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Anxiolytic Effects of *Taraxacum Officinale* in Animal Model of Post-Traumatic Stress Disorder

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A B S T R A C T

Post-traumatic stress disorder (PTSD) severity is worsened by co-occurring conditions that also arise concomitantly with PTSD, as a result of the trauma exposure, of shared causal determinants or of PTSD itself. The anxiety disorder known as PTSD is very common and has been linked to a higher risk of hypertension and cardiovascular disease. Criteria A of the DSM-5, a person must have experienced or witnessed a major traumatic event (exposure to actual or threatened death, serious injury, or sexual assault). Prior to experiencing re-experiencing symptoms, a person must have at least one of the following: intrusive distressing memories, recurrent distressing dreams, dissociative reactions (such as flashbacks), intense or prolonged psychological distress upon exposure to reminders of the trauma, and marked physiological reactions to internal or external cues symbolizing or resembling an aspect of the traumatic event (Criterion B). There is evidence that many monoaminergic neurotransmitters may play some part in the pathophysiology or treatment of persistent sequelae following trauma. Monoaminergic neurotransmitters are generally centrally involved in the regulation of both alertness and emotion/mood. Stress procedure for chronic restraint stress (CRS) was employed for 30 days. EETO contains alkaloids, saponins, flavonoids, tannins, glycosides, sugars, steroids, terpenoids, and phenolic chemicals, according to preliminary phytochemical research. *T.officinale* extract caused anxiolytic-like activity in mice, particularly at 400 mg/kg, as it caused a significant alteration in their anxiety-like behaviours, including entries to open arms and time spent in open arms, when compared to the mice in the control groups.

Keywords: Post-traumatic stress disorder, Anxiolytics, Chronic Restraint Stress (CRS), Ethanolic Extract of *Taraxacum Officinale* (EETO), Elevated Plus Maze, Phytochemical Screening, *T. Officinale*

1. INTRODUCTION

Posttraumatic stress disorder (PTSD) is a severe, chronic, and disabling anxiety disorder that can develop as a result of witnessing a traumatic event [1]. PTSD is a debilitating anxiety disease occurring in about 2–9% of individuals after their exposure to life-threatening events like severe accidents, sexual abuse, combat, or natural catastrophes. Although selective serotonin reuptake inhibitor (SSRIs) antidepressants like fluoxetine are currently the first line choice in PTSD drug treatment, the response rates to SSRI treatment rarely exceed 60% and less than 20–30% of SSRI-treated PTSD patients achieve full remission [2].

"Post-traumatic stress disorder (PTSD) is a mental health condition caused by witnessing or experiencing a terrifying event" [3]

PTSD severity is worsened by co-occurring conditions that also arise concomitantly with PTSD, as a result of the trauma exposure, of shared causal determinants or of PTSD itself, and disproportionally affect disadvantaged populations [4].

This disorder may disrupt how individuals and families function, leading to serious medical, financial, and social issues [5]. The anxiety disorder known as post-traumatic stress disorder (PTSD) is very common and has been linked to a higher risk of hypertension and cardiovasculardisease [6]

1.1 DIAGNOSTIC DEFINITIONS

There are currently two major diagnostic definitions of PTSD.

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According to Criteria A of the DSM-5, a person must have experienced or witnessed a major traumatic event (exposure to actual or threatened death, serious injury, or sexual assault). Four symptom clusters should appear if someone has encountered or witnessed such an occurrence. Prior to experiencing re-experiencing symptoms, a person must have at least one of the following: intrusive distressing memories, recurrent distressing dreams, dissociative reactions (such as flashbacks), intense or prolonged psychological distress upon exposure to reminders of the trauma, and marked physiological reactions to internal or external cues symbolizing or resembling an aspect of the traumatic event (Criterion B). Second, one must actively avoid any internal or external (situations, discussions, memories, ideas) reminders of the trauma (Criterion C). Third, there must be at least two "alterations in cognitions and mood" symptoms, such as persistent and exaggerated negative thoughts about oneself or the world, persistently distorted perceptions of the event's causes or effects, pervasive negative emotions, noticeably diminished interest, a sense of being distant or estranged from others, and a persistent inability to feel positive emotions (Criterion D Last but not least, a person must exhibit at least two of the arousal symptoms listed below: hypervigilance, excessive startle reaction, problems with attention, and sleep disturbance (Criterion E). To

prevent the pathologization of typical stress reactions, people must experience these symptoms for longer than one month after being exposed to trauma [7].

