Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/21473
DOI URL: http://dx.doi.org/10.21474/IJAR01/21473

RESEARCH ARTICLE

NEUROBEHAVIORAL EFFECT OF ETHANOL LEAF EXTRACT OF CHROMOLAENA ODORATA AGAINST ACUTE KETAMINE-INDUCED COGNITIVE IMPAIRMENT IN MURINE MODELS OF SCHIZOPHRENIA

Olayemi K. Wakeel[1], Okoduwa J. Omoabhiena[2], Olajide S. Annafi[3], Olawale H. Mohammed[4] and Susan T. Okojie[3]

1. Department of Pharmacology and Therapeutic, Faculty of Basic Clinical Sciences, College of Health Sciences, Ladoke Akintola University of Technology Ogbomoso, Nigeria.
2. Department of Veterans Affairs, Harvard Medical School Post Graduate: Safety, Quality, Informatics and Leadership, Veterans Healthcare System Phoenix Arizona, USA.
3. Department of Pharmacology and Therapeutic, Faculty of Basic Medical Sciences, University of Ilesha, Osun State, Nigeria.
4. Department of Pharmacology and Therapeutic, Faculty of Basic Clinical Sciences, College of Health Sciences, Osun State University, Osogbo, Nigeria.

Manuscript Info

Manuscript History
Received: 23 May 2025
Final Accepted: 25 June 2025
Published: July 2025

Key words:-
Ketamine; Cognitive impairment; Schizophrenia; C. odorata; Schizoprenia

Abstract

Schizophrenia is a neurological disorder reportedly linked to oxidative imbalance and associated behavioral disturbances.Chromolaena odorata is one of the commonly used plants in Nigeria for the management of psychiatry disorder.This study aimed to evaluate the extract in ketamin e-induced cognitive impairment using mice. The effect of ethanol leaf extract of Chromolaena odorata at doses 500, 1000, and 1500 mg/kg on neurobehavioral deficits was assessed in mice using various behavioral paradigms: Y-maze, novel object recognition, forced swim test, open field test, and catalepsy test. C. odorata significantly increased explorati on time of the novel object and the percentage recognition index during the retention phase of the Novel Object Recognition Test($p < 0.05$). In the Y-maze test, the extract significantly increased ($p < 0.05$) both the number of actual alternations and the percentage of spontaneous alternations. It also significantly decreased ($p < 0.05$) the duration of immobility in the forced swim test. The results of open field test revealed a significant decreased ($p < 0.05$) in the number of crossings in both the central and peripheral squares. Additionally, the extract did not prolong the duration of catalepsy induced by haloperidol in the glass bar test.C. odorata extract contains phytochemicals that may impr ove cognitive function and reduce negative symptoms in individuals with schizophrenia.These findings suggest that C. odorata probably exerts its antipsychotic like activity through a neuroprotective compens atory mechanism of action, and as such, it could be relevant in the management of schizophrenia.

Corresponding Author:- Olayemi K. Wakeel
Address:- Department of Pharmacology and Therapeutic, Faculty of Basic Clinical Sciences, College of Health Sciences, Ladoke Akintola University of Technology Ogbomoso, Nigeria.

……..

Introduction:-

Schizophrenia is an incapacitating ailment, generally characterised by stereotypic behaviour, bizarre behaviours or positive symptoms, depressive or negative symptoms and cognitive symptoms with the global burden around 1% (Fineberg et al., 2013). Dopaminergic deregulation, hypofunction of NMDA receptors and GABAergic activity, diminished cholinergic firing. The increased oxidative stress and neuroinflammation have been shown to play a pathophysiological role in schizophrenia. Typical (first generation) and atypical (second generation) antipsychotic agents are currently being use for the management of schizophrenia, which are also effective against hallucinations, delusions and thought disorders.

First-generation antipsychotics are only effective in the management of positive symptoms of schizophrenia and are also associated with extrapyramidal effects. In contrast, second-generation antipsychotics are beneficial in cognitive symptoms of schizophrenia with lesser extra-pyramidal effects, but may cause diabetes mellitus, cardiovascular disorders and agranulocytosis. Though antipsychotics have been used clinically for several decades, most of them have incomplete efficacy. They are also coupled with many adverse effects as well as an increased risk of psychotic relapse. Thus, there is a great need for therapeutic interventions for managing psychiatric disorders, which will not only provide symptomatic relief but also halt the progression of the disease. Natural medicinal agents are the powerhouse of various bioactive constituents which possess medicinal properties, biochemical specificity, and chemical diversity that make them essential remedies for various human disorders including schizophrenia[2]. Various medicinal herbs have been specifically studied in different neuropsychiatric disorders and many others have shown promising results based on their therapeutic potential and safety profile(Allman, 1959).

