

## Evaluation Antiepileptic activity of *Rumex acetosa* L and Histopathological changes in mice brain

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### ABSTRACT:

The neurological condition known as epilepsy is defined by convulsive seizures. 50–70 million People all throughout the world are affected and safer drugs with better anticonvulsant properties and more Accessibility is still required. The adverse effects of antiepileptic drugs remain a major issue notwithstanding developments in pharmacotherapy, since they may reduce adherence and quality of life. Herbal remedies are becoming increasingly well-liked as alternative and complementary medicines as a result. The goal of this research was to investigate albino mice for the antiepileptic properties of the leaf extract *Rumex acetosa* L. in methanol.

**Method:** The Soxhlet extraction method was used to extract the leaves of *Rumex acetosa* L. using methanol. Testing for phytochemicals was done on the extract. The chemical components were separated using TLC and column chromatography. FTIR and GCMS-MS were used to examine fractions. The antiepileptic and acute oral toxicity of methanolic extract were evaluated. An intraperitoneal dose of 35 mg/kg PTZ in saline solution was used to induce seizures in order to test for antiepileptic activity. Swiss albino mice were given dosages of 200 and 400 mg/kg body weight of the methanolic extract to assess its antiepileptic properties using the PTZ procedure. Diazepam, at a dosage of 2 mg/kg, is the usual medication utilised. Microscopy-based histopathological analysis of brain tissue samples to look for cellular abnormalities, inflammation, or other pathological changes that could be linked to antiepileptic effects

**Result:** Alkaloids, steroids, glycosides, amino acid flavonoids, carbohydrates, and phenolic tannins are among the phytochemicals found in methanolic extracts of the leaves of the *Rumex acetosa* L. plant. Yields 8 % in methanol extract; FTIR and GCMS-MS tests show different chemicals. At 200 and 400 mg/kg body weight, *Rumex acetosa* L extract produced p-values < 0.05 for epileptic score, p < 0.001 for convulsion latency, and p < 0.001 for convulsion duration. The protection value as a percentage was p < 0.001. Furthermore, the extract has dosage-dependent action, meaning that its activity rises with increasing dose. According to a brain histopathology investigation, there is some neuroprotective action. Conclusion: *Rumex acetosa* L plant leaf methanolic extracts shows significant Antiepileptic activity

**Key Words:** *Rumex acetosa*, Antiepileptic activity, Histopathology, Caryophyllene, GABA, CB2 receptors, PTZ Model

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### Introduction:

About 70 million individuals worldwide suffer from epilepsy, making it one of the most prevalent chronic neurological conditions.<sup>[1,2]</sup> Recent advances in neuroimaging and genetics have shown brain network dysfunctions and circuits linked to a neurological condition known as epilepsy. It is frequently classified as a chronic disease where a large number of neurones fire quickly and concurrently, resulting in increased brain electrical activity that is tracked, frequently leading to a seizure. Furthermore, the illness is frequently observed to have social, behavioural, cognitive, and psychological effects.<sup>[3]</sup> Seizures can have many different types and causes. Connected to epilepsy, for which the selection of antiseizure medications. (ASD) is used in many ways.<sup>[4]</sup> The anticonvulsant qualities of ASDs, such as ion channel

regulation, make them useful by inhibiting connections between glutamate-mediated neurotransmitters, and increasing GABA transmission inhibitors. But almost one-third of Patients with epilepsy often develop resistance to ASD and other disorders. Display a range of negative consequences, including pancreatitis, audiovisual issues, and even declines in the liver and kidneys, demonstrating that ASDs have unfavourable side effects and are ineffective at managing or lessening seizures caused by epilepsy. The constraints of contemporary ASD Therapies emphasise that a new method of treating the condition is required. While limiting their adverse effects.<sup>[5]</sup> The perennial herb sorrel (*Rumex acetosa*), belongs family Polygonaceae sometimes referred to as spinach dock or narrow-leaved dock, is grown as a garden herb or leafy vegetable (pot herb). Yakuwa (Hausa), Emagi (Nupe), and Isapa