It's important to note that the DSM-5 definition of PTSD has expanded the condition's definition beyond the conventional focus on terror responses to also encompass other emotional responses to stress. In reality, a large number of PTSD patients, particularly those who were in the military or who were first responders, exhibit emotional reactions other than fear [8].

Instead of using the DSM-5 to guide mental diagnoses, many regions of the world use the International Classification of Diseases (ICD) of the World Health Organisation. Because diagnosticians working in settings with limited resources frequently can't devote enough time to each patient, the ICD typically takes a simpler approach to mental diagnoses than the DSM. The recently accepted ICD-11 diagnostic standards for PTSD purposefully adopt a narrow focus on fear circuitry symptoms, which include reliving the traumatic event, avoiding reminders of it, and perceiving a greater-than-usual threat (reflected by various types of arousal). The idea that reliving the memories of the traumatic event in the present is a key element of PTSD lies at the heart of this concept [9].

1.2 TYPES OF PTSD:-

Not everyone experiences the same symptoms or responds to traumatic events in the same way. Everyone responds differently. Both PTSD and stress disorders can present similarly and share symptoms. However, there are some variations in how each type is handled [10].

- Normal Stress Response
- Acute Stress Disorder
- Uncomplicated PTSD
- Complex PTSD
- Comorbid PTSD[11]

The proximal or precipitating event can be easily identified, despite the fact that the exact cause of PTSD is unknown [12].

There are many factors that can contribute to someone developing posttraumatic stress disorder. These consist of going through a traumatic experience like,

- Rape
- A near-death experience
- Natural disasters: Those who live through hurricanes, earthquakes, wildfires, and other devastating natural disasters may experience trauma, like losing a loved one or their home.
- Severe illness or injury
- The death of a loved one

1.3 PATHOPHYSIOLOGY:-

Increased oxidative stress, dysregulation of the neuroendocrine system, inflammatory response, and hypothalamic-pituitary-adrenal axis are additional characteristics of PTSD that may contribute to cognitive decline (e.g., via increased neuronal death) [13].

Early studies in patients with PTSD showed autonomic reactivity, indicated by increased heart rate and skin conductance in response to trauma-related cues, and exaggerated startle responses. These findings recapitulated symptoms of general hyperarousal and distress following traumatic reminders in PTSD. Indeed, several pharmacological challenge studies with yohimbine (an α2- adrenergic receptor antagonist) showed exaggerated neurochemical and behavioural responses consistent with central noradrenergic hyper-reactivity in PTSD [4,14].

The monoamines, which include dopamine (from which noradrenaline is derived), histamine, serotonin, and melatonin, are a larger class of structurally related neurotransmitters that also include noradrenaline [15]. There is evidence that many monoaminergic neurotransmitters may play some part in the pathophysiology or treatment of persistent sequelae following trauma. Monoaminergic neurotransmitters are generally centrally involved in the regulation of both alertness and emotion/mood [16].

The neurotransmitter and neurohormonal functioning are altered in posttraumatic stress disorder, according to the pathophysiology of the condition. Despite their ongoing stress, people with PTSD have been shown to have normal to low cortisol levels and elevated levels of corticotrophin-releasing hormone (CRH). The anterior cingulate cortex releases norepinephrine in response to CRH stimulation, which increases

the sympathetic response and causes an increase in heart rate, blood pressure, arousal, and startle response [17].

Stress results impaired in the hypothalamic-pituitary-adrenal (HPA) axis's negative feedback. Additionally, it demonstrates that PTSD patients have altered functioning of other neurotransmitter systems like GABA, glutamate, and serotonin [18].

The hypothalamic–pituitary–adrenal (HPA) axis and sympathetic nervous system constitute the body's fundamental stress response; however, contrary to initial predictions of elevated stress hormones in PTSD, an unusual pattern of low basal (unstimulated) cortisol levels and raised catecholamine levels is evident and has been widely replicated in trauma survivors with PTSD. Epigenetic, molecular and endocrine studies of glucocorticoid signalling and glucocorticoid receptor sensitivity later confirmed a distinct set of HPA axis alterations that reflect exaggerated negative feedback sensitivity in PTSD [19].

