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Neuropsychopharmacological Effects of Leaves and Seeds Extracts of *Datura fastuosa*

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Abstract: Neuropsychopharmacological effects of aqueous extracts of leaves and seeds of *Datura fastuosa* (*D. fastuosa*), a solanaceae recently introduced in Congo as ornamental plant, were studied in rat and mice by oral administration using classical methods. Results revealed that extracts of *D. fastuosa* were well tolerated by rats. No mortality was observed until 3200 mg kg^{-1}. The doses of 400 and 800 mg kg^{-1} of leaves and seeds extracts increased motor activity, reduced slightly the duration of barbituric sleeping, antagonized catalepsy and ptosis induced by haloperidol and the immobility induced by forced swimming. *D. fastuosa* exhibited analgesic effect in acetic acid test with tolerance phenomenon in the leaves but not in the seeds extracts. Only the leaves extract reduced rectal temperature, apomorphin hypothermia and increased water drinking.Those results showed that, at the low doses, *D. fastuosa* has some antidepressant profile.

Keywords: *Datura fastuosa,* aqueousextract, leaves, seeds, neuropsychopharmacology

INTRODUCTION

Datura fastuosa (*D. fastuosa*) is a solanaceae, recently introduced in Congo with a large ornamental use. The Datura genus is known for anti-asthmatic, sedative and anti-rheumatismal properties[1]. Datura are also largely used for their psychodysleptic properties. In Congo, some informations have been reported about the using of *D. fastuosa* by population for hallucinogen and onirogen effects which recall those reported by literature with others Datura species[1-4].

Purpose of this study is to evaluate the neuropsychopharmacological effects of *D. fastuosa* in rat and mice by using classical methods.

MATERIALS AND METHODS

Animals: Wistar rats and albino mice of either sex, weighing, respectively between 150-200 g and 20-30 g maintained in standard environmental conditions and fed with standard laboratory diet and water ad libitum, were used.

Plant material: *D. fastuosa* collected in march 2002 in Brazzaville was identified by the botanist of the Center of Study on Vegetal Resources (Dr Felix KOUBOUANA). 1 g of leaves and seeds, respectively were dried at the room temperature for about one week and pounded. The powders were dissolved in distilled water to obtain the solutions of 1% (w/v). These solutions would be administered orally to rats or mice at different doses.

Toxicity study: 200, 400, 800, 1600 and 3200 mg kg^{-1} of leaves or seed extracts were administered to rats. Mortality was noted after 24, 48 and 72 h.

Effects of *D. fastuosa* on spontaneous motor activity: Motor activity is evaluated by using a slight modification of method of Martin *et al.*[5].

Briefly, 6 groups of rats received orally, respectively distilled water (0.5 ml kg^{-1}), haloperidol 5 mg kg^{-1}, extracts of leaves and seeds of *D. fastuosa* at the doses of 400 and 800 mg kg^{-1}. Sisty minutes after drugs administration, animals were submitted to spontaneous motor activity in a cage constituted by 50 squares. Number of squares

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crossed by animal with the four paws in 10 min. determined motor activity.

Effects of *D. fastuosa* on barbituric sleeping: After oral administration of distilled water, haloperidol and extracts of *D. fastuosa* at the doses above mentioned, pentobarbital (50 mg kg^{-1}) was injected intraperitonealy. Threshold and duration of sleeping were determined as described previously[6].

Effects of *D. fastuosa* on rectal temperature: 60 minutes after administration of extracts of *D. fastuosa*, rectal temperature was determined.

Effects on apomorphin stereotypies: 60 minutes after administration of extracts of *D. Fastuosa*, intensity of stereotypies induced by s.c injection of apomorphin (1 mg kg^{-1}) was evaluated during 60 minutes by using Shibuya *et al*. Method[7].

Effects on apomorphin hypothermia: Six groups of rats received orally respectively distilled water, clomipramin (16 mg kg^{-1}), extracts of *D. fastuosa* (400 and 800 mg kg^{-1}). Sixty minutes after drugs administration, apomorphin (16 mg kg^{-1}) was s.c. injected and the rectal temperature was measured during 4 h.