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(Yoruba) are some of the colloquial names.<sup>[6]</sup> The leaves' acidic flavour, as well as its therapeutic and dietetic qualities, are attributed to a significant amount of potash binoxalate. Sorrel leaves, both fresh and dried, are useful in medicine. Sorrel is used as a cooling beverage for all feverish conditions because of its diuretic and refrigerant properties. 268 compounds from 29 *Rumex* species have been released thus far. Important chemical components with a wide range of pharmacological actions, including anti-inflammatory, antioxidant, antibacterial, and anticancer properties, include anthraquinones, flavonoids, tannins, stilbenes, naphthalene, diterpene alkaloids, terpenes, and lignans.<sup>[7,8]</sup> Chicken pox sores, skin affected by boil shingles, poison ivy rashes, blisters, acne, and other skin lesions have all historically been treated with water from boiled sorrel. It is meant to reduce discomfort, stop itching, and hasten the healing process. It was thought that consuming sorrel water flavoured with a little honey would help reduce fever and treat sinus infections.<sup>[9]</sup>

**Material and Method**

Methanol, Diazepam, PTZ , Normal saline.

**Preparation of Plant Material**

Fresh *Rumex acetosa* (Polygonaceae) plant collected, leaves of plant were separated, cleaned, air-dried in a shaded environment. Soxhlet extraction was used to extract 100 g of the crude powder from 250 ml of

methanol. Dry extract was obtained by evaporating the solvent. For use in later research, the resultant extract was kept in a jar with a clear label.

**Phytochemical Analysis**

Phenolic, flavonoid, glycoside, carbohydrate, terpenoid, alkaloid, and amino acid tests are all positive in phytochemical analysis.

**Isolation and Purification of Extract**

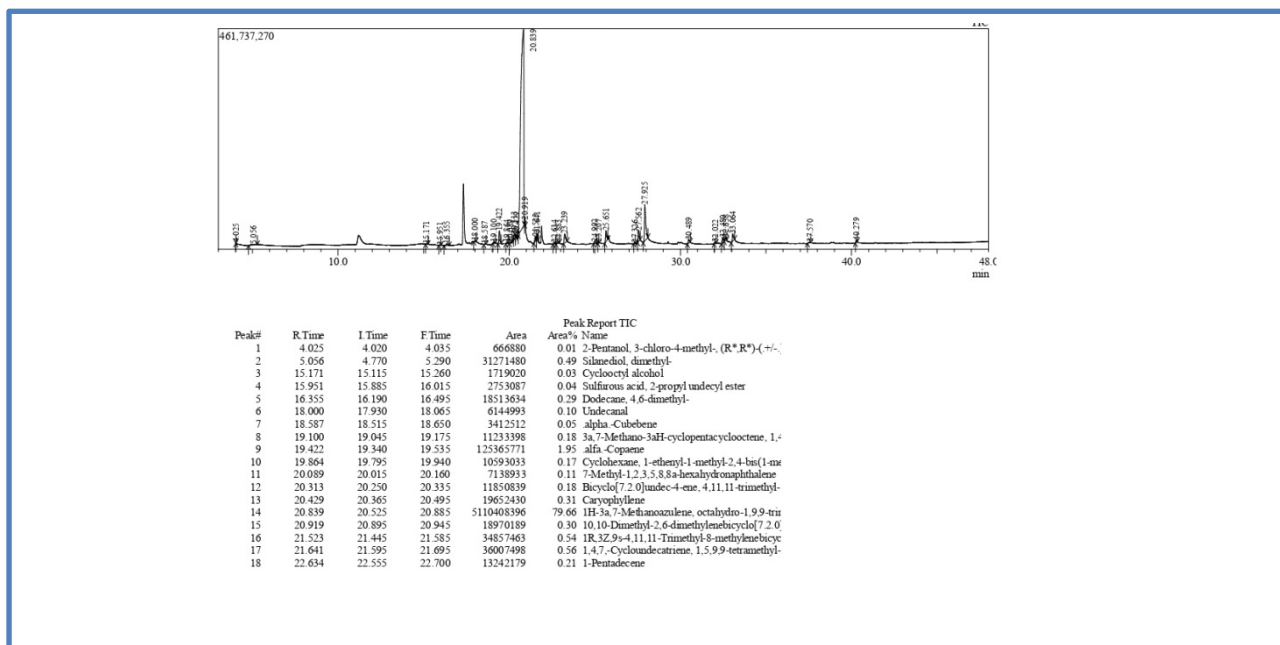
One or more fractionation processes based on various chromatographic techniques were the main methods used to separate and purify plant components. Column chromatography (CTs), thin layer chromatography (TLCs),

