Volume 5 (1): 1-15

Research Article

Evaluation of the effects of decoction of *Ficus mucuso* trunk stem bark (Moraceae) on lipopolysaccharide-induced schizoaffective psychoses in mice (*Mus musculus*).

Évaluation des effets de la décoction d'écorce de tronc de *Ficus mucuso* (Moraceae) sur les psychoses schizo-affectives induites par le lipopolysaccharide chez la souris (*Mus musculus*).

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Received on: October 2, 2023 Revised on : October 3, 2024 Accepted on : June 7, 2025

Section Editor: Prof. Michel Archange Fokam

Abstract

Background and objectives: *Ficus mucuso* is a tropical plant belonging to the Moraceae family. It is used in traditional medicine in Western, Eastern, and Adamaoua regions of Cameroon to treat diabetes, epilepsy, and psychosis. This study aims to evaluate the effects of the decoction of *Ficus mucuso* bark fragments on mouse models of schizoaffective disorder induced by lipopolysaccharide.
Materials and methods: The plant material used was *Ficus mucuso* bark, which was harvested in Manwi (Ngaoundéré). Forty-two mice with a body weight of 18–30 g were used. Schizoaffective disorder was induced by the intraperitoneal administration of lipopolysaccharide (0.83 mg/kg) for 21 days, after which the mice were treated with decoction at doses of 21.8, 43.5, 87, or 174 mg/kg, or haloperidol (2.5 mg/kg). The anxiolytic and memory effects, antioxidant potency, and phytochemical profile were evaluated.
Results: The evaluation of the pharmacological properties showed that *Ficus mucuso* reduced anxiety by significantly increasing the percentage of entries and the time spent in the open arms at the 21.8 and 43.5 mg/kg doses. At these doses, it also improved memory and learning capacity. The antioxidant power of *Ficus mucuso* was demonstrated by a significant decrease in MDA and a significant increase in GSH and CAT at doses of 21.8 and 43.5 mg/kg, as well as at 87 mg/kg. These results are comparable to those of haloperidol (2.5 mg/kg). The phytochemical profile reveals the presence of alkaloids, flavonoids, polyphenols, and saponins.
Conclusion: The different results demonstrate that *Ficus mucosa* and haloperidol have comparable effects, which justifies their use in traditional medicine.

Keywords: *Ficus mucuso*, anxiety, memory, lipopolysaccharide, schizoaffective disorder.

Résumé

Contexte et objectifs : *Ficus mucuso* est une plante tropicale de la famille des Moraceae. Elle est utilisée en médecine traditionnelle dans les régions de l'Ouest, de l'Est et de l'Adamaoua au Cameroun pour traiter le diabète, l'épilepsie et la psychose. Cette étude vise à évaluer les effets de la décoction de fragments d'écorce de *Ficus mucuso* sur des modèles murins de trouble schizo-affectif induit par le lipopolysaccharide.
Matériaux et méthodes : Le matériel végétal utilisé était l'écorce de *Ficus mucuso*, récoltée à Manwi (Ngaoundéré). Quarante-deux souris d'un poids corporel de 18 à 30 g ont été utilisées. Le trouble schizo-affectif a été induit par l'administration intrapéritonéale de lipopolysaccharide (0,83 mg/kg) pendant 21 jours, après quoi les souris ont été traitées avec une décoction à des doses de 21,8; 43,5; 87 ou 174 mg/kg, ou avec de l'halopéridol (2,5 mg/kg). Les effets anxiolytiques et sur la mémoire, le pouvoir antioxydant et le profil phytochimique ont été évalués.
Résultats : L'évaluation des propriétés pharmacologiques a montré que le *Ficus mucuso* réduisait l'anxiété en augmentant de manière significative le pourcentage d'entrées et le temps passé dans les bras ouverts aux doses de 21,8 et 43,5 mg/kg. À ces doses, il améliorait également la mémoire et la capacité d'apprentissage. Le pouvoir antioxydant du *Ficus mucuso* a été démontré par une diminution significative du MDA et une augmentation significative du GSH et du CAT aux doses de 21,8 et 43,5 mg/kg, ainsi qu'à 87 mg/kg. Ces résultats sont comparables à ceux de l'halopéridol (2,5 mg/kg). Le profil phytochimique révèle la présence d'alcaloïdes, de flavonoïdes, de polyphénols et de saponines.
Conclusion : Les différents résultats démontrent que le *Ficus mucuso* et l'halopéridol ont des effets comparables, ce qui justifie leur utilisation en médecine traditionnelle.

Mots-clés : *Ficus mucuso*, anxiété, mémoire, lipopolysaccharide, trouble schizo-affectif.

1. Introduction

Schizophrenia is a heterogeneous psychiatric disorder that affects approximately 1% of the global population (Monte et al., 2013; Ben-Azu et al., 2024). It is a chronic and debilitating brain disorder characterized by cognitive and functional deficits (Ermakov et al., 2021; Ben-Azu et al., 2024), as well as psychotic symptoms (Ior et al., 2021). Schizophrenia is characterized by abnormalities in dopaminergic, glutamatergic, serotonergic, GABAergic, and cholinergic neurotransmission (Howes et al., 2015; Omeiza et al., 2023). Abnormalities in neuroimmune and neurotrophic proteins in the hippocampus, prefrontal cortex, and striatum (Ben-Azu et al., 2021, 2023). Its pathophysiology remains unclear, with various associated pathologies such as anxiety, depression, and amnesia (Ben-Azu et al., 2018b). Studies suggest that oxidative stress plays an important role in the aetiology and pathophysiology of schizophrenia (Ben-Azu et al., 2016; Yadav et al., 2018; Ior et al., 2021). This stress can lead to the direct denaturation of blood-brain barrier (BBB) junction proteins. Schizoaffective disorders are known as one of the different types of schizophrenia characterized by the simultaneous presence of bipolar, psychotic, and affective symptoms (Peselow & Kumari, 2008). These disorders can occur spontaneously or in response to life events or trauma (Malaspina et al., 2013). However, nearly half of those affected receive no treatment (Nayer, 2013). These disorders impact various aspects of life, including work, social interactions, and functional autonomy. Those affected face ridicule, discrimination, and stigmatization, and are often perceived as a danger to society. In medicine, treatment relies on the use of antipsychotics, mood stabilizers, and antidepressants, but these are costly and inaccessible to the population and present enormous side effects (Azorin et al., 2005; Tréhout et al., 2023). In response to these challenges, communities often resort to traditional medicine, a practice that remains vital in underdeveloped regions, where it provides a diverse array of plant-based remedies for various ailments (Khan et al., 2011). In Africa, for example, *Securidaca longipedunculata* and *Khaya senegalensis* are used to treat psychosis (Pierre et al., 2020). Medicinal plants are a plausible alternative source of new compounds for the search for bioactive molecules (Beppe et al.,

