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Journal of Ethnopharmacology 54 (1996) 37–40

Journal of ETHNO-PHARMACOLOGY

Absence of alkaloids in *Psychotria carthagenensis* Jacq. (Rubiaceae)

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Received 15 September 1995; accepted 26 May 1996

Abstract

Psychotria viridis and *P. carthagenensis* are often discussed in relation to the hallucinogenic beverage *Ayahuasca*, used for religious, medicinal and social purposes. The significance of including *Psychotria* species in this beverage has been understood on the basis of substantial amounts of tryptamine alkaloids detected on leaves of both *P. viridis* and *P. carthagenensis*. Nevertheless, there is a long lasting debate over the identification of which *Psychotria* species are actually traditionally employed. We here report that a *P. carthagenensis* leaf ethanol extract was found to be devoid of alkaloids. The extract significantly decreased mice body temperature (350 and 500 mg/kg). Toxicity assessment revealed that the extract induced sedation and slight ptoses (75% of animals treated with 1000 mg/kg). Lethality was not observed within 48 h. The data indicate that *P. carthagenensis* does have bioactive compound(s), possibly active at the central nervous system, but unlikely to be tryptamine alkaloids as in the case of *P. viridis*. Therefore, if *P. carthagenensis* is indeed used by *ayahuasqueros*, its chemical and pharmacological significance have yet to be elucidated.

Keywords: Psychotria carthagenensis; Alkaloids: Toxicity

1. Introduction

Psychotria viridis Ruiz et Pav. and *P. carthagenensis* Jacq. are often spoken of in the literature in relation to the hallucinogenic beverage *Ayahuasca*, basically prepared from the bark of *Banisteriopsis caapi* (Spruce ex Griseb.) Morton (Malpighiaceae) (McKenna et al., 1984; Schultes and Rauffauf, 1990). The beverage is prepared by decoction and used for religious, medicinal and social purposes (Rivier and Lindgren, 1972; Luna, 1984; Schultes and Rauffauf, 1990; Liwszyc et al., 1992). Its use is widespread throughout the Amazon, where it is known as

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PII S0378-8741(96)01448-1

Ayahuasca in Peru, *Yagé* in Colombia, and in Brazil as *Caapi*, *Santo Daime* or *Daime*.

The significance of including *Psychotria* species in this beverage has been elucidated from the chemical and psychopharmacological points of view. *B. caapi* contains β-carbolines (in particular harmine, harmaline, and tetrahydroharmine), while the beverage also contains *N*,*N*-dimethyltryptamine (DMT). DMT, as well as other tryptamine derivatives, is a potent hallucinogen often found in several indigenous snuffs (Holmstedt and Lindgren, 1979). Nevertheless, DMT is inactive orally due to degradation by peripheral monoamine oxidase (MAO). The β-carbolines, however, have been shown to be highly active reversible inhibitors of MAO, as well as hallucinogenic when ingested in significant amounts. Moreover, these β-carbolines may protect DMT from peripheral MAO deamination, meriting DMT presence in a beverage prepared for oral use (McKenna et al., 1984; Schultes and Rauffauf, 1990). According to Rivier and Lindgren (1972), the analysis of leaves of both *P. viridis* and *P. carthagenensis* revealed substantial amounts of DMT and traces of *N*-monomethyltryptamine (MMT) and 2-methyl-1,2,3,4-tetrahydro-β-carboline (MTHC); the analysis of *B. caapi* revealed β-carbolines (harmine, harmaline and tetrahydroharmine) and, in addition, harmol and 6-methoxytryptamine (6-MeO-T).

McKenna et al. (1984) reported an interesting aspect of *Psychotria* folk taxonomy. Most *ayahuasqueros* identify the 'proper' *chacrunas* (vernacular term for *Psychotria*) suitable for inclusion in the mixture, as those possessing *espinas* (spines), tiny spine-like extensions of the mid-rib on the abaxial surface of the leaf. These appear to be slightly swollen glandular structures which may be equivalent to the 'dolmatia' found in some *Psychotria* spp. These tiny dolmatia-like structures were pointed out by the *ayahuasqueros* interviewed as the key taxonomic feature used to differentiate *true* and *false chacrunas*, the latter considered of no value for the beverage. Accordingly in their analysis, all of the *Psychotria viridis* samples that possessed these structures contained DMT. The single specimen which lacked these structures did not contain tryptamines, nor other alkaloids. McKenna et al. (1984) suggested that this specimen may correspond to *Psychotria carthagenensis*, although the collection was sterile and the identification therefore tentative.

This study provides additional chemical and pharmacological data on *Psychotria carthagenensis*, that may be useful in clarifying the long lasting debate concerning its chemical profile and use in the hallucinogenic beverage *Ayahuasca*.

2. Materials and methods

2.1. Plant material

P. carthagenensis Jacq. (Rubiaceae) was collected in Pedro Osório (RS, Brazil) and identified by Mr E.A. Salazar. A voucher specimen (ICN 98863) has been deposited at the herbarium of the Botany Department, University Federal do Rio Grande do Sul, Porto Alegre.