**Column chromatography of methanol extract of plant *Rumex acetosa* linn**

For part isolation, five grams of extract were utilised. The chromatographic bed was covered with cotton wool after the extract was dissolved in a small amount of ether.

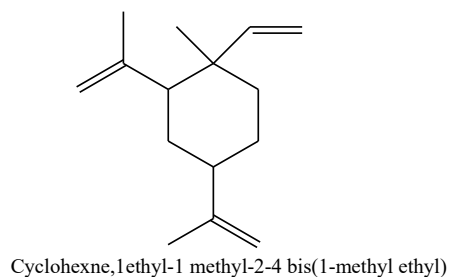
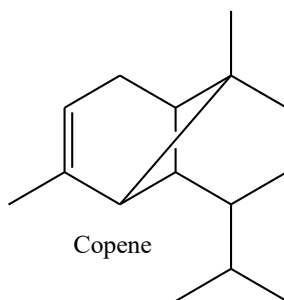
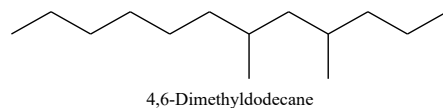
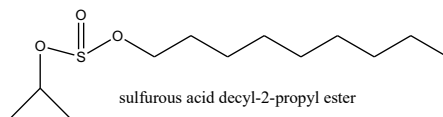
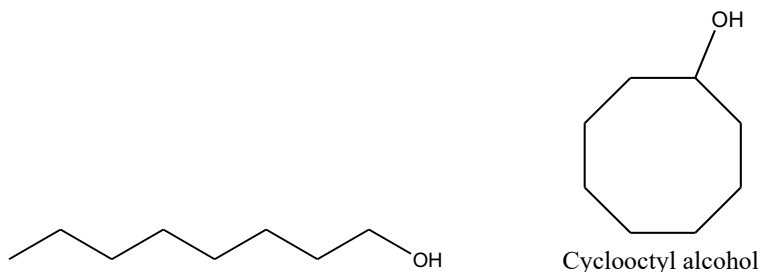
A mixture of increasingly polar solvents, starting with petroleum ether, was eluted to the column for isolation. Subsequently, n-Hexane: Ethyl acetate: Formic acid (5:4.5:0.5) set volume fractions (e.g., 20ml), cumulative fractions from the column were collected. Analytical techniques including FTIR and GC-MS-MS were used to further investigate its identification.

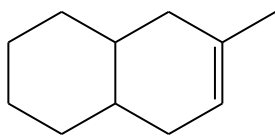
**Fig No 1.GCMS of Fraction RS in Methanol**



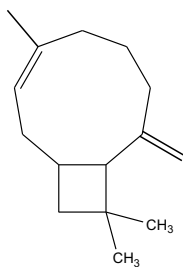
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Peak#	R Time	I Time	F Time	Area	Area%	Name
19	22.883	22.735	22.925	13927622	0.22	2-Tridecanone
20	23.239	23.180	23.390	109206867	1.70	Tridecanal
21	24.992	24.930	25.105	22443464	0.35	1,6,10-Dodecatrien-3-ol, 3,7,11-trimethyl-
22	25.207	25.175	25.240	5118278	0.08	Heptadecane
23	25.651	25.585	25.755	101660933	1.58	Tetradecanal
24	27.326	27.275	27.370	5345241	0.08	1-Nonadecene
25	27.562	27.495	27.660	89507128	1.40	2-Pentadecanone
26	27.925	27.835	28.105	388764647	6.06	Pentadecanal-
27	30.489	30.410	30.575	29944241	0.47	Hexadecanal
28	32.022	31.970	32.085	9512457	0.15	Oxirane, hexadecyl-
29	32.480	32.400	32.555	44577097	0.69	7-Hexadecenal, (Z)-
30	32.638	32.565	32.715	32909931	0.51	2-Heptadecanone
31	33.064	32.975	33.175	73847033	1.15	Eicosanal-
32	37.570	37.425	37.615	9296685	0.14	Octadecanoic acid, 3-hydroxy-2-tetradecyl-, m
33	40.279	40.225	40.335	15703865	0.24	Bi-1-cyclohexen-1-yl, 3,3,3',5,5',5'-octane
				6415567224	100.00	

