

Full Length Research Paper

# Effect of administration of aqueous and ethanolic extracts of *Enantia chlorantha* stem bark on brewer's yeast-induced pyresis in rats

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The phytochemical screening of aqueous and ethanolic extracts of the stem bark of *Enantia chlorantha* Oliv as well as the antipyretic effect of the solvent extracts at 25, 50, 100 and 200 mg/kg body weight was investigated in albino rats. Phytochemical analysis of the aqueous and ethanolic extracts of *E. chlorantha* stem bark revealed the presence of phenolics, flavonoids, alkaloids, glycosides and saponins. The concentrations of these phytochemicals in the ethanolic extracts were slightly higher than in the aqueous extracts. The 50 - 200 mg/kg body weight of the solvent extracts produced significant reduction ( $P < 0.05$ ) in rectal temperature of the hyperpyretic rats. The antipyretic activities of the solvent extract at these doses also compared favourably ( $P > 0.05$ ) with the indomethacin dosed groups. This study showed that the aqueous and ethanolic extracts of *E. chlorantha* stem bark at 50 - 200 mg/kg body weight possess antipyretic activity and thus supports the folklore use of the plant in the management of fever.

**Key words:** *Enantia chlorantha*, brewer's yeast, antipyretic, rectal temperature.

## INTRODUCTION

Pyresis is a clinical condition that results in increase in body temperature. Pyrexia or fever arises as a secondary impact of infection, malignancy or other diseased states (Chattopadhyay et al., 2005). High fever enhances faster disease progression by increasing tissue catabolism, dehydration and existing complaints (Spacer and Breder, 1994). Antipyretic drugs reduce elevated body temperature and are known to act centrally on the temperature regulation center in the brain or peripherally, through vasodilation and heat dissipation. They also act by inhibiting the synthesis of prostaglandin E<sub>2</sub> (Flower and Vane, 1972; Kurokawa et al., 1998). Several antipyretic agents including medicinal plants have been used for many years. One of those medicinal plants that have been used in many localities in Nigeria to manage fever is *Enantia chlorantha*.

*E. chlorantha* Oliv (family-Annonaceae) locally known as Awogba, Oso pupa or Dokita igbo (Yoruba), Osomolu (Ikale), Kakerim (Boki) and Erenba-vbogo (Bini), is widely distributed along the coasts of West and Central Africa. It is also very common in the forest regions of Nigeria. It is an ornamental tree which may grow up to 30 m high, with dense foliage and spreading crown. The outer bark which is thin and dark brown is fissured geometrically while the inner bark is brown above and pale cream beneath. The stem is fluted and aromatic while the elliptic leaves are about 0.14 – 0.15 m long and 0.05 – 0.14 m broad (Iwu, 1993).

The decoction of the root along with the roots of *Fleurya aestuans*, *Polyathia suaveolens* and old leaves of *Palisota hirsuta* and *Carica papaya* is used in the management of malaria and jaundice. The stem bark is also used for treating leprosy spots, as haemostatic agent and uterus stimulant. The possible use of the plant in conditions such as rickettsia fever, typhoid fever and infective hepatitis or jaundice has also been reported (Gill, 1992). The active principles have been implicated to be alkaloid-berberine, saponins and tannin (Gill, 1992).

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Several studies have shown that the stem bark of *E. chlorantha* possess wide spectrum antimicrobial activity including against *Klebsiella aeruginosa* (Adesokan et al., 2007), antimalarial and antipyretic properties (Agbaje and Onabanjo, 1991), but the antipyretic activity study carried out by Agbaje and Onabanjo (1998) used *K. aeruginosa* to infect mice and rabbits. Although, the antipyretic potentials of *E. chlorantha* stem bark has been explored, it is still not clear whether the effect is due to its antibacterial activity or solely an antipyretic effect.

This study, therefore, is aimed at ascertaining the sole antipyretic activity of *E. chlorantha* stem bark using brewer's yeast and to compare the antipyretic efficacy of the solvent (water and ethanol) extracts of *E. chlorantha* stem bark. Several authors (Olajide et al., 2000; Mutalik et al., 2003; Chattopadhyay et al., 2005; Zakaria et al., 2007) have used brewer's yeast to induce pyrexia in rats, hence, the use in this study.

## MATERIALS AND METHODS

### Experimental animals

Fifty albino rats (*Rattus norvegicus*) of both sexes with average weight of  $150\text{ g} \pm 5$  were obtained from the Animal Holding Unit of the Faculty of Basic Medical Sciences, College of Health Sciences, University of Ilorin, Ilorin, Nigeria. The animals were housed in clean metabolic cages, placed in well-ventilated house conditions (Temperature:  $28 - 31^{\circ}\text{C}$ ; photoperiod: 12 h natural light and 12 h dark; humidity: 50 - 55 %). They were also allowed free access to rat pellets (Bendel Feeds and Flour Mills Ltd., Ewu, Nigeria) and tap water. The cages were cleaned of waste once daily.

