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Full Length Research Paper

Pharmacological profile of aqueous extract of *Bridelia ferruginea* stem bark in the relief of pain and fever

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The pharmacological effects of the aqueous stem bark extract of *Bridelia ferruginea* were studied in rodents. Investigations were carried out on analgesic and antipyretic properties employing different experimental models in mice and rats. The analgesic activity was measured using the acetic acid induced-abdominal constriction and tail immersion tests. The antipyretic effect was assessed using the yeast-induced pyrexia test. It was found that *B. ferruginea* (25 to 100 mg/kg, *i.p*) at both doses produced significant analgesic and antipyretic effects. The results clearly indicate that stem bark extract of *B. ferruginea* possess potential analgesic and antipyretic properties.

Key words: *Bridelia ferruginea,* nociception, pyrexia, medicinal plant.

INTRODUCTION

Bridelia ferruginea (Family: Euphorbiaceae) is an indigenous medicinal plant in Nigeria. It is commonly found in the savannah. It is usually gnarled shrub which sometimes reaches the size of a tree in suitable condition. Its common names in Nigeria include Kirni, Kizni (Hausa), Maren (Fulani), Iralodan (Yoruba), Ola (Igbo). Its habitat is the savannah, especially in the moister regions from Guinea to Zaire and Angola. The bark is dark grey, rough and often marked scaly (Rashid et al., 2000). *B. ferruginea* has diverse uses. The leaves have been used to treat diabetes. The plant is also used as a purgative and a vermifuge (Cimanga et al., 1999). The bark extract is being used for milk coagulation and also in lime juice for the formulation of traditional gargle "ogun efu" (Orafidiya et al., 1990). Adeoye et al. (1988) reported that the bark extract of the plant possess antimicrobial activities against some micro-organisms known to cause enteric and secondary upper respiratory water treatment has also been reported by Kolawole and tract infections, while Olajide et al. (1999) reported that the plant has anti-inflammatory activity. Its potential for Olayemi (2003). This present study intends to determine the analgesic and antipyretic activities of aqueous extract of *B. ferrginea* stem bark in experimental animal models.

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MATERIALS AND METHODS

Plant collection

B. ferruginea stem bark was collected in November, 2009, from Odenigbo, Nkalagu-Obukpa, Nsukka, Enugu State, Nigeria. The plant was identified and authenticated by Mrs. Jemilat A. Ibrahim, a taxonomist of the Department of Medicinal Plant Research and Traditional Medicine, National Institute for Pharmaceutical Research and Development (NIPRD), Abuja where herbarium specimen (No. NIPRD/H/6414) was deposited for future reference. The international plant name index is Euphorbiaceae Bridelia ferruginae Niger Fl. (W.J. Hooker). 511. 1849 (November to December, 1849) (IK).

Preparation of bark extract

The bark was cut into pieces and air-dried at room temperature for 7 days and ground to powder using pestle and mortar and soaked in distilled water over-night. The filtrate was dried on a water bath

and the yield calculated to be 50.29%. The extract was subsequently reconstituted in water at appropriate concentrations for the various experiments.

Animals

Swiss albino mice (18 to 25 g) and Wister rats (200 to 260 g) of either sex were used for the studies. The animals were bred in the Animal Facility Centre (AFC), Department of Pharmacology and Toxicology, National Institute for Pharmaceutical Research and Development (NIPRD), Abuja, Nigeria. The animals were kept in cages at room temperature and moisture, under naturally illuminated environment of 12:12 h dark/light cycle. They were fed with NIPRD formulated feeds and access to water *ad libitum*.

Phytochemical screening

The screening method was according to Trease and Evans (1983).

Acute toxicity studies

The acute toxicity LD_{50} was estimated in mice both orally and intraperitoneally following Lorke's method (1983). Dose levels used ranged from 100 to 5000 mg/kg, *p.o* and 10 to 2000 mg/kg, i.p of the aqueous stem bark extract. The LD_{50} was calculated as geometric mean of the dose that resulted in 100% lethality and that which caused no lethality at all. Toxicity signs such as nervousness, excitement, dullness or even death were observed for 24 h.