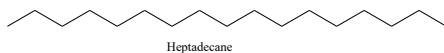




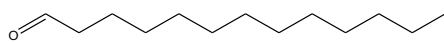
7-methyl-1,2,3,5,8,8a-hexahydronaphthalene



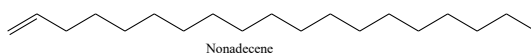
Bicyclo[7,2,0]undec-4-ene-4,11,11-trimethyl-8-methylene



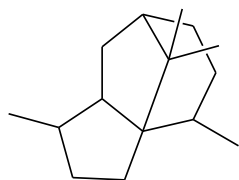
Heptadecane



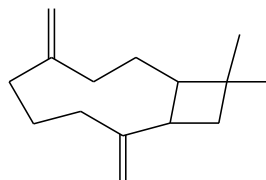
Tetradecanal



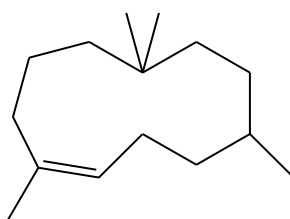
Nonadecene



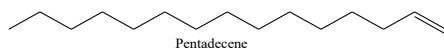
1H-3a,7-Mthanoazulene octahydro 1,9,9-trimethyl-4-methylene



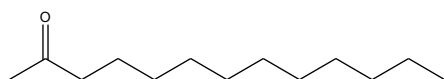
10,10-Dimethyl-2,6-dimethylene bicyclo[7,2]undecane



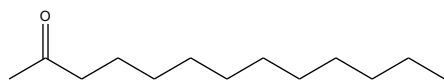
1,4,7-cycloundecatriene-1,5,9,9-tetramethyl



Pentadecene

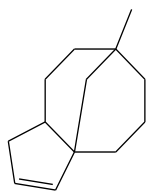
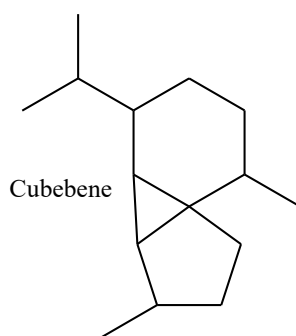
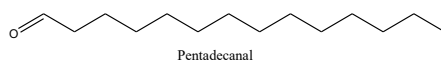
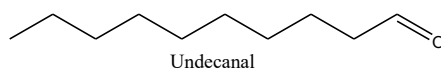
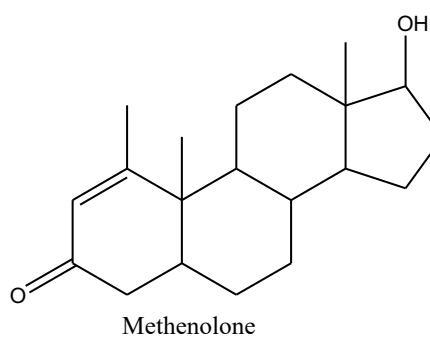
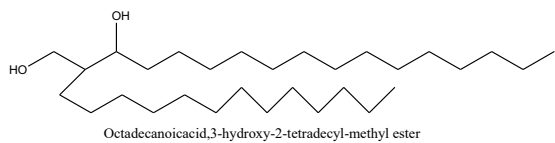
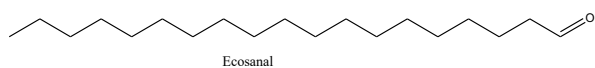
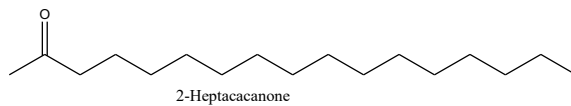
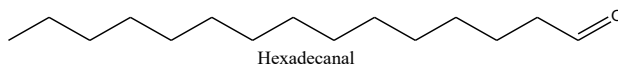
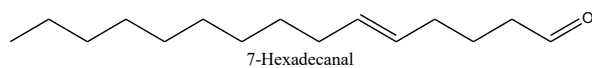
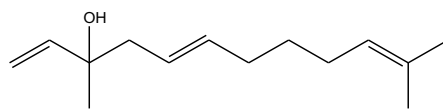


