Pharmaceutical Biology
1999, Vol. 37, No. 1, pp. 50–53

1388-0209/99/3701-0050$15.00

Isolation and Identification of Putative Hallucinogenic Constituents from the Roots of *Mimosa ophthalmocentra*

L.M. Batista[1], R.N. Almeida[2], E.V.L da-Cunha[2], M.S. da-Silva[2] and J.M. Barbosa-Filho[2]

[1]Laboratório de Farmácia e Biologia, Universidade Estadual da Paraíba, Campina Grande, Paraíba, Brazil
[2]Laboratório de Tecnologia Farmacêutica, Universidade Federal da Paraíba, João Pessoa, Paraíba, Brazil

ABSTRACT

A chemical investigation of the roots of Mimosa ophthalmocentra, *carried out in our laboratory, with the aim of monitoring the possible hallucinogenic activity, led to isolation and identification of three alkylamines* (N,N-*dimethyltryptamine*, N-*methyltryptamine and hordenine). The results explain the traditional use of this plant by several tribes in northeast Brazil to prepare a potent hallucinogenic drink in mystic-religious ceremonies.*

INTRODUCTION

The roots of *Mimosa ophthalmocentra* Mart. ex Benth. (Mimosaceae) are utilized in the hinterland of northeast of Brazil to prepare the "Wine of Jurema", a beverage used in mystic-religious ceremonies by several tribes, and as a traditional medicine for the treatment of wounds and for the prevention of inflammation (Lima, 1946; Agra,1977). Along with certain other *Mimosa* species, it bears the common name Jurema (*M. hostilis, M. nigra, M. jurema*), indicating that it is a "sensitive plant". The occurrence of tryptamine derivatives in these and other species has previously been reported (Lima, 1946; Gupta & Arias, 1979; Meckes-Laxoya & Lozoya, 1990; Moraes et al., 1990). Some years ago *N,N*-dimethyltryptamine (DMT) attracted the attention of several research workers by its hallucinogenic activity in man (Moussatché et al., 1970; Sai-Halász, 1962; Rosenberg et al., 1963).

The purpose of this paper is to report the isolation and identification of hallucinogenic constituents from the roots of *Mimosa ophthalmocentra*. No previous phytochemical investigations of this plant have been reported.

Keywords: Mimosa ophthalmocentra, Mimosaceae, *N,N*-dimethyltryptamine, *N*-methyltryptamine, hordenine, hallucinogenic activity, 5HT behavioral syndrome.

* Address correspondence to: Dr. J.M. Barbosa-Filho, Laboratório de Tecnologia Farmacêutica, Universidade Federal da Paraíba, 58051–970 João Pessoa, Paraíba, Brazil.

MATERIALS AND METHODS

Plant Material

Roots of *Mimosa ophthalmocentra* Mart. ex Benth. were collected in January 1996 at the Farm Pedro da Costa, 16 km from the city of Campina Grande, PB, Brazil and identified by M.F. Agra from the botany department of the Laboratorio de Tecnologia Farmaceutica. A voucher specimen (Agra 1131) is deposited in the Herbarium of the Universidade Federal da Paraíba.

Extraction Method

Dried ground roots (1000 g) were extracted with 80% ethanol at room temperature for 7 days. This extract (240 g), after being concentrated *in vacuo*, was dissolved in 3% hydrochloric acid, filtered and extracted several times with chloroform. The defatted aqueous acidic fraction was alkalinized with ammonium hydroxide to pH 9 and extracted again with chloroform. The $CHCl_3$ extract was washed with water, dried (Na_2SO_4) and the solvent evaporated to afford the total tertiary alkaloids (TTA, 30 g). This was chromatographed over a column of neutral alumina, using a gradient of hexane/chloroform/methanol. The fractions which showed hallucinogenic activity were purified by preparative TLC and three compounds were isolated.

