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Study of Anti Melancholy Effect of *Tridax procumbens* Leaf Extracts

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The current study was intended to assess the antidepressant action of Successive extraction of Petroleum ether (PEETP), Chloroform (CHETP), ethylacetate (EAETP), Ethanolic (EETP) & Aqueous (AETP) extracts of *Tridax procumbens (TP)*by Tail suspension test (TST). The 25-30g over night fasted mice were selected and divided into six groups. Dose was fixed as per OECD 425 Guidelines acute toxicity studies. Extracts and standard were administered 1 hr prior to study,time period and percentage diminution of immobility were noted. The CETP & EAETP 200 mg/kg extracts shows significant ($p<0.01$) reduction of immobility time was observed when compared to control. Both EETP 200 mg/kg effect and escitalopram (10mg/kg) shows the more significant ($P<0.001$) when compared to negative control. AETP was shows $p<0.05$ significant whereas

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PEETP no significant to negative control, the studies result recommends that ethanol extract pronouncedantidepressant effect. It may be the presences of Phtoconstituents attribute the level of Neurotransmitter like 5 hydroxy tryptamine and noradrenaline.

Keywords: Antidepressant; tridax procumbens; tail suspension test; mice; immobility.

1. INTRODUCTION

Depression, characterized by low mood and reduced activity, significantly impacts individuals' thoughts, behaviors, and well-being [1,2]. It is a prevalent chronic condition affecting millions worldwide, as highlighted by WHO statistics. The global burden of mental and behavioral disorders is substantial and expected to increase further [3-5]. Depression correlates strongly with suicide, with millions of attempts annually [3,6,7]. Despite the availability of numerous antidepressants, treatment efficacy remains inadequate, often accompanied by undesirable side effects such as weight fluctuations [8-10]. Seeking improved outcomes with fewer adverse effects, this study explores the potential of *Tridax procumbens*, an Ayurvedic plant, as an alternative therapeutic option for depression [11-13].

2. MATERIALS AND METHODS

2.1 Preparation of Extracts and Preliminary Phytochemical Screening

Plant material, specifically leaves of *Tridax Procumbens L*, was gathered in Namakkal District, Tamilnadu, and authenticated by Dr. Raju, an Associate Professor at Kandar Arts College, Paramathi Velur. The leaves underwent a process of shade drying until fully dehydrated. Subsequently, the dried leaves were coarsely powdered and sieved to obtain a uniform powder. A quantity of 500 grams of this powdered material was subjected to successive extraction using Petroleum ether, Chloroform, Ethyl acetate, ethanol, and aqueous solvents through maceration. The resulting compounds were concentrated via vacuum drying, and any remaining solvent traces were eliminated by placement in desiccators. Chemical tests were conducted to identify the constituents present in the leaf extracts of *Tridax Procumbens L*[6].

2.2 Acute Oral Toxicity Studies

Acute oral toxicity studies were conducted in accordance with OECD-425 guidelines, utilizing Leaf extracts of *Tridax Procumbens* L on albino mice of both sexes, chosen randomly for the study. Prior to dosing, animals underwent a fasting period, with food withheld overnight for rats and for 3-4 hours for mice, while water remained accessible. After fasting, the animals were weighed, and the test substance was administered accordingly. Following administration, food deprivation for an additional 3-4 hours was applied to mice. Each step of the study involved three animals. The starting dose, chosen from fixed levels of 5, 50, 500, and 2000 mg/kg body weight, was administered. Animals were closely observed after dosing, with particular attention given during the initial 4 hours and periodic checks over the first 24 hours. Any animals exhibiting severe distress or mortality were promptly removed from the study for humane reasons. If mortality occurred in two out of three animals at a particular dose, it was considered toxic. Further confirmation involved repeating the same dose, and if mortality persisted, it was assigned as the toxic dose. Conversely, if no mortality was observed, the procedure was reiterated with higher doses to determine toxicity levels [7].

2.3 Experimental Design for Anti-Depressant Activity

Mice were allocated into distinct control and experimental groups, each consisting of six individuals (n=6). Administration of drugs/vehicle took place 30 minutes before the commencement of the study. The groups were delineated as follows: Group I: Served as the negative control and received 1% DMSO. Group II: Acted as the positive control, receiving the standard drug Escitalopram orally at a dose of 10 mg/kg. Group III: Administered *Tridax procumbens* Petroleum Ether Extract orally at a dose of 200 mg/kg. Group IV: Administered *Tridax procumbens* Chloroform Extract orally at a dose of 200 mg/kg. Group V: Administered *Tridax procumbens* Ethyl Acetate Extract orally at a dose of 200 mg/kg. Group VI: Administered *Tridax procumbens* Ethanol Extract orally at a dose of 200 mg/kg. Group VII: Administered *Tridax procumbens* Aqueous Extract orally at a dose of 200 mg/kg.