2.2. Preparation of extract

Dried (30°C) milled leaves (10 g) were extracted by reflux with 80% ethanol for 60 min and filtered through a Büchner funnel. The procedure was repeated, the resulting filtrates combined and concentrated under reduced pressure (40°C). The dried ethanol extract (2.9 g) was screened for alkaloids by precipitation tests with Draggendorf's, Bertrand's, Bouchadart's and Mayer's reagents (Costa, 1972; Matos, 1980).

2.3. Pharmacological evaluation

Male adult Swiss mice, 25–30 g (food and water 'ad libitum'), were used throughout the study.

2.3.1. Hypothermic effect

Protocols were based on Dalmmeier and Carlini (1981). Groups of four mice were treated (i.p.) with saline, Tween, or extract (100, 350 and 500 mg/kg). Body temperature, measured by inserting the sensor probe of a digital thermometer into the rectum (1 cm), was recorded before drug treatment (time 0) and 15, 30, 60 and 120 min after drug administration. Room temperature was

maintained at 22–24°C. Results were analyzed by means of two-way ANOVA followed by Duncan test.

2.4. Toxicity

Mice (4/dose) were treated (i.p.) with 1000 mg/kg of extract and observed over a 60-min period for intensity of spontaneous activity, reaction to touch and ptoses. Ptoses was graded according to the scale of Rubin et al. (1956). Lethality was recorded at 1, 24 and 48 h thereafter.

3. Results

The extract presented a negative reaction for alkaloids in all tests. The body temperature decreased significantly with 350 mg/kg and 500 mg/kg (Fig. 1). The toxicity assessment revealed that 75% of treated animals showed sedation and slight ptoses (not higher than 1 in a 0–4 scale). Lethality was not observed in 48 h.

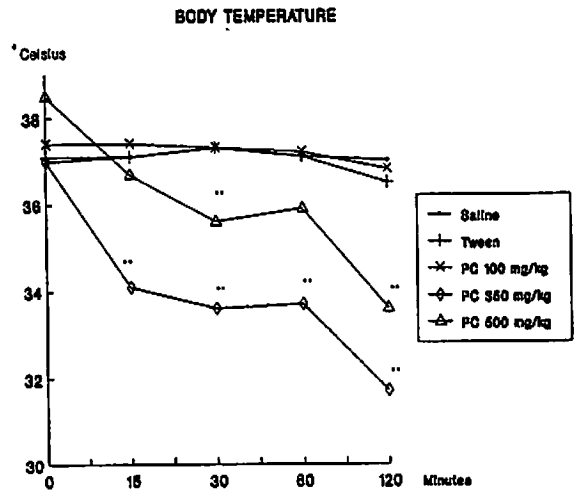

Fig. 1. Effects of *Psychotria carthagenensis* ethanol extract (PC) on body temperature. Extract diluted in Tween and administered i.p. Values expressed as mean °C. $^{*}P < 0.05$ and $^{**}P < 0.01$, ANOVA, compared to controls.

4. Discussion

The genus *Psychotria* is very closely allied to *Palicourea* (Rubiaceae) (Schultes and Rauffauf, 1990). Several species of *Psychotria* and *Palicourea* are reported as fairly to highly toxic, usually affecting cattle. Toxicological studies of *Palicourea marcgravii* St. Hill. demonstrated that the nervous system is the major organ affected (Górniak et al., 1989). The Makuna Indians do consider *Psychotria carthagenensis* as a toxic species (Schultes and Rauffauf, 1990). Our study showed that body temperature decreased after the administration of *P. carthagenensis* ethanol extract. The ability to decrease body temperature can be interpreted as an indication of central activity. In addition, the decrease in spontaneous activity and ptoses observed during toxicity evaluation are common to central nervous system depressors (Contar et al., 1985). Nevertheless, lethality was not observed even with higher doses.

In the search for analgesic compounds of natural origin, strong opioid-like analgesic activity was detected in alkaloids from *Psychotria colorata* (Willd. ex R. et S.) Muell. Arg., used by Amazonian caboclos (Brazil) as a pain killer (Elisabetsky et al., 1995). Following the combination of ethnopharmacology and chemotaxonomy in the quest for medically useful compounds, a broader screening was launched hoping to identify other *Psychotria* alkaloids with opioid-like activity. Interestingly enough, out of the six species of *Psychotria* native to and collected in the state of Rio Grande do Sul, only *P. carthagenensis* was devoid of alkaloids (Leal, 1994). The obvious difference in climate and other environmental conditions, in this case, does not seem to be the reason for absence of alkaloids. Several samples of *P. carthagenensis* collected in different regions of Rio Grande do Sul State and a sample brought from the Amazon Valley (State of Acre) were also devoid of alkaloids (Amélia Henriques, personal communication).

The data reported here indicate that *P. carthagenensis* does have bioactive compounds,

but these are unlikely to be tryptamine alkaloids as in the case of *P. viridis*. If *P. carthagenensis* is indeed selected and used by *ayahuasqueros*, its chemical and pharmacological significance have yet to be elucidated.

Acknowledgements

The authors wish to thank Enrique Araújo Salazar for collection and identification of botanical material and Ionara Siqueira and Luciane Costa-Campos for assistance in neurotoxicity tests. This work was supported by grants from CNPq, CAPES and PROPESP/UFRGS.

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