induced stereotyped behavior in a dose-dependent manner. Furthermore, the extract did not produce marked cataleptic behavior at the tested doses. Taken together, these findings provide preliminary experimental evidence that *F. carica* fruit extract may possess antipsychotic-like activity without producing substantial motor rigidity under the experimental conditions used.

Ketamine is widely employed as a pharmacological model of schizophrenia-like behavioral abnormalities because of its antagonistic action at N-methyl-D-aspartate (NMDA) receptors. Current understanding of schizophrenia indicates that glutamatergic dysfunction interacts with dopaminergic, serotonergic and GABAergic systems rather than being attributable exclusively to dopamine abnormalities [9,10]. Recent reviews have further emphasized that the behavioral effects produced by ketamine in rodents depend considerably on the dose, duration and experimental protocol used [9]. Sub-chronic ketamine administration in rats has been shown to produce hyperlocomotion and alterations in cognitive and behavioral functions, supporting its utility for investigating schizophrenia-like phenotypes [11]. Therefore, the marked behavioral abnormalities observed in the ketamine-treated group in the present study are consistent with the established pharmacological characteristics of the ketamine model.

The increased stereotyped behavior observed following ketamine administration represents an important finding in the present investigation. Repetitive movements, turning, head movements and other stereotypic responses are commonly used as behavioral indicators of psychosis-like disturbances in rodents. Ketamine-induced behavioral abnormalities have been associated with disturbances in glutamatergic signaling and downstream changes in dopamine neurotransmission [10,12]. Experimental and meta-analytic evidence indicates that ketamine can increase dopaminergic activity in the rodent brain, particularly in cortical regions, providing a possible neurochemical basis for some of the psychotomimetic behavioral effects produced by NMDA receptor antagonism [12].

Treatment with *F. carica* fruit extract significantly reduced ketamine-induced stereotyped behavior, with a greater reduction observed at the higher tested dose. The dose-dependent nature of this response strengthens the possibility that the extract

possesses genuine pharmacological activity rather than producing a nonspecific behavioral effect. Although the precise mechanism responsible for this activity remains unknown, modulation of neurotransmitter systems involved in schizophrenia-like behavior may be one possible explanation. In particular, attenuation of ketamine-induced behavioral abnormalities could theoretically involve modulation of dopaminergic and glutamatergic neurotransmission. However, the present study did not directly determine dopamine receptor occupancy, neurotransmitter concentrations, or receptor-binding activity; therefore, a direct dopamine receptor antagonistic mechanism cannot be conclusively established from the current findings.

The present observations are consistent with the broader literature showing that plant-derived bioactive compounds can attenuate ketamine-induced schizophrenia-like behaviors. For example, diosgenin has been reported to exert antipsychotic effects in a ketamine-induced murine model, with the effects associated with alterations in oxidative stress and cholinergic transmission [13]. Similarly, silymarin, a polyphenolic flavonoid with recognized antioxidant and neuroprotective properties, was reported to attenuate behavioral and biochemical abnormalities in a ketamine-induced mouse model of schizophrenia [14]. These findings are particularly relevant to the present study because *F. carica* fruit contains a range of polyphenolic and flavonoid constituents that may exert antioxidant and neuromodulatory effects.

Recent evidence also supports the importance of oxidative stress and neuroinflammation in schizophrenia-like states. Ansari et al. reported that oxidative stress and neuroinflammatory processes may contribute to the pathophysiology of schizophrenia and may represent potential targets for novel therapeutic approaches [15]. More recent evidence has further highlighted the interaction between oxidative stress, neuroinflammation, and neuronal dysfunction in schizophrenia [16]. In a ketamine-induced mouse model, Fujikawa et al. demonstrated that risperidone attenuated ketamine-associated behavioral abnormalities together with changes in reactive oxygen species regulation and microglial activity [17]. These findings suggest that oxidative and inflammatory pathways may participate in ketamine-induced behavioral alterations and may also contribute to the actions of compounds with antipsychotic-like properties.

