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Research Article

Antipyretic Activity of Some Nigerian Medicinal Plants in Rats.

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ABSTRACT
Preparations of *Grewia crenata, Striga hermontheca and Gongronema latifolium* have been used in traditional medicine for treatment of pain for many years and their efficacies are widely acclaimed among the Hausa communities of northern Nigeria. The aim of the study was to assess the activity of hydromethanolic extract of these plants in baker's yeast-induced pyrexia in rats. The effect of the extracts on pyrexia was appreciable and significant at 1 to 3 hours at the highest dose of 400 mg/kg (*Grewia crenata>Striga hermontheca>Gongronema latifolium*). However, paracetamol (10 mg kg^{-1}) used as the reference drug caused a greater reduction in the rectal temperature of the rats at the onset (i.e. first two hours after administration) which was significant when compare to both control and extract treated groups. In summary, these findings support the use of these extracts in traditional medicine for treatment of pain.

Keywords: Antipyretic, *Grewia crenata, Striga hermontheca, Gongronema latifolium*

INTRODUCTION

Over 75% of the world population relies mainly on plants and plant extracts for health care and more than 30% of the entire plant species, at one time or other, were used for medicinal purposes[1]. The World Health Organization (WHO) encourages the inclusion of herbal remedies that have been proven to be efficacious and safe, into primary health care[2]. The use of plants for medicinal remedies is an integral part of the African cultural life, and this is unlikely to change in the years to come. Over the past decade, herbal medicine has become a topic of global importance, making an impact on both world health and international trade. Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population. This is particularly true in developing countries, where herbal medicine has a long and uninterrupted history of use. Continuous usage of herbal medicine by a large proportion of the population in developing countries is largely due to the high cost of Western pharmaceuticals and healthcare. Recognition and development of the medicinal and economic benefits of these plants are on the increase in both developing and industrialized nations[3]. In addition, herbal medicines are more acceptable in these countries from their cultural and spiritual points of view[4].

Grewia crenata is a large flowering plant and is today placed by most authors in the mallow family Malvaceae. Folk medicine makes use of some species, which are reputed to cure upset stomachs and some skin and intestinal infections, and seem to have mild antibiotic properties. However, no data were found regarding the pharmacological and phytochemical evaluation of this plant. *Striga hermontheca* (Del.) Benth. (Scrophulariaceae) also known as witch weed is a noxious parasite of pearl millet and sorghum[5]. An erect herb, sparsely branched, usually 30–40 cm high, traditionally used as food sauces, condiments, spices, flavourings, and products such as dyes, stains, inks, tattoos and mordants. Whole plant is used for medicinal purpose in the treatment of diabetes, leprosy, cutaneous and subcutaneous parasitic infection and pain-killers[5]. *Gongronema latifolium* Benth Hook, (Asclepiadaceae) is an herbaceous shrub, with yellow flowers and the stem that yields characteristic milky exudates when cut. It is used in Sierra Leone as chew-sticks, and cut up and boiled with lime juice, or infused in water over three days, the liquor is taken as a purge for stomach-pains, and symptoms connected with worm-infection[6]. In Ghana the leaves are rubbed on the joints of small children to help them to walk, and in Southern Nigeria the leaves serve as vegetable. The use of crude leaf extract of this shrub in maintaining healthy blood glucose levels have been reported[7]. Scientific studies have established the hypoglycaemic, hypolipidaemic and antioxidative effects of aqueous and ethanol extracts of *G. latifolium* leaf[8,9].

Anti-inflammatory, analgesic, and antipyretic drugs are a heterogeneous group of compounds, often chemically unrelated (although most of them are organic acids), which nevertheless share certain therapeutic actions and side effects. Acute inflammatory process involves the synthesis or release of mediators at the injured site. These mediators include prostaglandins, especially of the E series, histamine, bradykinins, leukotrienes and serotonin, all of which also cause pain and fever[10]. Inhibition of these mediators from reaching the injured site or from bringing out their pharmacological effects will normally ameliorate the inflammation and other symptoms associated with it[11]. Most of the anti-pyretic drugs inhibit COX-2 expression thus inhibiting PGE2 biosynthesis to reduce elevated body temperature. They are however

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TABLE 1: Antipyretic effect of hydromethanolic extract of *Grewia crenata* leaves in rats

