

Antipyretic Activity of *Abutilon mauritianum* (Jacq.) Roots in Wistar Rats

Tosan Charles Akapa*¹, Adeoti Olayinka Kehinde¹, Ojewuyi Oluwayemisi Beatrice², Olayemi Joseph Olajide³

¹ Department of Biochemistry, Faculty of Science, University of Ilorin, Ilorin, Nigeria.

² Department of Biological Sciences, College of Natural Sciences, Al-Hikmah University, Ilorin, Nigeria.

³ Department of Anatomy, Faculty of Basic Medical Science, University of Ilorin, Ilorin, Nigeria

E-mail: Tosanakapa@gmail.com (*Corresponding author)

ABSTRACT

Purpose: Ethanolic extract of *Abutilon mauritianum* roots (EEAMR) was evaluated for its antipyretic activity.

Methodology: The antipyretic activity was done using changes in rectal temperature influenced by brewer's yeast (10mg/kg) and lipopolysaccharide (0.3µg/kg) induced pyrexia in rats. Forty-two male wistar albino rats weighing 160.39 ± 9.23 g were used for the study and randomized into seven groups of six rats each. In the first experiment, all the rats were induced with pyrexia using 10 mg/kg body weight of brewer's yeast subcutaneously. Group I (negative control) was given 0.5 ml of distilled water. Rats in groups II (positive control), III and IV were given 100mg/kg p.o paracetamol (PCM), 150 and 300 mg/kg p.o of EEAMR respectively. In the second experiment, the rats were induced with pyrexia using 0.3 µg/kg body weight of lipopolysaccharide (LPS) intravenously. Group I (negative control) was given 0.5 ml of distilled water while groups II (positive control) and III were given 100mg/kg p.o paracetamol (PCM) and 600 mg/kg p.o of EEAMR respectively. **Results:** The extract significantly lowered ($P < 0.05$) the elevated rectal temperature in the brewer yeast and lipopolysaccharide induced pyretic models which was also dose dependent. The antipyretic effect of the extract was comparable to the standard antipyretic drug paracetamol (PCM).

Conclusion: This revealed that the extract has an antipyretic activity and supports its use in managing fever.

Key Words: *Abutilon mauritianum*, brewer's yeast, lipopolysaccharide, paracetamol.

1. INTRODUCTION

Pyrexia or fever is one of the most rampant clinical signs and is characterized by an increase of body temperature above the normal range $36.5\text{--}37.5\text{ }^{\circ}\text{C}$ ($97.7\text{--}99.5\text{ }^{\circ}\text{F}$) as a result of an elevation in the temperature regulatory set-point [1]. This condition is caused as a secondary impact of infection, tissue damage, malignancy or other diseased conditions [2]. This is described as the body's natural defense mechanism to create an uncondusive environment where infectious agents or damaged tissue cannot withstand [3]. This elevation in set-point triggers increased muscle tone and chills. Occurrence of fever is due to a disturbance of the hypothalamic "thermostat" which ultimately leads to body temperature set point to be raised. Readjustment to normal set point by temperature regulating system (mechanism such as dilation of superficial blood vessels) functions to reduce the body temperature [4]. Centres in the hypothalamus regulate normal body temperature to ensure balance between heat loss and heat gain.

Antipyretics are medications that are used to reduce fevers. Ibuprofen a known antipyretic medication is effective in reducing fevers in children [5]. Its antipyretic action is more effective than acetaminophen (paracetamol) in children. Ibuprofen and acetaminophen in combination may be safely used in children with fever [6, 7]. Body temperature when elevated by factors such as exercise or increase in ambient temperature cannot be managed with medications like paracetamol [8]. Most antipyretics inhibit COX – 2 expression primarily to reduce PGE₂ biosynthesis whose action is involved in an elevated temperature [9, 10]. Some other agents used as medications include NSAIDs, opioid etc. However, renal, gastrointestinal, hepatic, central nervous system, dermatological diseases and other several side effects have been attributed to chronic usage of most these agents [11].