2023). Some plants, such as *Terminalia macroptera* (Ior et al., 2021), *Hallea ciliata* (Njapdounké et al., 2016), and Cissus quadrangularis (Moto et al., 2018), have already been shown to have therapeutic effects on psychiatric disorders. Similarly, Ficus mucosa, which belongs to the Moraceae family, is used in traditional African and Chinese medicine to treat epilepsy (Bankeu et al., 2010), diabetes (Chukwuma et al., 2015), insomnia (Okongola et al., 2016), and diabetic renal failure (Brown, 2019). Given these effects, could this plant be used to treat schizoaffective disorders? The present study aimed to evaluate the effects of *F. mucuso* trunk bark decoction on lipopolysaccharide-induced schizoaffective disorders in mice.

2. Materials and Methods

2.1. Animal Material

Naïve male and female white mice weighing between 18 and 30 g were used. They were purchased from the National Veterinary Laboratory of Garoua (LANAVET) and raised in the animal facility at the University of Ngaoundéré. The mice were kept under ambient conditions of 25 ± 1 °C and 60-70% humidity, with adequate ventilation, and on a 12-hour light/dark cycle. They had free access to food and water.

2.2. Plant Material

The bark of the *F. mucuso* trunk was collected in Manwi, Vina (Ngaoundéré, Cameroon). Identification of the specimen was carried out at the National Herbarium of Cameroon in Yaoundé, through comparison with the A.J.M. Leeuwenberg No. 9668 botanical collection, which is registered under No. 44030/HNC.

2.3. Chemical Material

Lipopolysaccharide Escherichia coli O111: [B4 (0.83 mg/kg) Sigma Aldrich, Co_Spruce Street, St Louis, USA].

- Haloperidol [(2.5 mg/kg) Sigma Aldrich, Co_Spruce Street, St Louis, MO, USA.]

2.4. Distribution and treatment of animal

The mice were divided into 7 homogeneous groups (n=6), including 3 males and 3 females. They were acclimatised to the laboratory for 72 hours before the start of the treatment. The different tests were conducted each day between 8:00 pm and 6:00 am. The experiment was conducted according to the following distribution and experimental plan (Figure 1):

- Group I (normal control): received distilled water (*p.o*).
- Group II (negative control): received lipopolysaccharide (0.83 mg/kg, *i.p*).
- Group III: received *F. mucuso* decoction (21.8 mg/kg, *p.o*),
- Group IV: received *F. mucuso* decoction (43.5 mg/kg, *p.o*),
- Groupe V: received *F. mucuso* decoction (87 mg/kg, *p.o*),
- Groupe VI: received *F. mucuso* decoction (174 mg/kg, *p.o*),
- Group VII (positive control): received Haloperidol (2.5 mg/kg, *p.o*).

LPS (0.83 mg/kg) was co-administered to all the mice, except those in the normal control group, for 27 days. Medications and various doses of *F. mucuso* decoction were prepared and administered intraperitoneally (*i.p*) and orally (*p.o*), one hour before each test at a volume of 10 ml/kg body weight.

After treatments, the mice were returned to their original cages to reduce neophobic responses due to the experimental environment. Behaviour tests were conducted as outlined below, and the experimental devices were cleaned with ethyl alcohol (70°C) after each animal's passage. All experiments were conducted in accordance with the guidelines of the National Ethical Committee (No. FWA-IRB00001954) and the internationally accepted principles for the use and care of laboratory animals presented in US guidelines. Every effort was made to minimise suffering and the number of animals used.

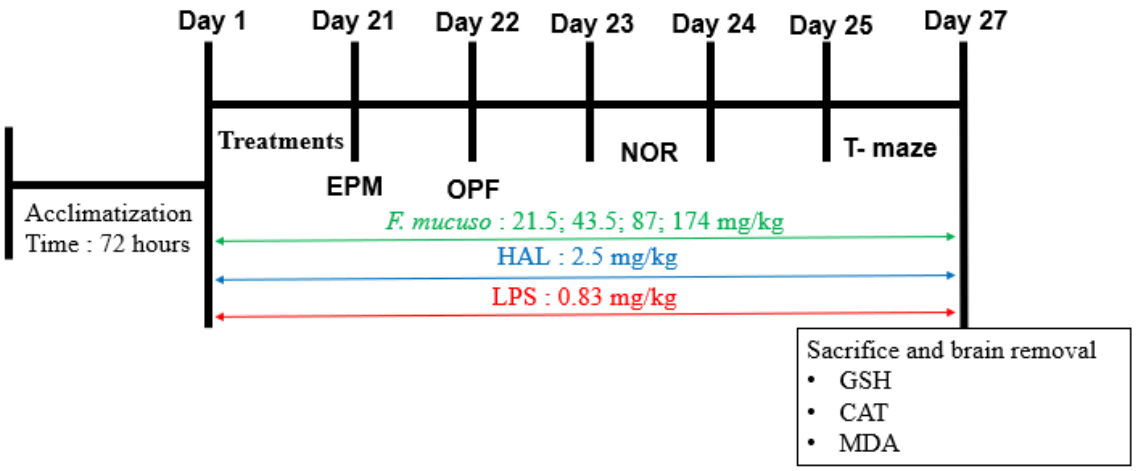

Figure 1 : Experimental Design

EPM: Elevated Plus Maze; OPF: Open Field; NOR: New Object Recognition; HAL: Haloperidol; LPS: Lipopolysaccharide

2.5. Preparation of the Decoction

40g of powder was introduced into 400 mL of distilled water and brought to a boil for 20 minutes at 100°C. One hour after cooling, the mixture was filtered using Whatman No.1 filter paper. After drying, 2.9 g of dry extract was obtained, with an extraction yield of 7.25 %. Considering the administration volume of 10 mL/kg and accounting for dilution factors, the doses used were 21.8, 43.5, 87, and 174 mg/kg, respectively. The traditional healer's dosage procedure was adhered to.

