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PRELIMINARY STUDIES ON ANTIPYRETIC AND ANALGESIC PROPERTIES OF *TAVERNIERA ABYSSINICA*

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ABSTRACT. In an attempt to ascertain the pharmacological basis of the use of the marketed traditonal drug Taverniera abyssinica *A. Rich. (Amharic name* Dingetegna*), crude extracts as well as purified substances of this plant were tested for their antipyretic and analgesic properties. Antipyretic activity was determined on rats made hyperthermic by yeast injection and analgesic activity was determined by the hot plate, as well as the acetic acid induced writhing, methods. The study showed that the plant possesses significant antipyretic and analgesic activities.*

In the folk medicine of central Ethiopia, the roots of a plant known in Amharic as 'Dingetengna' are commonly presecribed for the "treatment of sudden illness", particularly stomachache, headache and fever. The mode of administration usually involves chewing of the roots and swallowing the juice. A survey of 19 medicinal plant markets of central Ethiopia by Kloos et al (1) showed that a number of traditional drug vendors were selling this plant for the purposes stated above.

Based on information obtained from vendors, it was possible to locate the plant which was then unequivocally identified as *Taverniera abyssinica* (Leguminosae). A voucher specimen of the plant was deposited in the National Herbarium, Addis Ababa University, under the cipher Mesfin T. 3687. *T. abyssinica* is a shrub that grows up to 2 m high in bushland or on limestone at altitudes ranging from 1700-2150 m. This species has so far been recorded only from Ethiopia (2). Furthermore the genus *Taverniera* is a relatively small genus with only 15 species, found in arid regions from Egypt to India (2). Three other species are also known to occur in Ethiopia.

The plant material used in this study was collected from a locality known as Tinishu Muti Kebele near the town of Melka Konture, 52 km west of Addis Ababa along the Butajira road at an altitude of 2150 m. We were informed by the local people that traditional drug vendors collect the roots of the plant from this area. We established by chemical methods (3) that the constituents of the roots of *T. abyssinica* were identical to the constituents of the marketed traditional drug sold in the main market under the name of 'Dingetegna'. In this study, therefore, roots purchased from the market were also used. As there is no prior report on either the chemistry or the pharmacology of this plant, we set out to study both aspects. The results of the chemical study, which were reported recently (3), led to the isolation and identification of some of its constituents, prominent in which are the isoflavonoids formononetin 1 and afrormosin 2 and the pterocarpans medicarpin 3 and 4hydroxymedicarpin 4. In this paper we report the results of the pharmacological studies on the crude extracts as well as on some of the purified substances.

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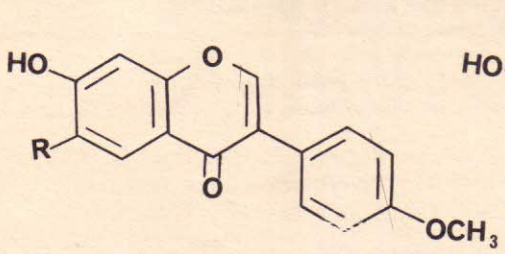
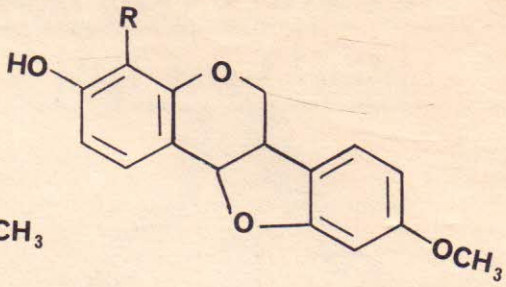
Structures of formononetin (1), afrormosin (2), medicarpin (3) and 4-hydroxmedicarpin (4)





1 R = H

2 R = OCH_3

3 R = H

4 R = OH

MATERIALS AND METHODS

Animals: Male Wistar rats (110-120 g) and Swiss mice (22-25 g) were housed in plastic cages at 22-25°C and maintained on a standard pellet diet (Nossan S.r.1, Correzzana, Italy) and water ad libitum.

Extraction: Air-dried and powdered roots of *T. abyssinica* (400 g) were extracted using a Soxhlet apparatus with ethanol for 8 hrs. The solvent was completely removed in vacuo to yield the crude extract (extract 1) which was used in the study. Another batch of the roots was extracted by the same method first with petroleum ether which, after solvent removal, yielded extract 2 followed by chloroform (extract 3) and finally ethanol (extract 4).