Lately, focus on the medicinal uses of plant has increased all over the world and a large amount of evidence has been collected to show great potential of medicinal plants used in various folk medicine [12]. *Abutilon mauritianum* belongs to the family, Malvaceae. It is widely distributed in the drier parts of tropical Africa from Senegal eastward to Eritrea, Ethiopia and Somalia, and southward to Angola, Zambia, Zimbabwe Mozambique and South Africa. The plants vanacular names are Bush mallow and country mallow in English, Mauve des champs in French, Furu and kawo in Nigerian traditional languages. In traditional medicine, infusion of the root is taken as a cooling drink in case of fever or pyrexia in Nigeria. The root is chewed as an expectorant, a root decoction is drunk against bronchitis and cramp in the stomach, and a decoction of the root and bark for the treatment of diarrhoea, stomach ache, coughs and colds in East Africa [13]. However, there is no scientific report available in support of the antipyretic activity of ethanolic extract of *Abutilon mauritianum* roots

(EEAMR). Hence, the purpose of the present study was to investigate the antipyretic activity of ethanolic extract of *Abutilon mauritianum* roots and justify the traditional claim.

2. MATERIALS AND METHODS

2.1 Drugs and chemicals

Paracetamol was purchased from Aspar Pharmaceutical Limited. Brewer's yeast and lipopolysaccharide (LPS) were procured from Lessaffre Red Star bakers. All other chemicals were of analytical grade.

2.2 Collection of the plant material and identification

The roots of *Abutilon mauritianum* used in this study were obtained from The Federal Polytechnic, Bida, Niger State, Nigeria. The Identification and authentication of plant material was carried out by Mr Bolu Ajayi, a botanist at the Herbarium Unit of Department of Biological Sciences, University of Ilorin, Nigeria in line with the criteria stipulated by International Committee for Botanical Nomenclature.

2.3 Preparation of plant extract

Abutilon mauritianum roots were dried at room temperature until a constant weight was obtained then pulverized into fine powder. 100g powder was macerated in 1000ml ethanol (95%) for 72 hours. The mixture was filtered and evaporated to dryness under reduced pressure in a rotary evaporator. The extract was reconstituted into doses of 150, 300 and 600 mg/kg body weight which were used for the experiment.

2.4 Experimental animals

Forty-two wistar male rats weighing 160.39 ± 9.23 g were randomized into seven groups (n= 6). Two sets of experiments were conducted. In the first experiment, four groups were used to evaluate the antipyretic activity of EEAMR in brewer's yeast while in the second experiment, three groups were used to evaluate the antipyretic activity of EEAMR in lipopolysaccharide induced pyrexia. All rats were housed in clean aluminum cages contained in well ventilated housing conditions (temperature of 22 ± 3 °C; photoperiod of 12 h; and humidity of 50%-55%). The experimental animals were made use of according to the Guide for the Care and Use of Laboratory Animals [14] and in accordance with the principles of Good Laboratory Procedure (GLP) [15]. They were allowed free access to pelletized rat feeds (Bendel Feeds and Flour Mills Ltd., Kwara State, Nigeria) and water *ad libitum*. acclimatization period to laboratory condition was for seven days before the commencement of the experiment.

2.5 Experimental model and animal grouping for antipyretic study

2.5.1 Yeast induced pyrexia

The method described by Adams *et al.* [16] was used. Pyrexia was induced in all the rats (that had been deprived of feeds for 6 h but were adequately supplied with water *ad libitum*) by subcutaneous administration of 20% w/v of brewer's yeast at a dose of 10 mg/kg body weight near the groin of the animals. A digital thermometer (Sato Keiryoki Mfg. Co., Ltd., Japan), 3 - 4 cm into the rectum after 19 hrs and only rats that showed an increase of at least 0.6 °C or more in the rectal temperature were used for the study. Group I the pyrexia negative control was administered distilled water only. Group II (positive control) was treated with 100 mg/kg of paracetamol p.o. Group III and IV were treated with 150 and 300 mg/kg of *Abutilon mauritianum* roots p.o. respectively. Rectal initial temperature before the induction of pyrexia and also the temperature at 0, 1, 2 and 3 hours after administration were recorded by a digital thermometer [17].