2-Tridecanone



Tridecanal

“Evaluation Antiepileptic activity of Rumex acetosa L and Histopathological changes in mice brain”



3a,7 Methano-3a H-cyclopentacyclooctane 1,4,5,6,7,8,8,9,9a octahydro 1,1,7-trimethyl

### ACUTE TOXICITY STUDIES <sup>[10]</sup>

When the limit test was conducted with a dose of 2000 mg/kg b.w. leaves, *Reumx actosa* L leaves extract, no mortality was seen in mice. The dose selected for Antiepileptic activity is 200mg and 400 mg/ kg body weight.

### ANTICONVULSANT ACTIVITY (PTZ INDUCED CONVULSION) <sup>[11, 12 13,14]</sup>

For the evaluation of Antiepileptic activity, mature male Swiss albino mice (7–10 weeks old, weighing 35–45 g) were used. The experimental animals were obtained from the Laboratory Animal Research Centre and housed under standard laboratory conditions at 20–24°C with a 12-hour light/12-hour dark cycle, with free access to food and water throughout the study. All experimental procedures were conducted in accordance with the guidelines approved by the Institutional Animal Care and Use Committee (IAEC/AMCP/04/387/2023-2024). The animals were randomly divided into five groups (n = 6 per group): normal saline (control), Disease control, diazepam (2 mg/kg +PTZ), and treatment groups. The treatment groups received oral administration of *Rumex acetosa* (200 and 400 mg/kg). <sup>[16, 17]</sup>

- 0 - No Respons . 1 - Immobilization and staring stage
- 2 - Head nodding .3 - Rearing accompanied by forelimb clonus and wet dog shakes

4 - Falling and wobbling stag .5 - Jumping circling or rolling .

6 - Severe tonic clonic seizures.

The mice were killed nearly 30 minutes after the final treatment, and their brains were stored at -8°C in formalin solution until they were needed again. (Naseer *et al.*, 2013).

### Hematoxylin and Eosin Staining <sup>[15]</sup>

Each group's (n = 4) tissue sections were fixed in 4% formaldehyde with PBS (0.1 M) and then cleaned with water. Ethyl alcohol dilutions ranging from 70 to 100% were used to dehydrate brain slices. Brain tissues were then preserved in paraffin after being cleaned with xylene. Blocks of paraffin were divided into 4 µm pieces, deparaffinized using xylene, and then hydrated using dilutions of ethyl alcohol ranging from 100 to 70%. After staining sections with Harris' haematoxylin solution (Sigma-Aldrich, St. Louis, MO, United States) for three minutes and eosin Y (Sigma-Aldrich) for one minute, brain tissues were cleaned with water, dehydrated using a series of graded ethyl alcohols, mounted and captured on camera using an Olympus microscope (Olympus, Tokyo, Japan).