2.6. Phytochemical Screening

Phytochemical screening was conducted on the *F. mucuso* trunk bark decoction using qualitative colorimetric methods for the determination of flavonoids, alkaloids, saponins, polyphenols, steroids, and triterpenes (Dohou et al., 2003; Bidie et al., 2011).

2.7. Pharmacological Tests

Elevated Plus Maze (EPM) Test

The EPM, developed by Handley and Mithami (1984), validated for both rats and mice (Pellow et al., 1985; Lister, 1987), serves as a device for measuring anxiety in rodents. The apparatus used was described by Njapdounké et al. (2016). One hour after treatment on the 21st day, mice were placed in the centre of the maze platform, and each mouse's behaviour was observed for 5 minutes. Classical variables (Lister, 1987; Pellow et al., 1985) such as the number of entries, time spent in each arm, and time spent in the centre, along with ethological variables from the comparative repertoire (Rodgers & Johnson, 1995), including rearing, head dipping, and freezing, were recorded.

Open Field Test

The open field test is used to assess locomotor and exploratory activity as well as emotional reactivity in rodents (Bronikowski et al., 2001; Blizard, 1989). The experimental device used was described by Njapdounké et al. (2016). It measures (40 x 40) and is divided into 16 squares that divide the interior surface, with 1 central square (10 x 10) and a 19 cm high wall on all sides. Mice were placed in the centre of the arena, and behaviour was observed for 5 minutes. Recorded parameters included the number of crossings, rearing, grooming, and time spent in the centre.

Object Recognition Test

The NOR test, initially described by Ennaceur and Delacour (1988), evaluates long-term memory in mice. The principle involves presenting a mouse with object A, and 24 hours later, presenting it simultaneously with object B for 5 minutes. Mice naturally tend to preferentially explore the new object (B) compared to the familiar object (A). The device used was an open field with object recognition (Dermers et al., 2018), measuring (40 x 40) and divided into 16 squares, with 1 central square (10 x 10) and a 19 cm high wall. The test consisted of familiarization, acquisition, and retention phases. The recorded parameters included exploration time, number of objects, and latency time for finding object (A). The retention phase occurred 24 hours after acquisition, where objects (A) and (B) of different sizes and colors were presented for a 5-minute exploration. The number and exploration time of objects (A) and (B) were recorded, and the recognition index (IR) was calculated as the percentage of the exploration time of the new object (B) compared to the exploration time of both objects. An IR of 50% corresponds to chance, and the higher the index, the better the performance.

T-Maze Test

The T-shaped labyrinth is constructed from wood, with a white interior and black exterior. It comprises a departure compartment and two arrival corridors measuring (30 x 10 x 25) cm. Opaque guillotine doors, placed at the exit of the departure compartment and at the entrance of each of the arrival corridors, control access to the different areas of the maze. At the end of each arrival compartment (7 x 1) is a feeder that can contain a food booster (Robert et al., 2002). This test assessed the effects of our system on the level of exploration, learning, and memory of naive mice placed in this apparatus. The mice were placed in the starting arm of the T-maze for 1 hour. This task has three phases: familiarization, acquisition, and retention (Robert et al., 2002). The following parameters were recorded during the 5 minutes of observation. In the familiarization phase, the number and time spent in the preferred arms and the number and time spent in the discriminated arm were recorded. In the acquisition phase, parameters included the number and time spent in the preferred arm, latency to find the preferred arm, and time spent in the preferred arm. In the maintenance phase, the number and time spent in the arm, the number and time spent in the discriminated arm, and the number of returns to the starting arm were recorded.

Assessment of Oxidative Stress Markers

The mice were sacrificed by decapitation on the 27th day. Brains were immediately collected, rinsed in a saline solution (0.9% NaCl), and centrifuged at 10,000 rpm for 15 minutes; the supernatant was obtained. Analyses were performed to determine specific biochemical parameters.

Measurement of Malondialdehyde (MDA) levels in mice treated with lipopolysaccharide

Lipid peroxidation (MDA) was assessed following the protocol outlined by Ohkawa et al. (1979).

Determination of Catalase Activity in mice treated with lipopolysaccharide

Catalase activity was determined using the method described by Nassima et al. (2010).

Measurement of Reduced Glutathione Levels in mice treated with lipopolysaccharide

The measurement of reduced glutathione was carried out following the protocol described by Ellman (1959).

2.8. Statistical Analyses

Data were processed using Microsoft® Office Excel 2010. Statistical analyses were conducted using GraphPad Prism for Windows software, version 5.01. Results are presented as means ± standard error of the mean (SEM) and comparisons were made using one-way ANOVA, followed by Tukey's post hoc test for

multiple comparisons when differences were detected. Differences were considered significant at a threshold of $p < 0.05$.

3. Results

3.1. Phytochemical Screening

The phytochemical screening of the decoction from the trunk contents of *F. mucuso* reveals the presence of polyphenols, saponins, alkaloids, and flavonoids.

