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Full Length Research Paper

The anti-inflammatory potential, heamatological and histological changes induced in rats due to the administration of methanolic extracts of *Ficus thonningii* leaves

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This study was designed to evaluate the anti-inflammatory potential, heamatological and histological changes induced in rats due to the administration of methanolic extracts of *Ficus thonningii* leaves. Fifteen wistar rats were divided into 3 groups of 5 rats per group to measure the anti-inflammatory activity using the inhibition of carageenan-induced oedema. For the acute oral toxicity test, twenty mice divided into 4 groups of 5 animals each were used. The doses of the extract given were 0.2, 0.4, and 1.0 g/kg body weight while the control group was given an equivalent volume of 2.5% v/v propylene glycol. The blood samples were collected for haematology before, mid-way and after 21 days. The body weights were also noted. Student "t"-test was used to determine the degree of significance between the treatment groups. The liver, kidney, spleen, ovary, uteri and lungs the animals were examined for histopathological changes. The extract of *F. thonningii* has anti-inflammatory properties that are comparable to aspirin and are significant (P<0.05) to Tween 80. There were no significant haematological and visible tissue pathological changes in the treated groups. *F. thonningii* appeared to be safe and can be recommended as a good source of feed for animals during dry season.

Key words: Anti-inflammatory*, Ficus thonningii*, heamatological and histological changes, rats.

INTRODUCTION

Herbs have been used as food and for medicinal purposes for centuries (Akinnyi and Sultanbawa, 1983). The use of medicinal herbs has however increased over the past few years and research interest has focused on various herbs that posses anti-platelets, anti-tumour or immune stimulating properties that may be useful adjunct in reducing the risk of disease and treatments (Craig, 1999). One of such plants is *Ficus thonningii* which has been listed by several authors as a plant being used for treatment of diseases ranging from wound treatment, fever, diarrhea, to gonorrhea and diabetes mellitus (Ajayi, 2008).

F. thoninningi, also known as the common wild fig is a plant that is widely used in local medicine and has been observed to posses analgesic and anti-inflammatory properties (Otimenyin et al., 2004). Although, any part of the plant can be used, there seems to be a preference for the leaves that exude latex, as the latex had always being taken as a sign of potency (Keay et al., 1974). Phytochemical analysis of *F. thonningii* revealed that this plant consists of many metabolites which includes carbohydrates, soluble starch, glycosides, steroids, unsaturated steroids, aglycones, tannins, saponins, flavonoids, titre peres and alkaloids, all these play an important and varied pharmacological actions that contribute to the therapeutic claims of the plant (Ndukwe et al., 2007).

Apart from the medicinal purpose, the plant also serves as source of feed to animals in the tropical environment as goats reared under extensive system of animal management heavily browse the leaves (Ademosun et al., 1988). The plant has been reported to be acceptable to ruminants as it has a crude protein higher than 7 g/100 kg (Bamikole et al., 2004). *F. thonningii* has also proven to be a standing feed reserve for rabbits especially during

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the dry season when there is feed scarcity (Jokthan et al., 2003). The ripe fruits are usually eaten by bats, bulbuls, parrots, pigeons and starlings. As there has been a re-surgence of interest in ethno-veterinary medicine and ethno-pharmacology and some of the plants consumed by humans and animals may be toxic with derangement in the heamatological values. Extracts from one of such plants, *F. thonningii* has been observed to possess anti-inflammatory and analgesic properties as claimed by the traditional healers, the extract inhibited egg-albumin induced edema and pain induced by hot plate respectively (Otimenyin et al., 2004).It has also been found to have astringent and purgative properties but its use as anti-diarrhoea drug should be used with caution as such attempt in rats lead to acute toxicity and subsequent death (Onwkaeme and Udoh, 2000).

The methanolic extracts of the leaves of *F. thonningii* had been reported to be active on *S. aureus* and *P. stauti* while the crude methanolic extract of the stem bark was active on *Escherichia coli* and the methanolic extract of the root was active on *Klebsiella pneumoniae, S. aureus* and *Bacillus substilis*. It has also been observed that concentrations of 50 mg/ml of the stem bark of the methanolic extract of the plant can kill these organisms (Ndukwe et al., 2007).However, the effect of this plant on the heamatological values and tissue pathology is very scanty in literatures (Musabayane et al*.,* 2007; Aniagu et al*.,* 2008). Aniagu et al. *(*2008) reported a non significant increase in body weight of rats given 250-500 mg/kg of *F. thonningii* and a significant increase in total leukocyte count and platelet values in male rats. The histological findings were that of testicular, lung and hepatic toxicosis (Aniagu et al*.,* 2008). However, the probable sex influence in the observations was not accorded due attention. Therefore, this study was designed to evaluate the anti-inflammatory potential, heamatological and histological changes induced in rats due to the administration of methanolic extracts of *F. thonningii* leaves in female laboratory animals.