2.5.2 Lipopolysaccharide induced pyrexia

Pyrexia was induced in the rats (already fasted overnight) by injecting 0.3 µg/kg lipopolysaccharide (LPS) (from *E. coli*) i.v. through the marginal ear vein dilated with xylene [18]. Immediately after administration of LPS, food was withdrawn and 19 hrs after; rise in rectal temperature was recorded. Only animals which developed satisfactory pyrexia (0.6 °C or more increase in rectal temperature) were used. Group I, the pyrexia negative control was administered distilled water. Group II (positive control) was treated with 100 mg/kg of paracetamol p.o. Group IV was treated with 600 mg/kg of *Abutilon mauritianum* roots p.o. A higher dose-level of 600mg/kg of the extract was tested in this model because a higher antipyretic effect was produced at the higher dose in the brewer yeast model. Basal rectal temperatures (T°C) before induction of pyrexia at a predetermined intervals and after administration of treatments at 0, 1, 2, and 3 hours (h) were recorded using a narrow bulb rectal thermometer (readings taken twice and averaged).

2.6 Acute toxicity test

Acute toxicity was carried out on the albino rats by up and down method [19]. The animals were fasted overnight and the extract at different doses of (500, 1000, 1500 mg/kg body weights) were administered orally. The animals were kept under observation continuously for 3 hours for general behavioural, neurological and autonomic profiles and finally after 24hrs.

2.7 Statistical analysis

The data were presented as mean SEM (n=6). Results obtained were analysed by one way analysis of variance (ANOVA) followed by Dunnett's t-test for multiple comparisons. The significant difference was considered at $P < 0.05$.

3.0 RESULTS

3.1 Acute oral toxicity study

Acute oral toxicity study indicates no mortality and sign of toxicity like change in skin and fur, eyes and mucous membrane, and also respiratory, circulatory, behavior pattern, convulsions, salivation, lethargy, sleep and coma were observed at the end of the study. Hence, EEAMR at a dose of 150 and 300 mg/kg body weights were selected for the yeast induced pyrexia while 600 mg/kg body weight was selected for lipopolysaccharide induced pyrexia.

3.2 Yeast induced pyrexia in rats

Subcutaneous injection of yeast suspension significantly ($P < 0.05$) increased the rectal temperature of rats compared to the initial rectal temperature. Administration of ethanolic extract of *Abutilon mauritianum* roots at 150 and 300 mg/kg significantly ($P < 0.05$) lowered the yeast induced elevated rectal temperature, this antipyretic effect was maintained from the 2nd to the 3rd hour and this compared favorably with the paracetamol (PCM) in a dose dependent fashion (Table 1).

3.3 Lipopolysaccharide induced pyrexia

Intravenous injection of lipopolysaccharide (LPS) significantly ($P < 0.05$) increased the rectal temperature compared to the initial rectal temperature. The ethanolic extract of *Abutilon mauritianum* at 600 mg/kg significantly ($P < 0.05$) attenuated the increased rectal temperature produced by LPS, this antipyretic effect was maintained from 1st to the 3rd hour and this compared favorably with the paracetamol (PCM) treated rats (Table 2).

