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Calming and against nociceptive impacts of the methanolic concentrate of the stem bark of *Ficus vallis-choudae delile* (*Moraceae*)

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Abstract

The methanolic stem bark extract of *Ficus vallis-choudae* was investigated for anti-inflammatory and anti-nociceptive activity. The anti- inflammatory effects were investigated using rat paw edema model, while the analgesic effects were studied using acetic acid induced writhing in mice. The results obtained revealed that the methanolic stem bark extract of *F. vallis – choudae* in doses of 50 and 100 mg/kg posses significant (P < 0.05) dose dependent anti-inflammatory effect and inhibit abdominal contractions caused by acetic acid in mice. The intraperitoneal LD50 in mice was found to be 470 mg/kg. The preliminary phytochemical screening revealed the presence of glycosides, flavonoids, tannins, alkaloids and saponins. The results of this study indicated the presence of biologically active substances which may be beneficial in the treatment of pain and inflammation.

Keywords: Acetic acid - induced writhing, Anti-nociceptive, Anti-inflammatory, *F. Vallis-choudae*, Rat paw edema.

INTRODUCTION

Presently interest in herbal medicine is enjoying renaissance. Medicinal plants are believed to be important source of new chemical substances with potential therapeutic effects (Farnsworth, 1989; Eisner, 1990). The study of plant species that have traditionally been used as pain killers should still be seen as fruitful and logical research strategy in the search for new analgesic drugs (Elisabetsky et al., 1995).

Ficus vallis-choudae, family *Moracceae* commonly known as Gimi (Hausa) in Nigeria, is a deciduous plant found mainly in the savanna region of West Africa. The stem bark is chewed with kola nut either to relieve thirst or as remedy for sore throat (Dalziel, 1995).

The various parts of the plant have been reported to be used in the treatment of stomach pain, paralysis, convulsion, epilepsy (Burkill, 1985). Few reports (oral communication) suggest that the stem bark is traditionally used to relieve pain and discomfort associated with hemorrhoids (Pile). The term “hemorrhoids” refers to a condition in which the veins around the anus or lower rectum are swollen and inflamed. Hemorrhoids are both inside and above the anus (internal) or under the skin around the anus (external). Hemorrhoids (piles) arise from congestion of internal and/or external venus plexuses around the anal canal (Guerrero, 2001).

There is no scientific report or verification of the use of this plant in the treatment of this condition. This study was therefore aimed at investigating possible anti-nociceptive and anti-inflammatory effect of the methanolic extract of *F. vallis-choudae* stem bark.

MATERIAL AND METHODS

Animal

Swiss albino mice weighing 18 - 25 g and Wistar rats weighing 150 - 200 g of both sexes available at the animal house, Department of Pharmacology, Ahamdu Bello University, Zaria, were used. They were housed under room temperature, relative-humidity and light/dark cycle, fed with excel feeds (feed masters Plc, Kaduna) and water *ad libitum*.

Table 1. Effect of methanolic stem bark extract of *F. Vallis Choudae* on acetic acid- induced abdominal contractions in mice.

Treatment (i.p.)	Dose (mg/kg)	No. of abdominal contractions/10 min	% inhibition
Saline (10 ml/kg)		38.2±3.4	
F. Vallis-choudae	50	5.0±1.2	86.9*
F. Vallis-choudae	100	5.4±3.3	85.8*
ASA	150	18.2±1.8	52.3*

*P < 0.05 compared to control.

Plant material

The stem bark of *F. vallis-choudae* was collected around Tsibiri Village, Sabongari Local Government Area, Kaduna State, Nigeria, in July 2003. The plant was identified and authenticated at the herbarium, Department of Biological sciences, Ahmadu Bello University, Zaria, Nigeria, where a voucher specimen (NO: 900348) was deposited for future reference.

Preparation of the extract

The bark was chopped, cleaned and air dried for 7 - 10 days. After that the size was reduced with a mortar and pestle into a fine powder. 100 g of the powder was extracted with 90% methanol (2.5 litres) using percolation process for 48 h. The liquid extract was then concentrated on a water bath to give a brownish solid extract with a mean yield of 10% w/w.

Phytochemical screening

Preliminary phytochemical analysis of the *F. vallis choudae* fresh extract was conducted using the standard screening method (Trease and Evan, 1997).