Identification of Alkaloids

Spectroscopic analysis of the alkaloids (uv, ir, eims, ^1H and ^{13}C NMR) provided results in close agreement with published values for *N,N*-dimethyltryptamine (Moraes et al., 1990; Poupat et al., 1976), *N*-methyltryptamine (Moraes et al., 1990; Poupat et al., 1976) and hordenine (Srinivasan & Lichter, 1976; Kruger et al., 1977). Co-chromatography of these samples with standards gave the same spots for all three compounds. All reference standards were obtained from Sigma Chemical Company.

Experiments for Evaluation of Hallucinogenic Activity through Serotonergic Syndrome

The pharmacological study consisted of an evaluation of the effects of extracts, TTA, fractions and compounds from *Mimosa ophthalmocentra* on the central nervous system of rats. In the 5HT syndrome, behavioral patterns such as resting tremor, hypertonus, reciprocal forepaw treading, hindlimb abduction, Straub tail, lateral head weaving, head shaking, hyperreactivity, hyperactivity and salivation were observed. If three of the above symptoms were present, the syndrome was considered as present. Groups of ten rats were dosed intraperitoneally (i.p.) with different doses of extracts, TTA, fractions or compounds. Following administration of the drugs, the animals were put into separate cages and observed for 120 min; their behavior was recorded (Batista & Almeida, 1997).

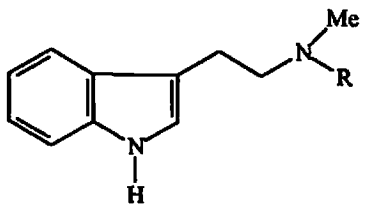
RESULTS AND DISCUSSION

Tryptamine and its derivatives with central effects commonly occur in *Mimosa* species. For this reason, chemical studies for the isolation of such alkaloids were guided by pharmacological monitoring of the hallucinogenic activity of the extract and fractions.

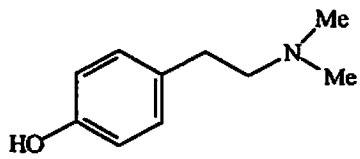
Hallucinogenic activity was considered present on the basis of the behavioural syndrome resulting in serotonergic central stimulation or the "Serotonergic Syndrome". This includes the following types of behavioral patterns: resting tremor, hypertonus, head shaking, hyperactivity, Straub tail, lateral head weaving, reciprocal forepaw treading and hindlimb abduction. The appearance of three of these symptoms was sufficient for the syndrome to be attributed.

The mechanism of action of the bioassay active response was suggested by pre-treatment of the group of experimental animals (rats) by antagonist serotonergic drugs. The use of only ketanserin, a $5HT_2$ antagonist, was sufficient to produce a complete block of the characteristic effects of the serotonergic syndrome. As a result, it is suggested that extracts, TTA, fractions and active compounds act at the $5HT_2$ receptor similar to other hallucinogenic drugs (Jacobs, 1976; Carline & Santos, 1981/1982).

