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Central Effects of the Constituents of *Mimosa opthalmocentra* Mart. ex Benth.

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SUMMARY. A fraction containing the total alkaloids (FTA) of the plant *Mimosa opthalmocentra* Mart. ex Benth. 50 and 100 mg/kg, i.p. and N,N,- Dimethyltryptamine (DMT), one of the compounds isolated, at 32, 64 and 128 mg/kg, i.p. produced the "5HT behavioral syndrome" in rats. Another substance isolated from the plant, *hordenin*, had no such effect. Pretreatment with ketanserin (10 mg/kg) inhibited all the behavioral syndrome elicited by FTA (100 mg/kg) and DMT (64 mg/kg) suggesting an action of the agents on 5HT2 receptors subtype in rat brain.

RESUMEN. "Efectos Centrales de los Constituyentes de *Mimosa opthalmocentra* Mart. ex Benth.". La fracción conteniendo los alcaloides totales (FTA) obtenidos de *Mimosa opthalmocentra* Mart. ex Benth. en dosis de 50 y 100 mg/kg por vía intraperitoneal (v. ip.) y N, N- Dimetiltriptamina (DMT) en dosis de 32, 64 y 128 mg/kg (v. ip.) produjo, en ratones, el "síndrome serotonérgico". En el caso de hordenina, el otro compuesto obtenido de *M. Opthalmocentra*, no mostró diferencias significativas en relación a los animals del grupo utilizado como control. En los ratones tratados con quetanserina (10 mg/kg) se observó un efecto inhibitorio del síndrome producido por medio del tratamiento con DMT y FTA. En conclusión, este efecto puede estar relacionado con la acción sobre los receptores 5 HT_2 en cerebro de ratones.

INTRODUCTION

Mimosa opthalmocentra Mart. ex Benth. is a plant which belongs to the Mimosaceae family and is popularly known as "Jurema Preta". The plant is widely spread througout the North-East of Brazil, and is used in mystico-religious cerimonies and also in folk-medicine as an antiseptic and anti inflammatory [1]. Since some Mimosaceae species demonstrate hallucinogenic activity, it was thought worthwhile to evaluate the central effects of this plant.

The purpose of this study consisted of an evaluation of the effects of a fraction containing total alkaloids (FTA), and of N,N, Dimethyl-tryptamine (DMT) and hordenine (HRD) obtained from the stem bark of *M. opthalmocentra*.

KEY WORDS: *Mimosa opthalmocentra*, Central activity, Alkaloids.
PALABRAS CLAVE: Mimosa opthalmocentra, Actividad central, Alcaloides.

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Materials and methods

Animals

Male Wistar rats wighing 250-300 g and male Swiss mice weighing 25-35 g were used throughout this study. The animals were randomly housed in appropriate cages at 25 ± 2 °C on a 12 h light/dak cycle (ligts on 06:00-18:00) with free acess to food (purina) and water. They were used in groups of ten animals each.

Plant material

M. ophthalmocentra was collected near the city of Soledade, State of Paraiba, Brazil, in july 1991 by Prof. Maria de Fátima Agra (Setor de Botânica/LTF, Universidade Federal da Paraíba, Brazil). The chemical study was carried out using the stem bark. From the chloroform extract of the bark was obtained a fraction containing total alkaloids (FTA). From this, two indole alkaloids and a phenolic amine were isolated. The infrared ^{1}H, ^{13}C NMR and mass spectra elucidated the structures of these compounds, viz., N, N-dimethyl-tryptamine (DMT); N Methyl-tryptamine (NMT) and hordenine (HRD).

Lethal dose 50%

The acute toxicity, LD50 dose in mice and rats, i.p., was determined according to Litchfield and Wilcoxon [2].

5 HT behavioral syndrome

This syndrome consist of behavioral patterns such as resting tremor, hypertonus, reciprocal forepaw treading, hindlimb abduction, Straub tail, lateral head weaving, head shaking, hyperreactivity, hyperactivity, and salivation. If 4 of the above symptoms were present these were scored on a 0-3 scale (0: absent, 1: weak, 2: medium, and 3: maximal)[3].