Effect on catalepsy and ptosis induced by haloperidol: sixty minutes after drugs administration, catalepsy and ptosis were evaluated by using Assis *et al*.[8] Method. The reaction time on horizontal metallic bar and ptosis intensity were determined during 4 h after i.p.injection of haloperidol (5 mg kg^{-1}).

Effect on immobility induced by forced swimming: Sixty minutes after oral administration of distilled water, clomipramin (16 mg kg^{-1}), leaves and seeds extracts of *D. fastuosa* (400 and 800 mg kg^{-1}), animals were submitted to forced swimming and the duration of immobility was determined for 3 min.

Study of an eventual tolerance on analgesic effect: 3 groups of mice received, respectively distilled water and Datura extracts (800 mg kg^{-1}) during 21 days. On the 7th,14th and 21th days, acetic acid (0,6%,10 ml kg^{-1}) were i.p. injected and writhing syndrom studied[9].

Effect on water consumption: Six groups of rats received orally, respectively distilled water, scopolamine 0.5 mg kg^{-1}, extracts of *D. fastuosa* 400 and 800 mg kg^{-1} 60 minutes after drugs administration, a feeding-bottle containing 200 ml of water was placed on the animal cage and the water consumption determined for 30 min.

Statistically analysis: All results were expressed as mean±SE. Statistical analysis was realized by using the Dunnett's test.

RESULTS

Toxicity: No mortality was observed 24, 48, 72 h after administration of leaves or seeds extracts of *D. fastuosa* at the doses of 20, 400, 800, 1600 and 3200 mg kg^{-1}.

Spontaneous motor activity: Results of the effects of *D. fastuosa* on spontaneous motor activity are presented in Table 1. Leaves extract at the two doses and seeds extract (800 mg kg^{-1}), increased significantly ($P < 0.01$), motor activity wchich is reduced by haloperidol ($P < 0.01$).

Rectal temperature: Only the doses of 800 mg kg^{-1} of leaves and seeds extracts of *D. fastuosa* reduced significantly the rectal temperature (Table 2).

Effect on barbituric sleeping: Only the threshold of barbituric sleeping (but not the duration) was significantly increased by Datura extracts (Table 3).

Table 1: Effects of *Datura fastuosa* on spontaneous motor activity

Products		Doses ml or mg kg^{-1}	Number of squares crossed
Control		5 ml kg^{-1}	131.20±20.60
Halopéridol		5 mg kg^{-1}	46.20±12.15 (***)
Datura fastuosa			
	Seeds	400 mg kg^{-1}	165.40±9.64
		800 mg kg^{-1}	232.80±12.69 (**)
	Leaves	400 mg kg^{-1}	266.00±12.69 (**)
		800 mg kg^{-1}	267.40±9.00 (***)

(n=5); **p< 0.01, ***p < 0.001 (comparing results with control)

Table 2: Effects of *Datura fastuosa* on rectal temperature

Products		Doses ml or mg kg^{-1}	Rectal Temperature (°c)
Control		5 ml kg^{-1}	37.28±0.11
Halopéridol		5 mg kg^{-1}	37.56±0.20
Datura fastuosa			
	Seeds	400 mg kg^{-1}	36.90±0.17
		800 mg kg^{-1}	36.72±0.14 (**)
	Leaves	400 mg kg^{-1}	36.89±0.65
		800 mg kg^{-1}	36.66±0.67 (**)

(n=5) ** p< 0.01 (comparing results with control)

Table 3: Effects of *Datura fastuosa* on barbituric sleeping

Products		Doses ml or mg kg^{-1}	Onset sleeping (min)	Duration of sleeping (min)
Control		5 ml kg^{-1}	3.00±0.31	102.00±10.05
Halopéridol		5 mg kg^{-1}	3.80±0.38	160.00±18.31 (**)
Datura fastuosa				
	Seeds	400 mg kg^{-1}	5.00±0.94 (*)	87.80±12.10
		800 mg kg^{-1}	4.20±0.37 (*)	84.80±13.02
	Leaves	400 mg kg^{-1}	6.20±0.58 (**)	82.40±14.73
		800 mg kg^{-1}	6.60±0.24 (**)	84.00±10.17

(n=5) *p < 0.01 (comparing results with control)

