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THE WATER EXTRACT OF *COLEUS BARBATUS* BENTH DECREASES GASTRIC SECRETION IN RATS

LYGIA A. FISCHMAN; L. A. SKORUPA*; CADEN SOUCCAR & A. J. LAPA/+

Escola Paulista de Medicina, Departamento de Farmacologia, Setor de Produtos Naturais, Rua Três de Maio 100, 04044 São Paulo, SP, Brasil *CENARGEM, EMBRAPA, 70000 Brasília, DF, Brasil

Coleus barbatus *(Labiatae) Benth is popularly used in Brazil "for the healing of liver and stomach diseases". The water extract (WE 1 to 10 g/kg, p.o.) of stem and leaves given to rats and mice did not induce signs of intoxication. Previous treatment of mice with WE (1 g/kg, p.o.) shortened the sleeping time induced by pentobarbital (50 mg/kg, i.p.) by 37%, although the extract alone did not increase the spontaneous activity nor did it induce hyperexcitability. In mice WE (2 g/kg, p.o.) increased the intestinal transit of charcoal by 30%, while reduced gastric secretions in rats treated with WE (2 g/kg intraduodenal) (3.9 ± 1.0 to 0.5 ± 0.2 ml/4 h, respectively). The treatment also reduced the total acid secretion from 34.4 ± 11.0 to 2.7 ± 0.5 mEq/l and raised gastric pH from 2.2 ± 0.3 to 6.5 ± 0.8. Treatment with WE (2 g/kg, p.o.) protected against gastric ulcers induced by stress (5.3 ± 1.6 and 1.5 ± 0.5 ulcers/cm^2), but it did not protect against indomethacin induced ulcers. The results show that the water extract of* C. barbatus *Benth produces mild stimulation of the central nervous system and increases intestinal movements. The extract also reduces gastric secretion indicating an antidyspeptic activity, and protects against gastric ulcers induced by stress.*

Key words: *Coleus barbatus* – boldus – gastric secretion – medicinal plant

Coleus barbatus Benth, family Labiatae, is a native Brazilian folk medicinal plant mainly known for its bitter taste. Because of its resemblance with the most used *Peumus boldus* (genuine boldo or Chilean boldo), the plant is named "false boldo". Medicinal teas of either plant are popularly used for gastrointestinal or hepatic disorders (Coimbra, 1958).

The main purpose of this study was to determine the pharmacological activities of *Coleus barbatus* Benth extract, particularly those related to the antispasmodic and antidyspeptic properties of the plant.

MATERIALS AND METHODS

The plant was collected in Brasília, DF, in a plantation grown at EMBRAPA, Ministry of Agriculture. The dried leaves were extracted with hot water (2%, 72 °C) for 30 min, the extract was concentrated under vacuum and freeze-dried. All tests were done using rats (200 to 250 g) and mice (30 to 40 g) of either sex. Isotonic contractions of *in vitro* rat jejunum and vas deferens were recorded at 30 °C, and kept in nutritive solutions of the following constitution, in mM: NaCl 135; KCl 5.0; $MgCl_2$ 1.0; $CaCl_2$ 1.8; $NaHCO_3$ 15.0; NaH_2PO_4 1.0 and Glucose 11.1 for jejunum preparations, and NaCl 64.0; KCl 81.7; NaH_2PO_4 0.36; $NaHCO_3$ 15.0; and Glucose 5.5 for vas deferens preparations. Cumulative concentration-response curves were constructed to acetylcholine (ACh, 10^{-10}–10^{-4}M) and norepinephrine (Nor; 10^{-10}–10^{-4} M) in either preparation, in the absence and presence of water extract (WE, 1 – 5 mg/ml). Cumulative dose-response curves to WE (1-5 mg/ml) were also obtained in both preparations.

In vivo pharmacological tests included: 1. General pharmacological screening in rats and mice (Malone, 1977); 2. Sleeping time induced by barbiturates (Carlini & Burgos, 1979); 3. Open-field test in mice; 4. measurement of the gastrointestinal transit time of charcoal (10%) in mice (Nodine & Siegler, 1964); 5. measur-

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+ Corresponding author.

ement of gastric secretion (volume, pH and total acidity) collected from pylorus ligated rats (Domer, 1971); 6. measurement of the protective effect of the extract against acute gastric ulcers induced by immobilization at 4 °C or by Indomethacin (10 mg/kg, s.c.) (Carlini, 1988).

The degree of gastric ulceration was scored as follows: loss of mucosal foldings, mucosal discolouration, edema or hemorrhage were scored 1 each; less than 10 petechiae scored 2; more than 10 petechiae scored 3; ulcers less than 1 mm scored number of ulcers x 2; ulcers more than 1 mm scored number x 3; perforated ulcers scored number x 4. The total score was taken as an index of ulceration.