Acetic acid induced writhing response in mice

The test was performed using the methods described by (Siegmund et al., 1957; Koster et al., 1959) with slight modification. The mice employed for this study were divided into 5 groups of 6 per cage and pre-treated with 25, 50 and 100 mg/kg of the extract using *i.p* for Groups 1, 2 and 3 while 10 ml/kg distilled water and 150 mg/kg of Aspirin was administered to Groups 4 and 5 respectively. After 30 min pre-treatment, each group was then pre-treated with 0.7% of an aqueous solution of acetic acid (10 ml/kg). The mice were placed in a transparent observation box and number of "stretching" per mouse was recorded during the following 15 min period. A significant reduction in number of writhing by any treatment as compared to control animal was considered as a positive analgesic response.

Tail immersion test in mice

The method described by Jansen and Jagenav (1959) with slight modification was adopted. The mice selected for this study were divided into 5 groups of 6 per cage and pre-treated with 25, 50 and 100 mg/kg of the extract intraperitoneally for Groups 1, 2 and 3, while 10 ml/kg distilled water and 10 mg/kg of morphine was administered to Groups 4 and 5 respectively. 30 min after drug administration, each mouse was restrained in horizontal cylinders leaving the tail hanging freely in a water bath maintained at 50 ± 1.0°C and the time taken for the mouse to remove its tail out of the water was recorded. The latency was evaluated at 0, 30, 60 and 90 min with 0 min being the initial reading.

Yeast-induced hyperpyrexia

The test was performed using the methods described by Mukerjee et al. (1996) and Akuodor et al. (2010a) with slight modification. The rats employed for the study were injected with 20 ml/kg of 15% (Danbaoli) yeast suspended in methyl cellulose solution to induce pyrexia. The rectal temperature of each animal was taken before and 24 h after yeast injection using clinical thermometer (Geon Corp, USA). Rats that did not show a minimum increase of 0.5°C in temperature, 24 h after yeast injection were discarded. Thirty selected rats were grouped into 5 and treated as follows: Group 1 received (20 ml/kg, *i.p*) distilled water, Group 2 (20 mg/kg, *i.p*) drugamol and Groups 3, 4 and 5 received (25, 50 and 100 mg/kg) of the extract respectively. The rectal temperature of each rat was again measured at hourly intervals for 5 h.

Statistical analysis

Results were expressed as mean ± S.E.M. The significance of difference between the control and treated groups were determined, using two-way analysis of variance (ANOVA), followed by student t-test. $P<0.05$ were considered to be statistically significant

RESULTS

Phytochemical screening

Phytochemical screening of the extract revealed the presence of alkaloids, cardiac glycosides, steroids, tannins and saponins.

Acute toxicity test

The LD_{50} of the extract was estimated to be 775 mg/kg *i.p* in mice. The behavioral sign of toxicity exhibited by the mice that received 1000 mg/kg of the extract and above are respiratory distress, increased abdominal contraction.

Acetic acid-induced abdominal constrictions

B. ferruginea significantly ($P<0.05$) and dose dependently decreased the number of writhing movement induced by the *i.p* administration of acetic acid solution as shown in Table 1.

Tail immersion test

B. ferruginea extract significantly attenuated the spinal pain sensation against conduction haet in mice. Moreover, this ameliorative effect of tail immersion response was observed in dose dependent manner. The maximum nociceptic effect was observed at higher dose (100 mg/kg) which was comparable to that of morphine (10 mg/kg) as shown in Table 2.

Antipyretic test

Administration of yeast suspension to rats produced

Table 1. Effect of *B. ferruginea* stem bark extract on acetic acid induced writhing in mice.

Extract	Dose (mg/kg)	Writhing	% Inhibition
B. ferruginea	25	11.0 ± 2.25	23.24
B. ferruginea	50	6.17 ± 1.05	56.94
B. ferruginea	100	1.67 ± 0.1	88.35
Control (N/S)	20	14.33 ± 3.32	-
Aspirin	150	2.5 ± 0.76	82.55

Results are mean ± S.E.M (n = 6),*P<0.05 as compared to the control.

Table 2. Effect of *B. ferruginea* stems bark extract on tail immersion in 50 ± 1°C hot water (mice).