Table 4: Effects of *Datura fastuosa* on hypothermia induced by apomorphin

Products		Doses ml or mg kg^{-1}	Temperature (°C) 1h	2h	3h	4h
Control		5 ml kg^{-1}	34.98±0.30	35.02±0.51	36.02 ±0.28	36.62±0.14
Clomipranin		16 mg kg^{-1}	36.76±0.15 (**)	37.02±0.16(**)	37.28 ±0.23(**)	37.12±0.12(*)
Datura fastuosa	Seeds	400 mg kg^{-1}	34.66±0.14	35.80±0.43	35.68±0.33	35.74±0.43
		800 mg kg^{-1}	34.58±0.07	35.16±0.17	36.06±0.25	36.82±0.14
	Leaves	400 mg kg^{-1}	34.72±0.15	36.40±0.25 (*)	37.18±0.12 (*)	37.10±0.04 (**)
		800 mg kg^{-1}	34.60±0.08	35.90±0.19	36.98±0.20 (*)	37.32±0.06(**)

(n=5) p< 0.05; ***p < 0.001 (comparing results with control)

Table 5: Effects of *Datura fastuosa* on catalepsy induced by haloperidol

Products		Doses (ml or mg kg^{-1})	Temperature (°C) 30 min	60 min	90 min	120 min
Control		5 ml kg^{-1}	5.01±0.28	6.81±1.61	5.37±0.66	7.02±1.35
Clomipranin		16 mg kg^{-1}	0.27±0.04 (**)	0.28±0.04(**)	0.45 ±0.09(**)	0.34±0.08(**)
Datura fastuosa	Seeds	400 mg kg^{-1}	1.06±0.23(***)	0.85±0.07	0.81±0.06(***)	1.01±0.05(**)
		800 mg kg^{-1}	0.43±0.02(***)	0.45±0.06(**)	0.68±0.08(***)	0.60±0.07(**)
	Leaves	400 mg kg^{-1}	0.51±0.04(**)	0.53±0.08 (**)	0.52±0.06 (**)	0.61±0.05 (**)
		800 mg kg^{-1}	0.33±0.07(**)	0.43±0.10(**)	0.59±0.19 (**)	0.87±0.29 (**)

(n=5) **p <0.01; ***p <0.001 (comparing results with control)

Table 6: Effects of *Datura fastuosa* on ptosis induced by haloperidol

Products		Doses (ml or mg kg^{-1})	Temperature (°C) 15 min	30 min	60 min	90 min
Control		5 ml kg^{-1}	1.00±0.00	1.60±0.20	1.80 ±0.20	2.20±0.20
Clomipramin		16 mg kg^{-1}	0.00±0.00	0.00±0.00	0.00 ±0.00	0.00±0.00
Datura fastuosa	Seeds	400 mg kg^{-1}	0.20±0.20(*)	0.20±0.20(*)	0.40±0.24(**)	0.20±0.20(**)
		800 mg kg^{-1}	0.00±0.00	0.40±0.20(**)	0.40±0.20(**)	0.80±0.20(**)
	Leaves	400 mg kg^{-1}	0.00±0.00	0.00±0.00 (**)	0.00±0.00 (**)	0.00 ±0.00 (**)
		800 mg kg^{-1}	0.00±0.00	0.00±0.00(**)	0.00±0.00 (**)	0.00 ±0.00(**)

(n=5) *p <0.05, **p < 0.01 (comparing results with control)

Table 7: Effects of *Datura fastuosa* on immobility induced by forced swimming

Products		Doses (ml or mg kg^{-1})	Duration of immobility (s)
Control		5 ml kg^{-1}	103.75±6.49
Clomipramin		16 mg kg^{-1}	20.20±1.65 (***)
Datura fastuosa	Seeds	400 mg kg^{-1}	44.40±2.20 (**)
		800 mg kg^{-1}	41.40±2.25 (**)
	Leaves	400 mg kg^{-1}	45.56±5.54 (**)
		800 mg kg^{-1}	39.80±3.87 (**)

(n=5) **p < 0.01; ***p < 0.001 (comparing results with control),

Effect on apomorphin stereotypies: On the contrary of haloperidol, the Datura extracts did not modified apomorphin stereotypies.