Chromolaena odorata is formerly known as Eupatoriu odoratum which belongs to the kingdom Plantae, family Asteraceae, genus Chromolaena, and species Chromolaena odorata L.(Boudjeko et al., 2015). The family Asteraceae or Compositae (known as the aster, daisy, or sunflower family) is the most prominent family of flowering plants, represented by about 950 genera and 20,000 species worldwide. C. odorata plants are distributed all over the world in almost all habitats. The common names for these plants are Siam weed, devil weed, eupatorium, Jack in the bush, Jack- in-the- bush, king weed, paraffin bush, and paraffin weed (Sirinthipaporn and Jiraungkoorskul, 2017). C. odorata has been introduced extensively to tropical Asia, West Africa and some parts of Australia (Zahara, 2019). In general, this plant can grow in a wide range of soil pH. However, it grows best in acidic soil areas that contain a high amount of potassium and phosphorus. Herbal plants are known to be rich sources of phytochemical ingredients that contribute to healthcare management.

Thereby, the demand for plant-based medicinal treatment using natural herbal plants has been shown to rise worldwide(Kumar et al., 2016).Chromolaena odorata has a wound healing properties,. Anti bacterial,anticancer(Kigi gha&Zige, 2013)anticonvulsant, antidiabetic, anti-diarrheal(Aba et al., 2015), anti-fungal, anti-inflammatory, antioxidant,Vijayaraghavan et al., 2017; Lee et al., 2020), and antiparasitic(Thoden et al., 2007), hemostatic and wound healingVaisakh et al., 2012), and hepatoprotective activities(Bissangouet al., 1997). Several studies have investigated the pharmacological properties of Chromolaena odorata leaf extract. Phytochemical constituent has revealed the presence of bioactive compounds such as:monoterpenes, sesquiterpenes hydrocarbons, triterpenes/steroi ds, alkaloids and flavonoids(Elion et al., 2017. The leaves of C. odorata also contain the highestconcentration of allelochemicals isolated from a plant, flavonoid aglycones (flavanones, flavonols, flavones) including acacetin, chalcones, eupatilin, luteolin, naringenin, kaempferol, quercetin, quercetagetin, and sinensetin(Anyasor et al., 2011), terpenes and terpenoids(Tilak et al., 2016).

Materials and Method:-

SPlant MaterialsThe leaves of C. odorata used in this experiment was collected in April Road 7, OAU, ILE-IFE, Osun State, Nigeria. It was identified by a botanist (Mr. G.A Ademoriyo) in the herbarium unit of the Botany Department, Faculty of Sciences, Obafemi Awolowo University, Ile Ife, Nigeria, where a voucher specimen was kept with the voucher number IFE-18267. The leaf was washed, air-dried, and then pulverized using a mortar and pestle.

Extraction Procedure

One hundred grams of the pulverized, air-dried leaf of C. odorata were dissolved in 500 mL of distilled water in a conical flask. The mixture was shaken vigorously and then allowed to stand for 72 hours. It was subsequently

filtered using Whatman (No. 1) filter paper, and the filtrate was evaporated at 50°C using a rotary evaporator(Eduador et al., 2000).

Animal materials

Male albino mice weighing approximately (20-25 g) grams were used for this study. The animals were housed in polypropylene cages maintained at room temperature. They were fed standard pellet feed and had access to water ad libitum. The albino mice were acquired from the LAUTECH Animal House, located within the College of Health Sciences at Ladoke Akintola University of Technology (LAUTECH) in Ogbomosho, Oyo State, Nigeria. The mice were kept in transparent, wire-gauged cages in a well-lit and adequately ventilated room, under standard environmental conditions consisting of a 12-hour light and 12-hour dark cycle. Prior to the commencement of the experiment, the mice were acclimatized for three weeks while continuing to receive standard pellet feed and water ad libitum.

Behavioural Observations

Behaviour assays were performed using method previously described(Hanieh et al., 2023). Briefly, mice, acclimatized previously were randomly selected and distributed into various groups of 7 animals (n = 7), i.e.: (a) hyperlocomotor activity (representing positive symptoms, evaluated using Open field test), (b) Forced Swim Test (representing negative symptoms) (c) Novel Object recognition test and Y-maze (representing cognitive symptoms). Drug administration was generally done one hour prior to ketamine treatment.

