Quest Journals
Journal of Medical and Dental Science Research
Volume 12~ Issue 3 (2025) pp: 14-21
ISSN(Online) : 2394-076X ISSN (Print):2394-0751
www.questjournals.org

Research Paper

"Impact of Cannabis Ethanol Extract on Hippocampal Structure and Spatial Memory: A Comprehensive Y-Maze Behavioral and Histological Analysis."

ANWARA, CHINEMEREM E[1]., EPETE, MICHEAL A[1]., OBIMMA, JACINTA N[2]., NKANU, IBAREREH I[1]., EKECHI, OBINNA H[3]., EGBUDU OSHITA E[4].

[1.] *Department of Anatomy, Ebonyi State University, Abakaliki, Nigeria.*
[2.] *Department of Physiology, Ebonyi State University, Abakaliki, Nigeria*
[3.] *Department of Anatomy, Federal University of Technology, Owerri, Imo State, Nigeria*
[4.] *Department of Anatomy and Forensic Anthropometry, University of Cross River State, Nigeria.*
Corresponding Author: NKANU, IBAREREH IREM

ABSTRACT
The hippocampus plays a crucial role in learning and memory and is highly sensitive to cannabinoid exposure. Cannabis sativa, known for its psychoactive and therapeutic properties, contains cannabinoids that interact with the endocannabinoid system, influencing cognitive functions, mood, and neuroplasticity. While some studies suggest neuroprotective benefits, others indicate potential hippocampal alterations leading to cognitive deficits, particularly in spatial short-term memory. However, the specific effects of cannabis ethanol extract on hippocampal structure and function remain inadequately understood. This study investigated the impact of cannabis ethanol extract on hippocampal histology and spatial memory performance in Wistar rats. Twenty rats were divided into four groups: a control group (A1) receiving standard chow and water, and three experimental groups (A2, A3, and A4) administered 50 mg/kg, 100 mg/kg, and 150 mg/kg of cannabis ethanol extract, respectively. Spatial memory performance was assessed using the Y-maze test, followed by histological analysis of hippocampal tissue. Results indicated a dose-dependent decline in spontaneous alternation and percentage alternation in cannabis-treated groups, suggesting impaired spatial memory. Histopathological evaluation revealed structural changes in the hippocampus, particularly at higher doses, raising concerns about potential neurotoxic effects. These findings emphasize the need for further investigation into the long-term implications of cannabis use on cognitive function and hippocampal integrity. Understanding these effects is essential for informing cannabis-based therapeutic applications and ensuring safe consumption guidelines.

Keywords: *Hippocampus, Cannabis sativa, spatial memory, Y-maze, cannabinoids, neurotoxicity, cognitive impairment.*

***R**eceived 27 Feb., 2025; **R**evised 05 Mar., 2025; **A**ccepted 07 Mar., 2025 © The author(s) 2025.*
P**ublished with open access at **www.questjournas.org

I. INTRODUCTION

The hippocampus, a crucial region for learning and memory (Wise et al., 2009), is particularly sensitive to cannabinoids derived from Cannabis sativa, which are known for their psychoactive effects (Atakan, 2012). Recent studies have highlighted the therapeutic potential of cannabis, as its active compounds interact with the endocannabinoid system to impact neurological functions such as memory, mood, and cognition (Burggren et al., 2019; Kim et al., 2019; Zou and Kumar, 2018). Research has shown that alterations in hippocampal neuroanatomy can lead to cognitive impairments, especially in spatial short-term memory (Camina and Güell, 2017; Sridhar et al., 2023).

However, despite a wealth of research, the precise effects of cannabis extracts on hippocampal structure and associated cognitive behaviors are still not fully understood (Nader & Sanchez, 2018). While Kumar et al., (2022) studied the anxiolytic and neuroprotective benefits of cannabinoids, others indicate

potential negative impacts on memory formation and retrieval at higher doses (Bhunia et al., 2023; Niloy et al., 2023, Nkanu et al., 2024). This disparity raises concerns about the safety of cannabis use, especially for vulnerable populations such as adolescents and those with pre-existing neuropsychiatric conditions (Lowe et al., 2019).

To clarify these ambiguities, there is an urgent need for comprehensive investigations into the effects of cannabis ethanol extracts on hippocampal histology and related behavioral outcomes, particularly focusing on spatial short-term memory (Sachs et al., 2015; Burggren et al., 2019; Lowe et al., 2019; Niloy et al., 2023). This study is designed to explore these effects in Wistar rats through histological analysis and Y-Maze behavioral assessments. The anticipated findings aim to significantly enhance clinical practices and therapeutic applications by providing clearer guidelines for cannabis use and improving treatments for cognitive health.