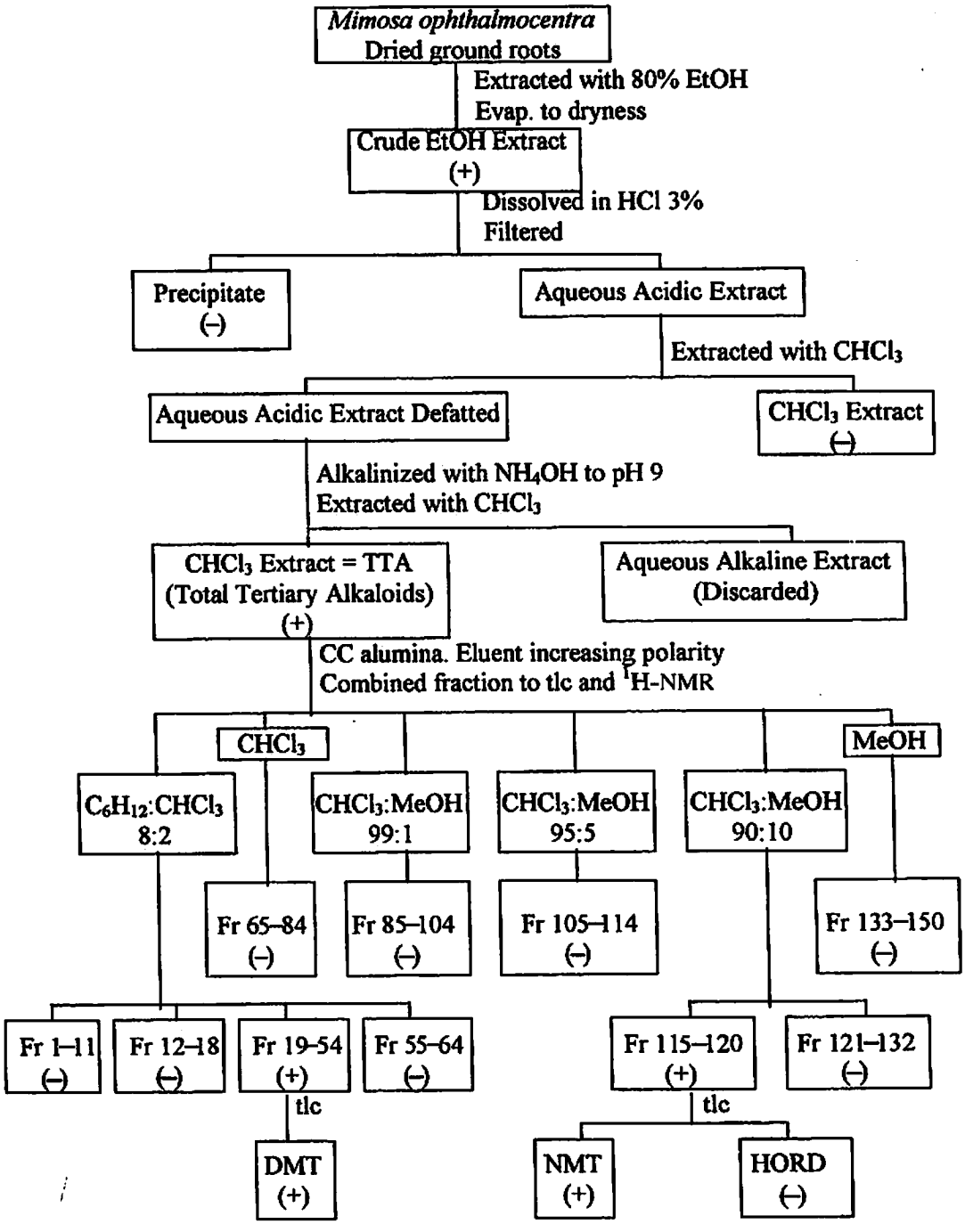
Initially, the hallucinogenic effect was observed when the crude ethanolic extract was tested in rats. This extract was subjected to acid/base partitioning and the total tertiary alkaloids (TTA) were found to have the highest pharmacological activity. The TTA were subjected to column chromatography on alumina using eluents of increasing polarity. A total of 150 frs. of ca. 75 ml each was collected and combined on basis of tlc and ^1H-NMR spectral data: C_6H_{12}:$CHCl_3$ 8:2 (Fr. 1–11, 12–18, 19–54, 55–64), $CHCl_3$ (Fr. 65–84), $CHCl_3$:MeOH 99:1 (Fr. 85–104), $CHCl_3$:MeOH 95:5 (Fr. 105–114), $CHCl_3$:MeOH 90:10 (Fr. 115–120, 121–132) and MeOH (Fr. 133–150). Evaporation of each fraction left a residue which was tested. The most hallucinogenic fractions (Fr. 19–54), and those with moderate activity (Fr. 115–120), were subjected to preparative tlc. Fractions 19–54 gave only *N,N*-dimethyltryptamine (DMT, 1600 mg; 1.6% of the plant material) and fractions 115–120 gave two compounds which were identified as *N*-methyltryptamine (NMT, 12 mg; 0.0012% of the plant material) and hordenine (HORD, 65 mg; 0.0065% of the plant material). All three compounds were evaluated, but only the indolalkylamine bases showed hallucinogenic activity, as illustrated in Scheme 1. Hordenine was inactive.



