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Preliminary Investigation of the Central Nervous System Effects of 'Tira-capeta' (Removing the Devil), a Cigarette used by some Quilombolas living in Pantanal Wetlands of Brazil†

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During an ethnopharmacological survey carried out among some Quilombolas living in Brazil, 48 plants with possible central nervous system (CNS) action were cited. A mixture of nine plants, known as 'Tira-capeta' (Removing the Devil) cigarette, has been utilized for years as a tonic for the brain. The effects observed after consuming this cigarette are: dizziness, lightness sensation, humor changes, yawns, heavy eyes, hunger, sleep and relaxation. This study aimed to verify the effects of a hydroalcohol extract of 'Tira-capeta' cigarette (ETC), as well as to evaluate the phytochemical profile. The phytochemical screening carried out through characterization reactions, thin layer chromatography and high efficiency liquid chromatography indicated the presence of tannins, phenolic acids, flavonoids, saponins and alkaloids; tannins and phenolic acids being the principal constituents. The pharmacological tests showed that ETC induced a biphasic effect, with intense initial stimulation of the CNS, followed by a general depressor state; decreased the latency for sleeping and increased the total sleeping time (50, 100 and 500 mg/kg), without causing prejudice in motor coordination (doses up to 200 mg/kg); induced catalepsy in mice, verified 10 and 50 min after drug administration (500 mg/kg). Also, no anxiolytic or anxiogenic effects were verified in rats submitted to the elevated plus-maze.

Keywords: ethnopharmacology; Quilombolas; neuroleptic; smoke; central nervous system; medicinal plants.

INTRODUCTION

Despite the existence of 178 *Quilombolas* communities in different biomes in Brazil (Fundação Cultural Palmares, 2006), few ethnopharmacological surveys of *Quilombolas* (descendants of Afro-Brazilian runaway slaves) and/or Brazilian Afro-descendants have been conducted. Exceptions are the studies by Camargo (1988, 1998), Voeks (1997) and recently by Albuquerque (2001) and Rodrigues and Carlini (2004).

The use of a great number of plants in a single prescription is very common among the *Quilombola*'s therapeutic practice, being also observed among the river dwellers from the Brazilian Amazon (Amorozo and Gély, 1988; Amorozo, 1993; Rodrigues, 2006), in African Yorubas (Verger, 1996), also in Ayurveda and Chinese therapeutics (Jaggi, 1969; Patwardhan *et al.*, 2005). This practice may produce synergistic or antagonistic effects (Williamson, 2001; Gilbert and Alves, 2003).

During an ethnopharmacological survey conducted among the *Quilombolas* from Sesmaria Mata-Cavalos, Municipality of Nossa Senhora do Livramento, in the State of Mato Grosso, Brazil, healers mentioned 82 plants utilized for 55 disorders (Rodrigues and Carlini, 2003). Of these 82 plants, 48 possibly have some effect on the central nervous system (CNS) and are grouped in 13 categories of use (followed in parenthesis by the number of plants indicated for each category): tonics for the brain (11), sleep disorders (11), depuratives (10), weight control, either to reduce appetite, to produce weight gain or weight loss (7), hallucinogens (6), rejuvenators, which present three simultaneous effects: aphrodisiac, memory enhancing and depurative (4), analgesics (4), anxiolytics (4), head diseases, i.e. general mental disorders, without a clear definition (3), memory enhancers (2), social relationships, including dating, marriage or separation from the spouse (2), antidepressants (1) and tonics for the body (1) (Rodrigues and Carlini, 2004). Of the 11 plants of the

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† This paper is dedicated to the memory of Marcelo Lima Joaquim, who worked as a technician at the Department of Psychobiology, and whose unexpected death in November 2006 was deeply felt by those involved in this study. His contribution to the present study and his unlimited dedication to our group will always be acknowledged.

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category tonics for the brain, nine are used as a cigarette known as 'Tira-capeta' (Removing the Devil) and can be consumed both by the healer and by the patients, including children. It is recommended for persons suffering from nervous breakdown due to overwork, being also used by teenagers and children to improve their performance in learning abilities. The cigarette produces a pleasant aroma, since most of the plants are strongly aromatic.

The purpose of the present study was to carry out phytochemical and pharmacological studies with 'Tira-capeta' extract.

