

Full Length Research Paper

Anti-pyretic, anti-inflammatory and anti-diarrhoeal properties of *Faidherbia albida* in rats

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***Faidherbia albida* Del. (local name: Gawo) is employed traditionally to treat disorders such as fever, diarrhoea, urticaria, vomiting, cough, rheumatism and haemorrhage. The present study was carried out to scientifically appraise some of the folkloric uses of the plant. The crude aqueous extract was studied for acute toxicity, its anti-pyretic, anti-inflammatory and anti-diarrhoeal effects using yeast-induced pyrexia, kaolin-induced oedema and castor oil-induced diarrhoeal models in rats. The extract was not lethal to the rats dosed at 5000 mg/kg body weight. At a dose of 500 mg/kg body weight, it significantly ($P < 0.05$) decreased yeast-induced pyrexia in rats. At doses of 250 and 500 mg extract/kg body weight, the extract significantly ($P < 0.05$) inhibited kaolin-induced acute inflammation and reduced frequency of diarrhea in the rats. These results indicate that aqueous extract of *F. albida* possesses potent anti-pyretic, anti-inflammatory and anti-diarrhoeal effects and thus pharmacologically justifies its folkloric use in the management of fever, rheumatic inflammatory conditions and diarrhoea.**

Key words: *Faidherbia albida*, aqueous extract, anti-pyretic, anti-inflammatory, anti diarrhoeal.

INTRODUCTION

Plants continue to serve as possible sources for new drugs and chemicals derived from various parts of plants. These can be extremely useful as lead structure for synthetic modification and optimization of bioactivity. Besides widespread use of botanicals as medicinal products in developing countries, such products are also becoming part of the integrative health care systems of industrialized nations known as “complementary alternatives system of medicines” (CAM). Safety and efficacy of natural herbal product is therefore a cause of concern to promote and rationalize their use.

The plant *Faidherbia albida* Del. (Family: Mimosaceae) is widely used in folk medicine in Africa. It is common and widely distributed across Senegal to Northern Nigeria, and extending from sub-Saharan Africa to Egypt and in East Africa southward to the Transvaal (Eggeling and Dale, 1952). It is known as Gawo among the Hausas of the Northern Nigeria. It is a large tree, 8 – 15 m high in Senegal (Berhant, 1975) and up to 25 m in Nigeria (Keay

et al., 1964). The roots can reach aquifers up to 80 m below the surface. Young trees have inverted cone-shaped crown, old trees with a hemispherical large canopy. Young branches and twigs are cream coloured to whitish, stipular spines are whitish, straight in axillary pairs somewhat at the base up to 5 cm long with a brown tip. The bark is grey, rough deeply fissured, becomes scaly with age and rich in tannins (Dalziel, 1937). The leaves are bipinnate, blue green with 3 – 12 pairs of pinnae carrying 6 – 23 pairs of leaflets up 12 mm long x 5 mm wide, partly overlapping. Contrary to all other native “acacias” *albida* sheds its leaves during rainy season and keeps them through out the dry season.

An infusion or decoction of the plant is made with other plants in Senegal to treat ‘diangara cayor’, an inclusive term covering many diseases (Kerharo and Adam, 1964). In Tanganyika and South West Africa, a decoction of the plant is taken for diarrhoea and as anti-emetic in fever (Wickens, 1969). The bark in decoction is used to cleanse new wounds, having an action akin to that of potassium permanganate, in the treatment of kidney pains, and mixed with other drugs for madness (Kerharo and Adam, 1974). In Nigeria, infusion (tea) of the plant is

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taken for fever, cough and to assist in childbirth (Singha, 1965). The Fulanis in Nigeria put it into a portion for chest pain (Jackson, 1973).

This study was carried out to investigate the anti-pyretic, anti-inflammatory and anti-diarrhoeal properties of the crude aqueous extract of *F. albida* in rats.

MATERIALS AND METHODS

Plant material

The leaves and stem bark of *F. albida* were collected from Gyamso Ward in Toro Local Government Council of Bauchi State, Nigeria during the month of January, 2005. They were identified and authenticated by Mr. Abdul-Karim of the Federal School of Forestry, Jos. A voucher specimen (number NIPRD/H/6151) was deposited at NIPRD herbarium for future references. The stem bark and leaves were cleaned, air-dried for 7 days and pounded into fine powder using mortar and pestle. The powder was stored in an airtight container and kept in a cool, dry place.

