Antipyretic and Analgesic Studies of the Ethanalic Extract of *Teclea nobilis* Delile

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The crude ethanol extract of the leaves of an African medicinal plant *Teclea nobilis* has been studied for its antipyretic, analgesic and anti-inflammatory activities. The extract exhibited marked antipyretic and analgesic activities while it was found to be weakly active against carrageenin oedema.

***Keywords*: *Teclea nobilis*; ethanol extract; analgesic; antipyretic activity.**

INTRODUCTION

Teclea nobilis Delile (Rutaceae), a shrub or understory tree 2–12 m high, is widely distributed in tropical Africa namely Ethiopia, Sudan, Somalia, Kenya, Uganda, Tanzania and also in Arabia. This plant is used in folk medicine of many African societies. Thus in South Africa, the bark of *T. nobilis* is reported to be a gonorrhoea remedy while in Tanzania, the leaves are used as cure for fever (Watt and Breyer-Brandwijk, 1962). Similarly in Ethiopian folk medicine the leaves are used to control pain. In order to shed some light on some of the locally reported medicinal properties of *T. nobilis*, we subjected the ethanol extract of this plant to some pharmacological tests, specifically antipyretic, analgesic and anti-inflammatory. Comparison was made against the standard drugs acetylsalicylic acid and phenylbutazone.

MATERIALS AND METHODS

Plant material. The leaves of *T. nobilis* were collected from Lepis State Forest, Arsi Province, Ethiopia at an altitude of 2100 m in April 1985. The plant was identified by Mr Zemede Asfaw and a voucher specimen is kept at the National Herbarium, Addis Ababa, under the cipher Zemede 535.

Preparation of ethanol extract. Powdered leaves of *T. nobilis* (500 g) were extracted in a Soxhlet apparatus using 95% ethanol for 8 h. The solvent was removed under vacuum to yield the crude ethanol extract used in the study. Complete removal of the solvent was achieved by further applying vacuum till constant weight was attained. In addition the extract was dried over anhydrous calcium chloride in a desiccator (Capasso *et al.*, 1983).

Animals. Male albino Wistar–Nossan rats (100–110 g) and male albino Swiss mice (22–24 g) were used. Animals were deprived of food overnight but were allowed water *ad libitum*, unless otherwise stated.

Antipyretic activity. This was determined in rats by the modified method reported by Turner (1965). The rats were trained to remain quiet in a restraint cage. A thermister probe was inserted 3 cm into the rectum and temperature recorded on a digital thermometer (Ellab a.s.).

After measuring the basal rectal temperature, animals were given s.c. injections of 10 mg/kg of a 30% w/v suspension of yeast in 0.9% w/v NaCl solution. Food was then withheld from the animals. At 15 h after yeast injection, the temperature of each rat was re-measured and animals showing a rise in temperature less than 0.6 °C were discarded. The remaining rats were then divided into groups and dosed with plant extract (25–100 mg/kg) or drug references (acetylsalicylic acid 25–100 mg/kg; phenylbutazone 30–120 mg/kg), at hourly intervals starting 2 h after dosing and continuing for 6 h. The rectal temperature of each rat was measured and compared with the pre-drug value. The mean change from the pre-drug over the 2–6 h period was then calculated for each animal and expressed as a percentage of the pre-drug yeast-induced temperature change recorded for the same animals. Finally the mean percentage was calculated for each group.

Antinociceptive activity. This was evaluated in mice using a standard hot plate method. Briefly, individual

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mice were placed on a heated surface at 50 ± 0.5 °C and the latency of their foot or anterior body-lifting response to the thermal stimulus was recorded. The animals showing a nociceptive threshold over 8 s were discarded. The remaining mice were then divided into groups and orally dosed with plant extract (25–200 mg/kg) or acetylsalicylic acid (25–100 mg/kg). Pilot studies suggested that the maximal antinociceptive activity of *T. nobilis* extract and reference drug occurred 90 min after the oral administration. On the basis of these observations, all compounds studied were tested 90 min after oral administration. The nociceptive threshold of each animal was compared to the initial one.

Anti-inflammatory activity. Inhibition of carrageenin paw oedema was used as a measure of anti-inflammatory activity. Oedema of the rat right-hind paw was produced and determined as described earlier (Mascolo *et al.*, 1987). Plant extract (25–300 mg/kg) and the standard drug acetylsalicylic acid (25–100 mg/kg) were suspended in 5% gum arabic (vehicle) and administered orally 1 h before eliciting paw oedema.

Drugs. The drugs used were: acetylsalicylic acid and phenylbutazone [Gianni, Milano], carrageenin [Viscarin 402, Marine Colloids Inc., Springfield, USA); yeast [Bertelli]. All other chemicals were analytical-grade preparations obtained from usual commercial sources.

Statistics. The data were analysed for significance by the Student's paired *t*-test (2-tailed).