2.4 Experimental Models of Anti-Depression

2.4.1 Tail Suspension Test (TST)

Before the commencement of testing, all animals underwent a fasting period of 12 hours. Following this, the vehicle/standard/test compounds were administered orally (p.o.), 30 minutes prior to testing. The experimental setup involved suspending mice from the edge of a shelf positioned 58cm above the table surface, achieved by affixing adhesive tape approximately 1cm from the tail tip. Immobility duration was then monitored for a 6-minute duration using a stopwatch. Initially, mice exhibited vigorous motor activity, eventually transitioning to a state of stillness. Immobility was defined as complete passivity and absence of motion during the observation period [8,9].

2.5 Statistical Analysis

The data underwent analysis utilizing one-way ANOVA, followed by Dunnett's multiple comparison test. A significance level of $p<0.001$ was deemed as statistically significant.

3. RESULTS

3.1 Preliminary Phytochemical Screening

The Preliminary Phytochemical analysis of various leaf extracts of Tridax procumbens L revealed the presence of constituents such as alkaloids, carbohydrates, flavonoids, polyphenols, among others.

3.2 Acute Oral Toxicity Study

Different doses of various extracts of Tridax procumbens L were orally administered to distinct groups of mice. The results indicated safety up to a dose of 2000 mg/kg, p.o., without inducing any toxic symptoms. Animals that survived were euthanized, revealing complete absorption of the drug through the gastrointestinal tract. Consequently, a dose of 200 mg/kg, equivalent to 1/10th of the Maximum Therapeutic Dose (2000 mg/kg), was selected for subsequent pharmacological models.

3.3 Functional Observational Battery (FOB)

The different extracts of Tridax procumbens L underwent Functional Observational Battery (FOB), a non-invasive method to identify gross functional deficits based on behavioral parameters. Table provided the scoring of various parameters. The results indicated normalcy in stereotypic behaviors. Parameters observed in the Functional Observational Battery for extracts at doses of 200 mg/kg, p.o. were documented as follows.

3.4 Tail Suspension Test

In both the standard (Escitalopram 10mg/kg) and ethanol extract (200 mg/kg) treated groups, the peak values of immobility time exhibited significant reductions to 72.22 ± 6.42 and 91.25± 3.94, respectively, compared to the control group's value of 192.80 ± 2.30. Notably, no significant variation was observed between the immobility times of the ethanol extract and escitalopram treated groups. However, both showed significant differences ($p<0.001$) compared to other extracts and the negative control. Chloroform and ethyl acetate extracts at 200mg/kg displayed less significant reductions ($p<0.01$) in immobility time compared to the negative control, with values of 112.31± 2.80 and 100.80 ± 5.66, respectively, although no significant differences were noted between these groups. The aqueous extract exhibited less significant reductions ($p<0.05$) compared to other extracts. Although the petroleum extract decreased immobility time, it did not show significance compared to the negative control.

4. DISCUSSION

Anxiety and depression pose significant challenges in communities, contributing to substantial morbidity [14-21]. Addressing these issues and finding effective remedies is imperative, given the limitations associated with currently available drugs. Tridax procumbens L has been traditionally used for treating nervous disorders, yet scientific evaluations of its pharmacological effects are lacking [22-27]. This study demonstrates that administering different extracts of Tridax procumbens L in mice induces antidepressant effects [28]. Animal models evaluating antidepressant drug activity often assess stress-precipitated behaviors, with forced swimming and tail suspension tests being the most widely utilized. These tests, sensitive and specific to major antidepressant classes, reflect despair states in animals, akin to human depression [29-33]. The tail suspension test (TST) particularly stands out for its low stress levels and high pharmacological sensitivity [34] compared to the forced swimming test (FST).

The administration of *Tridax procumbens* L resulted in a reduction in immobility time in mice subjected to tail suspension tests. Specifically, the ethanol extract of *Tridax procumbens* L at a dose of 200 mg/kg orally induced a notable antidepressant-like effect in the tail suspension test. However, both the chloroform extract (CETP) and ethyl acetate extract (EAETP) at 200 mg/kg exhibited increased immobility time compared to the ethanol extract, suggesting potentially lower efficacy in the release of neurotransmitters such as 5-Hydroxy Tryptamine or Noradrenaline [35-38].

Literature indicates that the antidepressant effects of the plant extract are mediated through actions on 5HT3 and α-adrenergic receptors, affecting the release or reuptake of neurotransmitters such as serotonin (5HT) and noradrenaline (NA). These modifications in neurotransmitter release are believed to contribute significantly to the observed antidepressant effects, particularly evident in the shortening of immobility time in tail suspension tests [39-48]. While dopamine increase has a minimal effect, the primary mechanisms underlying the antidepressant action involve modulation of serotonergic and adrenergic neurons, leading to increased neurotransmitter levels [49-56]. The extract's antidepressant activity may be attributed to its phytochemical composition, particularly flavonoids, tannins, phenolic compounds, alkaloids, and glycosides, abundant in the ethanol extract of *Tridax procumbens* L [57-59].

Table 1. Study period and observation parameters of acute toxicity studies

Initial once observation	First 30 min and periodically 24 hr
Special attention	First 1-4 hr after drug administration
Long term observation	Up to 14 days
Direct observation parameters	Tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma.
Additional observation parameters	Skin and fur, eyes and mucous membrane, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern etc.