Extract preparation

Two hundred gram of the powdered stem bark was weighed and soaked in 2000 ml of water and ethanol in ratio 1:1 for 48 h. The mixture was filtered using muslin cloth followed by Whatman filter paper (No. 1). The resultant filtrate was evaporated to dryness on steam bath to give a yield of 8.0 % (w/w) of the extract. Aliquot portions of the crude extract residue were weighed and dissolved in distilled water for use on each day of the experiment.

Animals

Male Wistar rats (150 – 200 g) obtained from Experimental Animal Department, University of Jos were used in the study. The rats were fed standard laboratory diet, given water *ad libitum* and maintained under laboratory condition of temperature $22 \pm 1^\circ\text{C}$, relative humidity 14 ± 1 and 12 h light: 12 h dark cycle. All experiments were performed according to the "Principles of Laboratory Animal Care" (NIH Publication No. 85; rev. 1985).

Phytochemical screening

Conventional standard protocols (Odebiyi and Sofowora, 1978; Trease and Evans, 1983) for detecting the presence of different chemical constituents in the plant extract were employed. Secondary metabolites tested include alkaloids, tannins, saponins, glycosides, flavonoids, digitalis, phenols, resins and volatile oils.

Acute toxicity (LD₅₀) study

Acute toxicity study was carried out using the method of Lorke (1983). In the first phase, nine rats randomly divided into three groups of three rats per group were given 10, 100 and 1000 mg extract/kg body weight orally (via a cannula), respectively. The rats were observed for signs of adverse effects and death for 24 h and then weighed daily for 14 days. In the second phase of the study, the procedure was repeated using three rats randomly divided into three groups of one rat each, given 1600, 2900 and 5000 mg extract/kg body weight, respectively. The rats were also observed for signs of toxicity, mortality and weighed for 14 days. The surviving animals were sacrificed, autopsied and examined macroscopically

for any pathological changes.

Anti-pyretic activity

Anti-pyretic activity of *F. albida* was carried out using the methods of Williamson et al. (1996). Rats were weighed and randomized into five groups of five rats per group. The baseline body temperatures of the rats were taken by inserting a clinical thermometer into their anal cavities for about 2 min. The steady temperature readings obtained were recorded as the pre-treatment temperatures. Pyrexia was induced in the rats by the administration of 1 ml/kg body weight of 15% brewer's yeast suspension intraperitoneally and 16 h later, the anal temperatures were measured again. Only rats with anal temperature elevated by 0.5°C were selected for the study. Normal saline 1 ml/kg body weight was administered to group I, while groups II, III and IV were treated with extract at 150, 300 and 500 mg extract/kg body weight, respectively. Group V was treated with 100 mg aspirin/kg body weight intraperitoneally. Anal temperatures were then measured and recorded every hour for a maximum of four hours.

Anti-inflammatory activity

The study was carried out using modified method of Winter et al. (1962). Rats were divided into five groups of five rats per group randomly. Distilled water 1 ml/kg was given to group I, which served as the control. Rats in groups II, III and IV were treated with 100, 250 and 500 mg extract/kg body weight respectively while the fifth group received 20 mg aspirin/kg body weight orally. Thirty minutes later, oedema was induced by administration 0.1 ml of 5% kaolin suspended in normal saline into the plantar surface of the right hind paw. The volume of oedema produced was measured in millimeter using a vernier caliper.

Anti-diarrhoeal activity

Anti-diarrhoeal activity of the extract was evaluated using the castor oil-induced diarrhoea model in rats (Awouters et al., 1978). Five groups of five rats per group were used. The rats were starved for 24 h prior to the experiment. Normal saline 1 ml/kg body weight was given to group I (control group) orally. Group II received 16 mg aspirin/kg orally while groups III, IV and V were treated with 125, 250 and 500 mg extract/kg body weight, respectively. One hour after the treatment, rats in all the groups were given 1 ml castor oil/100 g body weight orally. The rats in each group were then placed singly in cages having adsorbent paper beneath and examined for the presence and frequency of wet stool every hour for 4 h. Absence or delay in production of watery stool was regarded as protective or positive.

Statistical analysis

Results were expressed as the mean \pm standard error of mean (S.E.M). Statistical analysis of data was carried out using one-way analysis of variance (ANOVA) followed by Student's *t*-test. Differences in mean were considered to be significant when $p \leq 0.05$.

RESULTS

Phytochemical screening

Phytochemical analysis of the crude extract gave positive reactions for the following secondary metabolites:

Table 1. Effect of aqueous extract of *Faidherbia albida* on induced hyper-pyrexia in rats.

