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Studies on the Effects of the Stem Bark Extract of *Ficus thonningi o*n the Nervous System

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ABSTRACT: *Ficus thonningi* stem bark used by traditionalists for the treatment of mental illness was extracted with 70% ethanol and concentrated to dryness using vacuum evaporator. Rats were used to test the acute toxicity of the extract, effect of the extract on the thiopental sodium on sleep, muscle relaxation and the effect of the extract on convulsions induced by pentylenetetrazole and strychnine, while the local anaesthetic effect of the extract was tested in rabbits. The extract induced sleep in rats treated with high doses intraperitoneally. The LD50 of the extract was calculated to be 1440 mg/kg. Its effect on thiopental-induced sleeping time in rats was additive. It produced 80% protection in rats treated with convulsant dose of pentylenetetrazole (100 mg/kg s.c) and 20% protection in those treated with strychnine (2 mg/kg i.p.). It also induced significant muscle relaxant effects in rats and produced local anaesthetic effects in rabbits injected intradermally.

Key words: Acute toxicity, Pentylenetetrazole convulsion, Strychnine convulsion, Thiopental-induced sleep, Muscle relaxation, Local anaesthetic.

Introduction

The management of psychiatric disorders in Africa by traditional healers involves the use of both herbal and symbolic ritual treatments [1, 2]. Prior to the evolution of modern psychiatric care in Nigeria, the traditional healers were solely responsible for the treatment of mental illness [3], but today, there seems to be an interplay between western-oriented psychiatric institutions and traditional techniques. There is a general belief among the natives that mental illness occurs as a result of one of the following - heredity, curse, invoking the evil spirit and use of hard drugs. These accepted concepts of mental illness among both literate and non-literate Nigerians appear to be the primary reason for the patronage enjoyed by the traditional healers [1, 4, 5].

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With the recommendation by the WHO [6] for the use of alternative method for psychaitric treatment, there seems to be an up-surge in the use of herbs in the African subregion for this purpose.

In Borno State of Nigeria, the traditional healers use some of the following decoctions for psychotherapeutic management of mentally ill patients - *Boscia senegalensis* (root), *Ficus syncomorus* (stembark), *Zizyphus spina-christi* (leaf), and *Ficus thonnings* (stembark) [7].

Ficus thonningi Blume belongs to the family Moraceae [8]. The tree is of medium height, up to 15m, with short bole and wide-spread crown [9]. It possesses an aerial root found dangling from the branches and may grow into "large arcades" after reaching the ground. The bark of the tree is light-grey, smooth-slash pink and when cut produces a profuse latex [10]. The plant is widely distributed in tropical Africa especially in the savannah regions [11]. In Northern Nigeria the plant is locally known as "jaja" among the Kanuris. It is also known as "chediya" in Hausa and "bisketu" in Fulani. The stembark has been used extensively by herbalists and traditional doctors in the treatment of human ailments including colds, throat pain, diarrhoea, wound, fever, mental illness and to stimulate lactation.

In Nigeria, scientific information on the efficacy of the stembark extract of *Ficus thonningi* in treatment of psychiatric and other ailments in man is lacking. The purpose of this study was to determine the effect of the extract of *Ficus thonningi* on the nervous system.

Materials and Methods

Plant collection, identification and preparation of extract

Fresh stembarks of *Ficus thonningi* were collected in the month of November, 1996, from Maiduguri metropolis, in Borno State, Nigeria. The stembark was identified to be that of *Ficus thonningi* belonging to the family Moraceae by a botanist with the Department of Biological Sciences, University of Maiduguri, Maiduguri, Nigeria. The stembark was pounbded into powder with a mortar and pestle, after air-drying for 10 days. The powder has a characteristic brown colour with a pepperish taste. Two hundred and twenty-five (225) grammes of the powder were exhgaustively Soxhlet-extracted using 70% ethanol for 10 h at 65°C. The extract was then concentrated using a vacuum rotary evaporator. The concentrated extract was stored at 4°C until used.

Animals

White albino rats of both sexes weighing between 127.3 and 261.3g and male rabbits (2.08 to 2.25 kg) were purchased from National Veterinary Research Institute. Vom, Nigeria. They were housed in clean cages and allowed to adjust to the laboratory environment for a period of one week before commencement of the studies. Food (Nutrifeeds, Nig., Kano, Nigeria) and water were provided *ad libitum* the stabilization period.

Acute toxicity studies in rats

Twenty-five rats of both sexes were separated randomly into five equal groups (A, B, C, D and E). They were treated intraperitoneally with varying doses (200, 400, 800, 1,600 and 3,200 mg/kg) of ethanol-extracted stembark of *F. thonningi* dissolved in water. The rats were allowed access to food and water *ad libitum* and were observed for a period of 24 h for signs of toxicity and death. The symptoms of toxicity in each rat were recorded. The LD50 was calculated using the arithemetic method of Karber as modified by Aliu and Nwude [12].