Table 2. Preliminary phytochemical screening of various extracts of *Tridax procumbens L*

S. No	Constituents	Tests	PEETP	CETP	EAETP	EETP	AETP
1	Alkaloids	Mayer's test	-	+	+	+	+
		Dragendroff's test	-	+	+	+	+
		Hager's test	+	+	+	+	-
		Wagner's test	-	+	+	+	+
2	Sterols	Burchard test	+	+	+	-	-
		Salkowski	+	-	-	-	-
3	Carbohydrates	Molisch's test	-	-	+	+	+
		Fehling's test	-	-	+	+	-
		Benedict's test	-	-	+	+	+
		Barfoed's test	-	-	+	+	+
4	Glycosides	Legal test	+	+	+	+	+
		Keller kiallani test	-	-	+	+	+
		Borntrager's test	-	-	+	+	+
5	Fixed oils & Fats	Spot test	-	-	-	-	-
		Saponification test	-	-	-	-	-
6	Phenolic Compounds	Ferric chloride	+	+	+	+	+
7	Proteins & amino acids	Biuret test	+	+	+	+	+
		Ninhydrin test	+	+	+	+	+
		Millon's test	+	+	+	+	+
8	Terpenoids & Saponins	Foam test	-	-	-	-	-
		Hemolysis test	-	-	-	-	-
9	Tannins	Gelatin test	+	+	+	+	+
		$FeCl_3$ test	+	+	+	+	+
10	Gums &	Precipitation to	-	-	-	+	+

	mucilage	90%alcohol					
11	Flavonoids	Shinoda test	-	+	+	+	-
		Lead acetate test	-	-	-	+	-
		Ferric chloride test	-	+	+	+	+
		Zinc HCL test	+	+	+	+	+

+ve: Present, -ve: Absent

Table 3. Functional observation battery of extracts of *Tridax procumbens L*

S. NO	Behavioral Parameters	Normal Score	30 MIN	60 MIN	120 MIN	240 MIN
1	Spontaneous Motor Activity	4	4	4	4	4
2	Respiration	4	4	4	4	4
3	Ataxia	0	0	0	0	0
4	Inclined plane	0	0	0	0	0
5	Body tremor	0	0	0	0	0
6	Convulsions	0	0	0	0	0
7	Reactivity to Sound & Touch	0	0	0	0	0
8	Pinna reflex, Corneal reflex, Righting reflex	4	4	4	4	4
9	Analgesia	4	4	4	4	4
10	Writhing	0	0	0	0	0
11	Stereotype behavior	0	0	0	0	0
12	Body tone	4	4	4	4	4
13	Limb tone	4	4	4	4	4
14	Urination	0	0	0	0	0
15	Lacrimation	0	0	0	0	0
16	Salivation	0	0	0	0	0
17	Diarrhoea	0	0	0	0	0
18	Piloerection	0	0	0	0	0
19	Pupil size	4	4	4	4	4
20	Ptosis	0	0	0	0	0
21	Struab tail	0	0	0	0	0
22	Catalepsy	0	0	0	0	0
23	Hypothermia	0	0	0	0	0
24	Stratle response	0	0	0	0	0
25	Cyanosis	0	0	0	0	0
26	Exopthalmus	0	0	0	0	0

Table 4. Effect of *Tridax Procumbens* L on Immobility time in tail suspension test model of mice

Group	Treatment	Immobility time in seconds	% Inhibition
I	Negative control	192.80 ± 2.30	0
II	Positive control	72.22 ± 6.42***^{a}	62.54
III	PEETP 200mg/kg	186.26 ± 5.7 ^{nsd}	3.3
IV	CETP 200mg/kg	112.31 ± 2.8**^{b}	41.74
V	EAETP 200mg/kg	100.80± 5.66**^{b}	47.71
VI	EETP 200mg/kg	91.25 ± 3.94***^{a}	52.67
VII	AETP 200mg/kg	148.72 ± 5.51*^{c}	22.86

*Results were analyzed by one-way ANOVA using Dunnett's multiple comparison test; N=6 in each group; Significance at***p<0.001, **p < 0.01, *p<0.05, Mean Bearing same superscript do not differ significantly, mean bearing different superscript differ significantly. Non-Significance (ns) at p > 0.05 Vs negative*

5. CONCLUSION

Based on the successful outcomes of our experiments on mice, we are optimistic about the potential of the Ethanol leaf extract of Tridax procumbens L in treating depression and related mood disorders. Our findings suggest that this extract may exert its antidepressant effects by either inhibiting the reuptake of serotonin and noradrenaline or increasing the release of these

neurotransmitters non-selectively. These results provide pharmacological support for the traditional use of this plant in depression treatment. However, further extensive pharmacological studies are necessary to fully understand the antidepressant activity of the ethanol extract of Tridax procumbens L. Subsequent investigations should focus on isolating and identifying the chemical constituents and elucidating the mechanism of action responsible for its antidepressant effects.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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