Effect of ethanol leaf extract of Chromolaena odorata on **Novel object recognition test**

In assessing the efficacy of schizophrenia using animal models, Novel object recognition test is commonly usedrecognition(Rajashri et al., 2020; Sung et al., 2023). Mice were place individually in a box measured 32x30 cm with beige walls for 5 min habituation followed by injection with saline or extract (before or after acquisition) and returned to the chamber. Twenty minutes later mice were injected (i.p.) with saline or 100mg/kg ketamine and 30 min later, it was placed in a chamber with two identical objects for 10 min (acquisition session). After acquisition, mice was returned to home cages and 1.5 h later they were place back into the experimental chamber with retained and one novel object of about the same size but a different shape and color (recognition session). The acquisition and recognition sessions were video recorded and the time spent exploring the objects was scored by an observer who was blinded to the drug treatments. Exploratory behavior was defined as sniffing, touching and direct attention to the object. Exploration times were expressed as the means ± s.e.m. For the recognition session, the recognition index was calculated as (time for the exploration of the novel object divided by time exploring both the familiar and the novel object) multiply by 100

Effect of ethanol leaf extract of Chromolaena odorata on**Y-Maze**

The Y-maze can be used for short term working memory and locomotive activity. Spontaneous alternation is the measure of spatial working memory. To alternate among spatial location a mouse must remember its previous location(Akanmu et al., 2007). The effects of antipsychotic drug on cognitive function as an index for the cognitive dysfunction of schizophrenia are assessed using the method of Julia et al.,(2023). Six groups of mice (n = 6) were randomly selected and treated orally or by intraperitoneal injection; each mouse is only tested once. Group 1 was given distilled water (10ml/kg) once daily for 14 days. Group 2 to 6 were pretreated with sub-anesthetic dose of ketamine (20 mg/kg) once daily for 14 days. From 8th to 14th day of treatment, group 2 was treated with vehicle (10 ml/kg) once daily as negative control; group 6 (positive control) received risperidone 1mg/kg. Group 3 to 5 were given three graded dose of the extract till day 14th. Twenty-four hours after the last treatment (15th day), animals were assessed for behavioral activity on Y- maze. The apparatus consists of three identical arms (33 x 11 x 12 cm) in which arms are symmetrically separated at one twenty degree specifically each mouse is place at the end of arm A and allow to explore all the three arms (A, B, C freely for 5 minutes taking record of the number of arms visited and the sequence (alternation) of arm visits visually. An arm entry is defined as the entry of the body of mouse except its tail into an apartment. Alternation is defined as the entry into all three arms on consecutive device. The percentage alternation was determined as the ratio of actual alternation to visible alternation (defined as total number of arm entry minus two) multiply by 100(Akanmu et al., 2007). After each mouse observation the chamber will be clean with 70% ethanol.

Effect of ethanol leaf extract of Chromolaena odorata on**Forced Swimming Test**

Force swimming test, as described previously(Hanieh et al., 2023) in mice is a measure of despair behavior. In brief, mice were placed individually in glass cylinders (20 cm height, 10 cm diameter) containing 10 cm depth of water at

25 ℃. After 5 min, the animals were removed from water, dried and returned back to their home cages. They were again placed in the cylinder 24 h later and after the initial 1 min acclimatization period, the total duration of immobility was measured for 5 min. The duration of swimming during the 6 min test period was recorded by a camera mounted above the cylinders.

Effect of ethanol leaf extract of Chromolaena odorata on Open field test (Locomotor Activity)
Gross open field activity(Ghaderi et al., 2020) was studied using plexiglass arena, fitted with a video camera containing horizontal square lines on the floor of the arena. The number of interruptions of the central and peripheral square cross by the animals was interpreted as horizontal activity and locomotive behavior. Group 1 received only distilled water, while group 2-6 received ketamine with 3, 4, 5 receiving graded doses of extract and group 6 received risperidone 1mg/kg. Prior to the experiment, both the control and the treated animals were habituated in the experimental cage for15 min. After the initial habituation process, the activities of the animals were studied for 5 min. All cages were connected with video camera.

Effect of ethanol leaf extract of Chromolaena odorata on Catalepsy Test
The catalepsy procedure has been described previously(Prinsen et al., 2002;Zarrinkalam et al 2016). Animals will first be examined in the crossed-leg position test, and immediately thereafter in the bar test. In the crossed-leg position test, the hind limbs are placed over the ipsilateral forelimbs and the time during which an animal remained in this position was determined up to a maximum of 30 seconds. In the bar test, the forelimbs were placed on a horizontal, cylindrical metal bar (diameter 1.25 cm; height 10 cm) and the time during which both forelimbs remained on the bar was determined up to a maximum of 30 seconds. The bartest was repeated 3 and 6 min later and the mean of three trials was used for data analysis. Animals were returned to their cage between tests. Six animals were tested in each group. Positive control: Haloperidol, negative control: distilled water and test groups received 500, 1000 and 2000 mg/kg of the extract.