MATERIALS AND METHODS

Fieldwork. The fieldwork was conducted by one of the authors (E. Rodrigues) between 1998 and 2001, employing methods used in anthropology and botany. Informal interviews (Alexiades, 1996) were carried out with residents of Sesmaria Mata-Cavalos to determine to whom the people look for help in the case of illness. Four residents of Sesmaria were selected and participated in the interviews. The ethnopharmacological study was approved by the Ethics Committee of Universidade Federal de São Paulo (UNIFESP's Ethics Committee on Research n. 056/00) and residents of Sesmaria signed a written consent form to access *Quilombola* knowledge and botanical material. Samples of each plant mentioned by the interviewees were collected in compliance with methods recommended by Lipp (1989) and the plants were identified at the Botanical Institute of São Paulo (IB), where the vouchers were deposited. The phytochemical and pharmacological studies on animals were also approved by Ethics Committee on Research (n. 0147/07).

Botanical material. Parts of the nine plants used in the cigarette 'Tira-capeta' were collected in Sesmaria Mata-Cavalos by the researcher accompanied by one of the interviewees, the recently deceased spiritual and political leader, Mr Cezário. The leaves of the following plants [their respective vouchers] were collected: 'guiné' – *Petiveria alliacea* L. (Phytolaccaceae) [E. Rodrigues 823], 'eucalipto' – *Eucalyptus globulus* Labill. (Myrtaceae) [E. Rodrigues 525], 'alecrim-do-norte' – *Anemopaegma arvense* (Vell.) Stellfeld ex de Souza (Bignoniaceae) [E. Rodrigues 519], 'negramina' – *Siparuna guianensis* Aubl. (Monimiaceae) [E. Rodrigues 531], 'arruda' – *Ruta graveolens* L. (Rutaceae) and 'hortelã-da-várzea' – *Hyptis cana* Pohl ex Benth (Lamiaeae) [E. Rodrigues 530]. Also, the rhizomes of 'caiá-piá' – *Dorstenia asaroides* Hook. (Moraceae) [E. Rodrigues 878], the flowers of 'cravo-da-Índia' – *Syzygium aromaticum* (L.) Merr. & L. M. Perry (Myrtaceae) and finally, the skin of one bulb of garlic – *Allium sativum* L. (Liliaceae). After collection, the respective parts were cut in small pieces, mixed and exposed to the sun.

Preparation of the extract. The hydroalcohol extract of 'Tira-capeta' (ETC) was prepared by the turbolysis technique (Franco, 1990). Each 100 g of plant powder (ground in a grinding mill mesh 20) was extracted in 1000 mL of ethanol:water 50% (v/v). The extract was filtered with cotton and filter paper (weight 40 g/m^2), concentrated in a rota-evaporator and finally lyophilized. The dry extract was stocked in amber flasks (inside a desiccator in the refrigerator) and prepared fresh with distillated water at the time of the experiments.

Animals. Male Swiss albino mice (3–5 months, 35–50 g) and Wistar rats (3–5 months, 350–500 g), obtained from the Animal Facility of the Department of Psychobiology of UNIFESP were used. The animals were kept in a room under constant light/dark cycle of 12 h and controlled temperature (23 ± 2 °C); water and food were provided *ad libitum*, except during the testing period.

Drugs and administration. Haloperidol (Haldol®, Janssen-Cilag), sodium pentobarbital (Sigma) and diazepam (Compaz®, Cristália) were employed. All drugs (including ETC) were solubilized in distilled water and given at a volume of 10 mL/kg weight (mice) or 1 mL/kg (rats).

Phytochemical screening. The ETC was screened for alkaloids, phenolic acids, tannins, steroids, terpenoids, cardioactive glycosides, flavonoids, coumarins, saponins, lignans and iridoids following a classical thin layer chromatography (TLC) method (Stahl, 1969; Wagner, 1996; Harborne, 1998). The phytochemical screening, thin layer chromatography (TLC) and high performance liquid chromatography (HPLC) were carried out only to estimate which chemical classes prevailed in ETC, since the extract presents a mixture of parts from nine different plants. The gradient used as the mobile phase in reversed-phase HPLC was based on the publication by Jiang *et al.* (2006) with minor modifications.