Effect of extract on thiopental sodium on sleep

Twenty five rats were used for this study. They were separated into 5 equal groups (A, B, C, D and E). Stembark extracts of *F. thonningi* were given to rats in groups A to D at the doses of 50, 100, 200 and 400

mg/kg respectively, 30 minutes before the administration of 35 mg/kg of thiopental sodium. Group E served as the control and was given 35 mg/kg thiopental sodium only. All injections were administered intraperitoneally. The rats were given food and water *ad libitum* during the experiment. The time of thiopental administration, the time of onset of sleep (i.e., when they are unconscious and lose righting reflex) and the time of awakening were recorded. The results obtained were subjected to analysis of variance (ANOVA).

Effect of extract on muscle relaxation

Fifteen rats of both sexes weighing between 138 and 216 g were separated into 3 groups (A - C). The method of Kintano et al., as adopted by Asuzu and Abubakar [13] was used to study the muscle relaxation activity. The rats were placed one after another on the smooth surface of a board inclined at 35° to the horizontal and were allowed a minimum of 10 seconds to remain on the board. The rats in groups A, B and C were treated with increasing doses (100, 200 and 400 mg/kg) of the stembark extract respectively intraperitoneally. Thirty minutes after extract treatment, the rats were again placed on the inclined board and those rats that slipped down the board before 10 seconds were counted as positive for muscle relaxation.

Effect of strychnine and pentylenetetrazole-induced convulsions

Four groups (A, B, C, D) of five rats each were used for the study. They were housed in clean cages and given food and water *ad libitum.* A convulsive dose (100 mg/kg) of pentylenetetrazole (leptazole) was given to groups A and B subcutaneaously while groups C and D received a convulsive dose (2 mg/kg) of strychnine intraperitoneally. Groups B and D however, were pretreated with 400 mg/kg of the stembark extract 30 minutes before treatment with the convulsions. For each rat, onset of convulsions, and duration of convulsions were observed and recorded [14]. The results obtained were analyzed by ANOVA.

Local anaesthetic effect of the extract

To test the local anaesthetic effect of the extract, the method described by Shetty and Anika [15] was used. Four identical symmetrical and circular regions were shaved on the dorsum of the male rabbits, with two shaves circles on the thoracic region and the other two on the lumbar region, 24 h before the experiment. Two concentrations (0.3 mg/ml and 1.0 mg/ml) of xylocaine and the extract (25 mg/ml and 100 mg/ml) were prepared with distilled water and 0.2 ml each of 0.3 mg/ml and 1.0 mg/ml of xylocaine were injected intradermally in the right thoracic and left lumbar shaved regions respectively to form wheels which were encircled with a marker. Likewise, 0.2 ml each of 25 mg/ml and 100 mg/ml of the extract were injected intradermally in the shaved right lumbar and left thoracic regions respectively to form wheels which were also encircled with a marker. The encircled regions were each pricked with a needle 10 times at 5 min interval for 30 min starting at zero (0) time which was before injection of the drug or extract. The number of responses to pain or twiches by the rabbits when pricked with needle was recorded. The responses at the site of the injection indicate the degree of anaesthesia, which is expressed as the number of negative responses, i.e. of failure to twitch.

Results

Plant extraction

The ethanol extract of *F. thonningi* stembark was amber in colour. The yield of the extract was 7.4% w/w.

Acute toxicity

The stembark extract of *F. thionningi* produced behavioural sedation and induced sleep in treated rats at the dose of 400 mg/kg and above. The extract produced dose-related deaths (0/5, 200 mg/kg; 0/5, 400 mg/kg; 2/5, 800 mg/kg; 3/5, 1600 mg/kg and 5/5, 32000 mg/kg) in rats. Signs observed before death were loss of appetite, paralysis of hindlimbs, which progressed to forelimbs, sternal recumbency, difficulty in respiration, coma and death. Mortality was recorded 7.4 h after treatment of rats that received the highest dose (3200 mg/kg) of the extract. The intraperitoneal LD50 was calculated to be 1440 mg/kg.

Effect on thiopental on sleep

The stembark extract appeared to increase the sleeping time of thiopental although not dose dependently (Table 1). The time lapse between dosing with thiopental and induction of sleep decreased with administration doses of the extract.

Table 1: Effect of *F. thonningi* stembark extract on onset and duration of thiopental* sleep in rats

Treatment group	Dose of extract (mg/kg)	Onset of sleep (min) (mean ± SD)	Duration of sleep (min) (mean ± SD)
A	50	3.9 ± 1.3b	62.1 ± 7.8c
B	100	3.4 ± 0.8b	56.8 ± 6.6b
C	200	2.8 ± 1.2b	66.4 ± 5.6c
D	400	1.4 ± 0.5c	78.2 ± 10.1c
E	0	5.1 ± 1.8a	18.5 ± 4.2a

Effect on muscle relaxation

The stembark extract produced some muscle relaxation in rats in various treatment groups (Table 2). The muscle relaxation appeared to be dose-dependent.

Table 2: Effect of *F. thonningi* stembark on muscle relaxation in rats.