Data and Statistical Analysis
The data obtained are presented as means (± SEM) for each group of animals (n=6). Data from distilled water or normal saline-treated 'control' rats were utilized as the baseline. In all cases, the results from the extract- and reference drug-treated 'test' animal groups were compared to those from the normal saline groups. A one-way analysis of variance (ANOVA) was used to examine the differences between the 'test' animal groups and the vehicle-treated 'control' groups, using a 95% confidence interval. Following this analysis, Dunnett's post-hoc test was applied. A statistical significance level of $p \leq 0.05$ was set for all tests.

Results:-
The ethanol leaf extract of C. odorata significantly increased the percentage of spontaneous alternation at doses of 1000 and 2000 mg/kg compared to the control group ($p < 0.05$), as shown in Table 1. Additionally, Table 2 demonstrates that the extract dose-dependently increased both the duration of novel object exploration and the percentage recognition index when compared to the control group, with statistical significance ($p < 0.05$).
However, the extract also led to a significant decrease in the number of central and peripheral square crossings ($p < 0.05$), indicating reduced hyperlocomotor activity, as detailed in Table 3.

Table 4 shows a significant decrease in the duration of immobility at a dose of 1500 mg/kg, although this effect was not observed at the lower doses of the extract.

There was no significant increase in the duration of catalepsy induced by haloperidol across all doses of the extract when compared to the control group (Table 5, $p < 0.05$).
Furthermore, Table 6 indicates that there were no significant changes in any liver function parameters after 28 days of oral administration of the ethanol leaf extract of C. odorata at doses of 500, 1000, and 2000 mg/kg ($p < 0.05$).

Table 1: Effect of C. odorata ethanol leaf extract on acute ketamine induced spatial memory impairment in Y- maze

Treatments	Doses (mg/kg)	No. of alternation**		Spontaneous alternation%**
		NOAA	NOVA	
Control	0	3.5± 0.13	11.1±1.16	24.0
C. odorata	500	2.7 ± 0.06	8.9 ± 1.12	23.3
C. odorata	1000	5.3 ± 0.05	8.2 ± 0.07	39.3
C. odorata	2000	8.1±1.21	7.5 ± 1.23	52.0
Risperidone		18.7±1.35	6.9 ± 0.42	55.8

**Values are mean ± SEM (n=5).
*Values are statistically significant (P<0.05) compared with control using one-way ANOVA followed by Dunnett's post-hoc test.

Table 2; Effect of C. odorata extract on acute ketamine induced memory impairment in Novel object recognition test.

Treatments	Doses (mg/kg)	*A.* Exploration time(s)**		Recognition index %**
		TENO	TEFO	
Control	0	53.1± 4.06	75.1 ± 5.35	41.4
C. odorata	500	61.4 ± 4.13	72.5± 6.71	45.9
C. odorata	1000	61.8 ± 5.21	69.3 ± 5.28	47.1
C. odorata	2000	72.3± 5.23*	70.1± 5.63	50.8
Risperidone	1	75.6± 6.45*	73.8±7.35	50.6

**Values are mean ± SEM (n=5).
*Values are statistically significant (P<0.05) compared with control using one-way ANOVA followed by Dunnett's post-hoc test.

Table 3: Effect of C. odorata extract on acute ketamine induced hyperactivity in open field test.

Treatment	Doses (mg/kg)	N0. of central square cross**	N0. of peripheral square cross**
Control	0	8.4±1.35	17.83 ± 0.34
C. odorata	500	7.1± 1.05	8.50 ± 1.17*
C. odorata	1000	6.5± 0.79	6.61 ± 1.42*
C. odorata	2000	2.3± 0.21	3.66 ± 0.21*
Risp	1	0.45±0.48	0.65 ± 0.08*

**Values are mean ± SEM (n=5).
*Values are statistically significant (P<0.05) compared with control using one-way ANOVA followed by Dunnett's post-hoc test.

Table 4: Effect of C. odorata ethanol leaf extract on acute ketamine induced immobility in forced swim test.

Treatments	Doses (mg/kg)	Duration of immobility**
Control	0	5.72 ± 0.43
C. odorata	500	4.07 ± 0.21
C. odorata	1000	4.17± 0.03
C. odorata	2000	2.75 ± 0.19*
Risp1		1.97 ± 0.05*

**Values are mean ± SEM (n=5).
*Values are statistically significant (P<0.05) compared with control using one-way ANOVA followed by Dunnett's post-hoc test.