II. MATERIALS AND METHODOLOGY

Study Design

This experimental study investigated the effects of cannabis ethanol extract on hippocampal neuroanatomy and spatial memory in Wistar rats, combining Y-Maze behavioral tests, histological analysis, and statistical evaluation. This study was carried out in the Department of Anatomy, Ebonyi State University, Abakaliki.

Plant Procurement and Extracts

A matured Cannabis plant weighing 500g was obtained from the National Drug and Law Enforcement Agency in Abakaliki, Ebonyi State. It was washed, sliced, dried, and ground. A total of 206g of ground cannabis was mixed with 1500ml of absolute alcohol in a sealed container and left to steep for 72 hours. After filtration, the mixture was transferred to a Soxhlet apparatus for drying.

Preparation of Stock Solution for Administration

The cannabis plant extract stock solution was prepared daily by dissolving 1g of cannabis in 20 ml of water and adding 0.5 ml of Tween 80. Dosage volumes were determined according to the rats' body weight and the assigned group doses, as described by Nkanu et al. (2024).

Volume (ml) = weight of rat (kg) x standard dose per group (mg)/1000

Animal Procurement

Twenty Wistar rats (20), weighing between 70–160g, were sourced from the animal farm of the Department of Human Anatomy, Faculty of Basic Medical Sciences, Ebonyi State University. The rats were housed under a 12-hour light-dark cycle for a 72-hour acclimatization period with access to food and water. Afterward, they were weighed and randomly assigned to four groups: A1, A2, A3, and A4.

Animal Treatment

20 Wistar rats weighing between 70-160g were randomly grouped into groups A1, A2, A3, and A4. Each group contained 6 Wistar rats. Group A1 was the control which were exposed to only rat chow and water, group A2 were administered a low dose of 50mg/kg of cannabis ethanol stock solution, food, and water, group A3 were administered a medium dose of 100mg/kg of cannabis ethanol stock solution, food and water and group A4 were administered high dose of 150mg/kg of cannabis ethanol stock solution, food, and water. During the treatment period, neurobehavioral tests were conducted, with administration occurring over 40 days (Nkanu *et al*., 2024).

Groups	No of Animals (16)	Treatments
A1	4	Rat chow and water
A2	4	Rat chow, water, and 50mg/kg (low dose)
A3	4	Rat chow, water, and 100mg/kg (low dose)
A4	4	Rat chow, water, and 150mg/kg (low dose)

Table 1 shows the administration of normal food chow, water, and cannabis extracts in each group.

Behavioral Test

During Wistar rats' treatment using cannabis petroleum extract, spatial memory was conducted using a neurobehavioral test apparatus (Y-maze). Wistar rats were habituated before administering the cannabis ethanol extract.

Y Maze Test

During treatment, a Y-maze was used to assess short-term spatial memory. The maze dimensions were 30 cm in height, 40 cm in length, and 10 cm in width. Each rat was habituated before cannabis ethanol extract administration. The Y-maze comprised three arms, labeled A, B, and C. Each Wistar rat was placed at the start

of an arm to allow exploration of all arms. The number of arm entries and spontaneous alternations were recorded, and the percentage of alternation was calculated as follows:

Percentage alteration = {spontaneous alternation/ (total number of arm entries − 2)} × 100.

A spontaneous alternation was defined as the rat entering all three arms of the maze, while an arm entry was counted when the rat's hind paws fully entered an arm. To prevent potential bias from odor cues, each arm was cleaned with 5% alcohol before testing a new rat (Kraeute, 2019).

Animal Sacrifice and Tissue Preservation

After completing neurobehavioral assessments, the rats were sacrificed via cervical dislocation, followed by euthanasia through intra-cardiac perfusion. The brains were carefully extracted using forceps and preserved in 10% neutral buffered formalin.

Histological Analysis

Coronal slices, 1 mm thick, were taken from the hippocampal region of the brain, with precise localization using an atlas. The hippocampal tissue sections were then stained with Hematoxylin and Eosin (H&E) for visualization.