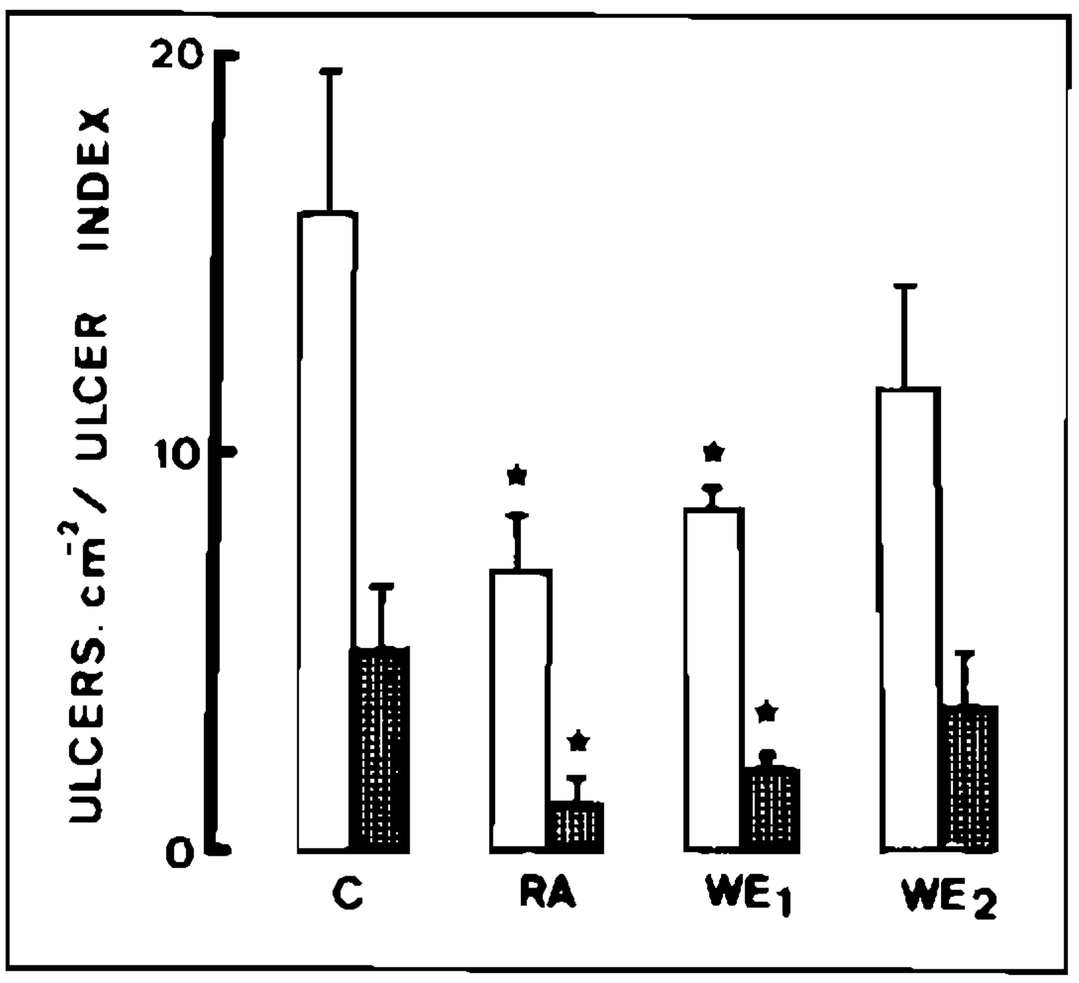
Results are given as means ± S. E. M. or S. D. when indicated. The significance of differences from controls was calculated by the Student "t" test ($P < 0.05$).

RESULTS

WE (0.1 to 10 g/kg, p.o.) caused ptosis, writhings, quietness and decrease of spontaneous motor activity of mice and rats. The effects were dose-dependent and more intense after i.p. injections. Previous oral administration of WE (1 and 2 g/kg) to mice reduced the sleeping time induced by pentobarbital (50 mg/kg, i.p.) by 20% and 25% of the control group (vehicle, 83.6 ± 4.6 min). The open-field test however, did not show different motility for control and treated mice. In rats treated with WE (2 g/kg, p.o.) the intestinal transit of charcoal was increased by 30% of control (from 66 ± 3% to 86 ± 4% of the total small bowel length).