Table 5: Effect of C. odorata extract on catalepsy duration in glass bar test.

Treatments	Doses (mg/kg)	Catalepsy (sec)**
Control	0	31.71 ± 3.41
C. odorata	500	29.35 ±3.27*
C. odorata	1000	28.9 ± 3.72*
C. odorata	2000	28.17 ±3.08*
Risp	1	11.31 ± 2.63*

**Values are mean ± SEM (n=5).
*Values are statistically significant (P<0.05) compared with control using one-way ANOVA followed by Dunnett's post-hoc test.

Table 6: Effect of C. odorata on liver function indices following 28 days subchronic oral treatment in mice

Treatment	Dose(mg/kg)	ALK(m/l)	AST(m/l)	ALT(m/l)	T.P(g/l)	Albumin(g/l)
Control	0	75.31±2.11	53.06±4.21	61.42±5.57	56.63±3.42	28.37±2.21
C. odorata	500	69.25±7.25	56.37±4.05	67.42±5.45	61.13±4.53	31.53±3.35
C. odorata	1000	61.32±5.40	51.25±4.23	52.35±3.34	48.31±3.71	35.81±2.07
C. odorata	2000	62.05±4.09	54.27±4.39	61.15±5.64	55.75±4.47	31.21±2.43

**Values are mean ± SEM (n=5).
*Values are statistically significant (P<0.05) compared with control using one-way ANOVA followed by Dunnett's post-hoc test.

Discussion:-

Medicinal plants, with their antioxidant properties and fewer side effects, remain the preferred choice compared to synthetic chemical compounds. Hence, we select the C. odorata plant for its vast spectrum of medicinal value, ranging from antiulcer to memory-enhancing properties. The study has evaluated the effects of C. odorataagainst the ketamine induced experimental psychosis model in mice.

In this study, we evaluated the effects of C. odorata, which is known to possess neuroactive properties, for the management of insanity and lactation-enhancing effects. Pharmacological, post-mortem, neuroimaging and clinical studies have implicated the glutamatergic N-methyl-D-aspartate (NMDA) receptor in the pathology of schizophrenia(Anushika et al., 2017). NMDA receptor antagonists such as MK 801, phencyclidine and ketamine induce schizophrenia-like symptoms in healthy humans(Jentsch & Roth, 1999) and augment psychotic symptoms in patients with schizophrenia(Hanieh et al., 2023). Most importantly, phencyclidine, as well as its derivatives, MK-801 and ketamine, also impaired cognitive function in both humans and animals(Nan et al., 2024), producing anomalies matching those present in schizophrenia(Upadhyaya et al., 2019). Therefore, in this present study, we have used the ketamine model to investigate the efficacy of C. odorata as a possible antischizophrenic agent.

In our findings, C. odoratawas able to reverse the ketamine-induced hyperactivity at doses of 1000 and 1500mg/kg; however, it showed a delayed response in blocking ketamine effects at the 100mg/kg dose. The stimulation of high locomotor activity has been mainly achieved through the administration of dopamine agonists, and the dopamine antagonists counteract the motor activation induced by the systemic administration of NMDA(Lorrain et al., 2003; Dehbani, 2019). Furthermore, dopamine release in the nigrostriatal neurons remains in direct presynaptic control of glutamate via both AMPA and NMDA receptors located in neuronal terminals of dopamine neurons. An indirect inhibitory regulation of dopamine release was also demonstrated due to the combined stimulatory effect of N-methyl-D-aspartate on the medium-sized GABAergic efferent neurons.

Also, a possible mechanism by which ketamine might produce these adverse behavioural effects, at least partially, has been related to the blockade of NMDA receptors located on inhibitory GABAergic neurons in the mesolimbic and subcortical brain regions(Lorrain et al., 2003). This disinhibitory action has been reported to facilitate neuronal activity and excessive DA release in the limbic striatal regions(Saykin et al., 1991). Our finding revealed that C. odorata can attenuate dopamine levels in the striatal areas but does not normalise D2 receptor gene expression suggests that C. odoratamay modulate dopamine, thereby showing efficacy against the positive symptoms of schizophrenia. Cognitive impairments such as deficits in executive function, attention, working short-term memory, and long-term memory are core symptoms in patients with schizophrenia(Lueptow, 2017).