The phytochemical profile of *F. carica* provides a plausible basis for its observed pharmacological activity. Previous investigations have demonstrated that fig fruits contain a variety of bioactive compounds, particularly phenolic acids and flavonoids. Arvaniti et al. reported that gallic acid, chlorogenic acid, rutin, quercetin derivatives and epicatechin are among the important phenolic constituents identified in fresh and dried figs [18]. Similarly, *Kebal et al*. demonstrated the presence of phenolic acids and flavonoids, including rutin and quercetin, in *F. carica* fruit extracts and reported significant antioxidant activity [19]. The composition and concentration of these constituents may vary according to cultivar, fruit color, maturity, processing conditions and extraction procedure [18,19].

The phytochemical screening performed in the present study demonstrated the presence of flavonoids, steroids, alkaloids, glycosides, terpenoids and saponins in the *F. carica* fruit extract. These constituents may act individually or synergistically to produce the observed behavioral effects. Flavonoids and phenolic compounds are particularly relevant because of their antioxidant and potential neuroprotective properties. A recent comprehensive review of figs described their diverse phytochemical composition, including flavonoids, phenolic acids, carotenoids and tocopherols, and summarized evidence for antioxidant and other biological activities [20]. Similarly, reviews of the *Ficus* genus have documented antioxidant, anticonvulsant, neuroprotective and other pharmacological effects associated with diverse secondary metabolites [21]. Thus, the behavioral activity observed in the present study may reflect the combined action of multiple constituents rather than a single pharmacologically active compound.

Recent experimental findings further support the neuroprotective potential of *F. carica*. Oktay et al. reported that *F. carica* seed oil exhibited neuroprotective effects in a Wistar rat model of diabetic neuropathy, which was attributed to its content of fatty acids, phenolic compounds and antioxidant/anti-inflammatory components [22]. Although seed oil and fruit extract are pharmacologically distinct preparations, this study supports the broader concept that bioactive constituents derived from *F. carica* can influence neuronal function and protect against pathological processes. In addition, recent reviews of *F. carica* polysaccharides have highlighted antioxidant and immunomodulatory activities, further demonstrating the pharmacological diversity of the plant [23].

The catalepsy findings provide an additional and important aspect of the present investigation. Catalepsy is commonly employed in rodents as an experimental indicator of extrapyramidal motor effects associated with strong dopamine D_2 receptor blockade. Antipsychotic drug-development models consider catalepsy as an index of potential extrapyramidal symptom liability [24]. In the present study, *F. carica* fruit extract did not produce pronounced cataleptic behavior at the tested doses. This finding suggests that the reduction in stereotyped behavior was unlikely to be solely

attributable to severe motor suppression. In other words, the extract appeared to reduce abnormal ketamine-induced behavior without producing substantial rigidity under the conditions of the experiment.

This observation may be pharmacologically relevant when compared with conventional antipsychotic therapy. While dopamine D_2 receptor blockade is an established mechanism underlying the antipsychotic activity of many agents, excessive blockade is associated with extrapyramidal adverse effects. Therefore, a candidate compound capable of attenuating psychosis-like behavior without marked catalepsy could potentially possess a favorable behavioral profile. Nevertheless, the absence of catalepsy in the present study should not be interpreted as definitive evidence that *F. carica* is devoid of extrapyramidal or other adverse effects. Such conclusions require dedicated neurological, toxicological and chronic-treatment studies.

An especially relevant recent finding comes from research on another species of the same genus. A 2026 study investigated the antipsychotic effects of an aqueous lyophilisate of *Ficus mucuso* in a ketamine-induced mouse model of schizophrenia and reported improvement in behavioral abnormalities together with changes in oxidative and neurochemical parameters [25]. Although *F. mucuso* is different from *F. carica*, this study is significant because it provides independent evidence that a *Ficus* species may possess activity against ketamine-induced schizophrenia-like behavioral alterations. The present findings with *F. carica* therefore extend this emerging evidence from the *Ficus* genus to the fruit extract of *F. carica*. Importantly, direct extrapolation between species should be avoided because phytochemical composition, extract characteristics and pharmacological potency may differ substantially.