In vitro rat jejunum contracted to increasing single doses of WE (1-5 mg/ml). This tonic effect was about 43% of the maximum induced by ACh and was not blocked by atropine (10^{-8} M). The EC50 obtained from cumulative dose-response curves of ACh in presence of 2.5 and 5.0 mg/ml WE were increased by 5 and 10 fold, respectively. Simultaneously the maximal contraction induced by the agonist was reduced by 20% and 70%. The effects were reversed after washing. The rat vas deferens also contracted with incubation of WE (1-5 mg/ml). This tonic effect was not blocked by atropine (10^{-8} M) but is was partially reduced by tolazoline (10^{-4} M). In presence of WE (1 and 2 mg/ml) the maximum contraction to Nor was reduced by 28% and 50% without changes of the EC50. Higher doses of WE (5 mg/ml) blocked the response to Nor.

Pretreatment of rats with WE (2 g/kg, p.o.) 1 h before, reduced the index of ulceration and the number of ulcers induced by restrain and cold by 51% and 72% of control values, respectively (Fig.). The treatment did not decrease gastric ulcerations induced by indomethacin (10 mg/kg, s.c.) (1.9 ± 0.1 and 2.9 ± 1.0 ulcers. cm^{-2} for control and treated groups, n = 5) nor did it reduce the index of ulceration (9.0 ± 0.3 and 11.6 ± 2.3, respectively).



Effect of administration of the water extract of *Coleus barbatus* Benth on gastric ulceration in rats. Ulcers. cm^{-2} (dark columns) and index of ulcerogenesis (white columns) in rats immobilized for 2 h at 4 °C. Control (C); rats treated orally 1 h before with the water extract of *C. barbatus* Benth (WE1 – 1 g/kg; WE2 – 2 g/kg), and rats treated with ranitidine (RA – 50 mg/kg). Columns and vertical bars are means ± S. E. M. of 5 animals each. ★ – indicates difference from control ($P < 0.05$).

TABLE

Effects of intraduodenal administration of *Coleus barbatus* Benth water extract (WE) on gastric secretion in rats induced by histamine (10 mg/kg, s.c.)

Treatment	Volume (ml)	pH	Gastric acidity (mEq/l)
Control	7.2 ± 0.8	1.4 ± 0.1	77.6 ± 36.0
WE (1 g/kg)	1.2 ± 0.7*	2.8 ± 0.5*	8.1 ± 5.7[a]
WE (2 g/kg)	2.2 ± 1.2*	2.5 ± 0.3*	9.5 ± 3.0[a]
Ranitidine	1.0 ± 0.3*	3.4 ± 0.9*	4.1 ± 3.3[a]

Results are means ± S. D. of animals.
a: different from control ($P < 0.05$).

Either intraperitoneal or intraduodenal administration of WE (1 and 2 g/kg) to rats submitted to pylorus ligature reduced the volume and the total acidity, while increased the pH of the gastric content. Intraduodenal administration of WE (1 and 2 g/kg) also reduced the volume and total acid secretion induced by histamine (10 mg/kg, s.c.), increasing the pH of the gastric content (Table).

DISCUSSION AND CONCLUSIONS

The most consistent results obtained in the present experiments were related to the effects of the water extract of *C. barbatus* Benth on the gastric secretion. In fact, the data showed unquestionably that the plant extract inhibits the gastric secretion of hydrochloric acid and protects against ulcerations induced by stress. The mechanism of this action however, is still unclear. It was shown that direct surface protection of the stomach mucosa is not the cause since the extract was still active after either intraperitoneal or intraduodenal administration. Furthermore, the extract inhibited effectively the hypersecretion induced by histamine; however, it did not protect the gastric mucosa against ulcers induced by indomethacin.

In vitro experiments were done in order to detect anticholinergic activity. Indeed, in the rat jejunum stimulated by acetylcholine the extract shifted competitively the EC50 of the agonist to higher values. This effect however, was superposed on two other ambiguous actions; a non-competitive inhibition of the smooth muscle contraction and a tonic effect not blocked by atropine. This latter effect is probably related to the unusual writhing observed in rats after oral administration of the extract, and to enhanced motility of the intestinal musculature accelerating the intestinal transit. Those effects however, do not explain other data obtained *in vivo* and *in vitro*. A possible high concentration of K^+ in the extract was eliminated by titration of the ion; further studies will require chemical purification of the extract.

In conclusion, the results so far obtained confirm that the extract of *C. barbatus* has an antidyspeptic activity which mechanism deserves more studies.

Finally, it remains to recall that the extract decreased the sleeping time induced by barbiturates without stimulating or changing the spontaneous activity in mice. This effect suggests that the extract changes the pharmacokinetics of pentobarbital, in which case a close examination on the influence of *C. barbatus* on hepatic functions should be considered.

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