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Methanol Stem Bark Extract of *Tamarindus indica* Exhibited Antidepressant Activity in Mice

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background: Depression is one of the most common psychiatric disorders affecting nearly 17% of the world population and the existing antidepressant drugs used in clinical settings are largely associated with serious side effects. *Tamarindus indica* (Fabaceae) is a plant that has been used ethno-medicinally as a remedy for depression.
Objectives: The objective of this study was to determine the antidepressant activity of methanol stem bark extract of *Tamarindus indica* using mice, also to determine the LD_{50} and phytoconstituents of same extract.
Methods: Fresh leaves of *Tamarindus indica* were collected, pulverised and extracted using 70% v/v methanol. Phyto-constituents of the extract were screened and Median lethal dose (LD_{50}) was determined using standard protocols. Antidepressant effects of the extract were investigated using Tail suspension test (TST) and forced swimming test (FST) models.
Results: The results of median lethal dose revealed the LD_{50} value of 470 mg/kg body weight and the phytochemical screening showed the presence of saponins, alkaloids and glycosides. The extract at the doses of 75 and 150 mg/kg body weight significantly ($p<0.05$) and dose-dependently decreased the immobility time in tail suspension test (TST) as compared to control. In forced swim test, the extract significantly ($p<0.05$) decreased the immobility time only at the highest tested dose (150 mg/kg) when compared to placebo group.
Conclusion: Methanol stem bark extract of *Tamarindus indica* contains secondary metabolites that possess antidepressant action and thus, justifying the traditional use of this plant in the treatment of mental disorders including depression.
Keywords: Depression, Antidepressants, LD_{50}, Tail Suspension Test and Forced Swimming Test

INTRODUCTION

Depression is a common chronic recurrent syndrome, characterized by lack of motivation or enthusiasm, loss of energy, retardation of thinking and activity, as well as profound feeling of gloominess, despair and suicidal thought (Yunusa *et al.*, 2018). It is an illness characterized by persistent sadness, loss of interest and ability to perform daily activities for a period of over two weeks; at worst leading to suicide which is the second cause of death in people aged 15-29 years globally (WHO, 2017). Depression is one of the most common psychiatric disorders affecting nearly 17% of the world population (Jun, 2016).. Several million individuals in the world do experience depression in their lifetime and this translates to about 21% of the world population (Zhang, 2014). Depression affects many African populations and the incidence is more pronounced in Nigeria (Freedman, *et al.* 2013), affecting 3.9% of the Nigerian population (WHO, 2017). Existing Antidepressants like the SSRTI and MAOI are associated with numerous adverse effects

which make it pertinent for search of a safe, cheap and readily available agent with minimal side effect.

Tamarindus indica (Fabacaea) is an evergreen tree reaching a height of about 24m, with pale yellow and pink flowers (Bhadoriya *et al.*, 2011). It grows on dry climate, mostly found in West, East and South Africa (Hartl, *et al.*, 2010). Epidemiological studies have consistently demonstrated that tamarind-derived food is rich in bioactive phytochemicals and possess a protective effect against oxidative stress (Librandi *et al*., 2007, Ovaskainen *et al*., 2008; Galili and Hovav 2014).

METHODOLOGY

Animals

Fifty (50) mice (18-25 g) of both sexes were purchased from the animal facility, Department of Pharmacology, Bauchi State University, Gadau. They were kept in a standard wire cage, under conducive environment. They were housed and fed on a standard pellet food and water and maintained at standard laboratory condition in accordance with principles of laboratory animal care (NIH publication, 1985). The protocol was reviwed and approved by Bauchi State University Ethics committee (BASUG/ETAPV/2020/0004).

Drugs and Chemicals

Imipramine (Tofranil®, Assos Pharma., Batch no: 1608010 Expiry date: 08/2021) was used as a standard drug. Other chemicals used include methanol (sigma chemical Co. St Louis, USA) and distilled water. All drugs and chemicals were locally purchased.

Plant collection, authentication and extraction

Fresh *Tamarindus indica* stem barks were collected from Gadau village, of Itas/Gadau Local Government area of Bauchi State in July 2019. The plant material was identified and authenticated by Dr. Haladu Aliyu Gagman of the herbarium section, Department of Biological Science, Bauchi State University Gadau. A voucher specimen (0010) was deposited in the herbarium of Biological Science Department as a reference.

The fresh stem barks were shade dried at room temperature and grounded to fine powder using a mortar and pestle. About 250 g of the fine powdered material was weighed and extracted in 2 L of 70 % v/v methanol using cold maceration; the mixture was stirred and shaken occasionally for three days (3 days). The mixture was filtered using whatman's filter paper No. 1, evaporated to dryness with an electric oven at 50 ^{0}C to get residue and then air dried. The extract was weighed and kept in an air tight container, labelled as "MSET'' (*Tamarindus indica* stem bark extract) until used.