MATERIALS AND METHODS

Animals and experimental methods

The animals used in this study were rats weighing between 110 and 150 g. They were all females and were maintained at the animal house of the Faculty of Veterinary Medicine, University of Ibadan. They were age-matched and kept in rat cages and fed rat pellets and allowed free access to clean fresh water in bottles *ad libitum.*

Anti-Inflammatory activity evaluation

Fifteen rats (Wistar strain) divided into 3 groups of 5 animals per group were used in this study. The inhibition of carageenan-induced oedema on the sub-plantar region of the paw of the rats was used to measure that anti-inflammatory activity of the extracts. The albino weight of the extracts in 40% v/v Tween 80 was administered orall to each group of five male albino rats by means of a cannulaAspirin 100 mg/kg body weight suspended in 40% v/v and 0.5 ml of the vehicle. That is 40% v/v Tween 80 was used as negative controls respectively on groups of five rats each. The extracts and controls were given to the rats an hour before injecting the sub-plantar region of the left hind paw of each rat with 0.1 ml of 1% w/v carageenan solution in normal saline. Increase in linear paw circumference, as measured by a micrometer screw guage, was taken as an index of increase in paw volume which is a measure of the oedema. Inhibitory activity was calculated according to the formula:

$$\text{Percentage Inhibition} = \frac{\{D_t - D_o\}_{control} - \{D_t - D_o\}_{test}}{\{D_t - D_o\}_{control}}$$

Where:
D_t = linear paw circumference 4 h after carageenan injection.
D_o = linear paw circumference at 0 h (just before carageenan injection.
$\{D_t - D_o\}_{control}$ = values obtained for 0.5 ml of 40% v/v Tween 80
$\{D_t - D_o\}_{test}$ = values obtained for each extract.

Acute oral toxicity test

Twenty mice were divided into 4 groups of 5 animals each. To each of four groups was given 0.2g/, 0.4g, 1.0 g/kg body weight respecttively of the extracts dissolved in 2.5% v/v propylene glycol. The fifth group was given an equivalent volume of 2.5% v/v propylene glycol as control. Treatment of the animals was in accordance with the Principles of Laboratory Animal Care (NIH Publication 85-93, revised1985).All the animals were observed for mortality for 21 days feed and water was administered *ad libitum.*

Determination of heamatological parameters

The blood samples were collected before the giving of the extract, mid-way in the research and after 21 days. The haemoglobin concentration was done as described by Schalm et al. (1975) using the cyanomethaemoglobin method. Packed cell volume (PCV) was done by conventional method of filling the capillary tube with blood as described by Schalm et al. (1975) and read with a microhaematocrit reader. Erythrocyte count was determined by the haemocytometer method as described by Coles (1986). Total leucocytes and leucocyte differential count were also determined. Erythrocyte indices were determined from values obtained from red blood cell count, haemoglobin concentration and packed cell volume values.

Histopathology

The animals were sacrificed with use of cervical dislocation and the liver, kidney, spleen, ovary, uteri and lungs of all the animals were harvested and fixed in 10% buffered formalin in labeled bottles. Tissues were processed routinely and embedded in paraffin wax. Sections 5 microns thick were cut, stained with haematoxylin and eosin and examined under light microscope.

Determination of weight gain

The body weight of the rats were taken before the commencement of the work, midway into the study and lastly before been euthanised at day 21 for tissue changes.

Statistical analysis

Student t-test was used to determine the degree of significance between the treatment groups.

Table 1. Evaluation of anti-inflammatory activities.

Extract + Tween 0	Aspirin + Tween 80	Tween 80
D_t Average = 1.42	D_t Average = 1.31	D_t = 2.87
D_0 Average = 0.45	D_0 Average = 0.48	D_0 Average = 0.46
Difference = 0.97	0.83	2.41

D_t Av = Average values obtained for linear paw circumference 4 hours after carageenan injection. D_0 Av = Average values obtained for linear paw circumference 0 hours [just before carageenan injection].