Data Analysis

Data obtained were expressed as mean ± standard deviation, paired sample t-test was employed for the comparison of means within groups, and P values were set as $p<0.001$.and 0.05 at two-tailed significant using the IBM Statistical Package for the Social Sciences Version 23.00 (IBM SPSS) and Microsoft Office Excel 2013 for charts.

III. RESULTS

Behavioral Observation using Y Maze

Descriptive statistics of Short-Term Spatial Memory Behavioral Assessment among various groups Exposed to Cannabis Ethanol Extracts using Y-maze

Groups/treatment	Spontaneous Alteration			Percentage Alteration		
	Mean ± S.D	t-value	P-value	Mean ± S.D	t-value	P-value
GRA1 (control)	1.33±0.58	4.00	0.057	17.04±5.13	5.75	0.029
GRA2 (50mg/kg)	0.33±0.58	1.00	0.423	5.56±9.62	1.00	0.423
GRPA3 (100mg/kg)	0.33±0.58	1.00	0.423	8.33±14.43	1.00	0.423
GRPA 4 (150mg/kg)	0.67±0.58	2.00	0.389	22.22±25.46	0.25	0.270

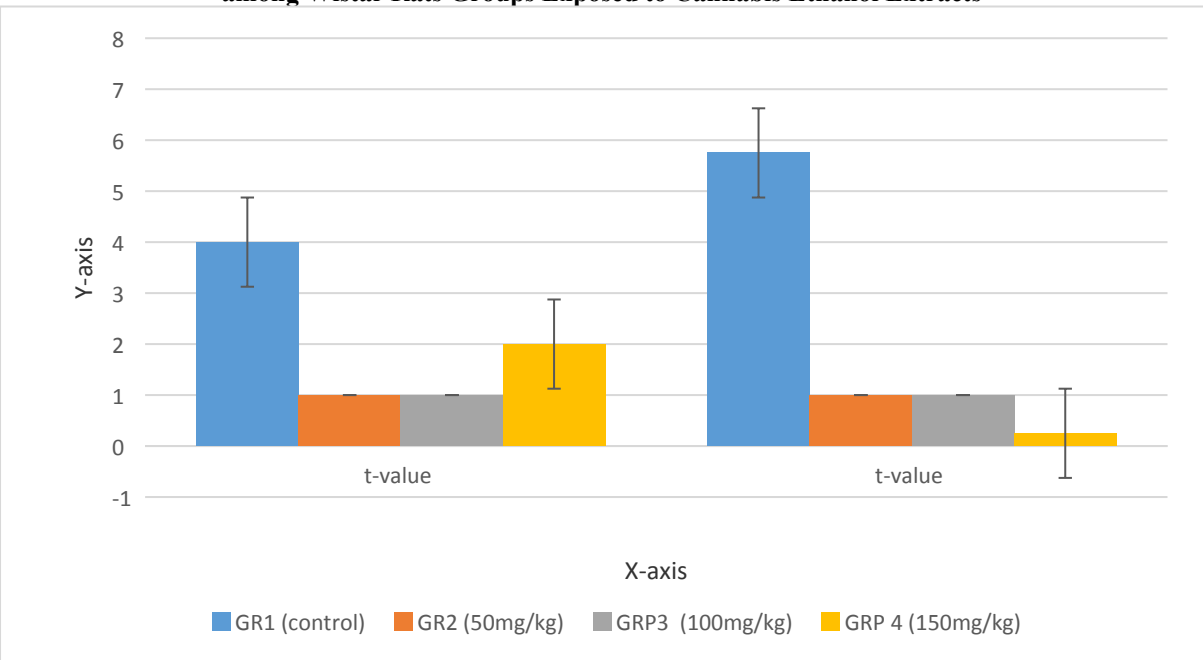
*Group A1 statistical results are higher than groups A2, A3, and A4. Group A1 P-value is significant while groups A2, A3, and A4 are not significant at a level of two-tailed.

Table 2 summarizes the short-term spatial memory performance of Wistar rats in the Y-maze after exposure to various doses of cannabis ethanol extracts. The two main measures are spontaneous alternation and percentage alternation, which indicate the rats' spatial memory abilities.

The control group displayed the highest level of spontaneous alternation of 1.33s ± 0.58, which may indicate better short-term spatial memory. The cannabis-exposed groups 2, and 3 showed a general reduction and similarity in spontaneous alternation (0.33 ± 0.58) while Group 4 spontaneous alternation score is slightly higher (0.67 ± 0.58) than in Groups 2 and 3 but remains lower than the control, suggesting that cannabis extract might impair memory performance, although the differences were not statistically significant as p-value is higher than 0.05 and 0.001.