Groups	Treatment	Dose (mg/kg)	Baseline Temp.	Post-yeast Temp.	Time (h)			
					1	2	3	4
I	Normal saline	1.00 ml	37.0 ± 0.85	40.0 ± 0.89	40.0 ± 0.89	40.0 ± 0.89	39.50 ± 0.59	39.4 ± 0.66
II	Extract	150.00	37.5 ± 0.86	39.8 ± 0.54	39.4 ± 0.23	39.1 ± 0.27	38.7 ± 0.25	38.3 ± 0.22
III	Extract	300.00	37.0 ± 0.64	40.1 ± 0.72	39.2 ± 0.13	39.0 ± 0.34	38.2 ± 0.62	37.5 ± 0.27*
IV	Extract	500.00	37.0 ± 0.71	40.1 ± 0.68	39.0 ± 0.06	38.5 ± 0.26*	37.8 ± 0.13*	37.2 ± 0.14*
V	Aspirin	100.00	37.0 ± 0.66	40.2 ± 0.43	38.4 ± 0.48*	37.6 ± 0.55*	37.2 ± 0.47*	36.8 ± 0.20*

Values are expressed as Mean ± SEM, n = 5.

*Statistical difference between treated and control groups [(F_{5,18}) = 8.00; P < 0.05].

Table 2. Effect of aqueous extract of *Faidherbia albida* on kaolin-induced rat paw oedema expressed as percentage inhibition.

Groups	Treatment	Time (h)			
		1	2	3	4
I	Control	-	-	-	-
II	Extract 100 mg/kg	23.07	22.58	25.00	31.03
III	Extract 250 mg/kg	46.15*	45.16	46.67*	51.72*
IV	Extract 500 mg/kg	52.31*	54.84*	60.00*	63.79*
V	Aspirin 20 mg/kg	44.62	45.16	51.67*	56.90*

Values are expressed as Mean ± SEM, N = 5.

*Statistical difference between treated and control groups [(F_{3,12}) = 35.60; P < 0.05].

saponins, tannins and alkaloids. Glycosides, flavonoids, digitalis, phenols, resins and volatile oils were absent.

Acute toxicity studies

Behavioural changes observed in the rats at 2900 and 5000 mg extract/kg body weight in the course of the study were salivation, rubbing of nose and mouth on the floor of the cage and restlessness. The animals gained weight throughout the study duration. No death was recorded in the rats at all the doses used. Gross pathological study showed no abnormality in all the organs examined. The oral LD₅₀ was found to be ≥ 5000 mg extract/kg body weight.

Anti-pyretic activity

The administration of 500 mg extract/kg body weight of the extract significantly (p < 0.05) reduced the body temperature of the rats from post yeast temperature of 40.1 ± 0.68 to 37.8 ± 0.13 and 37.2 ± 0.14 in the 3rd and 4th h respectively compared to control. Aspirin also reduced the rectal temperature of the yeast treated rats in the 1st, 2nd, 3rd and 4th h of the study. This reduction was found to be significantly (P < 0.05) different from both control and the extract treated rats (Table 1).

Anti-inflammatory activity

The extract showed inhibition of the kaolin-induced rat paw oedema in a dose-dependent manner throughout the duration of study. At 500 mg extract/kg body weight, the extract significantly (P < 0.05) inhibited formation of oedema in rat paw than aspirin throughout the duration of the study (Table 2).

Anti-diarrhoeal activity

Doses of 250 and 500 mg extract/kg body weight significantly (p < 0.05) protected the rats against castor oil-induced diarrhoea throughout the period of study dose-dependently. Aspirin at 16 mg/kg was also observed to protect the rats against castor oil-induced diarrhea in the 1st and 2nd h of the study significantly (Table 3).

DISCUSSION

The absence of death in the groups of rats treated with the extract at 5000 mg/kg body weight suggests that the extract is practically non-toxic acutely and is safe in rats (Matsumura, 1975).

Aspirin (100 mg/kg) and the extract at 300 mg/kg induced some reduction in pyrexia which was only significant

Table 3. Effect of aqueous extract of *Faidherbia albida* on castor oil-induced diarrhoea in rats.

Groups	Treatment	Dose (mg/kg)	Time (h)			
			1	2	3	4
I	Normal saline	-	0 (0%)	0 (0%)	0 (0%)	0 (0%)
II	Extract	125.00	0 (0%)	0 (0%)	2 (40%)	3 (60%)
III	Extract	250.00	5 (100%)*	5 (100%)*	5 (100%)	5 (100%)*
IV	Extract	500.00	5 (100%)*	5 (100%)*	5 (100%)	5 (100%)*
V	Aspirin	16.00	5 (100%)*	5 (100%)*	4 (80%)	4 (80%)

Values are expressed as percentage inhibition, N = 5.