3.2. Effects of *Ficus mucuso* on the Elevated Plus Maze

As shown in Figure 2, the number of entries into the open arms decreased from 9.1 in the control group (distilled water) to 2.1 in the negative control group (LPS 0.83 mg/kg). The number of entries for *F. mucuso* increased to 21.1 and 18.8 in mice treated with doses of 21.8 and 43.5 mg/kg, respectively. *F. mucuso* has an anti-stress effect and acts as a GABA receptor antagonist.

Figure 3A shows how the plant affects two aspects: percentage of entries and time spent in the open arms. The percentage of entries decreased from 68.7% in the normal group to 21.3% in the negative group (LPS at 0.83 mg/kg), while the time spent in the open arms decreased from 67.2% to 30.0%. Haloperidol and *F. mucuso* decoction increased the number of entries into the open arms to 98.7%, 83.3%, and 80.1%, respectively, in mice treated with 21.8 and 43.5 mg/kg doses. Similarly, an increase in the percentage of time spent in the open arms was observed with doses of 43.5 and 174 mg/kg at 72.2% and 86.3%, respectively. Figure 3B shows the percentage of entries and time spent in the closed arms. These percentages increased from 31.2% and 8.1% in the normal group to 78.6% and 48.6%, respectively, in the negative (LPS) group. Doses of 21.8 and 43.5 mg/kg increased the percentage of entries into the closed arms from 16.6% to 19.8%. However, the *F. mucuso* decoction reduced this percentage to 13.2%, 17.2%, and 32.6% in mice treated with 43.5, 87, and 174 mg/kg, respectively.A decrease in the time spent in the centre and the total number of entries into the arms, an increase in the number of entries into the closed arms, head dipping, and rearing were observed in mice that received lipopolysaccharide. Treatment with different doses of *F. mucuso* had opposite effects on these parameters (Table 1). These results show that the plant reduces stress.

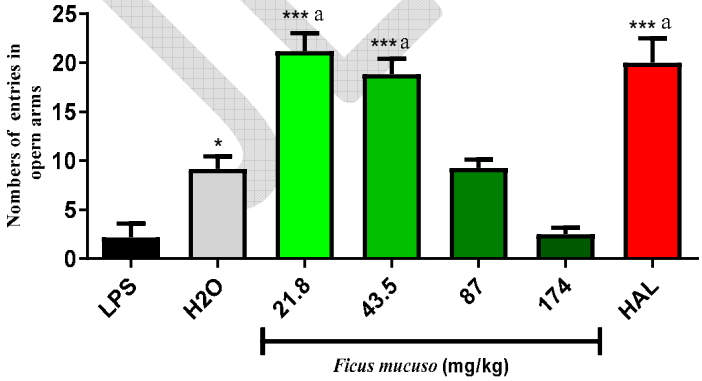

Figure 2: Effects of *Ficus mucuso* bark decoction on the number of entries in the open arms

*Each bar represents the mean ± SEM, N=6. ***p ≤ 0.001, **p ≤ 0.01, *p ≤ 0.05 significant difference compared to the negative control, a p ≤ 0.001 significant difference compared to the normal control, ANOVA followed by Tukey's test. H_2O: distilled water, LPS: lipopolysaccharide, HAL: haloperidol.*

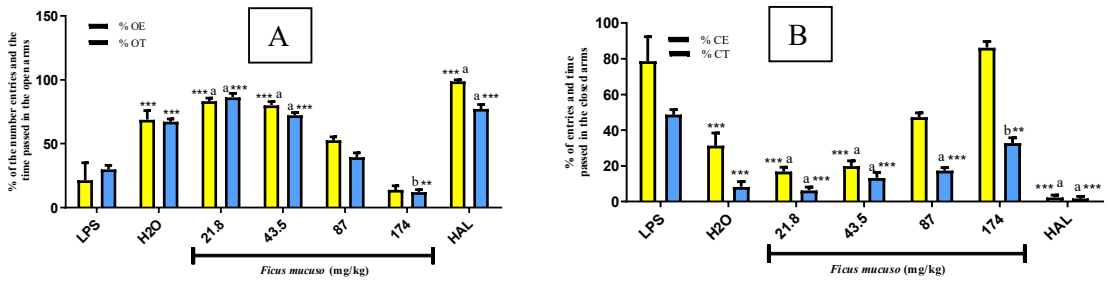

Figure 3: Effects of *Ficus mucuso* on the percentage of entries and time spent in open and closed arms
*Each bar represents the mean ± SEM, N= 6. ***p ≤ 0.001, *p ≤ 0.05 significant difference compared to the negative control, a p ≤ 0.001 significant difference compared to the normal control, ANOVA followed by Tukey's test. H_2O: distilled water, LPS: Lipopolysaccharide, HAL: haloperidol.*

Table 1: Effects of *Ficus mucuso* on other behavioural and ethological parameters in the Elevated Plus Maze.

Groups	Total number of entries	Number of closed arm entries	Head-dipping	Rearing	Centre time
LPS (0.83 mg/kg)	8.6 ± 0.2	77.09 ± 43.0	10.8 ± 1.3	42.5 ± 3.5	64.0 ± 8.6
H_2O (ED)	11.0 ± 0.6***	37.8 ± 1.2*	26.3 ± 3.0***	20.3 ± 5.8**	215.6 ± 26.4*
F. m (21.8 mg/kg)	25.3 ± 1.8*** a	16.6 ± 2.5*** a	10.8 ± 0.4*c	21.8 ± 3.6** b	210.7 ± 28.8**b
F. m (43.5 mg/kg)	23.6 ± 3.2*** a	19.7 ± 2.1*** a	10.5 ± 1.9	18.1 ± 3.5** b	186.8 ± 36.3** b
F. m (87 mg/kg)	18.5 ± 1.4*c	50.1 ± 2.0	2.2 ± 1.3	23.7 ± 3.3* c	23.0 ± 4.6
F. m (174 mg/k	18.0 ± 1.4*c	67.7 ± 22.9	9.2 ± 3.5	27.2 ± 3.9	6.5 ± 4.1
HAL (2. mg/kg)	20.5 ± 2.5** b	2.2 ± 1.3*** a	3.5 ± 1.1** b	3.5 ± 1.4*** a	117.0 ± 39.5** b

Each bar represents the mean ± SEM, N= 6. ***p ≤ 0.001, **p ≤ 0.01, *p ≤ 0.05 significant difference compared to the negative control, a p ≤ 0.001, b p ≤ 0.01, c p ≤ 0.05 significant difference compared to the normal control, ANOVA followed by Tukey's test. H2O: distilled water, LPS: lipopolysaccharide, HAL: haloperidol, F.m = Ficus mucuso.

