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Neuropharmacological effects of the aqueous extract of *Nauclea latifolia* root bark in rats and mice

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Abstract

The present study evaluated the neuropharmacological effects of the aqueous extract of *Nauclea latifolia* root bark in rodents. Effects on the spontaneous motor activity (SMA), exploratory behaviour, pentobarbital sleeping time, apomorphine-induced stereotypic behaviour and motor coordination (rota-rod performance) were investigated. The extract (50–200 mg/kg p.o.) significantly ($P < 0.05$) decreased the SMA and exploratory behaviour in mice and prolonged pentobarbital sleeping time in rats dose-dependently. The extract also remarkably attenuated the intensity of apomorphine-induced stereotypy dose-dependently in mice, but had no effect on motor coordination as determined by the performance on rota-rod. These results indicate the presence of psychoactive substances in the aqueous extract of the root bark of *Nauclea latifolia*.

Keywords: *Nauclea latifolia*; Exploratory behaviour; Spontaneous motor activity; Pentobarbital sleep; Apomorphine-induced stereotypic behaviour; Motor co-ordination

1. Introduction

Nauclea laltifolia Smith (family: Rubiaceae) occur wildly in Savanna forests of continental Africa where it is known as African peach or African fig. The plant has been used by the natives of East and West Africa in traditional medicine for treatment of various ailments (Dalziel, 1957). For instance, the pulverized root and bark have been used to treat sores (as topical application by washing of the affected parts) and gonorrhoea in Sudan, Ghana, Ivory Coast and Nigeria. Similarly, a decoction of the root bark is commonly employed in the treatment of stomach disorders, cough and, in particular, malaria fever (Irvine, 1961). In malaria ethnopharmacy, the root bark is the preferred part of the plant used. This part is usually harvested, sun dried and pulverized to obtain a powder. About 250 g of the powdered material is macerated in 'gin' (local alcoholic beverage) or hot water and administered twice daily for 7 days. Clinically, on a pilot scale, the freeze-dried cold-water extract is formulated into capsules and administered orally at a dose range of 16–25 mg/kg.

Previous scientific studies of the plant revealed that both the methanol and ethanol extracts of the dried fruit, stem and root bark possess spasmolytic and anti-bacterial activity (Ogunlana and Ramstad, 1975). The hot water extract of the root and stem bark of the plant was found to be active against *Plasmodium falciparum* in vitro (Gbeassor et al., 1989). Further investigations in our laboratory revealed that the cold water extracts of the leaves of *Nauclea latifolia* as well as some of its fractions were active against *Plasmodium berghei* in vivo in addition to their spasmolytic effects (Gamaniel et al., 1997). Udoh et al. (1998) reported the cardiovascular effect of the root and leaf extract of *Nauclea latifolia*. Recent

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investigations corroborate the spasmolytic, anti-plasmodial and anti-parasitic effects of the plant (Benoit-Vical et al., 1998; Traore-Keita et al., 2000; Fakae et al., 2000; Onyeyili et al., 2000; Tona et al., 2000). These activities support the traditional notion of the use of this plant.

As a step towards development and eventual introduction into clinical use as anti-malarial, we set out to investigate possible central nervous system (CNS) effect of high acute doses of *Nauclea latifolia* using mice and rats. The results will provide additional safety pharmacology data on the aqueous extract of *Nauclea latifolia*.

2. Materials and methods

2.1. Plant material and preparation of extract

The roots of *Nauclea latifolia* were collected from Idu, in the Federal Capital Territory, Abuja, Nigeria for this study. Taxonomic identification was established by Mallam Muazzam Ibrahim, of the National Institute for Pharmaceutical Research and Development Herbarium, Abuja where voucher (Number 4251) specimens were preserved for reference. The root bark was separated and cleaned, then sun-dried and pulverized using a mechanical grinder. The powdered material was extracted with distilled water by cold maceration for 24 h, then filtered through Whatman no. 1 filter paper and freeze-dried using LYOVAC, GT2 (Germany). This gave a yield of 9.50% (w/w). The freeze-dried extract was then subsequently reconstituted in distilled water at appropriate concentrations for the various experiments.