Preliminary phytochemical analysis

Phytochemical analysis was carried out according to standard procedures as described by Sofowora (1984).

Acute toxicity study (LD_{50} determination)

Median lethal dose (LD_{50}) was determined using Lorke's method (1983).

Antidepressant studies

Tail suspension test (TST)

Twenty five (25) mice were randomly divided into 5 groups of 5 mice each (n=5) and were pre-treated with the following; Group 1 received normal saline 10 ml/kg i.p, groups II, III, IV received MSET extract at doses of 150, 75 and 37.5 mg/kg body weight respectively, while group V received Imipramine at a dose of 10 mg/kg. The mice were suspended 50 cm above the ground with the help of an adhesive tape placed approximately 1 cm away from the tip of the tail, 30 minutes post treatment. The period by which the mouse remains passively motionless was recorded during the six minutes test period. A decrease in the immobility time was considered antidepressant like activity.

Forced swim test (FST)

This test was carried out according to the method described by Porsolt *et al*, (1977). Twenty-five mice were randomly divided into 5 groups of 5 mice each. The first group (I) was pre-treated with normal saline 10 mg/kg i.p, groups II, III and IV were pre-treated with 150, 75 and 37.5 mg/kg of the extract (MSET) i.p, while group V received imipramine 10 mg/kg. Thirty minutes post treatment; all the mice were forced to swim individually in an open and transparent glass container (30 cm high and 20 cm wide), containing fresh water of 15 cm height and maintained at 25 ± 1^{O}C. After an initial two minutes (2 min) period of vigorous activity, each animal assumed a typical immobile posture. The total duration of immobility was recorded for the next four minutes of the total six minutes testing period. Mice were considered immobile when they ceased struggling to escape and thus, remain floating motionless on water, making only those movements necessary to keep their heads and body above the water. A decrease in the immobility time typified antidepressant like effects.

Data analysis

Data analysis was conducted using SPSS, statistical software version 22. Data were presented as texts, table and charts where applicable. Results were expressed as mean ± standard error of mean (M ± SEM) and analyzed using one-way analysis of variance (ANOVA) followed by Dunnette's post hoc test. P values of < 0.05 were considered statistically significant.

RESULTS

3.1 Median lethal dose (LD_{50}) **value**

The intra-peritoneal (ip) median lethal dose (LD_{50}) of the methanol stem bark extract of *Tamarindus indica* was estimated to be 470 mg/kg body weight.

Phytochemical constituents

The preliminary phytochemical analysis of the stem bark extract revealed the presence of glycosides, saponins, alkaloids and phenols while tannins, flavonoids and anthraquinones were absent (Table 1).

Table 1: Phytochemical constituents of methanol stem bark extract of *Tamarindus Indica*

Constituents	Inference	Observation
Tannins	-	**Absent**
Glycosides	+	**Present**
Flavonoids	-	**Absent**
Saponins	+	**Present**
Alkaloids	+	**Present**
Anthraquinones	-	**Absent**
Phenols	+	**Present**

Key: + = Present, - = Absent

Tail suspension test (TST)

Tamarindus indica methanol stem bark extract at the doses of 150 and 75 mg/kg body weight significantly and dose dependently decreased the immobility time when compared to the control group (Fig. 1).

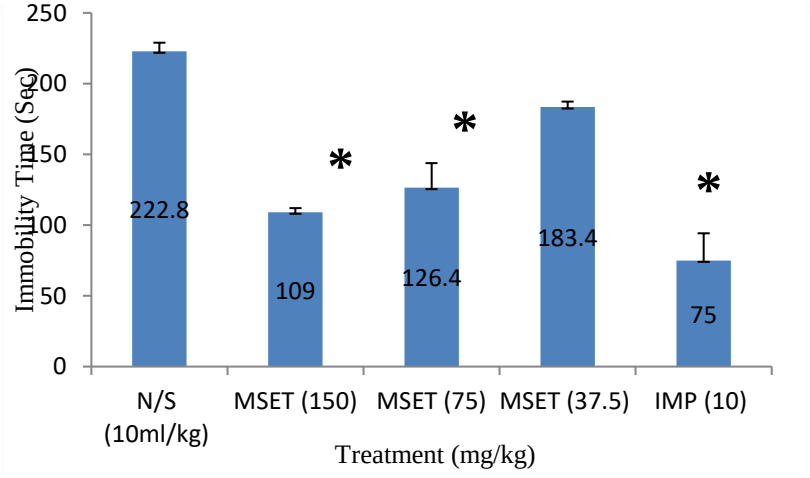

Fig. 1: Effects of methanol stem bark extract of *Tamarindus indica* (MSET) on Immobility Time in Mice Tail Suspension Test (TST)

Data presented as mean ± SEM, N=6, N/S=normal saline, MSET= Methanol stem bark extract of *Tamarindus indica* IMP= Imipramine, *= significantly different from control at p<0.05 using one-way analysis of variance (ANOVA).