Table 2: Effects of *Ficus mucuso* on mice behaviour in the Open Field Test

Groups	Grooming	Crossing	Rearing	Centre time
LPS (0.83 mg/kg)	6.0 ± 0.9	16.1 ± 4.8	52.8 ± 7.9	2.1 ± 0.4
H_2O (ED)	13.1 ± 1.5**	96.8 ± 15.7**	19.8 ± 4.5**	18.6 ± 4.5**
F. m (43.5 mg/kg)	13.0 ± 1.7** b	135.7 ± 11.3*** a	19.8 ± 3.3* c	14.0 ± 3.2** b
F. m (87 mg/kg)	6.5 ± 1.2	68.2 ± 21.8	50.7 ± 9.5	8.2 ± 3.4
F. m (174 mg/kg)	9.2 ± 0.7	37.0 ± 15.1	73.5 ± 12.0	5.7 ± 1.6
HAL (2.5 mg/kg)	15.0 ± 1.2** b	177.0 ± 11.9* c	13.0 ± 4.3* c	17.7 ± 3.4* c

Each bar represents the mean ± SEM, n= 6. ***p ≤ 0.001, **p ≤ 0.01, *p ≤ 0.05 significant difference compared to the negative control, a p ≤ 0.001, b p ≤ 0.01, c p ≤ 0.05 significant difference compared to the normal control, ANOVA followed by Tukey's test. H_2O: distilled water, LPS: lipopolysaccharide, HAL: haloperidol, F.m = Ficus mucuso.

Table 3: Effects of *Ficus mucuso* on latency time to find A and B, exploration number of A and B, and recognition index

Groups	Time of latency A	Time of latency B	Number of exploration A	Number of exploration B	IR
LPS (0.83 mg/kg)	38.5 ± 9.0	15.8 ± 3.1	13.3 ± 2.2	4.6 ± 1.0	14.3 ± 2.1
H_2O	10.3 ± 2.9**	4.0 ± 1.3**	6.0 ± 1.3*	19.3 ± 1.2***	16.9 ± 13.7*
F. m 21.8 mg/kg	5.5 ± 1.8*** a	3.5 ± 1.3*** a	2.8 ± 0.7*** a	16.3 ± 2.7** b	81.5 ± 16.6** b
F. m 43.5 mg/kg	13.4 ± 2.2** b	7.0 ± 1.7** b	3.8 ± 1.1** b	16.6 ± 2.7** b	80.5 ± 8.8** b
F. m 87 mg/kg	8.5 ± 1.7** b	8.5 ± 1.2	6.7 ± 2.4	12.5 ± 3.7	33.3 ± 9.7
F. m 174 mg/kg	7.6 ± 2.0** b	7.6 ± 2.0	7.6 ± 2.0	11.0 ± 1.0	26.5 ± 0.2
HAL (2.5 mg/kg)	8.5 ± 2.1*** a	2.0 ± 0.7*** a	2.0 ± 1.1*** a	20.2 ± 1.8*** a	86.8 ± 7.1** b

Each bar represents the mean ± SEM, n= 6. ***p ≤ 0.001, **p ≤ 0.01, *p ≤ 0.05 significant difference compared to the negative control, a p ≤ 0.001, b p ≤ 0.01, c p ≤ 0.05 significant difference compared to the normal control, ANOVA followed by Tukey's test. H_2O: distilled water, LPS: lipopolysaccharide, HAL: haloperidol, F.m = Ficus mucuso.

3.3. Anxiolytic Effects of *Ficus mucuso* evaluated by the Open Field Test

The number of righting movements in mice was reduced, and the time spent in the centre was increased by lipopolysaccharide (0.83 mg/kg). *F. mucoso* and haloperidol significantly reduced the number of mice standing on their hind legs, while increasing the time spent in the centre, grooming, and crossing the open field (Table 2). These results suggest improved locomotor and exploratory activity, indicating the plant's potential to alleviate stress and anxiety in mice. *F. mucuso* acts as an antagonist to LPS.

3.4. Effects of *Ficus mucuso* evaluated by Object Recognition

Lipopolysaccharide induced an increase in the latency time required to locate objects (A) and (B), and a reduction in the number of times object (A) was explored (Table 3). The *F. mucuso* decoction was administered at doses of 87 and 174 mg/kg for (A), and at doses of 21.8 and 43.5 mg/kg for (B). The results showed a significant reduction in latency, with values of 8.5 and 7.6 s being achieved in the first group, and 3.5 and 7.0 s in the second group. However, *F. mucuso* decreased significantly from 2.8 to 3.8 at doses of 21.8 and 43.5 mg/kg for (A) and from 16.3 to 16.6, respectively, for (B). The IR increased from 81.5 to 80.5 in the group treated with 21.8 and 43.5 mg/kg for (B) (Table 3). The administration of the *F. mucuso* decoction significantly increased the duration of exploration of the new object. This suggests that the plant influences memory abilities involving unconscious recall, highlighting episodic memory and recognition.