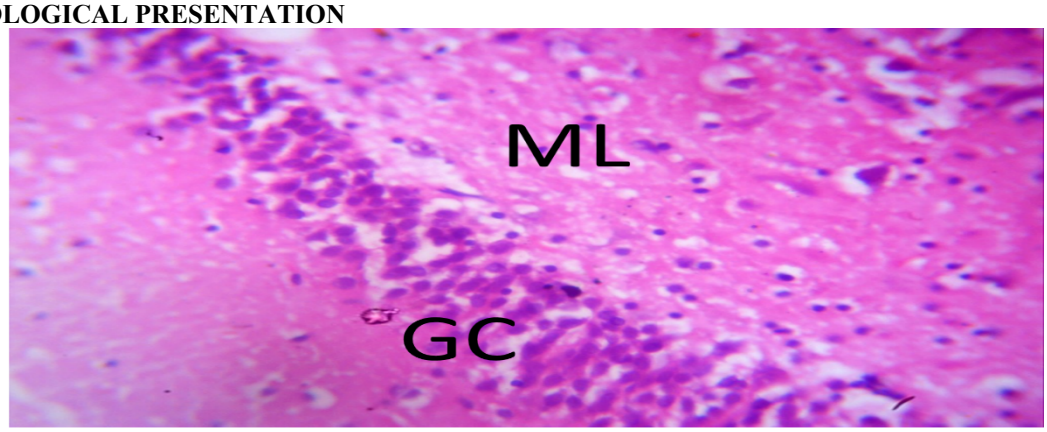
Control rats had a mean percentage alternation score of 17.04 ± 5.13, Group 2 exhibited a lower mean percentage alternation (5.56 ± 9.62), showing a decline in performance compared to the control group. Group 3 percentage alternation is 8.33 ± 14.43, slightly better than Group 2 but still below the control level. Group 4 displayed the highest mean percentage alternation among the treated groups (22.22 ± 25.46), exceeding the control's performance. This may be due to individual rat variability rather than a true treatment effect, as the P-value was not significant. Overall, the percentage alternation scores suggest that cannabis extract exposure may impair spatial memory in a dose-dependent manner, though the observed differences lack statistical significance except for the significant control group.

Fig 1. Chart Presentation of Descriptive Statistics on Short-Term Spatial Memory Behavioral Assessment among Wistar Rats Groups Exposed to Cannabis Ethanol Extracts

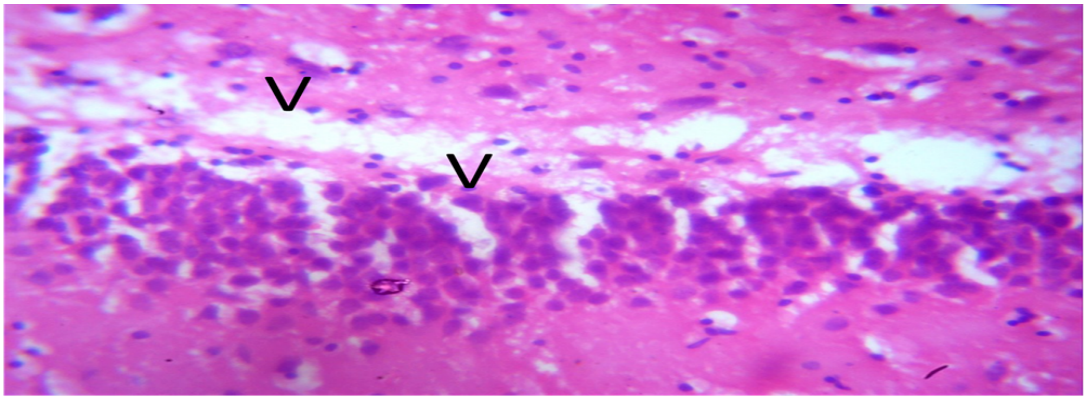


A chart presentation of Fig 1 shows that, the t-value and error bars on the top of each bar. The x-axis on the chart shows two sets of bars (spontaneous alteration and percentage alteration). The y-axis is represented in units of -1, 0, 1, 2, 3, 4, 5, 6, and 7. Group A1 (control) consistently shows higher values in both spontaneous and percentage alteration measures, suggesting that rats in this group may have better cognitive performance or exploratory behavior in the Y-maze test compared to the other groups because they were not treated with cannabis ethanol extracts. Groups A2 (50mg/kg) and A1 (control) show the lowest values in both measures, indicating reduced spontaneous and percentage alternations, which may reflect lower cognitive or exploratory behavior. Group A4 (150mg/kg) has moderate values, sitting between the high performances of Group A1 (control) and the lower performances of Groups A2 (50mg/kg) and 3 (100mg/kg).