Table 2. Percentage inhibition of the carageenan induced oedema of the extract compared with the control.

Extract	Aspirin
0.597%	0.655%
≈ 0.6%	≈ 0.7%

Table 3. Heamatological parameters.

Parameters	PRE				DAY 10				DAY 21			
	30 mg	60 mg	100 mg	Control	30 mg	60 mg	100 mg	Control	30 mg	60 mg	100 mg	Control
PCV(%)	35	37	35	33	36	38	38	34	36	38	42	43
RBC ($\times 10^6$/L)	10.5	12.4	12.3	11.6	10.5	12.5	12.5	11.6	10.5	12.5	12.3	11.6
WBC ($\times 10^3$/L)	28.2	26.8	26.8	26.4	28.2	28.7	29.2	26.4	28.7	30.6	31.8	26.5
LYM ($\times 10^3$/L)	22	16.6	20.1	20.1	19.7	22.4	20.4	16.4	17.2	23.9	21.6	18.6
NEU ($\times 10^3$/L)	6.2	10.2	6.7	6.3	8.5	6.3	8.7	10.0	11.5	6.7	10.2	8.0

Packed cell volume (PCV), Red blood cell (RBC) White blood cell (WBC) Lymphocytes (LYM) Neutrophils (NEU).

Table 4. Body weight changes.

	Pre	Mid	Late (AT DAY 21)
Control	135 g	136 g	137 g
30 mg	134 g	137 g	140 g
60 mg	138 g	142 g	146 g
100 mg	134 g	140 g	148 g

RESULTS

Evaluation of anti-inflammatory activity of *F. thonnigii*

The result of the evaluation of anti-inflammatory activity of *F. thonnigii* in Table 1 indicated that the plant has anti-inflammatory properties, which could be compared to that of aspirin, although this property is lesser with *F. thonnigii*. However, the anti inflammatory effect of the plant is significant when compared to the control ($P<0.01$).

In Table 2, the anti-inflammatory activity of the extract is comparable to that of Aspirin, although Aspirin has a greater inhibition percentage than the methanolic extract of *F. thonnigii.* Effects of *F. thoninngii* extract on heamatological parametersIn Table 3, there were no significant in the haematological parameters in the treated and control animals throughout the course of the investigations.

Histopathology

There were no visible gross and histopathological tissue changes in the liver, kidney, spleen, ovary, uteri and lungs of the treated groups. The effect of *F. thonningii* gradual changes in the body weight with increase in the amount of the extract given. The changes in body weight over the period of 21 days for test group is significant ($P < 0.05$) when compared to the control.

DISCUSSION

This study further reaffirms the anti inflammatory properties of *F. thoninngii.* In a similar study by Otimenyin et al. (2004), the methanolic extracts of the leaves was shown to possess anti inflammatory properties using egg-albumin induced oedema while in this study, the anti-inflammatory properties was proven using carageenean induced oedema.

The extract was found to have a dose dependent significant increase ($P<0.05$) in body weight over the period of the study. The fact that the consumption of this plant could lead to in increase in body weight may as well be the probable reason why goats in the tropical environment heavily browse this plant (Ademosun et al., 1988) and also due to the fact that the plant has a crude protein higher than 7 g/100 kg (Bamikole et al., 2001). The non-appreciable difference in the heamatological parameters in treated and control groups in this study is in contrast with that of Aniagu et al. (2008), who reported significant increase in the total leukocyte count and platelet values in male rats, this effect may be associated with the sex influence and this observation may need to be investigated.

There were no significant gross and histopathological changes in the liver, spleen, uteri, kidney and lungs of the treated animals over the period of this study. This shows that feeding the plants to mice at those dose rate appear to be safe. This observation is similar to that of Aniagu et al. (2008), who reported that short-term oral application of F. thonningii extract may not exert severe toxic effect in rats at doses lower than 500 mg/kg^{-1}. The extrapolation of this findings to humans and animals should be with caution as a possible testicular toxicity had been reported in rats (Aniagu et al., 2008).

In conclusion, the leaves of *F. thonningii* appeared safe for consumption both for animals and probably humans on a short term. The plant can also be recommended as a good source of feed for animals during dry season when the scarcity of pasture is iminent.

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