The findings of the present study are also compatible with earlier CNS research on *F. carica*. Bhanushali et al. previously demonstrated CNS-related pharmacological effects of an aqueous-acetonic *F. carica* extract in experimental animals, including effects on anxiety, muscle coordination, seizures, nociception and neurotransmitter-related parameters [26]. Although that study did not specifically establish antipsychotic activity, it provided early evidence that *F. carica* can influence central neurotransmission. The present study extends this earlier observation by demonstrating attenuation of ketamine-induced stereotyped behavior and evaluating catalepsy as an indicator of motor effects.

The potential involvement of dopamine and serotonin systems deserves consideration because both neurotransmitter systems contribute to the expression and treatment of psychotic symptoms. Contemporary models of schizophrenia emphasize complex interactions between glutamatergic and dopaminergic signaling, with alterations in dopamine transmission contributing particularly to positive symptoms, while glutamatergic dysfunction may influence positive, negative and cognitive manifestations [10,27]. Serotonergic mechanisms also interact with dopaminergic and glutamatergic pathways and contribute to the pharmacological actions of several atypical antipsychotic drugs. Consequently, the behavioral effects observed with *F. carica* may result from modulation of multiple neurotransmitter systems rather than a single receptor target. Nevertheless, this hypothesis requires direct confirmation using neurochemical estimation, receptor-binding studies or molecular approaches.

The antioxidant properties of *F. carica* may represent another possible mechanism. Recent analytical investigations have confirmed substantial phenolic and flavonoid content in *F. carica* fruit extracts and demonstrated measurable antioxidant activity [19,28]. A 2026 study further demonstrated that extraction conditions substantially influence the recovery of phenolic compounds and antioxidant activity from fig material [28]. Since oxidative stress and neuroinflammation are increasingly recognized as contributors to schizophrenia-related pathophysiology [15,16], the antioxidant properties of *F. carica* may potentially contribute to its behavioral effects. However, because oxidative-stress markers were not measured in the present investigation, this interpretation remains hypothetical.

The present study has several limitations that should be acknowledged. First, the study relied primarily on behavioral endpoints, and therefore the molecular mechanism responsible for the observed antipsychotic-like activity remains uncertain. Second, neurotransmitter levels, receptor interactions, oxidative-stress markers and inflammatory mediators were not directly measured. Third, the study evaluated an extract containing multiple phytoconstituents; consequently, the specific compound or combination of compounds responsible for the activity cannot be identified from the present data. Fourth, behavioral models of schizophrenia provide useful experimental screening tools but do not reproduce the full clinical complexity of human schizophrenia. Recent literature emphasizes that the ketamine model is influenced by dose, treatment schedule, animal strain, sex and behavioral paradigm [9,11].

Future investigations should therefore focus on identifying the active constituents of *F. carica* fruit extract and determining their pharmacological targets. Estimation of dopamine, serotonin, glutamate and GABA levels, together with evaluation of D_2 and 5-HT_2A receptor-related pathways, would help clarify the neurotransmitter

mechanisms involved. Measurement of malondialdehyde, reduced glutathione, superoxide dismutase, catalase and other oxidative-stress parameters could determine whether antioxidant mechanisms contribute to the observed activity. Assessment of inflammatory cytokines and microglial markers may further establish a possible neuroinflammatory component. Additional studies using prepulse inhibition, social-interaction, novel-object recognition and other validated schizophrenia-related paradigms would strengthen the pharmacological evidence.

Overall, the present findings demonstrate that *Ficus carica* fruit extract attenuated ketamine-induced stereotyped behavior in Wistar rats and did not produce pronounced catalepsy at the tested doses. These effects, together with the documented presence of flavonoids, phenolic compounds and other bioactive constituents in fig fruit, suggest that *F. carica* may represent a promising source of compounds with antipsychotic-like and neuroprotective potential. The findings are further supported by emerging evidence from other *Ficus* species and from studies of plant-derived compounds in ketamine-induced models of schizophrenia [13,14,25]. However, the present results should be regarded as preliminary preclinical evidence rather than proof of clinical antipsychotic efficacy. Detailed mechanistic, pharmacokinetic, toxicological and chronic-treatment studies, followed ultimately by appropriately designed clinical investigations, are necessary to determine whether *F. carica* has meaningful therapeutic potential in psychotic disorders.