N,N-Dimethyltryptamine - R = Me
N-Methyltryptamine - R = H



Hordenine



Scheme 1. Fractionation procedure for the extracts obtained from *Mimosa ophthalmocentra* with hallucinogenic activity (+) or negative activity (−).

The hallucinogenic effect in man of *N,N*-dimethyltryptamine is well known. In general, it produces anxiety, colored hallucinations, distortion in perception, loss of space and time reality, and some delusional experience (Moussatché, 1970; Saí-Halász, 1962; Rosenberg et al., 1963). These effects appear within 15–30 min and subside within 1–2 h. The results described within explain the traditional use of this plant by several tribes in northeast Brazil to prepare a potent hallucinogenic drink in mystic-religious ceremonies.

ACKNOWLEDGEMENTS

The authors express their thanks to Professor Maria de Fátima Agra for her assistance in identifying the plant material, and to Gilvane Goes for collection of plant materials. This investigation was supported in part by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). In addition, we acknowledge the use of NAPRALERT - Program for Collaborative Research in the Pharmaceutical Sciences, College of Pharmacy, University of Illinois at Chicago, Chicago, IL.

REFERENCES

Agra MF (1977): *Farmacopéia Popular da Paraíba*. Funarte, Editora da UFPB, Paraíba, Brazil. p. 21.

Batista LM, Almeida RN. (1997): Central effects of the constituents of *Mimosa opthalmocentra* Mart. Ex Benth. *Acta Farm. Bonaerense 16:* 83–86.

Carlini EA, Santos R (1981/1982): Screening psicofarmacológico para detecção de atividade tipo alcalóides indólicos alucinogênicos em extratos de *Ipomoea cairica* e *Ipomoea tuberosa. Oréades 8*: 375–384.

Gupta MP, Arias TD (1979): The occurrence of tryptamine and *N*-methyltryptamine in *Mimosa somnians. J Nat Prod 42*: 234–236.

Jacobs BL (1976): An animal behaviour model for studing central serotonergic synapses. *Life Sci 19*: 777–786.

Kruger TL, Cooks RG, McLaughlin JL, Ranieri RL (1977): Identification of alkaloids in crude extracts by mass-analyzed ion kinetic energy spectrometry. *J Org Chem 42*: 4161–4162.

Lima OG (1946): Observações sobre o "vinho de Jurema" utilizado pelos índios Pancarú de Tacaratú. *Arq Inst Pesq Agron 4*: 49–80.

Meckes-Lozoya M, Lozoya X (1990): *N,N*-Dimethyltryptamine alkaloid in *Mimosa tenuiflora* bark (tepescohuite): *Arch Invest Méd (Méx): 21*: 175–177.

Moraes EHF, Alvarenga MA, Ferreira ZMGS (1990): As bases nitrogenadas de *Mimosa scabrella* Bentham. *Química Nova 13*: 308–309.

Moussatché H, Carlini EA, Santos, M (1970): Behavioral effects of *N,N*-dimethyltryptamine in rats and mice. *Revista Brasileira de Biologia 30*: 483–489.

Poupat C, Ahond A, Sévenet T (1976): Alkaloids of *Acacia simplifolia. Phytochemistry 15*: 2019–2020.

Rosenberg DE, Isbeel H, Miner EJ (1963): Comparison of a placebo, *N,N*-dimethyltryptamine, and 6-hydroxy-*N,N*-dimethyltryptamine in man. *Psychopharmacol 4*: 39–42.

Sai-Halász A (1962): The effect of antiserotonin on experimental psychosis induced by dimethyltryptamine. *Experientia 18*: 137–139.

Srinivasan PR, Lichter RL (1976): ^{13}C NMR spectral studies of arecoline, hordenine, strychnine and brucine. *Org Magn Reson 8*: 198–201.

Accepted: October 18, 1998