Available online at www.sciencedirect.com
ScienceDirect
Journal of Ethnopharmacology 109 (2007) 348–353
Journal of ETHNO-PHARMACOLOGY
www.elsevier.com/locate/jethpharm

Ethnopharmacological communication

Acute and subacute toxicity of *Salvia scutellarioides* in mice and rats

Jorge H. Ramírez [a,*], Mauricio Palacios [a], Oscar Tamayo [b,1], Roberto Jaramillo [c], Oscar Gutiérrez [a]

[a] *Facultad de Salud, Sección de Farmacología, Universidad del Valle, Cali, Colombia*
[b] *Facultad de Salud, Programa de Medicina, Universidad Santiago de Cali, Cali, Colombia*
[c] *Centro Internacional de Entrenamiento e Investigación Medica (CIDEIM), Cali, Colombia*

Received 29 March 2006; received in revised form 11 July 2006; accepted 31 July 2006
Available online 12 August 2006

Abstract

The acute and subacute toxicity of the aqueous extract of *Salvia scutellarioides* (Lamiaceae) was studied in mice and rats. In the acute toxicity test, oral administration of 2 g/kg of *Salvia scutellarioides* produced neither mortality nor changes in behavior or any other physiological activities. In subacute toxicity studies, no mortality was observed when the two doses of 1 or 2 g/kg day of aqueous extract of *Salvia scutellarioides* extract were administered orally for a period of 28 days. In the blood chemistry analysis, no significant changes occurred, including glucose, creatinine, blood urea nitrogen (BUN), aspartate transaminase (AST), alanine transaminase (ALT), potassium, sodium, chloride, calcium, phosphorus, conjugated billirrubin, total billirrubin, total cholesterol, high density lipoprotein (HDL), triglycerides, total protein, albumin, prothrombin time (PT) and thromboplastin partial time (PTT) of both sexes. Hematological analysis showed no differences in any of the parameters examined (WBC count, platelet and hemoglobin estimation) in either the control or treated group of both sexes. The urinalysis was negative for glucose, ketonic bodies, casts, red blood cells, and albumin in the control and treatment groups. There were no significant differences in the body and organ weights between controls and treated animals of both sexes. Pathologically, neither gross abnormalities nor histopathological changes were observed.

Keywords: Lamiaceae; *Salvia scutellarioides*; Folklore medicine; Subacute toxicity; Herbal medicine

1. Introduction

Salvia scutellarioides Kunth Syn. *Salvia palaefolia* (Lamiaceae) is an abundant aromatic plant endemic in the pacific and central regions of Colombia, where it is commonly known as "mastranto". Infusions of the bark and leaves from *Salvia scutellarioides* are commonly used in folk medicine for their antihypertensive and diuretic properties (Piñeros et al., 1991; Garcia, 1992; Colmenares and Ramírez, 2001). Recently, our research group reported the effects of *Salvia scutellarioides* in lowering the blood pressure in L-NAME hypertensive rats (Ramirez et al., 2006b) and also their diuretic effect in normal rats (Ramirez et al., 2006a). Alkaloids, triterpenes and lignans were previously reported as chemical constituents from this plant (Gonzalez et al., 1990). Despite the wide use of *Salvia scutellarioides* in Colombian folk medicine, no study has been published in the scientific literature about its toxicological profile.

The present study was designed to determine the acute and subacute oral toxicity of the aqueous extract from bark and leaves of *Salvia scutellarioides* in Wistar rats. In addition, the effects of the administration of the plant in blood pressure of normotensive animals was also evaluated.

2. Materials and methods

2.1. Plant material

Salvia scutellarioides was acquired from a local herbal store in March 2003. Its identity was confirmed by Dr. Phillipe Silverstone (Department of Botanical Biology, Universidad del Valle) and a voucher specimen (JHR-01) was deposited at the Herbarium of the Natural Sciences Institute of the Universidad del Valle, Colombia. The bark and leaves of *Salvia scutellarioides* were dried at 38 °C for 72 h, followed by mechanical fragmentation for posterior storage in sealed container bags at 0 °C.

* Corresponding author. Tel.: +57 2 5185620.
E-mail address: jorgehramirez31@yahoo.com (J.H. Ramírez).
[1] Present address: Universidad Santiago de Cali, Sede San Fernando, Calle 4B 36-00, Edificio 116, Cuarto piso, Oficina 4035, Cali, Colombia.

0378-8741/$ – see front matter © 2006 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.jep.2006.07.040

2.2. Preparation of the extract

Infusions of the dried powdered bark and leaves of the plant (20 g) were extracted with distilled water (500 ml), followed by filtration and concentration (yield: 40%) with vacuum.

2.3. Acute toxicity

The acute toxicity of the extract of *Salvia scutellarioides* was evaluated in mice using the up and down procedure (OECD, 2001b).

