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SHORT COMMUNICATION

Antiulcerogenic Effects of *Tylophora conspicua* in Male Rats

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Studies were undertaken on the effect of a crude (TC) and an alkaloid fraction (TA) of the leaf extracts of *Tylophora conspicua* on indomethacin-induced gastric ulceration and gastric acid secretion in male albino rats. Both the TC and TA produced a dose-dependent inhibition of gastric ulceration. At a dose level of 40 mg/kg TC and TA were more effective (TA being more potent) than propranolol in inhibiting gastric ulceration. The highest dose of the extracts used (80 mg/kg) completely inhibited gastric ulceration. Intravenous administration of the TC and TA significantly decreased acid output at low dose (20 mg/kg), medium dose (40 mg/kg) and high dose (80 mg/kg) from the peak basal of 0.54 ± 0.02 mEq/L/min to 0.49 ± 0.02 mEq/L/min, 0.35 ± 0.01 mEq/L/min and 0.21 ± 0.02 Meq/L/min respectively. 80 mg/kg of TC and TA significantly reduced the histamine (1 mg/kg) induced gastric acid secretion. The results suggest that the antiulcer activity of *Tylophora conspicua* might be produced by gastric acid inhibition.

Keywords: Tylophora conspicua; gastric ulceration; gastric acids; rats.

INTRODUCTION

Several plants and herbs are used in folk medicine to treat gastrointestinal disorders, including peptic ulcers. Recently, there has been a growing interest in identifying new antiulcer agents from plant sources. For instance, recently we reported the antiulcer effects of *Entandrophragma angolense* in rats (Njar *et al.*, 1995).

In Ijebu-land, among the Yoruba speaking tribes of Western Nigeria, where the plant is found in abundance, concoctions prepared from the leaves of *T. conspicua* are commonly and frequently used as potent and highly effective compounds to ameliorate stomach upsets. Preliminary phytochemical screening carried out on the *Tylophora* extract showed that it contained mainly alkaloids and tannins. However, there is no information in the literature concerning the stomachic activity of this flora. As a part of our continued search for potent antiulcer agents from plant sources, this study was designed to investigate the effect of leaf extracts of *T. conspicua* on indomethacin-induced gastric ulceration in male albino rats. Attempts were also made to investigate the effects of *T. conspicua* on gastric acid secretion with a view to finding its probable mechanism of action.

MATERIALS AND METHODS

Animals. Adult male albino rats of the Wistar strain (180–200 g) obtained from the central animal house, College of Medicine, University of Ibadan were used after 7 days of acclimation to laboratory conditions. They were fed with normal rat chow (Ladokun Feeds Nigeria Ltd) and water *ad libitum*.

Preparation of extracts. Leaves of *T. conspicua* were obtained from the Forest Reservation of Ijebu-Ode, Nigeria and identified in the Department of Botany, University of Ibadan. A methanol extract of the plant was prepared using a Soxhlet extractor. A concentrated extract (TC) was obtained and lyophilized. An alkaloid extract (TA) was prepared by percolating the concentrated extract (TC) in 0.1 M HCl for 12 h before extraction with hexane (50 mL × 3). The residue obtained was extracted with $CHCl_3$ (50 mL × 3) and subsequently basified with NH_4OH (pH 9.0). More of the residual extract was again extracted with $CHCl_3$, and extracts were combined and purified as the alkaloid extract (TA). Solutions of TC and TA were prepared in sterilized water and 2% Tween 80, respectively.

Acute toxicity. Twenty-five male rats (180–200 g) divided into five groups were used. Increasing doses of the crude extract (TC) ranging from 100 mg/kg to 1000 mg/kg were given orally each as a single dose. The control group received 0.5 mL of sterilized water (vehicle for the crude extract). Another 25 male rats (180–200 g) divided into five equal groups were similarly treated with increasing doses (100–1000 mg/kg) of the alkaloid extract of *Tylophora conspicua* (TA). The control group received 0.5 mL, 2% Tween 80 (vehicle for the alkaloid fraction). The animals were starved for 16 h prior to administration of the extracts. All animals were observed for general behaviour over a period of 1

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Table 1. Effect of *Tylophora* extracts on ulcer index, percentage inhibition of ulceration and total gastric acidity

	Ulcer index[a]		% Inhibition of ulceration[b]		Mean total gastric acidity (meq/L)	
Treatment group $n = 5$	TC	TA	TC	TA	TC	TA
Normal saline/2% Tween 80	6.27 ± 0.91	6.57 ± 0.95	—	—	18.8 ± 1.01	19.7 ± 0.88
Propranolol 40 mg/kg	4.93 ± 0.83^c	5.43 ± 0.77^c	21.37	17.35	14.8 ± 0.93^c	16.3 ± 1.20^c
T. Extract 20 mg/kg	5.33 ± 0.87^c	4.67 ± 0.74^c	14.99	28.92	16.0 ± 0.87^c	16.0 ± 0.37^c
T. Extract 40 mg/kg	4.60 ± 0.68^c	3.33 ± 0.67^c	26.63	49.3	13.8 ± 0.73^c	14.0 ± 0.87^c
T. Extract 80 mg/kg	0.00	0.00				
	$0.00\pm$	$0.00\pm$	100	100	10.3 ± 0.47^c	10.0 ± 0.58^c

[a] Ulcer index $= \dfrac{\text{Mean degree of ulceration} \times \%\text{ of group ulceration}}{100}$

[b] Inhibition of ulceration $= \dfrac{\text{Ulcer index in control} - \text{Ulcer index in test}}{\text{Ulcer index in control}} \times 100$

TC, crude methanol extract of *Tylophora conspicua*; TA, alkaloid fraction of *Tylophora* extract.
[c] Significantly lower when compared with the respective control ($p < 0.05$).

week. The mortality rate within a 24 h period was recorded.