PTSD may increase your risk of developing other mental health issues, such as:

- Anxiety and Depression
- Issues with drugs or alcohol use
- Eating disorders
- Suicidal thoughts and actions

Anxiety disorders are prevalent mental illnesses that have pathological or severe anxiety as their main source of emotional or mood disturbance. An elevated state of fear and an exacerbated form of the acute stress response are the common denominator of all anxiety disorders [20].

The amygdala is a component of the neural circuitry involved in emotional learning, fear, and anxiety. Currently, it is thought that changes in dendritic and synaptic structure in stress-responsive brain regions mediate the fear and anxiety brought on by traumatic life events [21,22].

Anxiety disorder is posttraumatic stress disorder (PTSD). Symptoms appear soon after being exposed to a traumatic incident, fade with time in the majority of persons who initially exhibit them, and leave a sizable minority with chronic PTSD. Pharmacotherapy or psychotherapy can be used to treat PTSD [52]. Post-traumatic stress disorder (PTSD) was previously classified as an anxiety disorder (now classified as trauma and stressor-related disorders in DSM-V) that occurs as a result of a traumatic experience. Post-traumatic stress can occur as a result of an extreme situation, such as combat, natural disaster, rape, hostage situation, child abuse, bullying, or even a serious accident [23].

Stress:

Anxiety disorder can arise in response to life stresses, such as financial worries, chronic physical illness, social interaction, ethnicity, and body image, particularly among young adults. Anxiety and mental stress in mid-life are risk factors for dementia and cardiovascular disease during aging [24].

1.4 Cognitive Behavior Therapy Interventions for PTSD

- Exposure Therapy
- Anxiety Management Training
- Cognitive Restructuring
- Eye Movement Desensitization and Reprocessing (EMDR) [25]

One of the key components of supplementary medicine is herbal medicine.Three-quarters of people, according to the World Health Organization (WHO), rely on conventional and herbal treatments for daily healthcare. Due to their less negative effects than synthetic pharmaceuticals, herbal medications are currently more popular.The affinity of plant extracts and their isolated compounds for CNS receptors indicates an important role for medicinal plants in the treatment of neurological disorders [26].
Plants are the source of significant bioactive molecules that are chemically categorized as phenolics, alkaloids, carotenoids, organosulfur compounds, etc.

2. Materials and Methods

2.1 Collection of Plant Extract

Ethanolic leaves extract of *Taraxacum Officinale* (T.O) were purchased from Kshipra Biotech Private Limited 221, 2nd floor, Phadnis Complex near Kothari Market, 88/1 MG Road Indore 452007 MP.

2.2 Experimental Animals

Swiss albino mice of either sex weighing 25-35 gm was obtained from the animal house of Department of Pharmacology, Vidyabharti College of pharmacy Reg.No: 1504/PO/RE/S/11/CPCSEA , Amravati. All the animal are acclimatized to the animal house prior to use. They are kept in case in animal house with a 12 hr light: 12hr dark cycle at temperature (25°C 1°C) with 50+ 55% of relative humidity. Experiments was performed in accordance with the committee for the purpose of control and supervision of experimental animal (CPCSEA) guideline after the approval of the experimental protocol by the institutional animals ethical committee (IAEC). Animal are fed on pellets and tap water ad libitum. The care and

handling ofanimals in accordance with the internationally accepted standard guidelines of use of animals (CPCSEA).

2.3 Drugs and Chemicals

Standard drug: Diazepam 10mg/2ml ampule (Mfg.By Sun Pharma) purchased from Matoshree Medical Stores, Valgaon, Dist. Amravati, Maharashtra. 444801

2.4 Preparation of Doses

Diazepam was diluted to 1.5 mg/10 ml with distilled water. Three different concentrations (100 mg/kg, 200 mg/kg, and 400 mg/kg) of the EETO were prepared by dissolving the extracts in distilled water. All solutions were freshly prepared at the time of administration to the animals. Extract solution and vehicle (0.9 % NaCl) were given orally and standard drug (diazepam) intraperitoneally.

2.5 Phytochemical Analysis

The leaves extract undergoes different phytochemical tests for identification of different phytochemical such as Flavonoids, Alkaloids, Tannins, Steroid, etc.