Among these, learning and memory impairments are known to be particularly resistant to treatment by conventional antipsychotics(Sandeep, 2020). The Novel object recognition test is a widely accepted method for assessing recognition memory in mice based on their natural innate character for exploring novelty(Ezejindu et al., 2014). In this study, the groups treated with C. odorata displayed a clear preference for novelty. In contrast, the ketamine-treated group was unable to pass the novelty preference test, indicating memory impairment. Similar outcomes were observed with the percentage recognition index; the extract and Risperidone treated groups significantly enhanced the recognition index. This indicates the ability of the animals to retain a preference for the novel object. This

reveals that the C. odorata ameliorated object recognition memory that was impaired by ketamine. Based on these behavioural tests, it can be inferred that C. odorata improved the retention and recognition memory and can augment the effect of antipsychotic drugs on memory. Our findings also depict the memory-impairing properties of ketamine(Hanieh et al., 2023), which were reversed by C. odorata treatment and also by the standard atypical drug, Risperidone. The Y-maze can also be used for short-term working memory. Spontaneous alternation is the measure of spatial working memory.

To alternate among spatial locations, a mouse must remember its previous location(Akanmu et al., 2007).This study revealed that C. odoratawas able to increase the number of actual alternation and improve spontaneous alternation in Y maze which indicate a favorable effect toward cognition as glutamate via NMDA receptors mediates long term potentiation, memory formation and ketamine administration could decrease in glutamate content and reversal by C. odorata could correlate its memory improving aspects. The enhancement of immobility after administration of ketamine has been used previously as a model for the negative symptoms of schizophrenia, such as flattening of affect and avolition(Hanieh et al., 2023). Administration of C. odoratareduced the immobility duration in the forced swim test, similar to Risperidone.

The efficacy of atypical agents in the negative symptoms of schizophrenia has been attributed to their 5HT-2 receptor blocking ability; hence, our C. odorata possibly contained phytochemicals that antagonise the 5HT2a receptors in the brain. Urea and creatinine are the major biomarkers of renal toxicity. Accumulation of serum urea is used as the acute marker, and accumulation of serum creatinine is used in detecting chronic renal toxicity(Nikfarjam et al., 2016). In this study, 28 days of administration of C. odorata did not produce a significant alteration in the renal function indices. A similar finding was reported by Ezedinju et al, (2014) who evaluated the renoprotective effects of Moringa oleifera leaf extract on the kidneys of adult mice. They observed no changes in renal function indices and found no tissue lesions in their histopathological study.

The severity of chemically-induced liver damage can be used to evaluate or determine the level of biochemical markers of liver function, such as Alanine transaminase (ALT), Aspartate transaminase (AST), and Alkaline phosphatase (ALP)(Manzar et al., 2022), located in the cytoplasm, is released into circulation after liver cells are damaged. ALT and AST are also enzymes released as a result of hepatic injury, especially damage to the mitochondria of liver cells (Salem et al., 2017). Elevation of the level of these enzymes can be an indication of cellular damage, leakage and loss of functional integrity of the liver cell membrane. The result of this study displayed no significant differences in the level of liver enzymes when C. odorata-treated groups were compared with the distilled water group. This is an indication that the ethanol leaf extract of C. odorata is safe at the doses used in this study.

Conclusion :-

This study revealed that the plant extract used in this experiment is effective against ketamine-induced cognitive impairments. Additionally, the extract exhibited no extrapyramidal side effects typically associated with antipsychotic medications.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by us