Extract	Dose (mg/kg)	Latency			
		Pre-treatment		After treatment	
		0 min	30 min	60 min	90 min
B. ferruginea	25	10.0 ± 0.58	11.33 ± 0.56	12.0 ± 0.37	13.17 ± 0.79
B. ferruginea	50	10.33 ± 0.49	11.83 ± 0.79	13.17 ± 1.19	14.00 ± 0.10
B .ferruginea	100	11.33 ± 0.61	14.5 ± 0.76	16.17 ±1.90	19.33 ± 1.02
Control (N/S)	20	10.17 ± 0.45	10.00 ± 0.58	10.67± 0.33	10.5 ± 0.22
Morphine	10	10.66 ± 0.33	14.17 ± 0.54	16.17 ± 0.54	19.33 ± 0.56

Results are mean ± S.E.M (n = 6), *P<0.05 as compared to the control.

Table 3. Effect of *B. ferruginea* stem bark extract on yeast induced pyrexia in rats.

Extract	Dose (mg/kg)	Rectal temperature (°C)					
		After yeast injection		After drug administration			
		0 h	24 h	1 h	2 h	3 h	4 h
B. ferruginea	25	37.01± 0.30	37.66± 0.21	37.42± 0.27	37.33± 0.22	37.20± 0.30	37.12± 0.35
B. ferruginea	50	36.93± 0.18	37.57± 0.16	37.18± 0.39	37.02± 0.29	36.89± 0.30	36.83± 0.31
B. ferruginea	100	36.92± 0.36	37.55± 0.34	36.94± 0.28	36.82± 0.28	36.67± 0.23	36.53± 0.24
Control (N/S)	20	36.59± 0.22	37.57± 0.14	37.68± 0.13	37.76± 0.12	37.82± 0.11	37.91± 0.08
Drugamol	20	36.67± 0.04	37.67±0.08	37.38± 0.06	36.68± 0.05	36.22± 0.15	35.25± 0.13

Results are mean ± SEM (n = 6),*P<0.05 as compared to the control.

remarkable increase in rectal temperature 24 h after injection. The extract at the dose of 25, 50 and 100 mg/kg caused a more significant reduction in rectal temperature as shown in Table 3.

DISCUSSION

The present study reviewed some of the pharmacological basis for the use of stem bark of *B. ferruginea* in the relief of fever and pain. Acetic acid induced writhing response is believed to be produced by the liberation of endogenous substances notably metabolite of the arachidonic cascade (Formukong et al., 1998). The abdominal constrictions observed in the study are because of irritation of peritoneal cavity caused by administration of acetic acid. The acetic acid induced writhing allows the acid to act through central mechanism and motor performance of the animals. Therefore, the constituent of the aqueous extract of the stem bark reduced reasonably the duration of writhing in each mouse, and consequently the effects on arachidonate release and metabolism (Hossein and Hatri, 2003). In this study, the analgesic action of *B. ferruginea* can be attributed to the blockade of release of the endogenous mediators of pain. The results suggest that the extract has some inhibitory action on the cycloxygenase pathway which is initially involved in the synthesis of prostaglandin biosynthesis. Tail immersion test is very sensitive to centrally acting drugs (Carlission and Jurne, 1987). Tail

immersion test measures the complex response to a non-inflammatory, acute nociceptive input and is one of the models being used for studying central nociceptive activity. The opioid agents exert their analgesic effect through supra spinal and spinal receptors (Suffiness and Pezzuto, 1991; Nemirovsky et al., 2001). In both tail immersion and acetic acid induced nociceptive models, *B. ferruginea* stem bark extract exhibited anti-nociceptive activity which indicate both central and peripherally mediated analgesic properties.

Subcutaneous injection of yeast induced pyrexia by increasing the synthesis of prostaglandins and is a useful model for screening antipyretic effect of substances (Al-Ghamdi, 2001). It is note worthy that pyretic activity involves stimulation of the region in the hypothalamus that controls body temperature; through prostaglandins synthesized within the central nervous system and that the blood-brain barrier prevents drug molecules or other chemicals from entering the CNS (Zakaria et al., 2007a). Several researchers have used this method to record pyrexia 15 to 18 h after yeast injection, and then administered the antipyretic drug to be investigated (Asha and Pushpagandhan, 1999). The present result shows that the *B. ferruginea* possesses a significant antipyretic effect in yeast-provoked elevation of body temperature in rats, though its effect is not comparable to the standard drug drugamol. Based on the results obtained, it can be concluded that *B. ferruginea* stem bark extract possesses potential analgesic and antipyretic activities justifying the folkloric usage in the relief of pain and fever.