Acetic acid-induced writhings in mice

This test was conducted by employing the method described by Koster et al. (1959). Swiss albino mice were divided into four groups (5 mice per group). The first group served as control, while the second and third groups received the extract at doses of 50 and 100 mg/kg i.p, and the fourth group was given acetylsalicylic acid (ASA) at a dose of 150 mg/kg orally 30 min before acetic acid injection (0.75%, 1 ml / 100 g i.p). The mice were then placed in individual cages. The number of abdominal contractions was observed 5 min after stimulation for a period of 10 min. A writhe is indicated by abdominal constriction and full extension of hind limb. Percentage inhibition of writhing was obtained using the formula.

$$\text{Inhibition}(\%) = \frac{\text{Mean No. of writing (control – mean No. of writing(test)}}{\text{100 Mean No. of Writing control}} \times$$

Anti-inflammatory studies

This test was conducted by employing the method of Winter et al. (1962) as slightly modified by Akah and Nwambie (1994). Inflammation of the hind paw was induced by infecting 0.1 ml fresh egg albumin into the subplantar surface of the right hind paw of the rats.

The control group was given normal saline, the second group acetylsalicylic acid (150 mg//kg) while the remaining two groups received extract at doses of 50 and 100 mg/kg i.p. The measurement of the foot volume was done by a displacement technique with a digital plethysmometer (LE7150), before and every 20 min after the infection of egg albumin for 2 h.

Statistical analysis

The results of the experiment were expressed as mean ±SEM. Analysis of variance was performed and $p < 0.05$ was considered significant.

RESULTS

Phytochemical screening

Preliminary phytochemical analysis of the extract revealed the presence of flavonoids, glycosides, alkaloids, tannins and saponins.

Analgesic activity

The anti-nociceptive activity of *F. vallis choudae* was evaluated using acetic acid induced writhing in mice. The *F. vallis choudae* extract at doses (50 and 100 mg/kg) significantly ($p < 0.05$) decreased the number of acetic acid- induced writhes in mice (Figure 1). Highest percentage inhibition of writhes of 86.91% was observed at a dose of 50 mg/kg while ASA gave an inhibition of writhes of 52.36% (Table 1). All values were significant ($p < 0.05$) compared with control.

Anti-inflammatory activity

The *F. vallis choudae* extract caused an inhibition of egg-albumin induced edema over a period of 120 min. The effect appeared to be dose-dependent (Figure 2). However, ASA (150 mg/kg) also produced the peak inhibitory effect (23%) (Table 2) and the value is statistically significant ($p < 0.05$).

DISCUSSION AND CONCLUSION

The physiology of nociception involves a complex inter-

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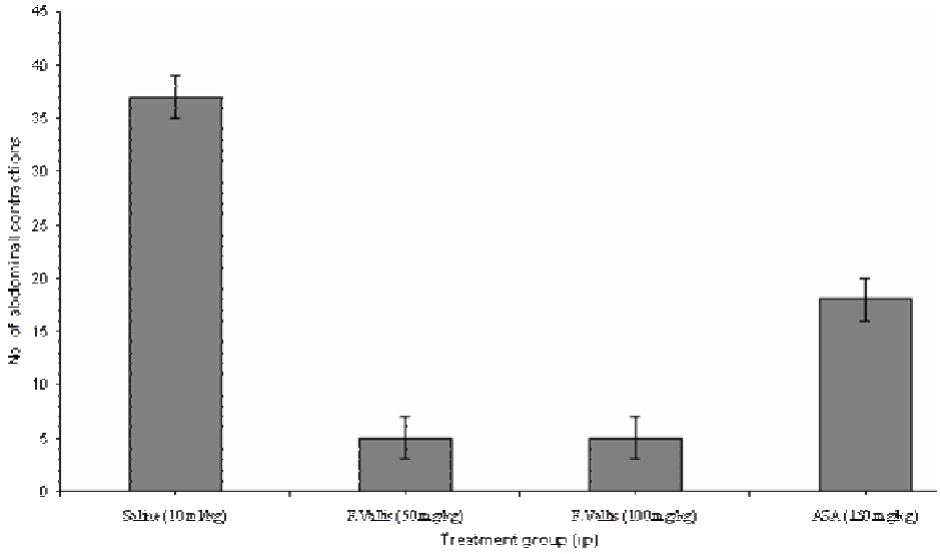

Figure 1. Effect of methanolic stembark extract of *F. vallis choudae* on acetic acid-induced abdominal contractions in mice (n = 20), $p < 0.05$.