Initial pharmacological screening. Groups of three mice each received ETC in doses of 10, 100 and 1000 mg/kg (oral) and 1, 10 and 100 mg/kg (i.p.) or water (controls) and were placed in wire cages for behavioral observation, according to Carlini (1972).

Pentobarbital induced sleeping time. Groups of 10 mice each received orally water (control) or ETC in doses of 50, 100 and 500 mg/kg, and after 1 h were administered with sodium pentobarbital (50 mg/kg, i.p.). The latency to sleep and the time between the loss and the recovery of the righting reflex were recorded (Mattei *et al.*, 1998).

Spontaneous motor activity. Groups of eight mice each received orally water (control) or ETC in doses of 50, 100 and 500 mg/kg. The animals were placed individually in boxes fitted with photoelectric cells immediately after the administration, and motor activity was cumulatively recorded at 10, 30, 60 and 90 min (Mendes *et al.*, 2002).

Motor coordination (rota-rod). Mice were previously selected on the rota-rod by their capacity to remain on the revolving bar (12 rpm) for 60 s, at least, in one of three trials. Groups of 10 animals each received orally water (control) or ETC in doses of 50, 100 and 200 mg/kg and were evaluated on the apparatus at 30 and 60 min after the administration, recording the time spent on the rod (maximum of 60 s) (Marques *et al.*, 2004).

Catalepsy test. Groups of 10 mice each received haloperidol (2.5 mg/kg, i.p.), ETC (50, 100 and 500 mg/kg, oral), or ETC 500 mg/kg (oral) plus haloperidol

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(2.5 mg/kg, i.p.). To measure catalepsy, the mice were placed with both forepaws on a horizontal glass bar located 5 cm above the floor. The total time the mice remained at the imposed position was recorded at 10–20 min and 50–60 min after the administration, according to Carlini *et al.* (1986), with small modifications.

Elevated plus-maze (EPM). Groups of 10 rats each received orally water (control), ETC in doses of 50, 100 and 200 mg/kg or diazepam (2.0 mg/kg, i.p.). After 45 min, the animals were placed on the EPM, being evaluated for 5 min with regard to the number of entrances in the open and closed arms and the time spent in each arm (Chacur *et al.*, 1999).

Statistical analysis. The initial pharmacological screening was analysed qualitatively. The results of motor coordination and catalepsy tests were analysed using the Kruskal–Wallis test, followed by Mann–Whitney. Data from the remaining tests were analysed by one-way analysis of variance (ANOVA), followed by the Duncan multiple range test. The results were expressed as mean ± SEM. The analysis were made using Statistica® program; the level of significance was set at $p < 0.05$.

RESULTS

Ethnopharmacological data

Although the main use of the 'Tira-capeta' cigarette is as a tonic for the brain, it also produces other pharmacological effects, according to the interviewees, being used against sinusitis, gastrointestinal and sleep problems and to diminish the use of cannabis. Cigarettes are also smoked by people suffering from nervous breakdown caused by overwork and are also used by children and teenagers to improve learning abilities at school, or to avoid cold. Therefore, we understand that the plants used in the cigarette can belong to more than one category of use, cited in Introduction section, such as tonics for the brain, sleep disorders and memory enhancers.

Mr Cezário's grandmother was an Indian who used to utilize this cigarette in her patients when Cezário was a child and at that time, he observed her practice. According to him, she used to exhale the cigarette's smoke over the patients in order to calm them down. Moreover, he explained that nobody could consume more than three cigarettes per day (nearly 1 g per cigarette) since it could produce aggressive behavior.

According to some consumers, while smoking a small cigarette, the immediate dizziness; lightness sensation, head rolling round, from one side to the other, laughing or crying (depending on the mood). These feelings lasted for a few minutes after finishing the cigarette. Next, the consumers yawned a lot and their eyes got heavy (ptosis), followed by a relaxed and sleepy sensation.

Mr Cezário explained that the main plant responsible for the effect of 'Tira-capeta' is 'caiá-piá' (*Dorstenia asaroides*); thus, if smoked alone, its effects could be more intense compared with a cigarette composed of the nine plants.