### Statistical Analysis

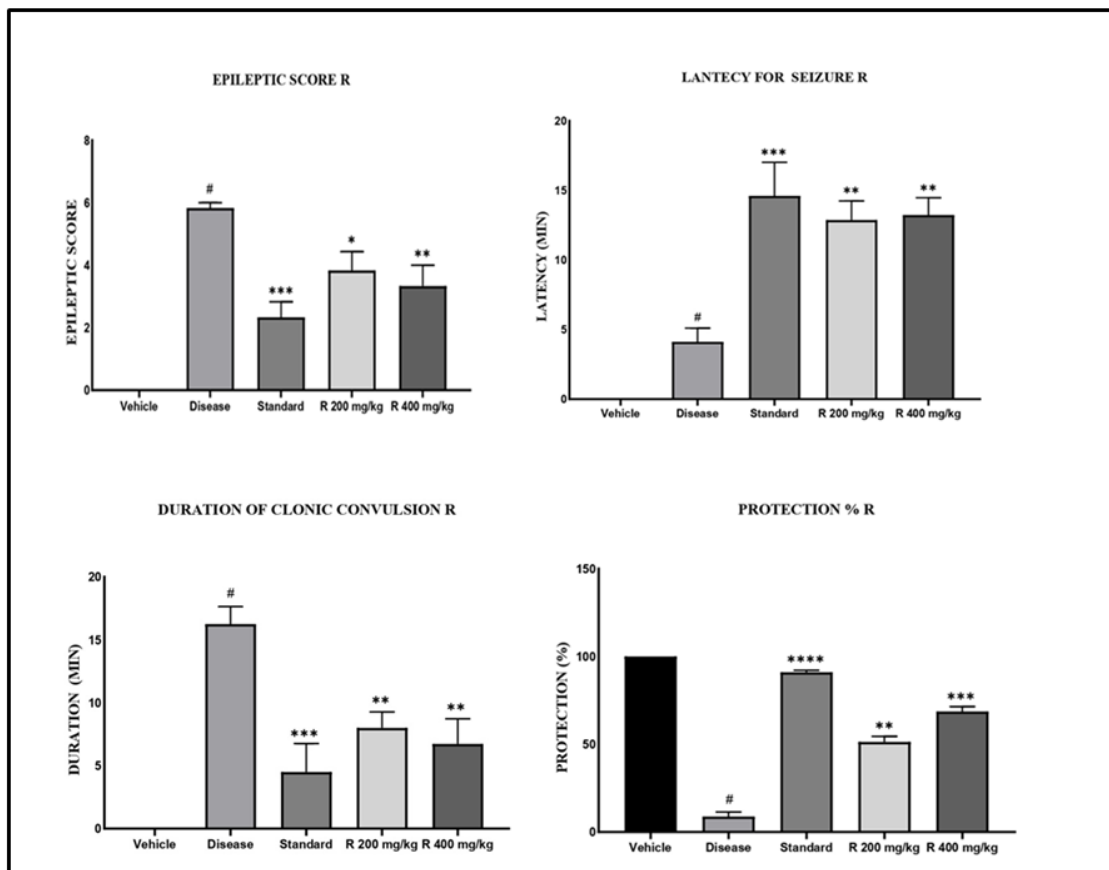
The results are displayed in tables and the collected data is represented as mean ± SEM. The Dunnett test and one-way ANOVA were used to evaluate the data. A significant p-value was defined as ≤0.05.

### RESSULT:

**Table No 1: Effects of *Rumex acetosa* linn methanolic extract on the Epileptic score, latency of convulsion, duration of convulsion, protection against seizures in mice.**

GROUPS	Number of Mice(n)	Epileptic (Racine scale)	Score scoring	Latency of Convulsion (min)	Duration of Convulsions (min)	of Protection Against Seizures (%)
DW +Saline	6	0	-	-	0	100
DW+ PTZ	6	5.833 ± 0.1667 #	4.115 ±0.9851 #	14.92 ± 1.003 #	8.833 ± 2.600 #	
PTZ+Diazepam	6	2.333 ± 0.4944 ***	14.61 ± 2.409 ***	4.502 ± 2.256 ***	91.00 ± 1.125 ****	
PTZ+200 mg/kg Extract	6	3.833 ± 0.6009 *	12.87 ± 1.373 **	7.995 ± 1.275 **	51.33 ± 3.159 **	
PTZ+400 mg/kg Extract	6	3.333 ± 0.6667 **	13.24 ± 1.237 ***	6.732 ± 1.991 **	68.67 ± 2.836 ***	

Results are expressed as Mean ± SEM (n = 6 mice per group). Epileptic sore, Latencies, duration of convulsion and Protection against seizures were analysis by one-way ANOVA, \* P < 0.05, \* \* P < 0.01; \* \* \* P < 0.001 significantly different compared with treated PTZ group, Diazepam 2 mg/kg, 200mg/kg *Rumex acetosa*, 400mg/kg *Rumex acetosa*, 35 mg/kg pentylenetetrazole