The compounds used in this study were isolated from the crude extracts employing chromatographic techniques and their structures were established by spectroscopic methods as previously described (3).

Antipyretic activity:

This was determined in rats according to the method described by Autore et al (4). Briefly, a thermister probe was inserted 3 cm into the rectum of each animal and temperature was recorded on a digital-thermometer (Ellab a.s.). After measuring the basal rectal temperature, rats were given subcutaneous injections of 10 ml/kg of a 30% w/v suspension of yeast (Bertelli) in NaCl 0.9%. At the fifteenth hour after yeast injetion rectal temperature of all the animals wa again recorded. Animals showing a rise in temperature less than 0.5°C were not included in the test. The remaining rats were then divided into groups of 6 to 8 animals each and dosed with plant extracts (25-200 mg/kg) or drug reference (acetylsalicylic acid, 25 and 100 mg/kg). Starting 2 hrs. after dosing, the rectal temperature of each rat was measured at hourly intervals until 4 hrs after dosing. The mean change from the pre-drug value over the 2-4 hrs period was 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.

Analgesic activity:

1. Hot plate method: The method used was described by Mascolo et al (5). Briefly, individual mice were placed on a heated surface maintained at 50 ± 0.5 °C and the latency of their foot or anterior body lifting response to thermal stimulus was recorded. Animals showing a nociceptive threshold over 8 secs were discarded. The remaining mice were divided into groups (6-8 animals each group) and orally dosed with plant extract (1200 mg/kg) or acetylsalicylic acid (30-60 mg/kg). Ninety minutes after oral treatment the nociceptive threshold of each animal was evaluated and compared to the initial one. The mean change was expressed as a percentage increase of reaction.

2. Acetic acid induced writhing: The method used was that described by Collier et al (6). The test sample was administered orally to mice, sixty minutes later each animal was injected intraperitoneally with acetic acid (50 mg/kg in sterile saline) and the number of "writhes" (or abdominal stretching movements) occurring in the following 20 min was recorded.

Acute toxicity: The acute toxicity of the crude ethanolic extract was evaluated in mice by administering the extract by gavage in volume of 10 ml/kg. The mice were fed ad libitum during the trial and kept under observation for seven days.

Drugs: Extracts and reference drug were suspended in 5% gum arabic (vehicle) and administered orally by gavage to fasting (12-14 h) animals. The control group received corresponding doses of the vehicle (10 ml/kg).

RESULTS

The effects of graded doses of ethanolic extract of *T. qbyssinica* on the rectal temperature of rats treated with yeast are shown in Table 1. This is based on mean normal rectal temperature which was found to be 36.4 ± 0.3 °C and a mean elevation of body temperature 15 hr. after yeast injection by 1.2 ± 0.4°C.

The extracts produced a dose dependent reduction of yeast induced pyrexia ($p < 0.05 - 0.01$). Furthermore an experiment to determine whether the extract was capable of exerting a hypothermic effect showed that the extract did not produce hypothermia at oral doses of 200 mg/kg.

The effects of extract 1 (different concentrations), and of extracts 2 to 4, on thermal stimulus induced in the mouse by heated surface are given in Table 2. Significant increase in the thermal response latencies of mice was exhibited by all extracts, with maximal response occurring 90 minutes after treatment. These effects are compared to that of the reference compound acetylsalicylic acid.

Similarly, the effects of the crude and the purified substances isolated from the plant, namely medicarpin, afrormosin and 4hydroxymedicarpin, on acetic acid induced writhing in mice are shown in Table 3. Significant activity was also noted in this test for the crude extracts and the compounds isolated from the plant.

The toxicity studies, carried out on the ethanolic extract, showed that the mice tolerated up to doses of 2.5 g/kg of the test extract. In fact, no mortality occurred in any of the animals and no side effects were recorded.

TABLE 1. Effect of ethanol extract of *T. abyssinica* and acetylsalicylic acid on yeast-induced pyrexia in rats

Treatment	Dose -mg/kg	Mean % reduction fever ± S.E.
Extract 1	25 (6)*	7 ± 3
	50 (7)	15 ± 5
	100 (8)	31 ± 6[a]
	200 (8)	63 ± 7[b]
Acetylsalicylic acide	25 (8)	21 ± 3
	100 (6)	65 ± 4[c]

*Figures in parenthesis represent number of experiments
[a] $p < 0.05$; [b] $p < 0.01$; [c] $p < 0.001$, Student T-test.