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REFERENCES

Akuodor GC, Idris-Usman MS, Mbah CC, Megwas UA, Akpan JL, Ugwu TC, Okoroafor DO, Osunkwo UA (2010). Studies on antiulcer, analgesic and antipyretic properties of the ethanolic leaf extract of *Gongronema latifolium* in rodents. Afri. J. Biotech., 9(5): 2316- 2321.

Adeoye AO, Abaeli AM, Owowumi CJ, Olukoya DK (1998). Antimicrobial activity of *Bridelia ferruginea* in: Book of abstract of the Symposium on drug production from natural product. Drug Research and Production Unit, Obafemi Awolowo University Ile-Ife, p. 24.

Al-Ghamdi MS (2001). The anti-inflammatory, analgesic and antipyretic activity of *Nijella sativa.* J. Ethnopharmacol., 76: 45-48.

Asha VV, Pushpagandhan P (1999). Antipyretic activity of *cardiospermum halicacabum*. Ind. J. Exp. Biol., 37: 411-414.

Carlisson Kh, Jurna I (1987). Depression by flupirtine, a novel on analgesic agent of motor and sensory response of nociceptive system in the rat spinal cord. Eur. J. Pharmacol., 143: 89-99.

Cimanga K, DeBruyne T, Apers S, Dietersh, Totte J, Kambu K, Tona L, Bakana P, Vanufford LQ, Benkelman C, Labadie R, Veietinck AJ (1999). Complement-inhibiting constituent of *Bridelia ferruginea* stem bark planta Med., 65: 213-217.

Formukong EA, Evans AT, Evans FJ (1988). Analgesic, and anti-inflammatory activity of constituents of *Cannabis sativa L*. inflammation, 12: (4): 1-10.

Hassein H, Hatri MY (2003). Antinociceptive and anti-inflammatory of effects of *Croces saiva* L. Stigima and Peals extracts in mice. BMC Pharmacol., 2: 1471-2210.

Jansen PAJ and Jagenav A (1959). A new series of potent analgesic Dextro 2, 2 diphenyl-3-methyl-4- morpholino-butyryl pyrrolidine related amides. J. Pharm. Pharmacol., 9: 381.

Kolawole OM, Olayemi AB (2003). Studies on the efficacy of *Bridelia ferruginea* benth bark extract for water purification. Niger. J. Pure Appl. Sci., 18: 387-1394.

Koster R, Anderson M, De Beer EJ (1959). Acetic acid for analgesic screening. Federation Proceeding, 18: 412-417.

Lorke D (1983). A new approach to acute toxicity testing. Archives of Toxicol., 54: 275-287.

Mukerjee PK, Das J, Saha K, Giri SN, Pal MI (1996). Antipyretic activity of *Welumbo neucifera* rhizome extract. Ind. J. Exp. Biol., 34: 275-276.

Nemirovsky A, Chen L, Zelma V, Jurna IC (2001). The antinociceptive effects of combination of spinal morphine with systemic morphine or buprenorphine. Anasthesia and Analgesia, 93(1): 197-203.

Olajide OA, Makinde JM, Awe SO (1999). Effect of aqueous extract of *Bridelia ferruginea* stem bark corrageenan-induced oedema and grand coma tissue formation rats and mice. J. Ethnopharmacol., 66(1): 113-117.

Rashid MA, Gustafson KR, Cardellina JH, Boyd MR (2000). A new podophyllojoxin Derivative from *Bridelia ferruginea*. Nat. Prod. Lett, 14: 285-292.

Siegmund EA, Cardmus RALUG (1957). Screening of analgesic including aspirin type compound based upon the antagonism of chemically induced writhing in mice. J. Pharmacol. Exp. Therapeutics, 119: 184-186.

Suffiness M, Pezzuto JM (1991). Assay related to cancer drug discovery. In: Methods in Plant Biochemistry, New York: Academic press: pp. 6-92.

Trease GE, Evans MC (1983). Textbook of Pharmacognosy, 12th ed. Bailliere, Tindall, London, pp. 343-383.

Zakaria ZA, Abdul Ghanzi ZDF, Raden Mohd, Nor RNS, Hasan Kumar G, Sulaiman MR, Mat Jais AM, Somuchit MN, Arifah AK, Ripin J (2007a). Anti-nociceptive, anti-inflammatory and antipyretic properties of aqueous extract of *Dicranopteris linearis* leaves in experimental animal models. J. Nat. Med., 62: 179-187.