**Fig No.2: Impact of *Rumex acetosa* Linn (200 and 400 mg/kg p.o.) on Epileptic score, Latency for seizure, Duration of clonic convulsion, % Protection**

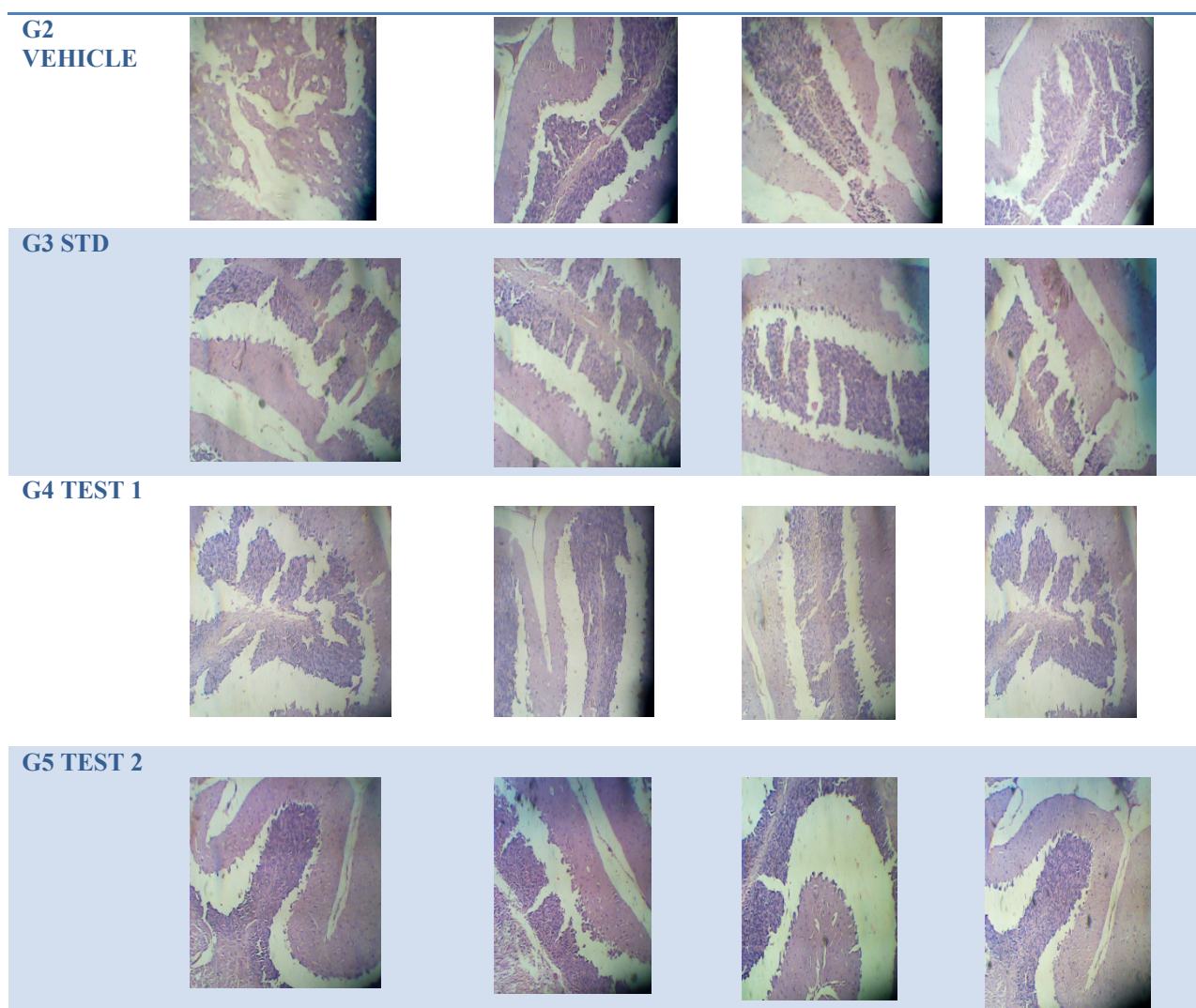
Percent Protection = [(Number of protected mice in control group - Number of protected mice in treated group) / Number of protected mice in control group] \* 100