Effect on apomorphin hypothermia: Table 4 presents effects of *D. fastuosa* on apomorphin hypothermia; only the leaves extract at the two doses antagonized (as clomipramin), apomorphin hypothermia.

Effect on catalepsy and ptosis induced by haloperidol: As clomipramin, *D. fastuosa* extracts antagonized significantly catalepsy and ptosis induced by haloperidol (Table 5 and 6).

Effect on immobility induced by forced swimming: As clomipramin, leaves and seeds extracts of *D. fastuosa* reduced significantly the duration of immobility induced by forced swimming (Table 7).

Study of an eventual tolerance on analgesic effect: Effects of leaves extract on acetic acid induced writhing syndrom were significantly reduced at the 21 day, when seeds extracts antagonized significantly the writhing at 7, 14 and 21 days (Table 8).

Effect on water consumption: Only the leaves extract increased significantly (as scopolamine) the water consumption (Table 9).

DISCUSSION

Many published studies have reported psychodysleptic properties of Datura genus in man[1-4] and in animal[10-11]. Those effects were attributed to central activity of tropane alkaloids, hyosciamine, scopolamine and atropine[4].

The present study which investigate neuropsychopharmacological effects of *D. fastuosa,* an ornamental plant recently introduced in Congo, show that those extracts are well tolerated by rat; until 3200 mg kg^{-1}, no mortality was observed. At the doses of 400 and

Table 8: Study of eventual tolerance of *Datura fastuosa*

Products		Doses (ml or mg kg^{-1})	Number of writhing movements D_0	D_7	D_{14}	D_{21}
Control		0.5 ml/20g	56.60±1.20	51.20 ±1.39	53.00±1.18	52.20±1.49
Datura fastuosa	Seeds	800 mg kg^{-1}	38.20±2.17(**)	35.00±1.67(**)	40.20±1.74(**)	39.20±0.89(**)
	Leaves	800 mg kg^{-1}	36.80±1.06(**)	37.20±1.73(**)	43.20±1.74(**)	52.00±0.81

(n=5) *p < 0.05; **p< 0.01 (comparing results with control)

Table 9: Effects of *Datura fastuosa* on water consumption

Products		Doses (ml or mg kg^{-1})	Volume of water consumpted (ml)
Control		5 ml kg^{-1}	2.80±0.48
Scopolamine		0.5 mg kg^{-1}	6.20±0.58 (**)
Datura fastuosa	Seeds	400 mg kg^{-1}	4.00±2.20
		800 mg kg^{-1}	3.80±0.37
	Leaves	400 mg kg^{-1}	5.40±0.74 (*)
		800 mg kg^{-1}	6.60±0.60 (**)

(n=5) *p < 0.05, **p < 0.01 (comparing results with control)

800 mg kg^{-1}, leaves and seeds extracts increased spontaneous motor activity, threshold of barbituric sleeping, with a slight reduction of the duration of this sleeping. In opposite of haloperidol, extracts reduced rectal temperature but did not modified apomorphin stereotypies wchich are classically antagonized by neuroleptics[12-13].

As clomipramin, antidepressant used as reference substance, extracts of Datura reduced apomorphin hypothermia, catalepsy and ptosis induced by haloperidol and the duration of immobility in the forced swimming test. These results bring extracts of Datura to antidepressants. The similarity between extracts of *D. fastuosa* and antidepressants was also observed on analgesic effect. As antidepressants[14-15], extracts of leaves and seeds of *D. fastuosa* exhibited a significant analgesic activity on the two tests used. Nemmani *et al.*[16], Panocka Massi *et al.*[17], Schreiber *et al.*[18] shows interference between antidepressants and opioids receptors. As opioids[19] analgesic effect of leaves extracts (but not seeds extracts) manifest tolerance.

Finally, leaves extract (but not seeds extract) increased water consumption. This observation is in agreement with the mouth dryness reported with Datura alkaloids[20] and antidepressants[21-22].

The present study revealed that aqueous extract of *D. fastuosa,* a solanaceae known for its psychodysleptic effects, has at low doses, the psychopharmacological properties similar than those of antidepressant drugs and qualitative and quantitative different could be observed between leaves and seeds extracts. Further pharmacological and chemical studies are necessary to confirm these results.

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