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Psorospermum Febrifugum Spach (Hypericaceae) Decoction Antagonized Chemically-induced Convulsions in Mice

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Abstract: *Psorospermum febrifugum* Spach is used in traditional medicine in Cameroon to treat epilepsy. The decoction of *Psorospermum febrifugum* slightly increased the total sleep time induced by diazepam (50 mg kg^{-1} i.p.). It also protected mice against pentylene tetrazol-, picrotoxin-and strychnine-induced seizures. Dose 300 mg kg^{-1} provided 83.3% of protection against pentylene tetrazol-induced clonic convulsions (the same protection as clonazepam 0.1 mg kg^{-1}). For the strychnine test, *Psorospermum febrifugum* protected 66.7% of mice at a dose of 1000 mg kg^{-1}. 83.3% of mice were protected against picrotoxin-induced seizures at a dose of 3000 mg kg^{-1}. The antagonism of chemically-induced seizures suggests that *Psorospermum febrifugum* decoction possesses anticonvulsant properties in mice.

Key words: Epilepsy, anticonvulsant, decoction, seizures, *Psorospermum febrifugum*

INTRODUCTION

Psorospermum febrifugum Spach grows in Savannah areas and tropical West Africa. It is found in Cameroon, Senegal, etc. It belongs to the family of Hypericaceae[1]. The plant has been reported to have therapeutic action against certain skin diseases, parasitic skin diseases and wound infections (http://uzweb.uz.ac.zw/medicine/pharmacy/pubs/1989.html; http://bodd.cf.ac.uk/BotDermFolder/BotDermG/GUTT.html). Psorospermin contained in *Psorospermum febrifugum* has been found to possess effect against leukemia in mice (www.pnas.org/cgi/content/full/9523/13531). In Cameroon, its leaves are used in the treatment of epilepsy. As *Psorospermum febrifugum* was reported possessing therapeutics properties in epilepsy disease in the traditional medicine and the fact that our laboratory is looking to identify and collect all medicinal plant used in the treatment of epilepsy, insomnia, anxiety and head ache, in Cameroon, *Psorospermum febrifugum* collected at Ngaoundéré (Cameroon) was tested for the determination of sedative and anticonvulsant properties in mice.

MATERIALS AND METHODS

Animals: Adult male mice (*Mus musculus* Swiss; 20-24 g; 6 per group) were used throughout this study. The animals were housed in standard cages at 25°C on a 12/12 h light-dark cycle. They were supplied with food and water *ad libitum*.

Plant material: The plant specimens of *Psorospermum febrifugum* used were collected in Cameroon in the vicinity of Ngaoundéré on November 2003. The National Herbarium of Cameroon recognized a voucher specimen.

Preparation of decoction: The decoction of *Psorospermum febrifugum* was obtained according to a method described below. The dried leaves of *Psorospermum febrifugum* were ground. The powder (10 g) was put for maceration in 25 mL of distilled water for 1 h. The mixture was boiled for 20 min. After cooling, the supernatant or decoction was collected and filtered. The stock solution obtained (19 mL) correspond to a concentration of 0.4 g mL^{-1}, that is 10 g of leaves in 25 mL distilled water and represent a 4.5% yield.

The decoction was administered intraperitoneally (i.p.) 1 h before the test. The following doses were used: 100, 300, 1000 and 3000 mg kg^{-1}.

Pharmacological tests

Diazepam-induced sleep in mice: The method described by Beretz *et al.*[2] and modified by Rakotonirina *et al.*[3] was used. Sleep potentiating effects of the plant was studied in mice that received diazepam at a dose of

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(50 mg kg^{-1}) 1 h after decoction and distilled water administration. Observing time between the disappearing and the recovery of the straightening reflex measured the sleeping time.

Pentylenetetrazol (PTZ) test: The method has been described previously[4,5]. Clonic seizures were induced in male mice by the i.p. injection of 70 mg kg^{-1} PTZ. The protective effect of the plant was recorded in mice treated 1 h before with the decoction. There were two control groups, one receiving placebo and a positive control group receiving 0.1 mg kg^{-1} clonazepam.

Strychnine (STR) test: STR convulsions followed by death were induced in male mice by the i.p. injection of 2.5 mg kg^{-1} STR nitrate. A protective effect of the decoction given i.p. 1 h prior to STR was recorded and compared to the one of 3 mg kg^{-1} clonazepam[4,6]. The number of animals, which survived more than 10 min served as criterion of protection.