Phytochemical screening

The phytochemical analyses of ETC indicated the presence of tannins, phenolic acids, flavonoids, saponins and alkaloids. The analyses obtained by HPLC 'fingerprint', using a wavelength of 270 nm for the detection of different chemical markers, showed that the main constituents exhibited retention times of 9.86 and 11.91 min, which when compared with standards, such as tannic acid, analysed in the same chromatographic conditions, indicated the presence of tannins (data not shown). The presence of flavonoids glycosides at 19.62 and 21.83 min and the flavonoids aglycones at 30.34, 33.11 and 38.84 min were also verified in ETC, by the HPLC analyses. The alkaloids appeared in low concentrations in both TLC and HPLC analyses (data not shown).

Initial pharmacological screening

Mice treated with ETC at doses of 100 and 1000 mg/kg (oral) or 100 mg/kg (i.p.) showed severe seizures and tremors beginning 3 to 10 min after drug administration. Also, during this period Straub tail was observed in almost all doses tested, followed by a decrease in motor activity. After the seizure, many animals showed ataxia, ptosis and remained lying on the floor. No deaths were recorded.

Pentobarbital induced sleeping time

The oral administration of ETC significantly diminished the latency and increased the sleeping time induced by pentobarbital, when compared with the control group ($p < 0.05$) (Fig. 1).

Spontaneous motor activity

Table 1 shows the motor activity observed after oral administration of different doses of ETC. A significant

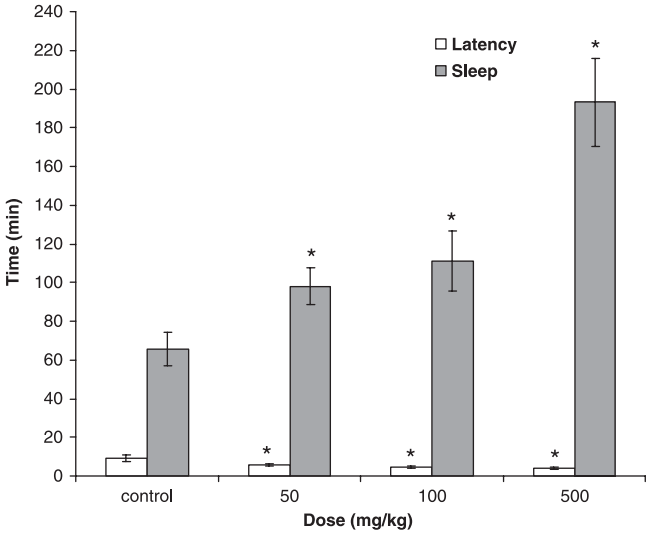

Figure 1. Effect of ETC administration on the latency to sleep and sleeping time (min) induced by pentobarbital (50 mg/kg). Data are presented as mean ± SEM ($n = 10$). * $p < 0.05$ compared with control group, ANOVA/Duncan.

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Table 1. Effect of ETC administration on the locomotor activity of mice. Data show the number of photoelectric beam interruptions at 10, 30, 60 and 90 min after drug administration (mean ± SEM, $n = 8$)

Group	Dose (mg/kg)	Time of observation			
		10 min	30 min	60 min	90 min
Control	–	1564 ± 101	2814 ± 248	4549 ± 492	5929 ± 757
ETC	50	1194 ± 120[a]	1933 ± 207[a]	2669 ± 378[a]	3472 ± 457[a]
ETC	100	1147 ± 94[a]	1939 ± 190[a]	3025 ± 357[a]	3526 ± 423[a]
ETC	500	475 ± 155[a]	593 ± 220[a]	719 ± 273[a]	1005 ± 323[a]

[a] $p < 0.05$ compared with control group, ANOVA/Duncan.

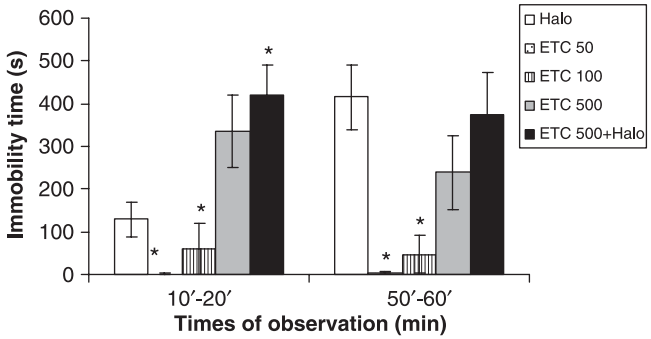

Figure 2. Effect of ETC administration, haloperidol (2.5 mg/kg) or ETC + haloperidol on the immobility time (s) of mice in the catalepsy test. Data are presented as mean ± SEM of 10 animals group. * $p < 0.05$ compared with control group, Kruskal–Wallis/Mann–Whitney.

reduction ($p < 0.05$) of motor activity was obtained with all doses utilized, at different periods of time, when compared with the control group.