DRUG	DOSE	HOURS BEFORE AND AFTER TREATMENT						
		BBT	0	1	2	3	4	5
Control	10ml/kg	37.50 ± 0.45	38.04 ± 0.22	37.96 ± 0.05	37.94 ± 0.08	38.02 ± 0.22	38.02 ± 0.11	38.14 ± 0.08
G.crenata leaves	200mg/kg	36.36 ± 0.05	38.24 ± 0.11	38.00 ± 0.19	38.04 ± 0.13	37.46 ± 0.18*	37.08 ± 0.12*	37.50 ± 0.21*
G.crenata leaves	400mg/kg	36.66 ± 0.34	38.02 ± 0.36	37.86 ± 0.12	37.74 ± 0.25*	37.44 ± 0.11*	37.68 ± 0.86*	36.26± 0.36*
Paracetamol	150mg/kg	37.32±0.16	38.18±0.14	37.62±0.07*	37.50±0.14*	37.68±0.27*	37.66±0.13*	37.96 ± 0.23

* Significantly different from the control at P<0.05 BBT: Basal body temperature

TABLE 2: Antipyretic effect of hydromethanolic extract of *Striga hermontheca* whole plant in rats

DRUG	DOSE	HOURS BEFORE AND AFTER TREATMENT						
		BBT	0	1	2	3	4	5
Control	10ml/kg	37.50 ± 0.45	38.04 ± 0.22	37.96 ± 0.05	37.94 ± 0.08	38.02 ± 0.22	38.02 ± 0.11	38.14 ± 0.08
Striga hermontheca	200mg/kg	37.58 ± 0.36	38.34 ± 0.21	38.22 ± 0.23	38.06 ± 0.21	38.16 ± 0.15	37.46 ± 0.32*	37.72 ± 0.34*
Striga hermontheca	400mg/kg	36.72 ± 0.12	38.46 ± 0.27	38.06 ± 0.22	38.12 ± 0.15	37.76 ± 0.05*	37.34 ± 0.07*	37.50 ± 0.17*
Paracetamol	150mg/kg	37.32±0.16	38.18±0.14	37.62±0.07*	37.50±0.14*	37.68±0.27*	37.66±0.13*	37.96 ± 0.23

* Significantly different from the control at P<0.05 BBT: Basal body temperature

toxic to the hepatic cells, glomeruli, cortex of the brain and heart muscle. A natural PGE2 inhibitory antipyretic remedy from medicinal plants with minimal toxicity is therefore essential.

In the same vein, these plants are used as herbal remedy for pain and inflammation. To the best of our knowledge the antipyretic activity of these selected plants has not been evaluated. Therefore the present study was designed to evaluate the antipyretic activity of hydro-methanolic extracts of these medicinal plants in rats.

MATERIALS AND METHODS

Collection of plant materials: Preliminary identification of three (3) selected plants (*Grongnema latilofolium, Grewia crenata And Striga hermontheca*) was carried out in the wild of Sokoto South by a botanist. Herbarium specimen were prepared and photographed to aid in the confirmation of the identity of the plants and deposited in the Herbarium, Botany unit, Department of Biological Sciences, Usmanu Danfodiyo University, Sokoto-Nigeria.

Preparation of plant extract: The plant materials were open-air dried under the shade and chopped into smaller pieces. The dried plant materials were pulverized into moderately coarse powder using pestle and mortar. A 400 g of the coarse powder was cold macerated with one liter of 50% v/v methanol in water for 72 hours with constant shaking in an air tight aspirator bottle. The resultant mixture was filtered using Whatman filter paper (No.1) and the filtrate concentrated to dryness *in vacuo* at 40^{o}C using a drying cabinet with a percentage yield of 34.6% (*G. crenata*), 82.2% (*S. hermontheca*) and 75.6% (*G. latifolium*). The dried extract collected was stored in a refrigerator and 30% concentration was prepared daily for use throughout the study.

Animals: Sprague - Dawley rats of both sexes (150-200g) were obtained from the National Veterinary Research Institute (NVRI), Vom, Nigeria. They were kept in well-ventilated environment and have free access to rodent pellets (Vital Feeds Ltd, Nigeria) and water *ad libitum*. The animals were allowed to acclimatize for 3 weeks and were fasted for six hours prior to experiments.

Antipyretic activity: Rectal temperature (T_R) were recorded by inserting a lubricated digital thermometer (external diameter: 3 mm, 0.1°C precision) 2.8 cm into the rectum of rats. Animals presenting initial rectal temperature between 36 and 37°C were selected for the antipyretic tests. Animals were selected for the experiment after confirmation of approximate constant rectal temperature for 7 days. The antipyretic activity of the extracts was evaluated based on Baker's yeast-

induced pyrexia in rats[12]. Pyrexia was induced by subcutaneous injection of 10 ml/kg of 15% w/v Baker's yeast suspension below the nape of the neck. The rectal temperature of each rat was measured at time, 0 hour, using a lubricated thermometer and before injection of the yeast. At 18 h following yeast injection, the different groups were treated with the vehicle, extracts (200 and 400 mg/kg) and standard drug, paracetamol (150 mg/kg). The rectal temperature was then recorded over a period of 5 hours.