Groups of ten rats were dosed intraperitoneally i.p. with varying doses of DMT (8, 16, 32, 64 and 128 mg/kg), FTA (12.5, 25, 50 and 100 mg/kg) or hordenine (20 and 40 mg/kg). Controls groups in each experiment received saline in a dose of 0.1 ml/100 g, i.p.

Following the drug applications the animals were put into the separate cages, continuously observed for 120 min and their behavior was recorded.

When antagonists methysergide, ketanserin, cyproheptadine or mianserin were used, there were injected in a dose of 10 mg/kg, i.p. 60 min prior to the injection of DMT (64 mg/kg, i.p) or FTA (100 mg/kg, i.p).

RESULTS AND DISCUSSION

In the first experiment the LD50 values (95% confidence range) by i.p route were determined in rats and mice treated with FTA, DMT or HRD (Table 1).

Table 2 shows that DMT and FTA treatment led to the appearance of the serotonergic syndrome. The behaviour occurred in a dose-dependent manner, after injections DMT (32, 64 and 128 mg/kg) or FTA (50 and 100 mg/kg). Hordenine treatment had no specific effect on this experimental model. Hind limb abdução, tremor and hypertonus were the most prominents signs observed at all developmental stages studied. The effects of 5 HT antagonists on serotonergic syndrom

Animals	Treatment	Lethal dose 50% (LD50) (95% confidence range mg/kg, i.p.)
MICE	FTA	87 (72-102)
	DMT	128 (104-152)
	HRD	> 100
RATS	FTA	92 (83-101)
	DMT	89 (77-101)
	HRD	> 100

Table 1. Acute toxicity of FTA and two of the substances isolated (DMT and HRD) from *Mimosa ophtalmocentra* stem bark in mice and rats. FTA: Fraction Total Alkaloids, DMT: Dimethyltryptamine, HRD: Hordenine

Treatment	Behaviour						
	Hind limb abduction	Tremor	Fore paw treading	Hypertonus	Head twitches	Straub tail	Hiperactivity
Control Solution	0	0	0	0	0	0	0
FTA							
8	1	0	0	0	0	0	0
16	2	1	0	0	0	0	1
32	2*	2*	0	2*	1	1	2*
64	3*	3*	1	3*	2*	2*	2*
128	3*	3*	1	3*	2*	2*	2*
Control Solution	0	0	0	0	0	0	0
DMT							
12.5	1	1	0	0	0	0	0
25	2	2	0	1	0	0	0
50	2*	2*	0	2*	1	0	1
100	3*	3*	0	3*	1	1	2*

Table 2. Serotonin syndrome elicited by DMT and FTA in rats. N = 10. * = Significant ($p < 0.05$) change from control.FTA: Fraction Total Alkaloids. DMT: Dimethyltryptamine

Behavioural serotonin syndrome	Pre-treatment				
	Control solution (0.1 ml/100 g)	Methysergide (10)	Ketanserin (10)	Cyproheptadine (10)	Mianserin (10)
Tremor	+	+	-	-	-
Hind Limb Abduction	+	+	-	+	-
Hypotonus	+	+	-	+	+
Hyperactivity	+	+	-	+	+

Table 3. Inhibition of DMT induced serotonin syndrome by Ketanserin pre-treatment in rats.
* = Statistically significant differences from control ($p < 0.05$) N = 10 - = No effect.
+ = Effect present

produced by DMT (64 mg/kg) or FTA (100 mg/kg) are shown in Table 3. Only pretreatment with ketanserin, a 5-HT2 antagonist markedly inhibited all the behaviours. With the possible exception of the hyperactivity component, the syndrome observed in rats following a variety of serotonergic manipulation represents a "pure" or specific behavioural reflection on central serotonergic activity [4]. In radioligand binding studies utilizing rat membrane preparations a correlation was initially found between hallucinogen 5 HT_2 receptor affinity for ^{3}H-Ketanserin binding and human hallucinogenic potency which suggests that their pharmacological properties are mediated through stimulation of these receptors [5,6]. In conclusion, both FTA and DMT from *M. opthalmocentra* presented 5-HT syndrome which may be related to an action on 5-HT receptor subtype in rat brain. These effects may account for the hallucinogenic action of the plant in humans.

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