Motor coordination (rota-rod)

Treatment of mice with doses of 50 to 200 mg/kg of ETC did not alter motor coordination in the rota-rod apparatus, when compared with the control group (data not shown).

Catalepsy test

Data shown in Fig. 2 reveal that the administration of ETC in doses of 50 and 100 mg/kg did not induce catalepsy in mice, whereas 500 mg/kg did. It is interesting to note that 10 min after drug administration, the catalepsy induced by ETC (500 mg/kg) plus haloperidol was higher than that produced by haloperidol alone ($p < 0.05$). This association produced a small increase in the immobility time 10 min after drug administration compared with ETC 500 mg/kg alone, but it was not significant ($p = 0.52$). Fifty minutes after drug administration, catalepsy induced by ETC 500 mg/kg (both, alone and associated) was not different from that induced by haloperidol.

Elevated plus-maze (EPM)

Treatment with ETC (50 to 200 mg/kg) did not change the rats' behavior in the EPM, when compared with the control group (Table 2). Diazepam (2.0 mg/kg, i.p.), used as a positive control, significantly increased the number of entries and the time spent in open arms, when compared with the control group ($p < 0.05$).

DISCUSSION

The use of cigarettes composed of a mixture of two or more plants to treat neurological disorders is common in some countries (Mohagheghzadeh *et al.*, 2006). The mixture of several plants, which is the usual practice in Asian traditional medicine, brings some advantages, such as the use of low doses of each plant, decreasing the possibility of toxicity. At the same time, the therapeutic effect may be reached by synergism as a consequence of the interaction among the constituents present in the plants (Williamson, 2001; Gilbert and Alves, 2003). Conversely, potentially toxic plants could hinder the effect of other plants that would, otherwise, be well tolerated if used alone.

For this reason, when mixing parts of plants in a single formula, it is very important to consider their

Table 2. Effect of ETC administration on elevated plus-maze behavior. Data are expressed as mean ± SEM ($n = 10$)

Group	Dose (mg/kg)	Time spent (s)		Number of entries		
		Open arms	Closed arms	Open arms	Closed arms	Total
Control	–	69 ± 11	177 ± 16	5.7 ± 1.2	8.8 ± 0.7	14.5 ± 1.7
ETC	50	72 ± 13	163 ± 15	6.7 ± 1.1	9.1 ± 1.2	15.8 ± 1.7
ETC	100	88 ± 20	141 ± 18	7.0 ± 1.7	7.4 ± 0.6	14.4 ± 1.6
ETC	500	104 ± 21	130 ± 22	7.2 ± 0.7	6.8 ± 1.2	14.0 ± 1.5
Diazepam	2	147 ± 18[a]	105 ± 15[a]	12.3 ± 2.2[a]	8.3 ± 2.0	20.6 ± 2.3

[a] $p < 0.05$ compared with control group, ANOVA/Duncan.

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respective doses. In the case of 'Tira-capeta', Mr Cezário explained that 'caiá-piá' – *Dorstenia asaroides* – smoked alone has a superior effect when compared with the cigarette, which is also composed of this plant, but in a lower dose, since eight other plants are used in the cigarette. Thus, although the data presented in this study are related to an extract composed of nine plants, in the future, they will be compared with others obtained from extracts composed by one (or more) of the nine plants, in order to examine which one of them is responsible for the main pharmacological effects observed. Moreover, the existence of synergism among them will also be explored.

It is important to point out that the amount of each plant in the mixture varies from preparation to preparation, because the interviewees do not use scales to quantify the amount of each plant in the cigarette. Instead, they use 'a handful' as a measurement, which makes it difficult to compute exactly how much of each plant is added to the cigarette. This is the reason why it is imperative to study each component of the cigarette alone, so as to obtain the pharmacological effect corresponding to a known dose of the extract and its participation in the final pharmacological effect.