A. Test for Glycoside

1. Legals Test

   The extract was hydrolysed with Hcl on a water bath. 1ml of pyridine was added to hydrolysate and few drops of sodium nitroprusside solution were added and then it madealkaline with NaOHsolution, appearance of pink to red colour shows the presence of glycoside.

2. Killer-killani Test

   2ml ofaqueous extract + glacial acetic acid, one drop 5% Ferric chloride and Concentrationsulphuric acid. Reddish brown colour appears at junction of two liquid layer and upper layers appears bluish green.

B. Test for Alkaloids

1. Mayer's Test
   1ml of extract in 1ml of Mayer's reagent (potassium mercuric iodide solution), Whitish yellow or cream colour precipitate observed, which shows the presence of alkaloid.
2. **Hager's Test**
   1ml of extract in 3ml of Hager's reagent. Yellow colour precipitate observed, which showsthe presence of alkaloid.
3. **Wagner's Test**
   1ml extract in 2ml of Wagner's reagent (Iodine in potassium iodide). Formation of reddish-brown precipitate, which shows the presence of alkaloid.
4. **Dragendroff's Test**
   1ml of extract in 1ml of Dragendroff's reagent (potassium bismuth iodide solution). Reddish orange precipitate was observed, which shows the presence of alkaloid.

C. Test for Flavonoid

1ml of extract + few drops of dil. NaOH was added. An intense yellow colour was producewhich become colourless an addition of few drop of dil. Hcl, indicate presence of flavonoids.

D. Test for Tannins

1. Ferric Chloride Test :-

About 0.5g of the dried powered sample were boiled in 20ml of distilled water in a test-tube and then filtered. A few drops of 0.1% ferric chloride added and observed for brownish green or a blue-black coloration.

2. Lead acetate Test

The extract (50 mg) is dissolved in of distilled water and to this 3 ml of 10% lead acetate solutions is added. A bulky white precipitate

indicates the presence of phenolic compounds.

E. Test for Terpenoids:

2.0 ml of chloroform was added with the 5 ml aqueous plant extract and evaporated on the water bath and then boiled with 3 ml of H2SO4 concentrated. A grey color formed which showed the entity of terpenoids.

F. Test for Saponin

Froth Test:

About 0.5gm of extract was dissolved in 10 ml of distilled water for about 30 seconds. The test tube was stoppered and shaken vigorously for about 30 seconds. The test tube was allotted to stand in a vertical position and observed over 30 minutes period of time. If a "honey comb" froth above the surface of liquid persists after 30 minutes for sample is suspected to contain saponins.

G. Test for protein.

Biuret test: 2 ml of NaOH and 4-5 drops of copper sulfate to the extract. Shake the test tube gently to mix the ingredients and allow the ingredients to stand for 5 minutes. Presence of bluish violet colour indicates presence of protein.

2.6 Treatment Protocol

Table 1. Grouping and Dosing of animals

Sr. No.	Group	No. of Animals	Treatment/Dose	Route of Administration
1	I (control -without CRS)	6	Normal saline 1ml/kg	Oral
2	II (control + CRS)	6	Normal saline 1ml/kg	Oral
3	III (DZPM + CRS)	6	DZPM (1.5mg/kg)	i.p
4	IV (EETO + CRS)	6	EETO (100mg/kg)	Oral
5	V (EETO + CRS)	6	EETO (200mg/kg)	Oral

2.7 Experimental Procedure

2.7.1 Stress Procedure

Stress procedure for chronic restraint stress (CRS) was employed for 30 days. CRS consisted of 1 hr session of restraint stress for selected days and the evaluation of behavioral testing for anxiolytic activity was done on 10^{th} day, 20^{th} day and 30^{th} day [27]. From day 1 to day 10 animals (except Grp I) were stressed for 7 days except day 8 and 9 and again stressed on day 10 for behavioral testing to determine anxiolytic activity and 10 days after testing same CRS procedure were applied for next 10 days except day 17 and 18 and again behavioral testing with CRS procedure on day 20 were carried out. After 20 days animals were not stressed from 21^{st} to 29^{th} days and then again stressed on 30^{th} day for behavioral testing. Restraint stress was carried out by placing the animal in a plastic restraint device (adjustable in size depending on the animal's weight) for 1 h. The area of the tube could be adjusted individually to each mice and the tube was held firmly in place without moving. There was a 1 cm hole in the far end for breathing [28].