*Statistical difference between treated and control groups [(F_{4,15}) = 31.98; P < 0.05].

at 240 min. However, at the high dose of 500 mg extract/kg body weight, a consistently significant decrease in rectal temperature with the lowest value (37.2 ± 0.14) was produced at 240 min. Antipyretics prevent rise in body temperature generally in response to microbial or endogenous pyrogens as excessive rise in body temperature may cause irreversible tissue damage and possibly death. The pyrogens either activate the enzyme cyclooxygenase (COX), which converts arachidonic acid to prostaglandin (PG), or make available the substrate for the enzyme. In any of these events, synthesis of prostaglandin Es (PGEs), especially PGE₁ is observed to be increased in the hypothalamus. Antipyretics compete with arachidonic acid at the active site of cyclooxygenase (Insel, 1996). During fever, arachidonic acid synthesis may thus be inhibited by antipyretics. Most of the currently available antipyretics inhibit both cyclooxygenase 1 and cyclooxygenase 2 (COX-1 and COX-2, respectively), inhibiting the synthesis of prostaglandin and thromboxane (Insel, 1996). Inhibition of COX-2 is thought to mediate, at least in part, the anti-pyretic action of aspirin and related antipyretic drugs while inhibition of COX-1 results in the unwanted side effects associated with this drug. The anti-pyretic action of *F. albida* may thus be dependent on its inhibition of PGE₁ synthesis.

Aspirin (20 mg/kg) and the extract at 250 mg/kg inhibited kaolin-induced rat paw oedema slightly, while high dose of 500 mg extract/kg body weight produced sustained significant (P < 0.05) reduction in volume of oedema formed throughout the duration of study. Inflammatory response (significant changes in skin temperature, paw volume and locomotion) to kaolin has been reported to be mediated by kinins and prostaglandins (Lewis et al., 1976). In the study, injection of commonly used NSAIDs were observed to significantly reduce inflammatory indices while histamine and 5-hydroxytryptamine (5-HT) were not effective. This observation is consistent with those of others (Gemmell et al., 1979; Masso et al., 1993), that PGs are the major mediators of kaolin-induced inflammation. The latter workers even suggested that kaolin-induced inflammation should be used as a model of inflammation for assessing

the efficacy of NSAIDs and other drugs acting via the same mechanism. The advantages of kaolin compared to other models of inflammation like carrageenan, are its longer duration of inflammation and being a clay mineral, it is unlikely to have antigenicity or to cause hypersensitivity reactions. It may therefore be suggested that the extract mediated remission of kaolin-induced rat paw oedema observed through inhibition of prostaglandins biosynthesis.

The extract inhibited castor oil-induced diarrhoea in rats in dose-dependent manner producing maximal inhibition at 250 and 500 mg/kg body weight, respectively. The gut wall contains prostaglandins E and F with prostaglandin synthetase activity mainly in the mucosa. In man, prostaglandins cause intestinal cramps and diarrhoea which is due to effect on intestinal smooth muscle and secretion. Ricinoleic acid, the active principle in castor oil caused changes in mucosal cell layer permeability, electrolyte transport and intestinal peristalsis, leading to hyper-secretory response and diarrhoea. It causes irritation and inflammation of the intestinal mucosa, leading to prostaglandin release, which results in an increase in the net secretion of water and electrolytes into the small intestine. Inhibitors of prostaglandin biosynthesis were also observed to delay castor oil-induced diarrhoea. Earlier studies by Ferreira et al. (1972), demonstrated that the inherent resting tone of the intestinal smooth muscle is maintained by continuous intramural generation of prostaglandins and the inhibition of PG biosynthesis by NSAIDs resulted in decrease of the resting tone.

Tannins and alkaloids observed to be present in the extract have been reported for their anti-diarrhoeal effects (Yu et al., 2000; Al-Rehaily et al., 2001) and may also be partly responsible for other pharmacological properties observed in this study.

In conclusion, this study has demonstrated that *F. albida* possesses anti-pyretic, anti-inflammatory and anti-diarrhoeal effects, which may be due to the presence of its phytochemical constituents (tannins and alkaloids) and its inhibitory effects on prostaglandin synthesis. The study also provides empirical evidence for its use in folkloric medicine.

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