The phytochemical screening (TLC and HPLC) indicated the presence of flavonoids, tannins, saponins, phenolic acids and alkaloids. The phytochemical analyses carried out by several authors with plants utilized in the 'Tira-capeta' cigarette reveal a wide variety of chemical constituents. *Petiveria alliacea* ('guiné') contained pimarene diterpenes (Peraza-Sanchez *et al.*, 2005), essential oils (Zoghbi *et al.*, 2002), flavonoids and triterpenes (Delle Monache *et al.*, 1996). In the *Siparuna guianensis* ('negramina') were found flavonoids (Leitão *et al.*, 2005), essential oils (Fischer *et al.*, 2005) and alkaloids (Simas *et al.*, 2001). *Ruta graveolens* ('arruda') contains alkaloids (Kuzovkina *et al.*, 2004; Michael, 2005), flavonoids (Saieed *et al.*, 2006), coumarins (Kostova *et al.*, 1999), furanocoumarins (Ekiert and Czygan, 2005), triacylglycerines (Asilbekova, 2001) and glycosides (Chen *et al.*, 2001). For *Dorstenia asaroides* ('caiá-piá') the phytochemical study showed the presence of furanocoumarins (Cardoso *et al.*, 1999). Phytochemical studies with *Syzygium aromaticum* ('cravo-da-Índia') showed the following constituents: essential oils (Juliani *et al.*, 2006), flavonoids (Nassar, 2006), gallic acid (Pathak *et al.*, 2004), phenylpropanoids (Miyazawa and Hisama, 2003) and tannins (Tanaka *et al.*, 1996). In the *Eucalyptus globulus* (eucalyptus) were found essential oils (Cimanga *et al.*, 2002); triterpenic acids and fatty acids (Pereira *et al.*, 2005; Guo and Yang, 2006), phloroglucinols (Singh and Bharate, 2006), flavonoids (Ikawati *et al.*, 2001) and condensed tannins (Ishida *et al.*, 2005). Many of the chemical constituents present in *Allium sativum* (garlic) are known (Amagase, 2006). From the garlic skin, the part used in 'Tira-capeta', were isolated phenylpropanoids (Ichikawa *et al.*, 2003, 2006) and flavonoids (Stajner *et al.*, 2006). Of the two remaining plants, *Anemopaegma arvense* ('alecrim-do-norte') and *Hyptis cana* ('hortelã-da-várzea'), there are no phytochemical data in the literature, but we suppose that they possess tannins, flavonoids and saponins, since they are the major constituents of ETC. A monograph on *Anemopaegma mirandum* (Cham.) Mart. ex DC. (synonym of *A. arvense*) describes the presence of tannic material and alkaloids in this plant (Teske and Trentini, 1995). The essential oils of *P. alliacea*, *S. guianensis*, *S. aromaticum* and *E. globulus* were not extracted by the same methodology used in the present study (open extraction) and for this reason were not screened in the phytochemical study of ETC.

Flavonoids were found in several of these plants, except in *D. asaroides*, *A. arvense* and *Hyptis cana*. Numerous flavonoids, including apigenin, chrysin, wogonin, baicalein and baicalin, have been shown to have anxiolytic effects in the EPM (elevated plus-maze) and VCT (Vogel conflict test) with a potency comparable to that of typical BDZ (benzodiazepine) agents (Zanoli *et al.*, 2000; Dhawan *et al.*, 2001, 2004; Rocha *et al.*, 2002; Liao *et al.*, 2003; Rodrigues *et al.*, 2006, in press). Unlike BDZ, the anxiolytic flavonoid does not induce sedation while producing antianxiety activity (Hui *et al.*, 2002). Flavonoids, also exhibit sedative effects (Zetola *et al.*, 2002; Rodrigues *et al.*, 2006, in press). Essential oils are found in *P. alliacea*, *S. guianensis*, *S. aromaticum* and *E. globulus*. Anxiolytic (Norte *et al.*, 2005; Komiya *et al.*, 2006; Rodrigues *et al.*, 2006, in press) and sedative (Re *et al.*, 2000; Freire *et al.*, 2006; Rodrigues *et al.*, 2006, in press) activities have also been attributed to these constituents.