4.0 DISCUSSION

Fever or pyrexia is said to be caused by several endogenous pyrogenic substances such as interleukins, tumor necrosis factor- α (TNF- α), macrophages and prostaglandins [20]. Tumor necrosis factor- α and phospholipase A₂ may possibly activate prostaglandin synthesis. Brewer's yeast forms a linkage to an immunological protein called Lipopolysaccharide-Binding Protein (LBP). This link causes the production of endogenous pyrogens ultimately leading to the synthesis and release of prostaglandins [21]. Generally, it is now accepted that prostaglandin E₂ (PGE₂) is the final fever mediator in the brain, particularly in the preoptic area of the anterior hypothalamus [22]. In a condition when body temperature increases, the temperature regulatory system dilates the blood vessels causing increased sweating to lower the temperature by nervous feedback mechanism. The antipyretics commonly prescribed for use today include acetaminophen or paracetamol, aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDS). The major action of antipyretics in their potential to inhibit the enzyme cyclooxygenase (COX) causing the synthesis of inflammatory prostaglandins to be interrupted [23]. They are known to also act by suppressing the production of pyrogenic cytokines such as TNF- α and IL- β [24]. It has been established that there are two pathways leading to the transcription and induction of cyclooxygenase. Both pathways are activated by cytokines e.g. IL-1 α , IL-6 and tumor necrosis factor (TNF) which trigger central mechanisms that act via the transcription factors such as nuclear factor (NF) κ B, signal transducer and activator of transcription (STAT-3) [25]. This study examined the antipyretic potential of ethanolic extract of *Abutilon mauritianum* roots (EEAMR) in experimental animal models. EEAMR significantly reduced the rectal temperature similar with standard antipyretic drug paracetamol, in a dose dependent fashion of brewer's yeast and lipopolysaccharide (LPS) induced pyrexia. On the basis of observation of data obtained from our study, we can say that the ethanolic extract of the plant roots showed most significant antipyretic activity at a higher dose of 600 mg / kg body weight compared to lower doses. Thus, it can therefore be inferred that EEAMR inhibits the synthesis of prostaglandins. The phytochemical analysis of the ethanolic extract of the *Abutilon maritinaum* leaves revealed the presence of flavonoids, saponins and tannins while glycosides were completely absent [26]. Previous studies have shown that antipyretic effect of *Dalbergia species* may be attributed to the presence of flavonoids [3]. Furthermore, flavonoids and tannins are known to inhibit prostaglandin synthesis as reported by Ramaswamy, 1985 [27]. We might therefore say that the flavonoids, tannins and other chemical compounds present in the plant's extract are the components responsible for the observed antipyretic effect. It is worthwhile to isolate the bioactive principles which are responsible for this activity; the process has begun in our laboratory.

5.0 CONCLUSION

The data obtained in this study indicates that the ethanolic extract of *Abutilon mauritianum* (Jacq.) roots exhibited antipyretic properties that were significant after yeast and lipopolysaccharides induced pyrexia. The inhibition of the synthesis and/or release of inflammatory mediators may be its main mechanism(s) of action. These findings justify the traditional use of this plant in the treatment of pyretic conditions and validate its claim

of being used in folklore medicine for the treatment of pyrexia. However, extensive studies are needed to evaluate precise mechanism(s) and active principles of the plant as a medicinal remedy for pyrexia conditions.

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Table 1: Effect of EEAMR in brewer's yeast induced pyrexia in rats.

Group	Dose	Initial rectal temp.	Rectal temperature after administration (°C)			
			0 (h)	1 (h)	2 (h)	3 (h)
I Control	0.5ml	36.35±0.16 ^a	40.02±0.47 ^a	40.22±0.07 ^b	40.11±0.04 ^b	40.06±0.03 ^b
II PCM	100mg/kg	36.87±0.17 ^a	40.07±0.22 ^a	38.71±0.46 ^a	38.12±0.01 ^a	36.63±0.09 ^a
III EEAMR	150mg/kg	36.58±0.03 ^a	40.31±0.16 ^b	40.15±0.13 ^b	38.10±0.04 ^a	36.53±0.11 ^a
IV EEAMR	300mg/kg	36.01±0.09 ^a	40.15±0.12 ^b	40.30±0.04 ^b	38.06±0.26 ^a	36.48±0.18 ^a

Data are mean ± SEM of six determinations. Values carry superscripts different from the control for each parameter that are significantly different (P < 0.05).

Table 2: Effect of EEAMR in lipopolysaccharide induced pyrexia rats.

Group	Dose	Initial Rectal temp.	Rectal temperature after administration (°C)			
			0 (h)	1 (h)	2 (h)	3 (h)
I control	0.5ml	36.33±0.04 ^a	39.99±0.02 ^a	40.02±0.20 ^b	40.00±0.06 ^b	40.13±0.20 ^b
II PCM	100mg/kg	36.36±0.33 ^a	39.36±0.33 ^a	37.50±0.07 ^a	37.36±0.04 ^a	36.07±0.01 ^a
III EEAMR	600 mg/kg	36.04±0.14 ^a	39.04±0.14 ^a	37.60±0.05 ^a	37.41±0.49 ^a	36.03±0.30 ^a

Data are mean ± SEM of six determinations. Values carry superscripts different from the control for each parameter that are significantly different (P < 0.05).