**Histopathology<sup>[15]</sup>**

Each animal in the saline group had tightly packed neurones with perfect outlines and translucent cytoplasm in the hippocampal CA1, CA3, dentate gyrus regions, and cortex, as seen by the haematoxylin and eosin-stained sections. Neurones were missing and organised erratically, and the granule cell layers in the

disease group were significantly diminished. The plant extracts (200 mg/kg and 400 mg/kg) considerably lessened these structural alterations in the hippocampus and prefrontal cortex, respectively, as compared to the saline group. Meningeal congestion, cerebral oedema, neuronal eosinophilia, meningeal inflammation, and cerebral congestion were not present in mice treated with amaranth. These findings suggest that the plant extract may possess neuroprotective properties, which could lessen the adverse effects of PTZ-induced neurotoxicity. To determine the mechanisms, more investigation is required.

GROUPS	IMAGES			
DISEASE G1				



**Fig No. 3** A photomicrograph of the PTZ group treated with saline, diazepam 2 mg/kg, 200 mg/kg *Rumex acetosa*, and 400 mg/kg *Rumex acetosa* following haematoxylin and eosin staining.

**DISCUSSION:** Phenolic, flavonoid, glycoside, carbohydrate, terpenoids, alkaloid, and amino acid were found in the methanol leaf extract of *Amaranthus cruentus*, according to preliminary phytochemical screening. Numerous phytochemicals, including polyphenols, tannins, flavonoids, steroids, terpenoids, saponins, and betalains, have been found in *Amaranthus cruentus*, according to earlier research. [16] The peak of caryophyllene in GCMS-MS analysis has been linked to various pharmacological actions and is specifically linked to certain therapeutic qualities. [17] Caryophyllene was found to have a complete agonist effect on cannabinoid type 2 (CB2) receptors and to increase GABA-mediated inhibitory neurotransmission. Low GABA levels are linked to epilepsy and seizures. Seizure activity results from depolarised cells in the cerebral cortex due to lower levels of inhibition. Seizures are treated with GABA agonists. Unlike CB1 receptors, activation of CB2 receptors did not appear to have any negative psychotropic effects from marijuana. It has been demonstrated that CB2 receptor activation modulates seizure activity and lowers neuroinflammation, a major role in the development of

epilepsy. [18, 19, 20] Therefore, the anticonvulsant effects seen in this study may be caused by this active chemical component in the methanolic leaf extract of *Amaranthus cruentus*. Several physiologically active elements in the leaf extract may be responsible for the anticonvulsant effect observed in this investigation. Pentylentetrazole blocks the gabaergic system, which results in convulsive episodes. By improving GABA-facilitated inhibition in the brain, diazepam, a drug used to treat absence seizures, can also lessen seizures brought on by PTZ. [21] As the main inhibitory neurotransmitter in the central nervous systems of mammals, GABA has been connected to convulsions because it increases chloride-ion conductance by opening the chloride ion channel, which inhibits neuronal response and activity. [22] The plant extract is believed to have anticonvulsant qualities because it shortens the duration of disturbances and delays the onset of convulsions, even if it significantly lowers the epileptic score. Significant anticonvulsant efficacy against PTZ-induced seizures was also shown by some protection against seizures. The results suggest that the plant extract's impact on the GABA system

may be responsible for its anticonvulsant effects, which are comparable to diazepam in the PTZ paradigm.<sup>[23]</sup>

**CONCLUSION:** The plant *Amaranthus cruentus* Linn, which is a member of the Amaranthaceae family, was chosen for this investigation. We found phenolic, flavonoid, glycoside, alkaloid, amino acid, steroid, protein, and carbohydrate phytochemical elements in the methanolic plant extract using phytochemical screening. These substances exhibit a variety of biological actions, indicating possible therapeutic uses. Caryophyllene is identified as an active component using spectroscopic investigation. The 400 mg/kg body weight dose of *Amaranthus cruentus* L. methanol

**Conflict of interests:** No conflict of interests

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