Among the plants used in 'Tira-capeta' extract four are aromatic, i.e. possess essential oils, which could be found in higher concentrations in the smoke, since they are volatile. Therefore, the biological activity of the 'Tira-capeta' cigarette, when burned, can be attributed to these constituents. However, other constituents could also be transformed in some active principle when burned. It is also important to consider the difficulties and technical limitations in reproducing the popular use, i.e. smoking, in animals. The non-volatile polar compounds generally represent the main group of metabolites in a crude plant extract and are extracted in polar solvent. The use of a 50% water:ethanol mixture as solvent is effective for the extraction of polar constituents.

The non-volatile fraction of *Lippia alba*, extracted in ethanol, presents sedative and myorelaxant effects because it presents the highest flavonoid content (Zetola *et al.*, 2002). Recent studies have found that oral administration of the aqueous extract of *Acorus gramineus* and inhalation of its essential oil dose-dependently suppresses the intensity of apomorphine-induced stereotypic behavior and locomotor activity, and extends the duration of sleeping time induced by pentobarbital (Vohora *et al.*, 1990; Koo *et al.*, 2003). Therefore, despite the fact that the most traditional use of the plant is the smoke resulting from the burning of nine plants and that four plants possess essential oils, we chose to assess the effects of the hydroalcohol extract on the CNS because of the flavonoids present in this extract.

From the pharmacological point of view, the extract presented an apparent biphasic effect, characterized by intense CNS stimulation in the initial minutes (with tremors and, in some cases, seizures) followed by a general depressor effect. The pro-convulsant effect of ETC suggests a strong glutamatergic or cholinergic effect, or a GABAergic inhibition, which consequence would be a depletion of the stock of neurotransmitters and lethargy after the seizure. The second phase was characterized by a general decrease of motor activity, despite a lack of impairment in motor coordination

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(examined by the rota-rod test). This noticeable depressor effect was indicated by the decreased latency to initiate sleep and increased pentobarbital-induced sleeping time. This result corroborates the popular mentioned effects: sleepiness and relaxation after smoking the 'Tira-capeta' cigarette.

The high dose of ETC (500 mg/kg) induced catalepsy, a typical effect of neuroleptic drugs (Baez *et al.*, 1979), suggesting a possible blockade of dopamine receptors. This effect, if confirmed, would corroborate the popular name of the smoke – 'Tira-capeta' ('Removing the Devil') – since some people believe that schizophrenics have the 'devil in the body'. This supposition is purely speculative, considering that no report of this kind of use was gathered in the ethnopharmacological interviews. Nonetheless, this hypothesis cannot be ruled out. A similar example is the famous *Rauvolfia serpentina* (L.) Benth. ex Kurz (Apocynaceae): called 'insanity herb' and employed in witchcraft, the plant is a source of reserpine, a pioneer substance used as a neuroleptic (Balick and Cox, 1996). The cataleptic effect might not only occur by blockade of nigrostriatal dopaminergic receptors, but also by interfering with other systems, such as the opioid (Kuschinsky and Hornykiewicz, 1972; Costall and Naylor, 1973). The Straub tail induced by ETC in the pharmacological screening suggests the involvement of this system.

Some plants present in the 'Tira-capeta' cigarette have a broad folk use. *Siparuna guianensis* is popularly employed as a calmative (anxiolytic) and hypnotic (Stellfeld, 1955; Lorenzi and Matos, 2002; Rodrigues and Carlini, 2003; Leitão *et al.*, 2005), which is in concordance with some of the popular uses of the 'Tira-capeta' cigarette. For this reason, we tried also to evaluate the anxiolytic property of ETC, but the extract failed to show positive results in the EPM.

The *Dorstenia asaroides* is used against the cold by Krahô Indians (unpublished data). Garlic (*Allium sativum*), which is also present in the 'Tira-capeta' cigarette, is employed to counteract cold and, in fact, there is a clinical study confirming this use (Josling, 2001). Consequently, it is possible that these two plants could be responsible for the alleged anti-cold effect attributed to the 'Tira-capeta'.