From the first day (day 1) 30 minutes before the stress procedure drugs were given once per day. Group I received normal saline without stress, Group-II received normal saline + CRS which served as control .Group-III received standard drug (DZP 1.5mg/kg) + CRS .Group-IV, Group- V and Group-VI received EETO + CRS (100, 200 and 400 mg/kg respectively).

2.7.2 Behavioral Test

On day 10th, 20th and 30th of experimental procedure the following anti-anxiety models assessed the effect of EETO for evaluation of anxiolytic activity. All assessment was done 30 minutes after CRS.

Elevated plus maze model

The EPM has been widely used as a tool in the investigation of the psychological and neurochemical basis of anxiety, for screening anxiety-modulating drugs. The elevated plus maze apparatus consisting of two open arms (35 x 5 cm) and two closed arms (30 x 5 x 15 cm) with an open roof which was 50 cm elevated from the floor used to observe anxiolytic behavior in animals. Animal placed on the elevated plus-maze apparatus 30 min after the stress procedure. Each animals were placed in the center of the elevated plus-maze with its head facing towards the open arms. The behavioral effects of the mice observed for 5 min with a different kind of parameter such as total time spent in open arms and the number of entries in the open arms were recorded. The animals were allowed to socialize during the entire experiment. These different parameters observed using MASTER MAZE software in our video tracking room [29].

3. RESULT

3.1 Phytochemical Analysis of Ethanolic Extract of *Taraxacum Officinale.*

Table 2. Preliminary Phytochemical Screening

Sr. No.	Phytochemical Analysis	Test Performed	Result
1	Glycosides	Killer-Killani Test Legals Test	**(+)**
2	Alkaloids	Mayer's test Wagner's test	**(-)** **(+)**
3	Tannins	Ferric Chloride Test, Lead acetate Test	**(+)**
4	Flavonoids	Alkaline Reagent Test	**(+)**
5	Saponins	Froth Test	**(-)**

Where, **(+)** Indicates Presence & **(-)** Indicates Absent

3.2 Pharmacological Study

Elevated Plus Maze Test:

Table 3. Anti PTSD effect of EETO on Elevated Plus Maze test in mice.

Group	Treatment	Number of entries into open arms (5 min observation)		
		10 th Day	**20 th Day**	**30 th Day**
I	Control saline(1 ml/kg)- without CRS	7.833 ± 0.6009	7.833 ± 0.6009	7.833 ± 0.6009
II	Contol saline(1 ml/kg) + CRS	2.833 ± 0.4773	2.333 ± 0.4944	4.333 ± 0.4944

III	DZPM(1.5 mg/kg) + CRS	6.833 ± 0.7032*	7.667 ± 0.8819*	9.333 ± 0.7149*
IV	EETO(100 mg/kg)+ CRS	3.5 ± 0.4282	4 ± 0.5774	4.833 ± 0.4773
V	EETO(200 mg/kg) + CRS	4.5 ± 0.7638	5.5 ± 0.7638*	6.5 ± 0.7638*
VI	EETO(400 mg/kg) + CRS	5.667 ± 0.6667*	7.167 ± 0.7032*	8.5 ± 0.7638*

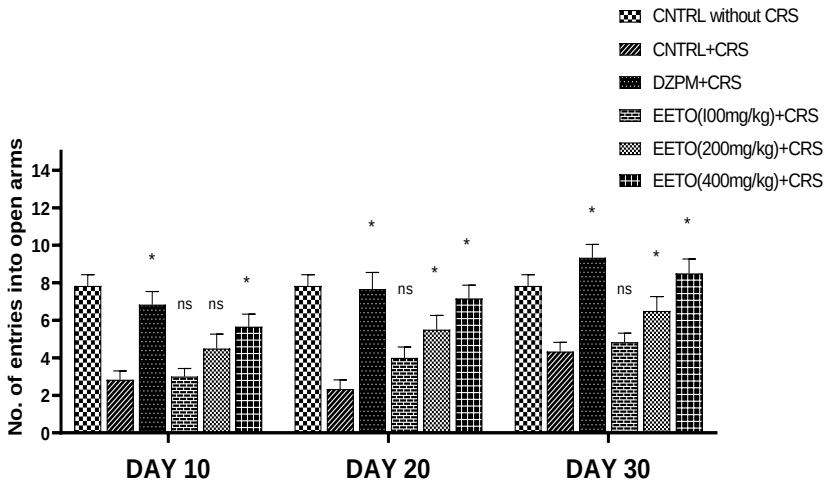

Figure 1. Anti PTSD effect of EETO on the numbers of entries into open arms in EPM test.