Mice of either sex (three females and three males, weight: 25–35 g, age: 6–8 weeks) received *Salvia scutellarioides* aqueous extract starting at 2 g/kg orally by gavage. The animals were observed for toxic symptoms continuously for the first 4 h after dosing. Finally, the number of survivors was noted after 24 h and these animals were then maintained for further 13 days with observations made daily.

2.4. Subacute toxicity

2.4.1. Experimental animals

Thirty Wistar rats (weight: 150–250 g; age: 6–8 weeks old) were randomly assigned into three groups ($n = 10$), five females and five males in each group. Groups of five rats were housed together in stainless steal cages (males separated from females) with 12 h light/dark cycle in a temperature and humidity controlled environment. Treatments were administered orally by gavage once a day for 4 weeks. The first group of animals, serving as control, received normal saline (5 ml/kg); the second and third group received the water extract of *Salvia scutellarioides* at doses of 1 and 2 g/kg, respectively. All animals were supplied with Fiel Purina Chow® and tap water *ad libitum* during the testing periods.

All rats were weighted and observed daily for physiological and behavioral changes. Any rat that died during the test period was tested pathologically, and all animals were examined at the end of the test period.

2.4.2. Observation and examination methods

Clinical signs were observed at least once a day through the 28 days of dosing. Body weight, water and food intake and weight gain were measured once a week. Systolic blood pressure (SBP) and mean blood pressure (MBP) were measured weekly in conscious, prewarmed, restrained rats by tail-cuff plethysmography using a piezoelectric transducer (Model 631 Six Channel Semi-automatic NIBP Test System. IITC, Inc., Los Angeles, CA). Diastolic blood pressure (DBP) was extrapolated from the SBP and MBP using the following formula:

$$\mathrm{DBP} = \frac{3\mathrm{MBP} - \mathrm{SBP}}{2}$$

2.4.3. Urine samples

On day 27th, the rats were placed in metabolic cages during 4–6 h; 3–5 ml of urine were collected for immediate urinalysis.

2.4.4. Blood analysis

On day 29th all surviving animals were fasted overnight, and anesthetized afterwards for blood collection from the right ventricle. Blood samples were collected into three tubes: (1) 3.2% buffered sodium citrate tubes; (2) heparinized centrifuge tubes; (3) dry non-heparinized centrifuge tubes. A blood analysis (hematology, coagulation and chemistry) was carried out. The blood in the sodium citrate tubes was used for prothrombin time (PT) and partial thromboplastin time (PTT) estimation. The heparinized blood was used for a hematological study which included red blood cell count (RBC), hemoglobin concentration (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelets (Plt),

Table 1
Systolic and diastolic blood pressures of rats in subacute toxicity of the aqueous extract from *Salvia scutellarioides*

Week	Control		*Salvia scutellarioides* (g/kg)			
	SBP	DBP	1		2	
			SBP	DBP	SBP	DBP
Male						
0	119.4 ± 3.8	83.4 ± 3.90	116.2 ± 2.33	86.8 ± 2.66	122 ± 4.74	92.9 ± 2.14
1	131.6 ± 7.25	84.8 ± 3.75	121 ± 9.82	79.3 ± 7.33	124.6 ± 3.26	92.8 ± 2.38
2	138.8 ± 5.51	104.9 ± 4.22	149.8 ± 10.1	97 ± 8	126.8 ± 5.2	94 ± 1.51
3	127.6 ± 8.27	93.7 ± 6.79	130.1 ± 2.91	94.4 ± 4.74	128.4 ± 5.07	90.3 ± 6.62
4	143 ± 1.61	102.8 ± 2.46	138.2 ± 3.65	107.9 ± 5.65	136.8 ± 7.17	99 ± 7.95
Female						
0	126.4 ± 2.94	93.4 ± 3.82	118.6 ± 1.99	87.7 ± 3.72	114.2 ± 5.52	83.3 ± 6.58
1	114 ± 4.47	82.8 ± 2.08	124.6 ± 4.64	85 ± 2.2	118.6 ± 4.38	83.2 ± 5
2	115.6 ± 4.15	88.6 ± 2.89	122.4 ± 7.8	83.4 ± 10.1	108 ± 5.33	74.7 ± 3.72
3	111 ± 7.32	82.2 ± 2.37	116.6 ± 6	77.3 ± 7.02	112.2 ± 7.17	78.3 ± 7.28
4	107.4 ± 5.81	74.4 ± 8.44	105.4 ± 4.57	74.5 ± 4.21	108.2 ± 3.64	81.5 ± 2.81

Data are expressed as mean ± S.E.M., $n = 5$. No statistical difference between control and *Salvia scutellarioides* ($P > 0.05$). SBP: systolic blood pressure; DBP: diastolic blood pressure.