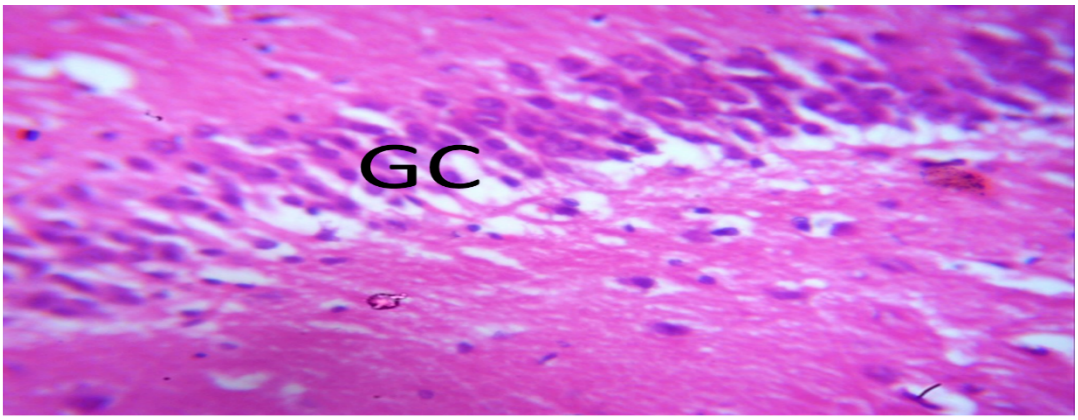
HISTOLOGICAL PRESENTATION



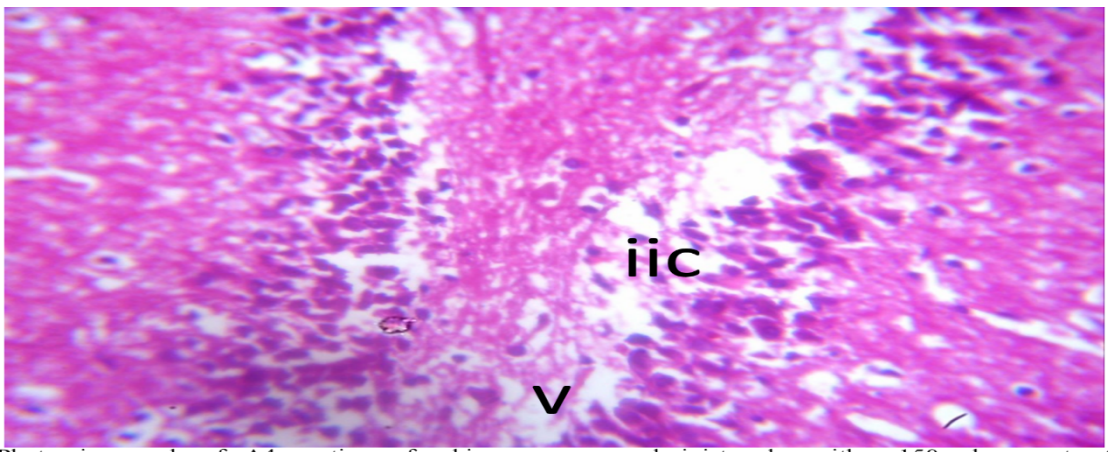
Photomicrograph of A control section of hippocampus (x400)(H/E)(CV) shows hippocampus with active granular cells(GC) and well perfused molecular layer (ML).



Photomicrograph of group A2 section of hippocampus administered with 50mgkg (x100x400)(H/E) shows moderate degeneration with moderate vacoulation(v) granular cell (GC) is moderately active



Photomicrograph of group A3 section of hipocampus administered with 100mgkg (x100x400)(H/E) shows neuronal tissue with moderate active granular cell.



Photomicrograph of A4 section of hippocampus administered with 150mgkg extract (x400)(H/E)(CV) shows moderate vacoulation (V) and moderate infiltration of inflammatory cells (IIC) .