Picrotoxin (PIC) test: The method has been described previously[4]. Seizures were induced in male mice by the i.p. injection of 7.5 mg kg^{-1} PIC. The protective effect of the plant was recorded in mice treated 1 h before with the decoction. There were two control groups, one receiving placebo and a positive control group receiving 0.4 mg kg^{-1} clonazepam.

Statistical analysis: The protection against PIC-, STR-and PTZ-induced seizures that was expressed as percentage of animals protected. The Fisher exact test (two-tail) was used to compare percentage of protected mice in each case.

In the total sleep time the mean values of the control group were compared to the mean values of the groups treated with the decoction using the correction for multiple t-test by Bonferroni method.

The ED_{50} was calculated using Prism 3.0 Software (Graph-Pad, San Diego CA).

Chemicals: PIC, PTZ, STR and clonazepam are from Sigma Chemical, USA.

RESULTS

Effect of *Psorospermum febrifugum* on diazepam-induced sleep: The total sleep time induced by diazepam increased slightly but significantly from 37.7 min in the control group to 45.5 and 51 min in the groups treated with the decoction at the doses of 1000 and 3000 mg kg^{-1}, respectively (Fig. 1).

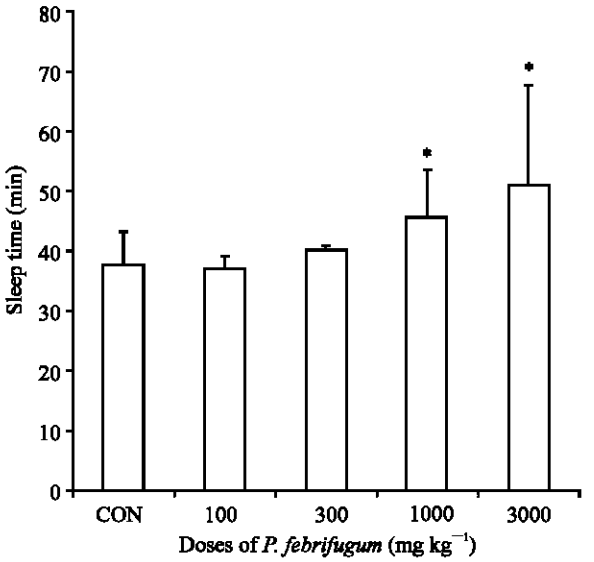

Fig. 1: Effect of *Psorospermum febrifugum* on diazepam-induced sleep in mice
The total sleep time (min) induced by diazepam (50 mg kg^{-1}, i.p.) in the presence of different treatments in mice. It is expressed as means + SD, n= 6 per dose, *= p<0.5 (Correction for multiple t-test by Bonferroni method). CON = distilled water

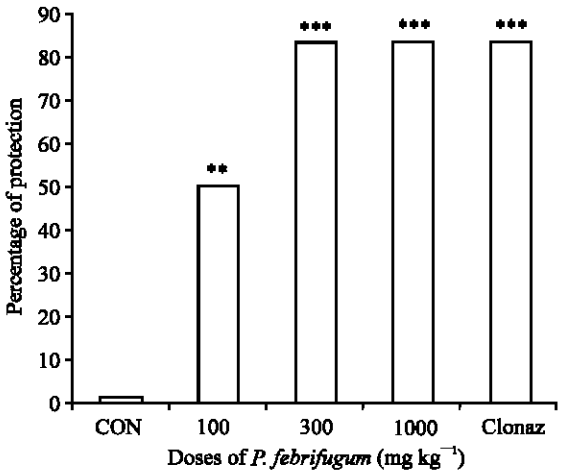

Fig. 2: Effect of *Psorospermum febrifugum* on PTZ-induced convulsions in mice
Psorospermum febrifugum significantly protected mice against PTZ-induced convulsions. N = 6 per dose, **= p<0.01, *** = p<0.001 (Fisher exact test: two tail). CON=distilled water. Clonaz= clonazepam 0.1 mg kg^{-1}

Effect of *Psorospermum febrifugum* on PTZ-induced seizures: The decoction of *Psorospermum febrifugum* prevented mice against PTZ-induced seizures. This effect