References:-

1. Fineberg,A.M.1., Lauren,E. M (2013). Inflammatory cytokines and neurological and neurocognitive alterations in the course of schizophrenia. Biol Psychiatry. 73(10):951-66. doi: 10.1016/j.biopsych.2013.01.001.
2. EllmanG.L. (1959) Tissue sulphydryl groups. Arch BiochemBiophys.;82(1):70-7. doi: 10.1016/0003-9861(59)90090-6.
3. Boudjeko, T., Megnekou, R., Woguia, A.L., Kegne, F.M., Ngomoyogoli, J.E., Tchapoum(2015),C.D. Antioxidant and immunomodulatory properties of polysaccharides from Allanblackia floribunda Oliv stem bark and Chromolaena odorata (L.). King and H.E. Robins leaves. BMC Res Notes.8:759
4. Sirinthipaporn, A., and JiraungkoorskulW(2017) .Wound Healing Property Review of Siam Weed, Chromolaena odorata. 'Pharmacogn' Rev. 11(21):35-38. https://doi.org/10.4103/phrev.phrev_53_16.PMID: 28503052
5. Zahara, M (2019). 'Description of Chromolaenaodorata medicinal plant: A Review'. IOP ConfSer Mater Sci Eng. 506(1 12):23-35
6. Kumar Shakya A. and Arvind Kumar Shakya C (2016). 'Medicinal Plants: Future Source of New Drugs'. Int J Herb Med. 4(4):59–64
7. Kigigha,L.(2013). T., Zige,D.V. Activity of Chromolaena odorata on enteric and superficial etiologic bacterial agents. Am J Res Commun. 1:266–76. [Google Scholar]
8. Aba, P.E., Joshua, P.E., Ezeonugu, F.C., Ezeja, M.I., Omoja, V.U., Umeakuana, P.U (2015). 'Possible anti-diarrhoeal potential of ethanol leaf extract of Chromolaenaodorata in castor oil- induced rats'. J Complement Integr Med.12:301–6.
9. Vijayaraghavan, K., Rajkumar, J., Bukhari, SNA., Al-Sayed, B., &Seyed, M A (2017). Chromolaenaodorata: A neglected weed with a wide spectrum of pharmacological activities. Mol. Med. Reports. 2017;15(3):1007–1016. https://doi.org/10.3892/mmr.2017.6133
10. Lee, K.H., Cha, M., Lee, B.H (2020) Neuroprotective efect of antioxidants in the brain. Int J Mol Sci 21(19):7152. https://doi.org/10.3390/ijms21197152.
11. Thoden, T.C., Boppre, M., Hallmann, J (2007). Pyrrolizidine alkaloids of Chromolaena odorata act as nematicidal agents and reduce infection of lettuce roots by Meloidogyne incognita. Nematology 9:343-9.
12. Vaisakh, M.N., and Pandey, A (2012. 'The Invasive Weed with HealingProperties: A review On Chromolaenaodorata'. Int J Pharm Sci. 2012;3(1):80–3.
13. Bissangou, MF., Ouamba, J.M (1997). Valorisationchimique de quelquesespècesaromatiques et médicinales du Congo (Ageratum conyzoïdes L, Chromolaena odorata King et Robinson,Hyptis suaveolens Poit et LippiamultitloraMoldenke). Pharm. Méd. Trad. Afr.9:70-84.
14. Elion Itou, R.D., EtouOssibi, A.W., Epa, C., Nsond, Ã.,Ntandou, G.F., Bokia, C.B., Ouamba, J.M., Abena, A.A (2017). Anti-inflammatory and analgesic effects of leaves of Chromolaena odorata. Afr. J. Pharm. Pharm. 11(17), pp. 217-223 https://doi.org/10.5897/.4753
15. Anyasor, G.N., Aina, D.A., Olushola, M., Aniyikawe, A.F (2011). Phytochemical constituents, proximate analysis, antioxidants, anti-bacterial and wound healing properties of leaf extracts of Chromolaenaodorata. Ann Biol Res. 2:441–51.
16. Tilak, R., Kumar, P., Rathee, R., Dubey,K.K.(2016). Screening of some medicinal plants for their antimicrobial activities. Int J Pharm Pharm Sci.8:202-6
17. Eduardo, G., Irene, I., Emillia, C., & Angel, V. (2000). Antipsychotic effect of aqueous stem bark extract of A. andongensis in Wistar albino rat. J. Ethnopharmacol. 70: 329- 333.
18. Hanieh, Y., Leila, A., Fahimeh S., Homa, H., Somayeh E., Zahra M (2023). Anti-Fatigue Effect of Viola odorata L. in Forced Swimming Test in Rat. Traditional and Integrative Medicine, 8(2):164-169 ISSN: 2476-5112,
19. Rajashri, K., Mudhol, S., ServaPeddha, M., andBorse, B.B (2020). Neuroprotective effect of spice oleoresins on memory and cognitive impairment associated with scopolamine-induced Alzheimer's diseasein rats, ACSOmega, 5(48), 30898–30905.
20. Sung B., Hyun Yeoul Ryu., Woo Nam., So Min Lee., Mi Ran Jang., Youn Gil Kwak, Gyoo Il Kang, Kyung Seok Song, Jae Won Lee (2023). The Neuroprotective Effects of Dendropanaxmorbifera Water Extract on Scopolamine-Induced Memory Impairment in Mice. Int J Mol Sci. 2023;24(22):16444. doi: 10.3390/ijms242216444.
21. Akanmu, M.A., Adeosun, S.O, Ilesanmi, O.R (2007). Neuropharmacological effects of oleamidein male and female mice. Behav. brain res.182(1):88-94.
22. Julia Eisenhardt de Mello., Karina Pereira Luduvico., Alessandra Dos Santos., Fernanda Cardoso Teixeira, Juliane de Souza Cardoso, Mayara Sandrielly Soares de Aguiar, Wilson Cunico, Marcia Vizzotto,

FrancieliStefanello, Roselia Spanevello(2023). Therapeutic potential of blackberry extract in the preventing memory deficits and neurochemical alterations in the cerebral cortex, hippocampus and cerebellum of a rat model with amnesia. Metab Brain Dis. 38(4):1261-1272. doi: 10.1007/s11011-023-01175-w.