All data are expressed as mean ± SEM (n = 6). One-way Anova followed by Tukey post hoc test. Values are statistically significant $^{*}P<0.05$ compared with (Control + CRS) group and non- significant as ns.

Table 4. Anti PTSD effect of EETO on Elevated Plus Maze test in mice.

Group	**Treatment**	**% Time spent into open arms (For 300 seconds)**		
		10 th Day	**20 th Day**	**30 th Day**
I	Control saline(1 ml/kg)- without CRS	44.05 ± 0.7716	44.05 ± 0.7716	44.05 ± 0.7716
II	Contol saline(1 ml/kg) + CRS	10.55 ± 0.4687	8.938 ± 0.4825	11.39 ± 0.4678
III	DZPM(1.5 mg/kg) + CRS	33.95 ± 0.3917*	43.72 ± 0.5465*	56.11 ± 0.6483*
IV	EETO(100 mg/kg)+ CRS	15.05 ± 0.4172*	18.22 ± 0.6298*	25.83 ± 0.4774*
V	EETO(200 mg/kg) + CRS	20.17 ± 0.6006*	24.11 ± 0.6417*	30.94 ± 0.4502*
VI	EETO(400 mg/kg) + CRS	30.17± 0.6006*	41.22 ± 0.6593*	50.39 ± 0.785*

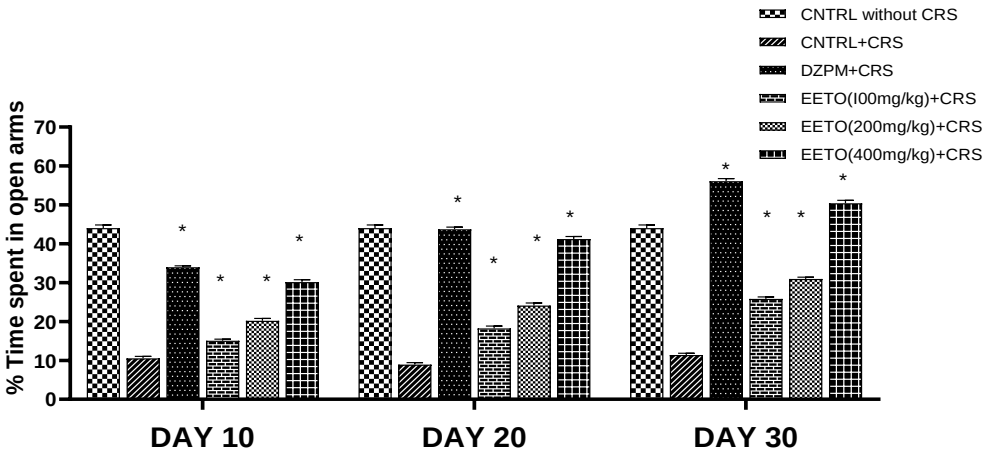

Figure 2. Effect of EETO on the percentage of time spent in open-arms.

All data are expressed as mean ± SEM (n = 6). One-way Anova followed by Tukey post hoc test. Values are statistically significant *P<0.05 compared with (Control + CRS) group and non- significant as ns.

As shown in the figure 1 and 2, the mice in CRS subgroups receiving the *T. Officinale* extract showed a significant difference in terms of anxiety behaviors using elevated plus-maze in comparison with those in the control group (Grp II). Diazepam showed significantly increased in the number of entries in open arms as well as time spent in open arms when compared with (Control + CRS) group. In the stress subgroups mice were showed the significant (P<0.05) increased entries in the open arms at 400 mg/kg on day 10 and on day 20 and day 30 extract showed significant (P<0.05) effect at 200 mg/kg and 400 mg/kg for open arms entries (figure 1). For percent time spent into open arms EETO shows significant (P<0.05) increased at all i.e.100 mg/kg, 200 mg/kg and 400 mg/kg doses (figure 2).