Forced swim test (FST)

Tamarindus indica methanol stem bark extract at the dose of 150mg/kg significantly decreased the immobility time when compared to the control group (Fig. 2).

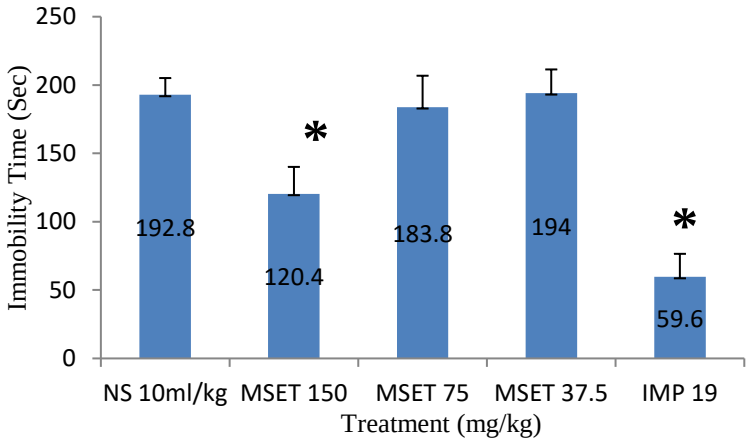

Fig. 2: Effects of methanol stem bark extract of *Tamarindus indica* (MSET) on Immobility Time in Mice Forced swim Test (FST)

Data presented as mean ± SEM, N=6, N/S=normal saline, MSET= Methanol stem bark extract of *Tamarindus indica* IMP= Imipramine, *=significantly different from control at $p<0.05$ using one way analysis of variance (ANOVA).

DISCUSSION

In the search for safe, effective, cheap and less toxic antidepressant from the stem bark of *Tamarindus indica*, some bioactive metabolites have been found to be present. Alkaloids, saponins, glycosides and phenols were present, tannins, flavonoids and anthraquinones were absent. Hamid *et al* in 2011 reported that secondary metabolites such as Saponins, alkaloids, flavonoids, polysaccharides and polyphenols have antidepressant activity. The antidepressant effect of the plant could be attributed to the presence of one or more of these bioactive compounds.

The antidepressant effect of the methanol extract of *T. indica* stem bark was assessed using the two most widely used animal models for antidepressant screening (Tail suspension and forced swimming test) which are quite sensitive and relatively specific to all classes of antidepressants (Santosh *et al.*, 2011). They are valuable tools in drug discoveries for high-throughput screening of prospective antidepressant compounds. These tests have been extensively used to screen antidepressant agent due to exposure of the animals to stress, which was reported to play a role in the likelihood of depression (Adem *et al.*, 2012). The observed antidepressant action with this extract was found to be greater in Tail suspension test (TST) as compared to Forced swim test (FST), this could be due to the fact that tail suspension test is less stressful than forced swim test and therefore may have greater pharmacological responses (Thierry *et al*., 1986). In the tail Suspension Test (TST), the activity of the extract at 150 and 75 mg/kg doses were observed to be greater than the control group (normal saline 10ml/kg) and almost close to standard drug (Imipramine 10 mg/kg) than in the force swim test. However, the lowest dose tested (37.5 mg/kg) produced no significant statistical reduction in immobility time when compared to the control. Previous studies have established that decrease in 5-HT and catecholamine neurotransmission in the brain is mainly responsible for the depressant-like effects of forced swim test and tail suspension test (Borsini and Meli, 1988) and alkaloids have been found to act as reversible inhibitors of mono-amine oxidase enzyme (Abdelfatah *et al*., 1997), thereby enhancing the brain concentration of biogenic amines (dopamine, serotonin, histamine, norepinepherine).

The pattern by which the extract reduced immobility time in both TST and FST was similar to that produced by imipramine, which suggests that the extract mechanism of antidepression could be linked to enhancement of neurotransmission via mono-aminergic pathway.

CONCLUSION

The study suggested that methanol stem bark extract of *Tamarindus indica* possess potential antidepressant effects which support its traditional use and could be of therapeutic interest for use in treatment of patients with depressive disorders.

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