Group	Dose of extract (mg/kg)	Percentage that showed muscle relaxation in the inclined board test
A	100	40
B	200	60
C	400	80

Effect on pentylenetetrazole and strychnine-induced convulsions

The stembark extract provided 80% protection to rats against pentylenetetrazole-induced convulsions, and produced 20% protection in rats treated with a convulsive dose of strychnine (Table 3). The mean onset of convulsions were increased by 29.6% and 57.4% by the extract in pentylenetetrazole and strychnine-treated rats, respectively. The mean time lapse between convulsion and death was increased by

Table 3. The effect of *F. thonningi* stembark extract on strychnine and pentylenetetrazole-induced convulsions

Extract pretreatment (mg/kg i. p)	Convulsant treatment	Mean onset of convulsion (min)	Mean onset of death (min)	Quantal death	Survival (%)
-	Leptazole (100 mg/kg s. c)	7.1 ± 0.25^{b}	15.7 ± 0.35^{a}	$^{5}/_{5}$	0
400 mg/kg*	Leptazole (100 mg/kg s. c)	9.2 ± 0.76^{c}	23.5^{b}	$^{1}/_{5}$	80
-	Strychnine (2 mg/kg i. p)	5.4 ± 0.93^{a}	16.7 ± 4.60^{a}	$^{5}/_{5}$	0
400 mg/kg	Strychnine (2 mg/kg i. p)	8.5 ± 0.50^{c}	28.3 ± 0.64^{c}	$^{4}/_{5}$	20

[a, b, c] Columns with different superscripts are significantly ($p<0.05$) different from each other (ANOVA)

*Only one rat died in this group

Table 4. The local anaesthetic effect of the *F. thonningi* stembark extracts in rabbits

Drug	Concentration (mg/ml)	Number of negative* responses over time (min)							Total out of 60	Percentage anaesthetized
		0	5	10	15	20	25	30		
Xylocaine	0.3	0	10	6	4	0	0	0	20	33.3
	1.0	0	10	10	9	8	7	5	49	82.6
F. thonningi	25	0	10	7	3	2	0	0	22	36.7
	100	0	10	10	10	3	3	2	38	63.3

* = Negative responses indicate failure to twitch
10 = Maximum anaesthesia
0 = No anaesthesia

49.7% in leptazole-treated rats and by 68.9% in strychnine-treated rats after treatment with the stembark extract. All the rats in the control groups (pentylenetetrazole and strychnine-treated rats) died.

Effect on local anaesthesia

The stembark extract produced local anaesthetic effects on rabbits into which it was injected intradermally. It showed 36.7% and 63.3% local anaesthetic effect at 25 mg/ml and 100 mg/mlrespectively, while xylocaine at 0.3 and 1.0 mg/ml showed 33.3% and 82.6% anaesthesia, respectively (Table 4). The local anaesthetic effect commenced 5 min after the extract was injected just as observed for xylocaine.

Discussion

Acute toxicity study of *F. thonningi* stembark showed that it produced mortality in experimental rats at high doses with an intraperitoneal LD50 of 1440 mg/kg. This is an indication of low toxicity. Substances with LD50 of 1000 mg/kg are classified as having low toxicity [16].

The ethanol extract of the stembark of *Ficus thonningi* showed depressant effects on both the peripheral and central nervous system.

The peripheral action of the extract was observed as local anaesthesia in rabbits. The local anaesthetic effect commenced five minutes after the extract was injected intradermally, just as was observed for xylocaine and the effect was still felt after 30 minutes (Table 4) with the concentration of 100 mg/ml of the extract. The local anaesthetic effect of the extract was, therefore, prolonged.

The central action of the stembark extract was demonstrated by its effects on thiopental sleeping time, strychnine and pentylenetetrazole-induced convulsions, and muscle relaxant activity. The extract appeared to have an additive effect with thiopental on sleep. It also showed that the extract had a depressant or sedative action on the central nervous system. This might explain why the traditional healers use the decoction from the plant for the treatment of psychiatric cases. Rats treated with 400 mg/kg and above of the stembark extract even went to sleep. The central depressant action of the extract was also demonstrated by the significant (80%) protection it conferred on rats treated with convulsive dose of pentylenetetrazole, inducing an anticonvulsant activity. The inablity of the extract to significantly protect rats treated with convulsive dose of strychnine may suggest a specific mechanism of action. Pentylenetetrazole acts on the brain stem selectively to augument its descending influences (medullary stimulant), while strychnine normally facilitate multi-synaptic reflexes [17]. It also suggests that the stembark extract acts differently from thiopental sodium which is a barbiturate and normally barbiturates are used to treat animals poisoned with strychnine. In addition, the extract possessed muscle relaxant activity as shown by its effect on the inclined board test, which can evaluate muscle relaxant activity [18].

The present work did not include identification of the active principles and its mechanism of action. This will be the subject of future work.

In conclusion, the ethanol stembark extract of *F. thionningi* induced significant depressant effects on both the peripheral and central nervous systems. Its effect on thiopental-induced sleep was additive and it induced anticonvulsant activity and produced muscle relaxant effect in rats.

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