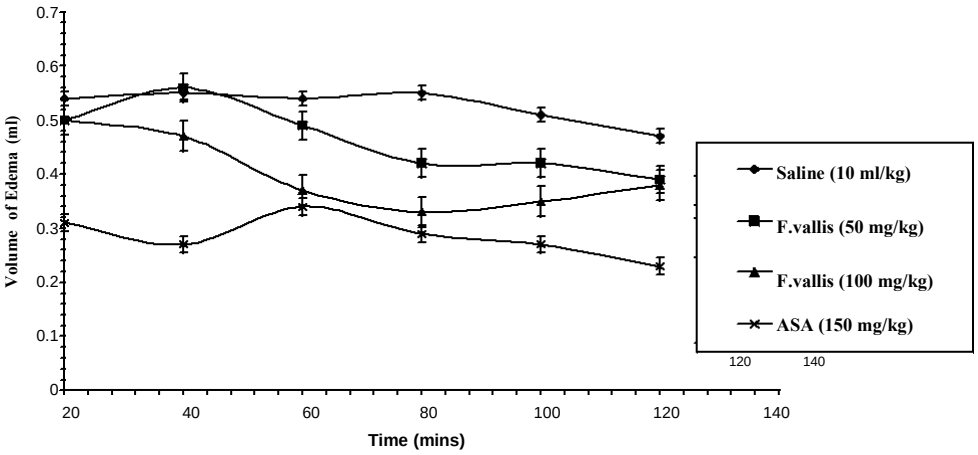

Figure 2. Effect of administration of methanolic stem bark extract of *F. vallis choudae* on egg albumin induced in rats (n = 18) $p < 0.05$.

Table 2. Effect of methanolic stem bark extract of *F. Vallis Choudae* on egg-albumin induced edema in rats.

Treatment (i.p.)	Dose (mg/kg)	Paw vol. (ml)	% inhibition
Saline (10 ml/kg)		0.53±0.01	
F. Vallis-choudae	50	0.46±0.02	11.54*
F. Vallis-choudae	100	0.40±0.02	12.00*
ASA	150	0.29±0.02	

*P < 0.05 compared to control.

action of peripheral and central nervous system (CNS) structures, extending from the skin, the viscera and the musculoskeletal tissues to the cerebral cortex.

Pathophysiology of pain shows alterations of normal physiological pathways, giving rise to hyperalgesia or allodynia (Riedel and Neeck, 2001). Modulation of nociception occurs at all levels of the neuraxis, thus eliciting the multidimensional experience of pain involving sensory

- discriminative, affective, motivational, cognitive and locomotor components. Acetic acid induced writhing test was used for detecting both central and peripheral analgesia. Intraperitoneal administration of acetic acid releases prostaglandins and sympathomimetic system mediators like PGE_2 and PGF_2 and their levels were increased in the peritoneal fluid of the acetic acid induced mice (Besra et al., 1996)

The present study has established the anti-nociceptive and anti-inflammatory effect of the methanolic stem bark of *F. vallis choudae*. The *F. vallis choudae* extract has significantly ($P < 0.05$) reduced the number of acetic acid-induced writhings in mice. The method employed in the anti-nociceptive studies, also called the abdominal constriction response, is very sensitive and is able to detect anti-nociceptive effects of compounds at dose level that may be inactive in other methods like the tail - flick test (Collier et. al. 1981). The abdominal constriction response is postulated to partly involve local peritoneal receptors (Bentley et al., 1983; Vongtau et al., 2000). The abdominal constriction produced after the administration of acetic acid is related to sensitization of nociceptive receptors to prostaglandins. It is therefore possible that the *F. vallis choudae* extract exert its effect probably by inhibiting the synthesis or action of prostaglandins.

The extract has also caused inhibition of albumin - induced edema in rats and this appeared to be dose - related ($P < 0.05$). The method used in determining anti-inflammatory activity is also useful in detecting activity in acute inflammation. Flavonoids isolated from some medicinal plants have been proven to posses anti-nociceptive and or anti-inflammatory effects (Duke, 1992) and it has been shown by Meli et al. (1990), Dicarlo et al. (1994) that flavonoids also inhibit gastric motility in a dose - dependent, manner. It is therefore possible that the inhibitory effects on anti-nociceptive and anti-inflammatory effects observed in the extract may be attributed in part to its flavonoid content.

Flavonoids also inhibit the phosphodiesterases involved in cell activation. Much of this effect is upon the biosynthesis of protein cytokines that mediates adhesion of circulating leukocytes to sites of injury. Flavonoids inhibit biosynthesis of prostaglandins, which are involved in various immunologic responses and are the end products of the cyclooxygenase and lipoxygenase parthways (Moroney et al., 1988). Protein Kinases are another class of regulatory enzymes affected by flavonoids. Inhibition of these enzymes provides the mechanism by which flavornoids inhibit inflammatory processes (Manthey et. al., 2001).

From the results obtained *F. vallis choudae* extract does posses significant anti-nociceptive and anti-inflam-matory activities. The association of both anti-nociceptive and anti-inflammatory effects is well documented for various non-steriodal anti-inflammatory agents (NSAIDS) (Gyires et al., 1985). The results tend to corroborate the traditional use of *F. vallis choudae* in the treatment of pain and discomfort associated with hemorrhoids. The results also suggest the presence of biologically active principles worthy of further investigation.

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