3.5. Effects of the Decoction of *Ficus mucuso* on Mice's Memory in the T-Maze

Figure 4A below illustrates that LPS induced an increase in latency during the habituation, acquisition, and retention phases. This time increased from 6.8, 4.1, and 6 seconds in the normal group to 19, 12, and 9.8 seconds in the negative group (LPS at 0.83 mg/kg). The *F. mucuso* decoction reduced this time to 4.5 seconds during habituation. During the acquisition phase, this time decreased to 2.3, 4, and 7 seconds in mice treated with 21.8, 43.5, and 87 mg/kg doses, respectively. During the retention phase, it was reduced to 20.0 and 5.2 seconds in mice treated with 43.5 and 174 mg/kg, respectively. Lipopolysaccharide induced a decrease in the number of returns to the reference arm (Figure 4B) and in the number of entries into the preferred arms during the habituation, acquisition, and retention phases (Figure 5A). The *F. mucuso* decoction increased the number of returns to the reference arm to 2.6, 5.3, 1.8, and 2.8, and 1.3 and 2 during habituation, acquisition, and retention, respectively. Similarly, the number of entries into the preferred arm increased to 16.0, 16.5, and 17.0. Figure 5B shows that lipopolysaccharide reduced the time spent in the discriminated arm during the three phases. In the group treated with *F. mucuso*, this time increased significantly, rising to 223.8 and 207.7 s with doses of 21.8 and 43.5 mg/kg. The same result was obtained with the haloperidol group. These observations show that the plant reduces stress by acting on the retention of information gathered. Mice have shown improvements in learning and memory after being given a decoction of *F. mucuso*.

3.6. Study of the Effects of the Decoction of *Ficus mucuso* Bark on Oxidative Stress Markers

Table 4 below summarizes the effects of *F. mucuso* extract on malondialdehyde (MDA), glutathione peroxidase (GSH), and catalase (CAT) activity. Lipopolysaccharide (0.83 mg/kg) increased the MDA level from 1.36 nmol/g to 1.20 nmol/g of tissue in the normal group. It decreased to 1.27 nmol/g of tissue in the treated group at a dose of 43.5 mg/kg of extract. Lipopolysaccharide reduced the concentration of glutathione in the homogenates from 486.76 nmol/g of tissue to 580.44 nmol/g of tissue in the normal group. *F. mucuso* increased this concentration to 582.3 and 573.9 nmol/g in the treated rats at doses of 21.8 and 174 mg/kg. This increase was 579.8 nmol/g tissue with haloperidol. Catalase activity decreased from 461.6 in the normal group to

407.5 nmol/g tissue in the negative group (LPS). There was an increase in this activity to 400.3 and 440.3 nmol/g in the group treated with doses of 87 and 174 mg/kg of decoction. This activity significantly increased with haloperidol up to 440.6 nmol/g of tissue.

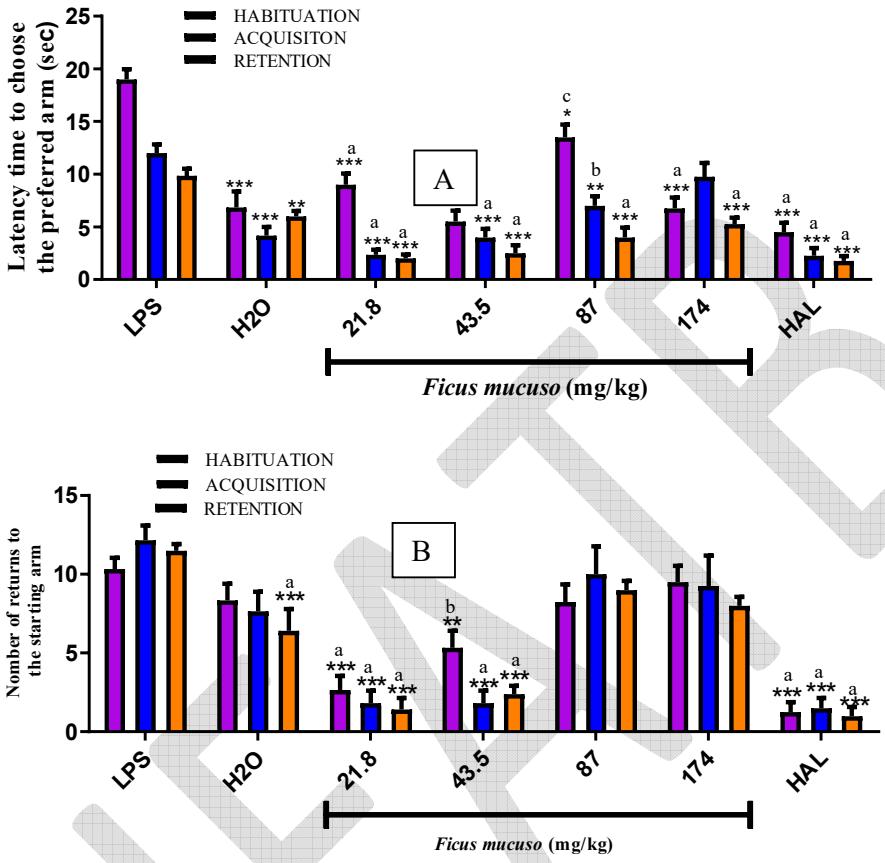

Figure 4: Effect of *Ficus mucuso* on latency time to choose the preferred arm.

*Each bar represents the mean ± SEM, n=6. ***p ≤ 0.001, **p ≤ 0.01, *p ≤ 0.05 significant difference from the negative control, a p ≤ 0.001, b p ≤ 0.01, c p ≤ 0.05 significant difference from the normal control, ANOVA followed by Tukey's test. H_2O: distilled water, LPS: lipopolysaccharide, HAL: haloperidol.*

Table 4: Effects of *Ficus mucuso* and lipopolysaccharide on the level of Malondialdehyde, Reduced Glutathione, and Catalase Activity in Mice