Other plants contained in 'Tira-capeta' cigarette possess a depressor effect, such as *Petiveria alliacea* and *Eucalyptus globulus*, both acting as analgesics (De Lima *et al.*, 1991; Lopes-Martins *et al.*, 2002; Silva *et al.*, 2003; Gomes *et al.*, 2005).

The aqueous and methanol extracts of *Ruta graveolens* (leaves) exhibited moderate inhibition of the enzyme acetylcholinesterase using Ellman's colorimetric method (Adsersen *et al.*, 2006), which may contribute to the memory and cognition improvement, one of the therapeutic indications of 'Tira-capeta'. Nevertheless, it is used as an abortifacient in many countries, including Brazil. This plant causes preimplantation embryonic loss and reabsorptions in the mouse (Gutierrez-Pajares, 2003; Freitas *et al.*, 2005).

Syzygium aromaticum is used by indigenous ethnic populations of different countries, such as, India, Indonesia and Mauritania for several therapeutic indications, as for example, diuretic, stomachache, tonic and condiment with carminative and stimulant properties (Nassar, 2006). Some studies have shown an aphrodisiac effect of this plant (Tajuddin *et al.*, 2004) and an improvement of learning and memory in rats (Dashti *et al.*, 2004). This kind of effect, as tonic, aphrodisiac, memory enhancer and to improve mental fatigue is generally described in plants used as adaptogens in popular medicine, among them 'alecrim-do-norte' or 'catuaba' (*Anemopaegma arvense*) (Mendes and Carlini, 2007), present in the 'Tira-capeta'.

Similarly, *Allium sativum* may also contribute to the alleged effect on memory due to its effect in protecting hippocampal cells from the neurotoxic action induced by β-amyloid; thus, reducing age-related learning disabilities and cognitive damage (Nishiyama *et al.*, 2001). One study indicates that, similar to diazepam, aged garlic extract prevents the alterations induced by stress, such as adrenal hypertrophy, hyperglycemia and the elevation of the corticosterone rate, without altering serum values of insulin (Kasuga *et al.*, 1999). Garlic (or garlic supplements) is consumed in many cultures for its hypolipidemic, antiplatelet and procirculatory effects (Kasuga *et al.*, 1999). However, since the smoke is prepared only with the skin of garlic bulbs (the bulb not being used in ETC), it is difficult to determine to what extent garlic might have exerted all or some of the effects described in the literature.

Although preliminary, the results of the present study indicated a possible biphasic effect of ETC (intense stimulation followed by a depressor effect). The fact that a stimulant effect (tremor and seizure) was observed in the initial minutes of the drug administration indicated a rapid absorption of the chemical constituents, involved with this biological activity. However, there is a likelihood that some active principles absorbed via the gastrointestinal tract would not be absorbed by inhalation (Rang *et al.*, 2004), i.e. by smoke, which is the popular form of use of 'Tira-capeta' by *Quilombolas*. The advantages of smoke-based remedies are the rapid delivery to and more efficient absorption of active principles into the brain (Rang *et al.*, 2004; Mohagheghzadeh *et al.*, 2006), justifying the rapid effect reported by the users, which is, in general, limited to the time spent smoking the cigarette. It is worth mentioning that oral administration, as used in the present study, induced stimulatory effects such as seizure in a short time. Smoke, in turn, is a gaseous product of incomplete combustion of organic substances. Substances that volatilize at low temperature can be easily and efficiently administered as smoke, and large amounts of the drug can be rapidly delivered to the brain, whereas large molecules probably are not absorbed, for they are more difficult to volatilize. Most psychoactive drugs exert their maximum effect when their levels in the blood are rapidly increasing. Because such drugs enter the bloodstream rapidly by the lungs, an extra inhalation can produce a sharp increase in the concentration of the drug in arterial blood, which is carried direct to the brain.

CONCLUSION

The present study, although preliminary, confirms the potential CNS effect of ETC, as well as the plants comprising the 'Tira-capeta' cigarette. The results suggest that ETC stimulates the glutamatergic and cholinergic systems and blockades the dopaminergic system. The

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effects observed are likely the result of a synergism among the different substances present in the extract of the plants contained in 'Tira-capeta' cigarette. A follow-up of this work will be focused on the confirmation of these effects and on new tests with extracts prepared from isolated plants or the mixture of those considered more important for the observed effects.

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