5. CONCLUSION

The current study shows that *Ficus carica* fruit extract significantly reduces ketamine-induced psychotic symptoms in Wistar rats, indicating antipsychotic action. Both positive and negative ketamine-induced behavioral symptoms, including hyperlocomotion and stereotyping, were successfully reduced by the extract. These results imply that *Ficus carica*'s phytoconstituents, including flavonoids and phenolic compounds, may play a role in its neuroprotective and antipsychotic properties, perhaps via influencing the glutamatergic and dopaminergic systems. The effectiveness was dose-dependent and somewhat comparable to conventional antipsychotic therapy.

These results suggest that *Ficus carica* could be a good natural option for the creation of safer and more potent antipsychotic medications. To identify the active ingredients, clarify the precise mode of action, and assess long-term safety and effectiveness, more research is necessary.

6. REFERENCES

1. Munawar, Md Shamsuddin, Evaluation of antipsychotic activity of some Indian medicinal plants.2022
2. Van Os, J., Hanssen, M., Bijl, R. V., & Vollebergh, W. (2001). Prevalence of psychotic disorder and community level of psychotic symptoms: an urban-rural comparison. *Archives of general psychiatry*, *58*(7), 663-668.
3. Sandhu, A. K., Islam, M., Edirisinghe, I., & Burton-Freeman, B. (2023). Phytochemical composition and health benefits of figs (fresh and dried): a review of literature from 2000 to 2022. Nutrients, 15(11), 2623
4. Bhanushali, M. M., Makhija, D. T., & Joshi, Y. M. (2014). Central nervous system activity of an aqueous acetonic extract of Ficus carica L. in mice. *Journal of Ayurveda and integrative medicine*, *5*(2), 89.
5. Sruthi, 2 Sunny, 3Hajra Naz, 4 Sakthivel Diuretic activity of ethanolic extracts of ficus carica fruits. *International Journal of Research in Pharmacology and Pharmacotherapeutics* Vol-1[1] 2012 [23-26].
6. M., Verma, R., Kumari, R., Singh, S., Verma, A. K., Dwivedi, A. K., & Palit, G. (2015). Antipsychotic activity of standardized Bacopa extract against ketamine-induced experimental psychosis in mice: Evidence for the involvement of dopaminergic, serotonergic, and cholinergic systems. *Pharmaceutical Biology*, *53*(12), 1850-1860.
7. Yadav, M., Parle, M., Jindal, D. K., & Sharma, N. (2018). Potential effect of spermidine on GABA, dopamine, acetylcholinesterase, oxidative stress and proinflammatory cytokines to diminish ketamine-induced psychotic symptoms in rats. *Biomedicine & Pharmacotherapy*, *98*, 207-213.
8. Priyadarshini, P., Pandey, P., & Raja, W. *Asian Journal of Phytomedicine and Clinical Research.*
9. Rice CA, Stackman RW Jr. Psychosis: the utility of ketamine as a pharmacological model of psychotic-like symptoms in rodents: a review of dosage regimens. Biology (Basel). 2026;15(3):222. doi:10.3390/biology15030222.
10. Howes OD, Murray RM. Schizophrenia: an integrated sociodevelopmental-cognitive model. Lancet. 2014;383:1677-1687.
11. Samizadeh MA, Abdollahi-Keyvani ST, Fallah H, Beigi B, Motamedi-Manesh A, Adibian S, et al. Sex difference alters the behavioral and cognitive performance in a rat model of schizophrenia induced by sub-chronic ketamine. J Psychiatr Res. 2024;178:180-187. doi:10.1016/j.jpsychires.2024.08.014.