2.2. Drugs

Apomorphine hydrochloride, pentobarbital sodium, diazepam (Sigma Chemical Co., USA), nitrazepam (Roche, Nigeria), sodium chloride (Fisher Scientific Co. USA).

2.3. Animals

Swiss albino mice (18–25 g) and adult Wistar rats (200–250 g) of either sex were maintained at the Animal Facility Centre (AFC), NIPRD, under standard environmental condition of temperature (22 ± 3), relative humidity (14 ± 1) and light/dark cycles (12/12 h). The animals were fed with Ladokun Feeds, Ibadan, Nigeria and water ad libitum.

2.4. Pharmacological evaluation

2.4.1. Studies on exploratory behaviour

The head dip test procedure of Perez et al. (1998) was used for this study. Mice were divided into five (5) groups ($n = 6$). Three Groups received graded doses of the extract (50, 100 and 200 mg/kg p.o). One group received nitrazepam (2 mg/kg i.p.) and the remaining group received normal saline (20 ml/kg p.o.) to serve as control. The animals were singly placed on LETICA (Spain) instrument with 16 evenly spaced holes and a counter (LE 3333) before and at 30 and 60 min post-treatment. The number of times mice dipped their heads into the holes during the 5 min trial was automatically counted both for control and treated groups.

2.4.2. Studies on spontaneous motor activity (SMA)

Adult mice of either sex were randomly divided into four groups of six mice per group. The base line activity counts of all the animals were taken twice. Three groups were given graded doses of the extract (50, 100 and 200 mg/kg p.o.). Animals in the remaining group received normal saline (20 ml/kg p.o.). Thirty minutes post-treatment, the animals were transferred individually to Letica activity cages (LE 886) connected to a multicounter (LE 3806) and after 1 min latency, activity counts were recorded for 6 min at 30, 60, 90 and 120 min (Amos et al., 2001b).

2.4.3. Studies on pentobarbital-induced sleep in rat

The effect of the extract on pentobarbital sleeping time was performed in five groups of rats ($n = 5$). Three groups received graded doses of the extract (50, 100 and 20 mg/kg p.o.). One group received diazepam (1 mg/kg i.p.), while animals in the control group were administered normal saline (20 ml/kg p.o.). Thirty minutes post-treatment, pentobarbital sodium (35 mg/kg) was administered i.p. to each rat. The onset and duration of sleep for each rat was recorded, the criterion for sleep being loss of righting reflex (Wambebe, 1985; Ramirez et al., 1998).

2.4.4. Apomorphine-induced stereotypic behaviour

The effect of the extract on apomorphine-induced stereotypic behaviour was investigated as described by Kenneth and Kenneth (1984). Briefly, three groups of mice of either sex ($n = 6$) were administered graded doses of the extract (50, 100 and 200 mg/kg p.o.), while animals in the control group received normal saline (20 ml/kg p.o.). Thirty minutes later, apomorphine (2 mg/kg i.p.) was administered to each mouse. Signs of stereotypic behaviour, which include mainly sniffing and gnawing, were observed and rated. The stereotypic episodes were scored as follows: absence of stereotypy (0); occasional sniffing (1); occasional sniffing with occasional gnawing (2); frequent gnawing (3); intense continuous gnawing (4); intense gnawing and staying on the same spot (5). The stereotypic behaviour was measured and scored after every minute and mean of 5 min period was calculated and recorded.

2.4.5. Studies on motor coordination (rota-rod performance)

This test was performed using a horizontal rotating rod (Ugo Basile 7560, Milano, Italy) set at a rate of 16 revolutions per minute. Mice that were able to remain on the rod longer than 3 min were selected and grouped into four ($n = 6$). Groups I–III received the extract at doses of 50, 100 and 200 mg/kg p.o., respectively. Animals in the remaining