Images 1-4 show a photomicrograph of the hippocampus's histological presentation following the administration of varying doses of a cannabis extract, revealing dose-dependent changes in the tissue structure which was taken at a magnification of x400. The study assessed four groups, each subjected to different cannabis extract doses: a control group and three experimental groups receiving 50 mg/kg, 100 mg/kg, and 150 mg/kg.

In the control group (Image 1), the hippocampus exhibited normal histological features, characterized by active granular cells (GC) and a well-perfused molecular layer (ML). These findings indicate the absence of any pathological changes, suggesting a healthy hippocampal structure. This serves as the baseline for comparison with the experimental groups.

The group administered 50 mg/kg cannabis extract (Image 2) displayed moderate degeneration in the hippocampal tissue. Notably, moderate vacuolation (V) was observed in the tissue, indicating some cellular damage. Despite this, the granular cells remained moderately active. These results suggest that the 50 mg/kg dose induced mild degenerative effects, including vacuolation, although the activity of the granular cells was not significantly reduced. The observed moderate changes point to the beginning of the cannabis extract's impact on hippocampal tissue.

In the group receiving a higher dose of 100 mg/kg (Image 3), the hippocampus showed moderate activation of the granular cells (GC). This increased activity of the granular cells suggests that the higher dose of cannabis extract may be stimulating certain aspects of hippocampal function, though the overall structure remained relatively intact. This moderate activation contrasts with the earlier observed degenerative changes and indicates a shift in the response to the extract as the dosage increases.

Finally, in the group administered the highest dose of 150mg/kg (Image 4), more significant histological changes were evident. In addition to moderate vacuolation (V), there was moderate infiltration of inflammatory cells (IIC) into the tissue. These findings suggest that the 150 mg/kg dose induced more pronounced vascular changes and an inflammatory response within the hippocampal tissue. The infiltration of inflammatory cells further implies that the highest dose resulted in notable pathological alterations, such as an immune response to tissue damage or stress caused by the extract.

IV. DISCUSSION

This study aimed to investigate the effects of cannabis ethanol extract on hippocampal neuroanatomy and spatial short-term memory, emphasizing dose-dependent alterations in histological structure and behavioral outcomes. Our findings shed light on how varying doses of cannabis extract influence hippocampal function and memory processes, adding to the growing body of research regarding the neurological effects of cannabis.

Histological analysis revealed dose-dependent changes in hippocampal tissue architecture. The control group exhibited a normal histological appearance, characterized by active granular cells and a well-perfused molecular layer, indicating healthy tissue. Such findings are consistent with prior studies where control animals demonstrated intact hippocampal architecture (Amin et al., 2013; Kumar et al., 2020). This baseline serves as a crucial point of reference for assessing the impact of the cannabis ethanol extract.

In the group administered 50 mg/kg of cannabis extract, moderate degenerative changes were observed, including mild vacuolation within the tissue. This suggests that low doses of cannabis may initiate early stages of cellular damage, a phenomenon noted in other studies focused on cannabinoid exposure (Nkanu et al., 2024; Rieder et al., 2010). Notably, despite evident vacuolation, the granular cells remained moderately active, indicating that this low dose did not entirely impair hippocampal function, yet it likely introduced subtle disruptions in cellular integrity. This finding aligns with research suggesting that low concentrations of cannabinoids may have neurotoxic effects without fully disrupting neural activity (Giedd, 2004; Bhunia et al., 2023).

At the 100 mg/kg dose, an increase in the activation of granular cells was observed, contrasting the degenerative changes from the lower dose. This increased cellular activity implies that, at this intermediate dose, the cannabis extract might stimulate certain aspects of hippocampal function, potentially enhancing neuroplasticity or synaptic activity (Puighermanal et al., 2009; Chowdhury, 2022). Despite this activation, the overall tissue structure remained largely intact, suggesting that moderate doses could balance stimulating neural activity while causing minimal disruptions to tissue homeostasis.

Conversely, the highest dose of 150 mg/kg resulted in pronounced histological alterations, with the tissue exhibiting moderate vacuolation, inflammatory cell infiltration, and signs of vascular changes. These findings indicate a more significant pathological response, likely including an immune reaction to stress or damage caused by the cannabis extract. Infiltration of inflammatory cells is particularly concerning, as it indicates a potential neuroinflammatory response, which could contribute to cognitive impairments associated with high doses of cannabis (Hou et al., 2019). These observations align with other studies suggesting that high concentrations of cannabinoids may induce neuroinflammation, exacerbating neuronal damage (Nader & Sanchez, 2018; Kumar et al., 2020).