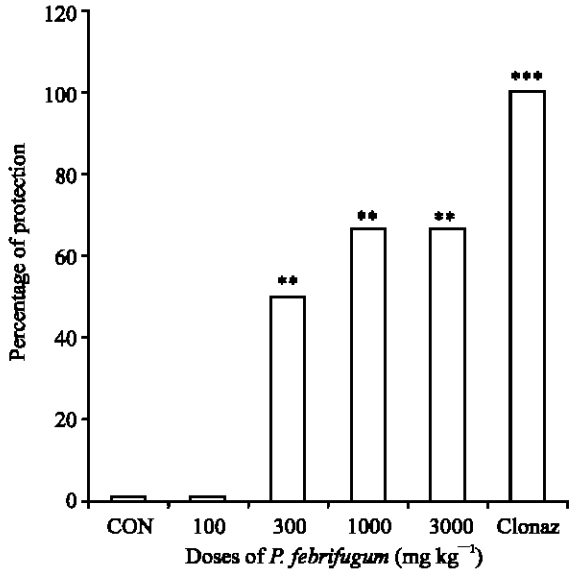

Fig. 3: Effect of *Psorospermum febrifugum* on STR-induced tonic seizures and death in mice
Psorospermum febrifugum significantly protected mice against STR-induced tonic seizures and death. N=6 per dose, **=p<0.01, ***= p<0.001 (Fisher exact test: two tail). CON = distilled water. Clonaz = clonazepam 3 mg kg^{-1}

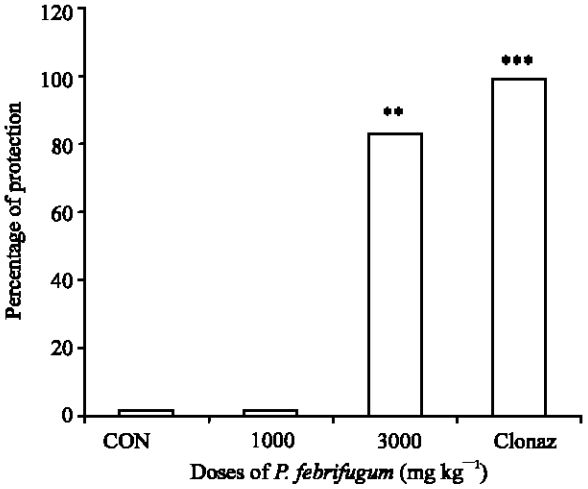

Fig. 4: Effect of *Psorospermum febrifugum* on PIC-induced convulsions in mice
Psorospermum febrifugum protected mice against PIC-induced seizures at a dose of 3000 mg kg^{-1}. N= 6 per dose, CON = distilled water. Clonaz = clonazepam 0.4 mg kg^{-1}.

(83.3% at a dose of 300 mg kg^{-1}) was as strong as the effect produced by clonazepam (0.1 μM), a potent anticonvulsant. Dose 100 mg kg^{-1} protected 50% of mice (Fig. 2). The ED_{50} was 107.7 (42.34-274.1).

Effect of *Psorospermum febrifugum* on STR-induced seizures and exitus: *Psorospermum febrifugum* decoction significantly increased the number of mice protected against STR-induced seizures and exitus. The percentage of protection were 50 and 66.7% at the doses of 300 and 1000 mg kg^{-1} i.p., respectively (Fig. 3).

Effect of *Psorospermum febrifugum* on PIC-induced seizures: The dose 3000 mg kg^{-1} provided a strong protection (83.3%) against PIC-induced convulsions in mice (Fig. 4).

DISCUSSION

The decoction of *Psorospermum febrifugum* increased only slightly the total sleep time induced by diazepam. This increase is not so strong (no potentiation) to allow the suggestion of the presence of sedatives properties in the decoction of *Psorospermum febrifugum.* The decoction of *Psorospermum febrifugum* antagonized chemically-induced seizures in mice. *Psorospermum febrifugum* significantly protected mice against PTZ-and STR-induced seizures in mice. The effect on PIC-induced seizures (83.3%) was found only at a dose of 3000 mg kg^{-1}. The inhibition by the decoction of *Psorospermum febrifugum* of STR-induced seizures suggests the involvement of glycine receptors[7] and the presence of anticonvulsant properties[8,9]. As PTZ have been shown to interact with the GABA neurotransmitter[10-12], the antagonism of PTZ-induced seizures suggests that the decoction of *Psorospermum febrifugum* might have effect on the GABA-ergic neurotransmission. It is known that PTZ test is of predictive relevance regarding the clinical spectrum of activity of experimental compounds[13,14]. It is also known that PTZ is assumed to identify anticonvulsant drugs effective against generalized clonic seizures[10,12-14]. For these two reasons it could be suggested that, *Psorospermum febrifugum* possess anticonvulsant efficacy against the above mentioned seizures types in man.

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