4. DISCUSSION

Exposure to a traumatic experience causes posttraumatic stress disorder (PTSD), a common psychiatric illness. Individuals with PTSD not only have major functional deficits, but they also have increased rates of physical morbidity and mortality, necessitating long-term pharmacological treatment. The issues with current synthetic chemical therapy are poor response, remission, and severe undesired side effects. As a result, the hunt for new drugs continues, and medicinal plants have emerged as a significant source of new medication development for this CNS illness. Over time, several pharmacological models have been used to analyse medicinal plants for neuropharmacological activity in order to identify botanicals and pharmaceuticals with positive benefits in the treatment of diverse CNS illnesses. Over time, several pharmacological models have been used to analyse medicinal plants for neuropharmacological activity in order to identify botanicals and pharmaceuticals with positive benefits in the treatment of diverse CNS illnesses.

The current study found that EETO significantly alleviated anxiety-like behaviours in a PTSD mouse model (i.e. CRS) as measured by the elevated plus-maze. It has been found that chronic restraint stress (CRS) procedure in PTSD model induced an anxiety-like behavior in mice even after days or may be after month [30]

EETO contains alkaloids, saponins, flavonoids, tannins, glycosides, sugars, steroids, terpenoids, and phenolic chemicals, according to preliminary

phytochemical research. The current study revealed that CRS exposure caused anxiety-like behaviour, as evidenced by the fact that CRS exposed mice/animals significantly decreased their percentage of time spent and number of entries into the open arms, increased the time spent in the dark section and decreased the duration of stay in the light section, and for the hole board there was increased immobility and decreased head dipping in comparison to the control group without CRS. The specific cause of PTSD is unknown at this time. PTSD pathology has been linked to changes in a variety of neurotransmitter and neuroendocrine systems, including serotonin (5-HT), norepinephrine (NE), and gamma amino butyric acid type A receptor (GABA-A), as well as dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, according to research into the underlying neurobiology. EETO reduced PTSD-like behaviour impairments induced by CRS. Our findings revealed that the T.officinale extract caused anxiolytic-like activity in mice, particularly at 400 mg/kg, as it caused a significant alteration in their anxiety-like behaviours, including entries to open arms and time spent in open arms, when compared to the mice in the control groups.

Many studies on the chemical elements of plant extracts suggest that plants containing flavonoids, alkaloids, phenolic acids, saponins, and tannins have anti-cancer properties. The EETO's phytochemical screening revealed the presence of flavonoids, tannins, and phenolic acid [31]. The precise mechanism of EETO is currently unknown. It is probable that phytoconstituents, particularly tannins and flavonoids, influence CRS-induced anxiety via GABA-A. There is a chance that EETO raises GABA levels in brain regions such as the hippocampus, amygdala, and prefrontal cortex.

Accumulating evidence suggests that serotonin (5-HT) and GABA abnormalities play a significant role in the aetiology of PTSD. Given the complex aetiology of PTSD, the importance of 5-HT and GABA in anti-PTSD therapy, and the interaction between these neurotransmitters, medicines that normalise 5-HT and GABA levels may have greater therapeutic efficacy. As a result, it is feasible to infer that the anti-PTSD-like actions of EETO are related to GABA levels in the brain.

A single mechanism may be active in any particular circumstance, or there may be intricate interactions between active constituents and various neurotransmitter systems in the brain. Because the effects of EETO seen in this study were acquired by employing an ethanolic extract rather than an isolated substance, it is critical to comprehend the effects of active ingredients in combination and isolation, as well as their interactions with other neurochemicals.

5. CONCLUSION

Herbal medications have grabbed the interest of the psychiatry research community in recent years due to their better compliance and lower side effects. This is largely owing to the fact that various herbal formulations have been demonstrated to be beneficial in both animal and human research for a variety of psychiatric diseases. Although the current model suggests that flavonoids may be an effective herbal candidate for treating PTSD, primarily through serotonergic activation, more research is needed to determine the exact molecular mechanisms underlying its effects and to better understand the neuropathological changes in PTSD.

In conclusion, the current findings suggest that CRS followed by frequent reminders is a reliable and long-lasting animal model for PTSD. T.officinale has possible anti-PTSD activity, and serotonin and GABA may play a role in T.officinale's anti-PTSD benefits.Flavonoids and tannins found in both plants must play a major influence in the findings of this study.T.oficinale may give appropriate pharmacotherapy and alternative treatment approaches when used as an adjuvant phytochemical material. In the future, research will be needed to determine the mechanism of action for the aforementioned activity.

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