23. Ghaderi A, Karimi SA, Talaei F, Shahidi S, Faraji N, Komaki A (2020). The effects of aqueous extract of Origanum vulgare on learning and memory in male rats. J HerbmedPharmacol. 9(3):239-244. doi: 10.34172/jhp.2020.31.
24. Prinssen, E.P., Colpaert, F.C., Koek, W (2002). 5-HT1A receptor activation and anti-cataleptic effects: high-efficacy agonists maximally inhibit haloperidol-induced catalepsy. Eur. J. Pharmacol. 453; 217-221.
25. Zarrinkalam, E., Heidarianpour, A., Salehi, I., Ranjbar, K., Komaki, A (2016). Effects of endurance, resistance, and concurrent exercise on learning and memory after morphine withdrawal in rats. Life Sci.157:19-24. doi: 10.1016/j. lfs.2016.05.034.
26. Anushika Sirinthipaporn, WanneeJiraungkoorskul (2017). Wound Healing Property Review of Siam Weed, Chromolaena odorata. Pharmacogn Rev.11(21):35–38. doi: 10.4103/phrev.phrev_53_16
27. Jentsch, J.D., Roth, R.H (1999). The neuropsychopharmacology of phencyclidine: from NMDA receptor hypofunction to the dopamine hypothesis of schizophrenia. Neuropsychopharmacol.120:201–225kuroxidative/nitrosative stress: current state. Nutr J 15(1):71. https://doi.org/10.1186/s12937-016-0186-5
28. Nan, S., Wang, P., Zhang, Y., and Fan, J (2021), Epigallocatechin-3-Gallate provides protection against alzheimer's disease-induced learning and memory impairments in rats, Drug Des Devel Ther, 2021, 2013–2024, doi: 10.2147/DDDT.S289473
29. Upadhyaya, S., Gangachannaiah, S., Chandrashekar, P.L (2019). Effect of Piper betel leaf extract on learning and memory in Aluminium chloride induced Alzheimer's disease in Wistar rats. Biomed Pharmacol J.12(3)
30. Lorrain, D.S., Baccei, C.S., Bristow, L.J, Anderson, J.J., Varney, M.A (2003). Effects of ketamine and N-methyl-D-aspartate on glutamate and dopamine release in the rat prefrontal cortex: modulation by a group II selective metabotropic glutamate receptor agonist LY379268. Neuroscience. 117:697–706.
31. Dehbani, Z (2019). Effect of a hydro-alcoholic extract of Melissa officinalis on passive avoidance learning and memory J HerbmedPharmacol2(3);34-41
32. Saykin, A.J., Gur, R.C., Gur, R.E., Mozley, P.D., Mozley, L.H, Resnick, S.M (1991). Neuropsychological function in schizophrenia. Selective impairment in memory and learning. Arch Gen Psych. 48:6.
33. Lueptow, L.M (2017). Novel object recognition test for the investigation of learning and memory in mice. J Vis Exp. 126:e55718. https://doi.org/10. 3791/55718
34. Sandeep, K.K (2020). Effect of methonolic extract of Vitex negundo on haloperidol induced catalepsy in albino mice. Int. J. of Basic & Clin.Pharmacol. 2020: 9(4) DOI: https://doi.org/10.18203/2319-2003.ijbcp20201188
35. Ezejindu, D.N, Udemezue, O.O, Akingboye, A.J. (2014). Renoprotective effects of moringa oleifera leaf extract on the kidneys of adult wistar rats. Am. J Eng. Res. 2014; 3(02):157-161
36. Nikfarjam, M., Bahmani, M., Naimi, A (2016). Native medicinal plants of Iran effective on memory and learning: a review. Int J PharmTech Res. 9(5):466-73.
37. Manzar, B.S., Sarah, S.V., Simin, K (2022). Protective Effect of Hydroalcoholic Extract of Clove on Thioacetamide-Induced Hepatotoxicity Animal Model.Galen Med J. Nov 11;11:e1603. doi: 10.31661/gmj.v11i.1603
38. Salem, A.M., Mahdy, K.A., Hassan, N.S., El-Saeed, G.S., Farrag, A.R., Monem, M.A (2017). Nigella sativa seed reduced galectin-3 level and liver fibrosis in thioacetamide-induced liver injury in rats. J Arab Soc Med Res. 2(12):46–46.