RESULTS

Subcutaneous injection of the pyrogenic dose of yeast produced elevated changes in rectal temperature of the rats as shown in the Table 1 - 3 respectively. All three plant extracts caused a dose-dependent decrease in rectal temperature when compared to the control. *Grewia crenata* leaves extract revealed a significant decrease ($p<0.05$) in temperature between 2 to 5 hours after administration (Table 1). *Striga hermontheca* and *Gongronema latifolium* showed significant decrease ($P<0.05$) in temperature at 3 to 5 hours (Table 2) and 3 to 4 hours (Table 3) after administration respectively. However, paracetamol (10 mg kg^{-1}) used as the reference drug caused a greater reduction in the rectal temperature of the rats at the onset (i.e. first two hours after administration) which was significant different ($P<0.05$) when compare to both control and extract treated groups. The antipyretic effect started as from the 1st hour after drug and extract administration and was sustained for 4 h while control showed no antipyretic effect in the entire period of experiment.

DISCUSSIONS

The extracts produced a significant reduction in yeast induced pyrexia in rats dose-dependently and its effect is comparable to that of the standard anti-pyretic drug (paracetamol) used in this study. Pyrexia is a result of secondary impact of infection, tissue damage, inflammation, graft rejection, malignancy or other diseased states. The infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediators (cytokines like interleukin 1 and 6 and TNF-α) which increase the synthesis of PGE2 near pre optic hypothalamus area thereby triggering the hypothalamus to elevate the body temperature[13].

Baker's yeast (a lipopolysaccharide which is a cell wall component of gram negative bacteria) is an exogenous pyrogen which binds to an immunological protein called Lipopolysaccharide-Binding Protein (LBP). The binding results in the synthesis and release of various endogenous cytokine factors such as interleukin 1 (IL-1), interleukin 6 (IL-6) and the tumor necrosis factor-alpha which in turn activate the arachidonic acid pathway and ultimately results in the synthesis and release of prostaglandin E_2 (PGE_2). PGE_2 is the ultimate mediator of the febrile response; it slows the rate of firing of warm sensitive neurons and results in increased body temperature. The set-point temperature of the body will remain elevated until PGE_2 is no longer present[14,15].

Antipyretic activity is a characteristic of drugs or compounds which have an inhibitory effect on prostaglandin-biosynthesis and an indispensible role of prostaglandins in the febrile response has been demonstrated[16,17]. The yeast-induced fever in rats employed to investigate the antipyretic activity of the extract showed all plants to caused a reduction in rectal temperature however, the effect was not as pronounced and sustained as compared to 400mg/kg G*rewia crenata* and paracetamol. Systemic inflammation is accompanied by changes in body temperature,[17,18] hence these results seems to support the view that G*rewia crenata, Striga hermontheca and gongronema latifolium* have some influence on prostaglandin-biosynthesis, because prostaglandin is believed to be a regulator of body temperature[17].

Although, S. hermontheca and G. latifolium exhibited weak anti-pyretic effect occurring at 400 mg kg^{-1} respectively, further studies with higher doses may be necessary to confirm its antipyretic activity. Fever is a result of a finely tuned, complex event that involves both the peripheral immune system and the brain, through which a series of inflammatory and metabolic processes are regulated[19,20] and it is now commonly accepted that prostaglandin E_2 (PGE_2) is the final fever mediator in the brain, specifically in the preoptic area of the anterior

TABLE 3: Antipyretic effect of hydromethanolic extract of *Gongronema latifolium* leaves in rats

DRUG	DOSE	HOURS BEFORE AND AFTER TREATMENT													
		BBT		0		1		2		3		4		5	
Control	10ml/kg	37.50 0.45	±	38.04 0.22	±	37.96 0.05	±	37.94 0.08	±	38.02 0.22	±	38.02 0.11	±	38.14 0.08	±
Gongronema latifolium	200mg/kg	37.08 0.21	±	38.22 0.06	±	38.22 0.16	±	38.32 0.19	±	37.74 0.22*	±	36.98 0.46*	±	38.38 0.18	±
Gongronema latifolium	400mg/kg	37.04 0.35	±	38.02 0.17	±	37.78 0.39	±	37.74 0.30	±	37.52 0.21*	±	37.40 0.27*	±	37.86 0.23	±
Paracetamol	150mg/kg	37.32±0.16		38.18±0.14		37.62±0.07*		37.50±0.14*		37.68±0.27*		37.66±0.13*		37.96 0.23	±

* Significantly different from the control at $P<0.05$ BBT: Basal body temperature

hypothalamus[21], thus it may be plausible to conclude that the extract inhibits the synthesis of prostaglandins, albeit to a very little extent.

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