12. Kokkinou M, Ashok AH, Howes OD. The effects of ketamine on dopaminergic function: meta-analysis and review of the implications for neuropsychiatric disorders. Mol Psychiatry. 2018;23:59-69. doi:10.1038/mp.2017.190.
13. Ben-Azu B, Adebayo OG, Fokoua AR, Oritsemuelebi B, Chidebe EO, Nwogueze CB, et al. Antipsychotic effect of diosgenin in ketamine-induced murine model of schizophrenia: involvement of oxidative stress and cholinergic transmission. IBRO Neurosci Rep. 2024;16:86-97. doi:10.1016/j.ibneur.2023.12.008.
14. Ben-Azu B, Fokoua AR, Annafi OS, Adebayo OG, Del Re EC, Okuchukwu N, et al. Effective action of silymarin against ketamine-induced schizophrenia in male mice: insight into the biochemical and molecular mechanisms of action. J Psychiatr Res. 2024;179:141-155. doi:10.1016/j.jpsychires.2024.09.003.
15. Ansari Z, Pawar S, Seetharaman R. Neuroinflammation and oxidative stress in schizophrenia: are these opportunities for repurposing? Postgrad Med. 2022;134(2):187-199. doi:10.1080/00325481.2021.2006514.
16. Trubalski M, Markiewicz-Gospodarek A, Żerebiec M, Poleszak J. Oxidative stress-mediated neuroinflammation in the pathophysiology of schizophrenia. Int J Mol Sci. 2025;26(22):11139. doi:10.3390/ijms262211139.
17. Fujikawa R, Yamada J, Maeda S, Iinuma KM, Moriyama G, Jinno S. Inhibition of reactive oxygen species production accompanying alternatively activated microglia by risperidone in a mouse ketamine model of schizophrenia. J Neurochem. 2024;168(9):2690-2709. doi:10.1111/jnc.16133.
18. Arvaniti OS, Samaras Y, Gatidou G, Thomaidis NS, Stasinakis AS. Review on fresh and dried figs: chemical analysis and occurrence of phytochemical compounds, antioxidant capacity and health effects. Food Res Int. 2019;119:244-267.
19. Kebal L, Pokajewicz K, Djebli N, Mostefa N, Poliwoda A, Wieczorek PP. HPLC-DAD profile of phenolic compounds and in vitro antioxidant activity of *Ficus carica* L. fruits from two Algerian varieties. Biomed Pharmacother. 2022;155:113738. doi:10.1016/j.biopha.2022.113738.
20. Sandhu AK, Islam M, Edirisinghe I, Burton-Freeman B. Phytochemical composition and health benefits of figs (fresh and dried): a review of literature from 2000 to 2022. Nutrients. 2023;15(11):2623. doi:10.3390/nu15112623.
21. Salehi B, et al. Ficus plants: state of the art from a phytochemical, pharmacological, and toxicological perspective. Phytother Res. 2021;35(3):1187-1217. doi:10.1002/ptr.6884.
22. Oktay S, Turkkol A, Bozkurt-Girit O, Bilgin MD, Bilgen M. Neuroprotective effects of *Ficus carica* seed oil in diabetic neuropathy: a preclinical study in Wistar rats. J Clin Pract Res. 2024;46(6):584-592. doi:10.14744/cpr.2024.11149.
23. Wu C, Liao B, Li C, Zhu Z, Duan B, Peng A, He F. Recent advances in isolation, structures, and bioactivities of *Ficus carica* L. polysaccharides: a review. Int J Biol Macromol. 2025;299:139887. doi:10.1016/j.ijbiomac.2025.139887.
24. Ellenbroek BA, Cools AR. Animal models with construct validity for schizophrenia. Behav Pharmacol. 2000;11(6):469-490.
25. Antipsychotic effects of aqueous lyophilisate of *Ficus mucuso* on ketamine-induced schizophrenia. 2026.
26. Bhanushali MM, Makhija DT, Joshi YM. Central nervous system activity of an aqueous acetonic extract of *Ficus carica* L. in mice. J Ayurveda Integr Med. 2014;5(2):89-96. doi:10.4103/0975-9476.131734.
27. Howes OD, Shatalina E. Integrating the neurodevelopmental and dopamine hypotheses of schizophrenia and the role of cortical excitation-inhibition balance. Biol Psychiatry. 2022;92(7):501-512.
28. Zulfiqar S, Butt MS, Chatha A, Hafiz MS. Phytochemical content and antioxidant activities of *Ficus carica* extracts. Int J Anal Chem. 2026;2026:3209992. doi:10.1155/ianc/3209992