Treatments (mg/kg)	MDA (µM/mg protein)	CAT (µM/mg protein)	GSH (mol/g brain)
LPS (0.83 mg/kg)	0.21 ± 0,00	0,10 ± 0.02	0,33 ± 0.006
H_2O	0,18 ± 0.00***	0,16 ± 0,01*	0,39 ± 0,00*
F. m 21.8 mg/kg	0,20 ± 0,00	0,19 ± 0,00** b	0,3 ± 0,00** b
F. m 43.5 mg/kg	0,19 ± 0.00* c	0,16 ± 0,00* c	0,38 ± 0,00* c
F. m 87 mg/kg	0,19 ± 0.00* c	0,16 ± 0,00* c	0,37 ± 0,00
F. m 174 mg/kg	0,20 ± 0.00	0,16 ± 0,00	0,39 ± 0,02* c
HAL (2,5 mg/kg)	0,19 ± 0.00** b	0,18 ± 0,00** b	0,39 ± 0.00** b

*Every bar represents the mean ± SEM, n= 6. *** p ≤ 0.001, ** p ≤ 0.01, * p ≤ 0.05, significant difference compared to the negative control, a p ≤ 0.001, b p ≤ 0.01, c p ≤ 0.05, significant difference compared to the normal control, ANOVA followed by Tukey's test. H_2O: distilled water, LPS: lipopolysaccharide, HAL: haloperidol, F, m= Ficus mucuso,*

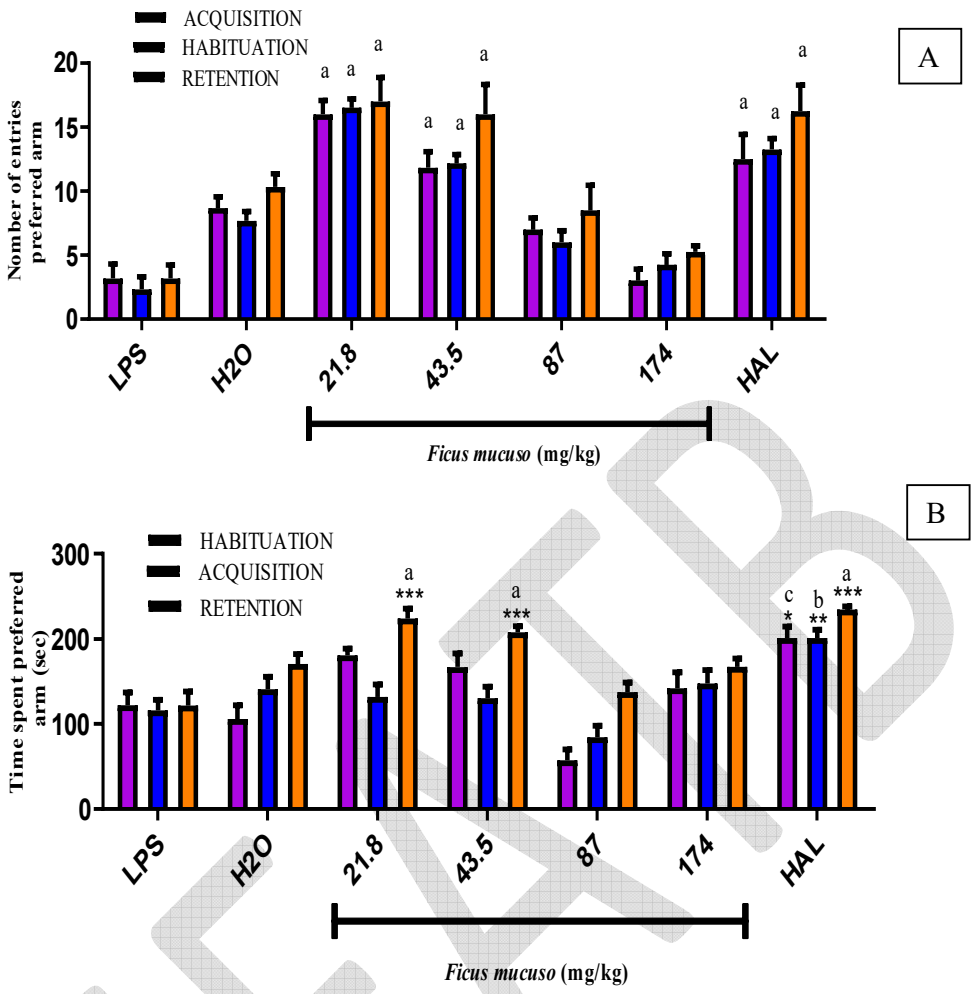

Figure 5: Effects of *Ficus mucuso* on the number of entries and latency time to select the preferred arm.

*Each bar represents the mean ± SEM, n=6. ***p ≤ 0.001, **p ≤ 0.01, *p ≤ 0.05 significant difference from the negative control, a p ≤ 0.001, b p ≤ 0.01, c p ≤ 0.05 significant difference from the negative control, ANOVA followed by Tukey's test. H_2O: distilled water, LPS: lipopolysaccharide, HAL: haloperidol.*

4. Discussion

The study aimed to evaluate the effects of *F. mucuso* decoction on schizoaffective disorders induced by lipopolysaccharide in mice. Behavioural tests such as the EPM, OPF, NOR, and T-maze test were used to assess anxiety and cognitive aspects of memory in schizoaffective disorders induced.

The results of the EPM suggest improved exploration by the mice, as evidenced by the significant increase in the number and percentage of entries, as well as the time spent in the open arms in mice treated with *F. mucuso* decoction, indicating an anxiety reduction (Moto et al., 2013, 2018; Rodgers & Dalvi, 1997). In addition, *F. mucuso* led to a notable decrease in righting, head diving, and time spent in the centre of the maze, indicating a reduction in the anxiety response in rodents (Rodgers et al., 1997; Njapdounke et al., 2016). Conversely, a decrease in the number, percentage of entries, and time spent in the closed arms was observed, indicating a stress reduction (Lister, 1990; Ngo et al., 2009). *F. mucuso* inhibits neuronal activity by antagonizing serotonin 5-HT2C and 5-HT3C receptors (Nayer et al., 2017). These results suggest that the plant has anxiolytic properties.

