

An aqueous extract of trunk bark of *Ficus religiosa* has anxiolytic activity

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Abstract: The aim of this study was to evaluate the anxiolytic potential of a water extract of trunk bark of *Ficus religiosa*. This was tested in rats using the Vogel conflict test system. 1 ml of different concentrations of the extract (12.5, 25, 125, 250, 500 mg/kg) or water (vehicle) was orally administered (three times per day) to different groups of rats and the average number of mild electrical shocks accepted per minute was determined as a measure of anxiolysis. The results showed a potent anxiolytic activity with a rapid onset. The anxiolytic activity was, however, not dose-related. The effect was also not accompanied by sedation (measured in terms of number of head dips, time per head dip, number of rear or locomotory activity in rat hole-board technique) or loss of motor coordination due to muscle relaxation (in terms of time for righting reflex). Further, the extract was non-toxic (in terms of haematology, rectal temperature, body weight and food and water intake) even when given three times a day for seven consecutive days. Overall, the results suggest that the anxiolytic effect is unlikely to have been mediated via a gamma-aminobutyric acid mechanism as with benzodiazepines. We conclude that it may be possible to isolate from this plant promising anxiolytic agents or develop lead compounds without undesirable side-effects.

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Introduction: Anxiety and anxiety-related disorders seem to be more frequent nowadays than during past centuries [1]. Yet only four main classes of drugs are available to relieve anxiety: benzodiazepines, serotonergics, dopamergics and beta blockers [2]. Of these, beta blockers can combat only physical symptoms of anxiety. Regular use of other three classes of drugs, especially benzodiazepines, not only induces physical or psychological dependence but may also lead to abuse [2,3]. Further, sudden cessation of these drugs often causes withdrawal symptoms [4]. There is a pressing need for the development of novel and selective anxiolytics lacking these unpleasant side-effects.

The tree of *Ficus religiosa* Linn. (Family: Moraceae known as Bo in Sinhala and in Arachu in Tamil) is a sacred plant venerated by Buddhists. A strong belief exists that this tree has anxiety relieving properties. It is possible that it contains anxiolytic constituents which could be developed into potential drugs or provide lead compounds for the

design and synthesis of selective and extremely potent pharmacotherapeutic agents for anxiety.

We therefore investigated the potential of a water extract of trunk bark of *Ficus religiosa* in rats using the Vogel conflict test system [5]. Trunk bark was selected since this is used therapeutically in traditional medicine for the treatment of ulcers, skin diseases and tooth ache and for promotion of fertility in women [4].

Materials and methods: Pieces of fresh trunk barks (length approximately 30 cm and breadth 3-6 cm) of *Ficus religiosa* were removed from a mature tree located in the University of Colombo campus during January, and April, 1998 using a kitchen knife. These were cut into small pieces (length 2.5 cm and breadth 1 cm) using a pen knife on the day of collection and was air-dried overnight at room temperature (30-32°C). This material was then subjected to reflux boiling in distilled water (1 : 3 w/v) for 3 h in a round bottom flask coupled to a Liebig's condenser and allowed to cool to room temperature.

The resulting dark brown extract was filtered using cotton wool. The filtrate was freeze-dried using a freeze-drier (Model LFD - 600 EC, Laytant Life Science, Tokyo, Japan) for 5 consecutive days (yield: 8%). The resulting reddish brown powder was dissolved in distilled water to obtain the required concentrations in 1 ml (500, 250, 125, 25 and 12.5 mg/kg) of solution. The pH was determined using a pH meter (TOA Electronics, Tokyo, Japan). The extract was stored at 4°C until use.

The presence or absence of steroids and triterpenoids, phenols, coumarines, alkaloids and amino acids and peptides were examined using standard chemical tests as described by Fransworth [6].

The experimental animals were healthy adult and cross-bred male rats (180-210 g) from our own colony. They were housed under standardized animal house conditions with free access to pelleted food (Vet house Ltd, Colombo, Sri Lanka) and tap water. The rats used in the evaluation of anxiolytic activity were deprived of water for 24 h before the commencement of the experiment.

63 rats were randomly divided into six groups. Group 1 ($n = 14$), group 2 ($n = 9$), group 3 ($n = 12$), group 4 ($n = 10$), group 5 ($n = 3$) were given 500, 250, 125, 25 and 12.5 mg/kg of extract, respectively and group 6 ($n = 15$) 1 ml of distilled water orally. 2 h following administration, these rats were individually placed in the plexiglass box (20 × 20 × 30 cm) of the Vogel conflict test system apparatus (Model VC-001, Muromachikikai, Co Ltd, Tokyo, Japan). The anxiolytic effect was evaluation in a 15 min testing session.

The intensity and duration of the electric shock used were 0.5 mA for 0.5 s respectively. After 15 min the test was