Behavioral data from the Y-maze test corroborated the histological findings, showing dose-dependent impairments in spatial short-term memory. The control group displayed the highest levels of spontaneous alternation and alternation percentages, indicating robust memory function consistent with previous reports of normal spatial memory performance in rodents (Cheng et al., 2014; Coles et al., 2020). In contrast, the groups receiving cannabis extract exhibited decreased spontaneous alternation and percentage alternation scores. Both Group A2 (50 mg/kg) and Group A3 (100 mg/kg) showed similar levels of impairment in spatial memory, suggesting that even moderate doses of cannabis extract could interfere with memory processes. These findings support research connecting cannabinoid exposure with cognitive deficits, especially regarding learning and memory (Hickman et al., 2018; Amini and Abdolmaleki, 2021).

Although Group A4 (150 mg/kg) showed a slight improvement in memory performance, the higher percentage of alternation was not statistically significant. It may relate to individual variability rather than a true treatment effect. This observation underscores the complexity of cannabis's effects on cognition, highlighting that higher doses may not consistently enhance performance and could lead to inconsistent behavioral outcomes (Coles et al., 2020; Niloy et al., 2023). Additionally, the lack of statistically significant differences across treatment groups suggests that while cannabis exposure can impair memory, the extent of this impairment may depend on individual animal variability and the duration of exposure.

V. CONCLUSION

This study provides crucial evidence that cannabis ethanol extract influences hippocampal neuroanatomy and spatial short-term memory in a dose-dependent manner. Lower doses (50 mg/kg) exhibited mild tissue degeneration, while moderate doses (100 mg/kg) seemed to stimulate hippocampal activity without substantial structural damage. However, high doses (150 mg/kg) were associated with significant histological changes, including neuroinflammation. These findings highlight the risks linked to cannabis consumption, particularly at elevated doses, underscoring the necessity for further research on the long-term effects of cannabis on cognitive function and brain structure. Understanding the mechanisms behind these dose-dependent effects will be pivotal in informing safe cannabis use, particularly in clinical and therapeutic contexts.

VI. RECOMMENDATION

Based on the findings of this study, we recommend cautious consideration of cannabis use, particularly at higher doses, due to its potential neurotoxic effects on the hippocampus and associated impairments in spatial memory. Future research should focus on elucidating the precise mechanisms underlying cannabinoid-induced neuroanatomical changes, including dose-response relationships and long-term cognitive impacts. Additionally, further investigations are needed to assess the therapeutic potential of cannabis-based compounds while minimizing adverse effects. Policymakers and healthcare providers should incorporate these findings into guidelines for cannabis use, particularly in vulnerable populations such as adolescents and individuals with neuropsychiatric disorders.

AUTHORS DECLARATION

The authors declare no conflicts of interest related to this study. The research was conducted independently, without any financial or personal relationships that could influence the findings, interpretations, or conclusions.

REFERENCES

[1]. Amin, Shaimaa N., Younan, Sandra M., Youssef, Mira F., Rashed, Laila A., Mohamady, Ibrahim, (2019). A histological and functional study on hippocampal formation of normal and diabetic rats.F1000Research, 9;2:151.

[2]. Amini, M., and Abdolmaleki, Z. (2021). The effect of cannabidiol coated by nano-chitosan on learning and memory, hippocampal CB1 and CB2 levels, and amyloid plaques in an Alzheimer's disease rat model. Neuropsychobiology 81, 171–183.

[3]. Atakan, Z. (2012). Cannabis, a complex plant: Different compounds and different effects on individuals. *Therapeutic Advances in Psychopharmacology*, *2*(6), 241-254.

[4]. Bhunia S, Kolishetti N, Arias AY, Vashist A and Nair M (2022) Cannabidiol for neurodegenerative disorders: A comprehensive review. Front. Pharmacol. 13:989717.

[5]. Burggren AC, Shirazi A, Ginder N, London ED, (2019). Cannabis effects on brain structure, function, and cognition: considerations for medical uses of cannabis and its derivatives. Am J Drug Alcohol Abuse, 45(6):563-579.

[6]. Camina E and Güell F (2017). The Neuroanatomical, Neurophysiological and Psychological Basis of Memory: Current Models and Their Origins. Front. Pharmacol. 8:438.