Acute indomethacin-induced gastric mucosal lesions. This was carried out as described earlier (Njar *et al.*, 1995). Male rats (180–200 g) were randomly assigned into six experimental groups of five animals each. One group served as the control and received sterilized water (0.5 mL), a second group received intraperitoneal propranolol (Sigma, 40 mg/kg) while the remaining groups received different doses of the crude extract orally. Food and water were withdrawn about 16 h before the commencement of the experiments. One hour after administering propranolol and 2 h after administration of water and extract, indomethacin (40 mg/kg, Mark, Sharp and Dohme) dissolved in 2% sodium carbonate in water was given intraperitoneally to all animals in all groups. The same procedures were carried out on rats placed on the alkaloid extract, except that the control group received 2% Tween 80 (vehicle for alkaloid extract) orally. Four hours after drug or vehicle administration, the animals were killed and their stomachs removed, weighed and opened along the greater curvature. The presence of spots and scoring of gastric ulceration was done according to the methods of Elegbe (1978) and Zaidi and Mukerji (1958). The total gastric acidity of rat gastric contents was determined according to the method of Lai (1964).

In another experiment, gastric acid secretion responses to intravenous injection of TC, TA and histamine (1 mg/kg) were carried out according to the method of Ghosh and Schild (1958).

Statistical analysis. The test of significance between the control and experimental groups was performed by the analysis of variance (ANOVA) using Duncan's multiple range test (Duncan, 1975).

RESULTS AND DISCUSSION

This study showed that *Tylophora conspicua* possesses antiulcer acitivity against experimental indomethacin-induced gastric ulceration in rats. Oral administration of TC and TA up to 1000 mg/kg did not produce any sign of toxicity in the rats. In addition no symptoms of stereotypic behaviour were observed over the 1 week period of study. There was no change in water or food intake (data not shown) when compared with the control. Moreover there was no change in daily body weight or organ weight during the next 3 weeks. The antiulcerogenic effects of TC and TA on indomethacin induced gastric lesions in rats are shown in Table 1. The extracts also produced a dose-dependent decrease in total gastric acidity. The gastroprotective action of TC and TA (80 mg/kg) was greater than that produced by propranolol (40 mg/kg) suggesting that the plant extracts were highly potent. The highest dose of the extract used in the acute toxicity (1000 mg/kg) and which did not cause any death was about twelve times that of the extract (TC and TA; 80 mg/kg) which conferred total protection against indomethacin-induced gastric mucosal lesion. This shows that *T. conspicua* has a wide margin of safety and oral administration of the plant concoction as done in traditional medicine may not have any adverse effect.

In view of the dose-dependent reduction in total gastric acidity by this extract (with the alkaloid fraction

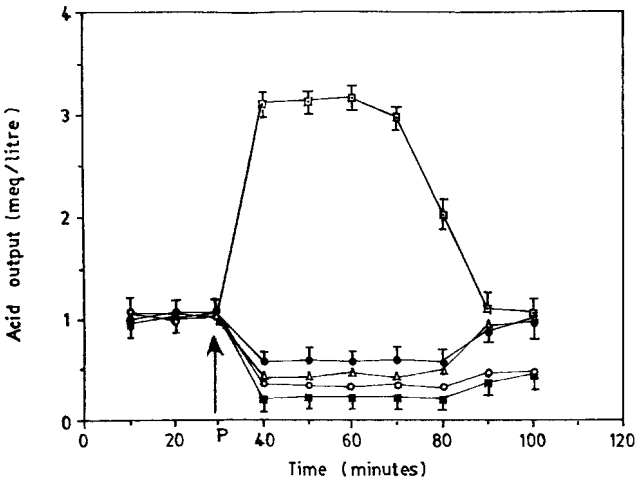

Figure 1. Effect of *Tylophora* extracts on gastric acid secretion *in situ*. P indicates point of drug and extract injection. histamine 1 mg/kg □; crude *Tylophora* extract (TC), 80 mg/kg △; alkaloid extract (TA), 80 mg/kg ■; TC plus histamine ● and TA plus histamine ○.

producing greater inhibition), it is thought that the antiulcer activity of the extract lies in its ability to inhibit gastric acid secretion. Consequently, the effects of these extracts on basal and histamine induced gastric acid secretion were studied. The results shown in Fig. 1, clearly suggest that these extracts probably act by inhibiting gastric acid secretion. The gastric acid stimulatory action of histamine is mediated by the H_2 receptor as demonstrated by a wealth of pharmacological studies (Batzri and Dyeri, 1981; Berglindh, 1977; Bottcher *et al.*, 1989; Dial *et al.*, 1981). Histamine stimulation of acid secretion is inhibited competitively by selective H_2 receptor antagonists (Hirschowitz and Molina, 1983). Since endogenous histamine formation and release in the gastric mucosa have been implicated in the pathogenesis of gastric ulcers, antihistamine agents may be useful in the prevention of such lesions (Parmar and Ghosh, 1981). Nunes *et al.* (1989) showed that tannins present in *Dalbergia monetaria* L. were histamine decarboxylase inhibitors and had been found to be antiulcerogenic. Phytochemical screening of *Tylophora* extract showed the presence of tannins, suggesting these compounds are antihistaminic and therefore the antiulcer agents of *Tylophora conspicua*.

Thus the data presented in this paper provide an experimental basis for the use of the *T. conspicua* as antigastrointestinal disorder agent. Future studies will focus on the phytochemical analysis of the extract with a view to isolating the antiulcer compounds.

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