The open field test is used to assess exploratory and locomotor behaviour in mice (Bronikowski et al., 2001; Blizard, 1989). Administration of *F. mucoso* and haloperidol revealed an increase in crossing, grooming, time spent in the centre, and a decrease in righting (Ngo Bum et al., 2009; Moto et al., 2013). The plant acts as an agonist of GABAergic receptors by inhibiting dopaminergic neurotransmission (Nayer et al., 2017). The effect of the plant suggests an increase in locomotion and exploratory activities, indicating an anxiety reduction (Ngo Bum et al., 2011; Moto et al., 2018). As a result, *F. mucuso* has anxiolytic properties.

The NOR test was used to assess the effect of *F. mucoso* on the recognition memory of mice. LPS treatment increased the time required to locate the new object (B) and a reduction in the IR and the number of times the object (B) was explored. However, the *F. mucoso* decoction reversed this trend, resulting in a prolonged exploration period (Nkemmo et al., 2020; Mani et al., 2022); an increase in IR (Ennaceur & Delacour, 1988; Kouémou et al., 2017), thereby improving recognition memory. These results are similar to those of Ennaceur et al. (2010), who demonstrated that children explore new toys more than familiar ones.

The T-maze is used to assess memory function based on an individual's ability to familiarize themselves with an environment, orient themselves, and perform memory tasks (Chapouthier et al., 2002). It is also used to evaluate exploration, learning, and memory levels in mice (Robert et al., 2006). Indeed, cognitive symptoms have been linked to both microglial activation and the inflammatory response (Adiko et al., 2013). *F. mucuso* decoction has been shown to reduce the time taken to find the preferred arm, suggesting that it enhances memory and mnemonic capabilities (Chapouthier et al., 2002). Furthermore, the number of returns to the starting arm decreases, indicating strong exploration (Nkemmo et al., 2020). This memory improvement has been demonstrated by mice remembering the location where they find satisfaction (Farshchi et al., 2010). As demonstrated by Nkemmo et al. (2020), improvements in memory resulting from increased exploration are linked to reductions in stress and anxiety. The group treated with the F. *mucoso* decoction showed an increase in the number and frequency of entries into the preferred arm, indicative of enhanced working memory.

Oxidative stress is an important factor in the pathophysiology of schizophrenia (Ben-Azu et al., 2016b; 2018a). Increased levels of reactive oxygen species can damage cells by inducing lipid peroxidation and protein damage. Antioxidants are substances capable of neutralising or reducing the damage caused by free radicals in the body, while maintaining non-cytotoxic concentrations of reactive oxygen species at the cellular level (Mohammedi, 2013; Taiwe et al., 2015). Schizophrenia is characterized by a state of widespread oxidative stress, which is believed to be a major contributing factor to the condition (Ben-Azu et al., 2019). This stress is often linked to an antioxidant system that is not functioning properly. LPS administration causes oxidative stress in mice by increasing malondialdehyde production and decreasing glutathione concentration and catalase activity in the brain. The decoction of *F. mucoso* reduced MDA levels and increased GSH and CAT levels. MDA, produced when polyunsaturated fatty acids are oxidised, is a useful marker of oxidative stress and cellular damage (Moto et al., 2018). The *F. mucuso* decoction acts as a peroxidation antagonist with high antioxidant power (Esfandiari et al., 2018) by reducing MDA concentration; this may be due to the presence of flavonoids and tannins in the extract. Glutathione is a cell-specific endogenous antioxidant enzyme (Kouémou et al., 2017). It plays an important role in protecting against oxidative damage to lipids, proteins, and nucleic acids by replenishing other antioxidants such as ROS, vitamin C, and vitamin E (Prakash et al., 2017; Ben-Azu et al., 2024). CAT is an enzyme that catalyzes the conversion of hydrogen peroxide into oxygen, which is then made available to the cell for oxygenation (Ben-Azu et al., 2022). A decrease in cerebral CAT levels is caused by the administration of LPS. The brains of mice are protected against oxidation by the increased activity of this enzyme, which is caused by the administration of *F. mucoso*. The

beneficial effects of this plant are due to its secondary metabolites, such as flavonoids, saponins, tannins, and alkaloids. These compounds have an anti-stress effect on the brain (Ben-Azu et al., 2016b; Prakash et al., 2017). These components can easily cross the blood–brain barrier (BBB) and exert antioxidant and neuroprotective activity in the central nervous system (Constant et al., 2012). The presence of metabolites and the positive effects obtained through behaviour and biochemical tests explain the plant's anxiolytic, antioxidant, and antinociceptive effects, partly justifying its traditional medicinal use in the management of psychoses, particularly schizoaffective disorders.

Conclusion

The aim of this study was to investigate the effects of *F. mucuso* decoction on schizoaffective disorders induced in mice. The plant demonstrated its anxiolytic effect by increasing locomotor and exploratory activities in the open arena and EPM. Similarly, it showed beneficial effects on memory and cognition in object recognition and the T-maze. The presence of flavonoids, alkaloids, and saponins was revealed by phytochemical screening. The presence of secondary metabolites gave our extract antioxidant properties by reducing MDA levels and increasing GSH and CAT levels at doses of 21.8 and 43.5 mg/kg. *Ficus mucuso* has antioxidant, anxiolytic, and anti-amnesic properties. The study suggests its potential application in traditional medicine as an alternative therapy for psychoses, particularly schizoaffective disorders.

Acknowledgments

We are grateful to the team of the Laboratory of Medicinal Plants, Health, and Galenic Formulations of the Faculty of Sciences at the University of Ngaoundéré for providing the technical resources that facilitated this research.

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How to cite this paper:
Tchiengang, DJ, Njapdounke, KJS, Nkemmo, TWS, Moto, OFC, Zogning, DLM, Jerye, S, Nezoumne, FN & Ngo Bum, E. (2025), Evaluation of the effects of decoction of *Ficus mucuso* trunk stem bark (Moraceae) on lipopolysaccharide-induced schizoaffective psychoses in mice (*Mus musculus*). *Journal of Experimental and Applied Tropical Biology, 5 (1): 1-15.*