[7]. Cheng, D., Spiro, A. S., Jenner, A. M., Garner, B., and Karl, T. (2014). Long-term cannabidiol treatment prevents the development of social recognition memory deficits in Alzheimer's disease transgenic mice. J. Alzheimers Dis. 42, 1383–1396.

[8]. Chowdhury, K. U., Holden, M. E., Wiley, M. T., Subramaniam, V., & Reed, M. N. (2024). Effects of Cannabis on Glutamatergic Neurotransmission: The Interplay between Cannabinoids and Glutamate. Cells, 13(13), 1130.

[9]. Coles, M., Watt, G., Kreilaus, F., and Karl, T. (2020). Medium-dose chronic cannabidiol treatment reverses object recognition memory deficits of APPSwe/PS1ΔE9 transgenic female mice. Front. Pharmacol. 11, 587604.

[10]. Hickman, S., Izzy, S., Sen, P., Morsett, L., and El Khoury, J. (2018). Microglia in neurodegeneration. Nat. Neurosci. 21 (10), 1359–1369.

[11]. Hou, Y., Dan, X., Babbar, M., Wei, Y., Hasselbalch, S. G., Croteau, D. L., et al. (2019). Aging as a risk factor for neurodegenerative disease. Nat. Rev. Neurol. 15 (10), 565–581.

[12]. Giedd JN., (2004). Structural magnetic resonance imaging of the adolescent brain. Ann N Y Acad Sci. 1021:77–85.

[13]. Kim D-J, Schnakenberg Martin AM, Shin Y-W, Jo HJ, Cheng H, Newman SD, Sporns O, Hetrick WP, Calkins E, O'Donnell BF., (2019). Aberrant structural-functional coupling in adult cannabis users. Hum Brain Mapp, 40:252–61.

[14]. Kumar, P. B. R., Kumar, A. P., Jose, J. A., Prabitha, P., Yuvaraj, S., Chipurupalli, S., et al. (2020). Minutes of PPAR-γ agonism and neuroprotection. Neurochem. Int. 140, 104814.

[15]. Lowe DJE, Sasiadek JD, Coles AS, George TP., (2019). Cannabis and mental illness: a review. Eur Arch Psychiatry Clin Neurosci, 269(1):107-120.

[16]. Nader DA, and Sanchez ZM., (2018). Effects of regular cannabis use on neurocognition, brain structure, and function: a systematic review of findings in adults. Am J Drug Alcohol Abuse, 44(1):4-18.

[17]. Niloy N, Hediyal TA, Vichitra C, Sonali S, Chidambaram SB, Gorantla VR, Mahalakshmi AM., (2023). Effect of Cannabis on Memory Consolidation, Learning and Retrieval and Its Current Legal Status in India: A Review. Biomolecules, 13(1):162.

[18]. Nkanu, I.I., Eteudo A.N., Anwara, C.E., Obun, C., Epete, M.A., Ekechi, H.O., Nweke O. I., (2024). Chronic Cannabis Extract Modulates Anxiety Behavior in Wistar Rats: VTA Histology and Catecholamine Analysis. International Journal of Pharmaceutical and Bio-Medical Science, 4(12): 910-918.
[19]. Puighermanal, E.; Marsicano, G.; Busquets-Garcia, A.; Lutz, B.; Maldonado, R.; Ozaita, A., (2009). Cannabinoid modulation of hippocampal long-term memory is mediated by mTOR signaling. *Nat. Neurosci*, *12*, 1152–1158
[20]. Rieder, Sadiye A., Chauhan, A., Singh U., *et al*., (2010).Cannabinoid-induced apoptosis in immune cells as a pathway to immunosuppression. Immunobiology, 215(8):598–605.
[21]. Sachs J, McGlade E, Yurgelun-Todd D., (2015). Safety and Toxicology of Cannabinoids. Neurotherapeutics, 12(4):735-46.
[22]. Sridhar S, Khamaj A, Asthana MK., (2023). Cognitive neuroscience perspective on memory: overview and summary. Front Hum Neurosci, 17:1217093.
[23]. Wise LE, Thorpe AJ, Lichtman AH., (2009). Hippocampal CB(1) receptors mediate the memory-impairing effects of Delta(9)-tetrahydrocannabinol. Neuropsychopharmacology, 34(9):2072-80.
[24]. Zou S, and Kumar U., (2018). Cannabinoid Receptors and the Endocannabinoid System: Signaling and Function in the Central Nervous System. Int J Mol Sci, 19(3):833.