RESULTS AND DISCUSSION

The inhibitory effect of the ethanol extract of the leaves of *T. nobilis* and selected reference drugs on fever, induced in rats, by yeast is shown in Table 1. Subcutaneous injection of yeast suspension markedly increased the rectal temperature 15 h after its administration (mean ± S.E.: 1.5 ± 0.4 °C, $n = 10$, $p < 0.05$). Oral treatment with plant extract (25–100 mg/kg), dose-dependently decreased temperature. In this test situation, plant extract was equipotent to acetylsalicylic acid and phenylbutazone. The IC_{25} (dose required to protect 25%) was 31.7 mg/kg. Corresponding values for acetylsalicylic acid and phenylbutazone were 37.5 and 36.0 mg/kg. An additional experiment, designed to investigate whether the ethanol extract of the leaves of *T. nobilis* was capable of exerting a hypothermic action in normothermic rats, was undertaken. The results obtained showed that the extract produced no significant hypothermia at oral doses of 25–100 mg/kg when compared with vehicle-treated controls over the same period of observations (2–6 h after drug administration). The extract (25–200 mg/kg) also demonstrated antinociceptive activity as judged by its ability to increase the thermal response latencies of mice kept on heated surface (Table 2). The IC_{25} of plant extract in this test was 26.1 mg/kg. The corresponding value for acetylsalicylic acid was 32.5 mg/kg. Table 3 demonstrates the dose-related effect of *T. nobilis* extract on carrageenin-induced oedema. Doses of 25–100 mg/kg of *T. nobilis* extract did not significantly modify carageenin oedema while high doses (200–300 mg/kg) produced a significant anti-inflammatory effect. The IC_{25} of plant extract was 157.5 mg/kg. The corresponding value for acetylsalicylic acid was 22.5 mg/kg. These results demonstrate that the ethanol extract of the leaves of *T. nobilis*

Table 1. Effect of *T. nobilis* extract, acetylsalicylic acid and phenylbutazone on yeast-induced hyperthermia in rats

Treatment	Dose (mg/kg, p.o.)	(*n*)	Mean % reduction of fever (±S.E.)
Vehicle	10 ml/kg	(6)	5.7 ± 2.8
T. nobilis extract	25	(8)	21.5 ± 5.0
(ED_{25} = 31.7)	50	(20)	34.5 ± 6.9[a]
	100	(12)	30.5 ± 7.0[b]
Acetylsalicylic acid	25	(6)	19.4 ± 4.1[a]
(ED_{25} = 37.5)	50	(10)	33.0 ± 7.0[b]
	100	(10)	54.4 ± 6.9[b]
Phenylbutazone	30	(6)	20.3 ± 5.9[a]
(ED_{25} = 36.0)	60	(10)	31.7 ± 7.4[b]
	120	(10)	59.3 ± 6.4[b]

S.E = standard error.
[a] $p < 0.05$.
[b] $p < 0.01$.

Table 2. Effect of *T. nobilis* extract on thermal stimulus induced in the mouse by hot plate

Treatment	dose (mg/kg, p.o.)	(*n*)	% increase of reaction time mean (±S.E.)
Vehicle	10 ml/kg	(5)	3.4 ± 1.1
T. nobilis extract	25	(8)	21.8 ± 4.0
(ED_{25} = 26.1)	50	(10)	33.7 ± 3.9[a]
	100	(10)	51.6 ± 4.3[b]
	200	(10)	71.0 ± 6.5[b]
Acetylsalicylic acid	25	(12)	20:8 ± 2.8[a]
(ED_{25} = 32.5)	50	(12)	35.1 ± 4.1[b]
	100	(12)	70.0 ± 7.5[b]

S.E. = standard error.
[a] $p < 0.05$.
[b] $p < 0.01$.

Table 3. Effect of *T. nobilis* extract and acetylsalicylic acid on carrageenin induced oedema in rats

Treatment	dose (mg/kg, p.o.)	(*n*)	*A* ± S.E.	% inhibition
Vehicle	10 ml/kg	(6)	3.85 ± 0.7	—
T. nobilis extract	25	(12)	3.65 ± 0.8	5.2
(ED_{25} = 157.5)	50	(12)	3.30 ± 0.8	14.3
	100	(12)	3.00 ± 0.7	22.1
	200	(12)	2.65 ± 0.6[a]	31.2
	300	(6)	2.45 ± 0.7[b]	36.4
Acetylsalicylic acid	25	(9)	2.83 ± 0.7	26.5
(ED_{25} = 22.5)	50	(10)	2.00 ± 0.3[b]	48.0
	100	(10)	1.50 ± 0.4[c]	61.0

A = mean oedema 1–4 h + $\frac{1}{2}$ mean oedema 5th h.
S.E. = standard error.
[a] $p < 0.5$.
[b] $p < 0.01$.
[c] $p < 0.001$.