### Plant material and authentication

The plant samples obtained from herb sellers at Baboko market, Ilorin, Nigeria was authenticated at the Department of Botany, Obafemi Awolowo University, Ile-Ife, Nigeria. A voucher specimen (IFE 13968) was deposited in the herbarium of the Department.

### Brewer's yeast

#### Brewer's yeast was obtained from Noble Brewery, Ijagbo via Offa, Nigeria.

Indomethacin and clinical thermometer; Indomethacin was a product of Sigma Aldrich Chemical, USA, while the clinical thermometer was supplied by UNESCO International, USA.

### Other reagents

All other reagents used were of analytical grade and were prepared in all glass distilled water.

### Phytochemical screening

Phytochemical screening of the plant stem bark was carried out using standard methods described for alkaloids (Harborne, 1973); steroids and phlobatannins (Trease and Evans, 1989); phenolics and flavonoids (Awe and Sodipo, 2001); saponins and cardiac glycosides (Sofowora, 1993); tannins (Odebiyi and Sofowora,

1978). Quantitative analysis of the detected phytochemicals were carried out for phenolics (Edeoga et al., 2005), flavonoids (Bohm and Kocipal-Abyazan, 1974), alkaloid (Harborne, 1973), saponins (Obadoni and Ochuko, 2001) and glycosides (El-Olemy et al., 1994).

### Preparation of aqueous and ethanolic extracts of *E. chlorantha* stem bark

The method described by Yakubu et al. (2005) was employed. Briefly, the plant stem bark was cut into pieces with the aid of a sterile knife and oven-dried at  $40^{\circ}\text{C}$  until constant weight was obtained. The dried pieces were then pulverized with an electric blender (Blender/Miller III, model MS-223, China). The powdered material was stocked in a plastic container from which 20 g each was separately percolated in 100 ml of cold distilled water and absolute ethanol for 48 h at room temperature with constant shaking. The extract was then filtered with Whatman No. 1 filter paper and the resulting filtrate for the water extract was concentrated on a steam bath to give 5.00 g of the residue (% yield of  $25.00\text{ g} \pm 0.05$ ) while the ethanolic extract after concentrating in a rotatory evaporator yielded 5.10 g (% yield of  $25.50\text{ g} \pm 0.08$ ). The residues were reconstituted in distilled water to give the required doses of 25, 50, 100 and 200 mg/kg body weight of the aqueous and ethanolic extracts.

### Induction of pyrexia

The method described by Adams et al. (1968) was used. Briefly, pyrexia was induced in the animals (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 to near the groin of the animals. The rectal temperature of the rats were measured 17 h after the brewer's yeast injection by inserting the thermometer, 3 - 4 cm into the rectum and only rats that showed an increase of at least  $0.5^{\circ}\text{C}$  rise in temperature were used for the study.

### Animal grouping and administration of chemical compounds

Fifty albino rats were grouped into 10 consisting of 5 rats each as follows:

Group A, the control, received orally 6.7 ml/kg body weight of physiological saline.

Group B, received orally 1 ml corresponding to 5 mg/kg body weight of the reference drug, indomethacin.

Groups C, D, E and F were orally administered with 1 ml each, corresponding to 25, 50, 100 and 200 mg/kg body weight of aqueous extract of *E. chlorantha* stem bark respectively, 17 h after induction of pyrexia.

Groups G, H, I and J were orally administered with 1 ml each, corresponding to 25, 50, 100 and 200 mg/kg body weight of ethanolic extract of *E. chlorantha* stem bark respectively, 17 h after induction of pyrexia.

The various groups of animals were administered with their doses and brewer's yeast preparation using plastic syringes attached to metal oropharyngeal cannula. The animals were allowed free access to rat pellets and tap water after their daily doses. The rectal temperature was measured at 60, 90 and 120 min after their doses. This study was reviewed and approved by the College of Health Sciences Ethical Committee on Animal Use and Care.

### Statistical analysis

Data were expressed as mean of five replicates  $\pm$  SD except for

**Table 1.** Phytochemical constituents of aqueous and ethanolic extracts of *Enantia chlorantha* stem bark.

Phytochemicals	% Concentration	
	Aqueous extract	Ethanolic extract
Phenolics	1.12±0.00	1.32±0.02
Flavonoids	0.40±0.02	0.44±0.01
Alkaloids	2.76±0.02	2.88±0.02
Glycosides	0.086±0.01	0.11±0.01
Saponins	1.60±0.02	1.72±0.03
Tannins	Not detected	Not detected
Phlobatannins	Not detected	Not detected
Steroids	Not detected	Not detected

Values are mean ± SD; n = 3

the phytochemical screening. The values were subjected to student's t-test and data were considered statistically significant at  $P < 0.05$  (Mahajan, 1999)

## RESULTS

Phytochemical screening of the aqueous and ethanolic extracts of *E. chlorantha* stem bark revealed the presence of phenolics, flavonoids, alkaloids, glycosides and saponins while tannins, phlobatannins and steroids were not detected. Despite producing the same phytochemicals by the solvents, the ethanolic extract produced slightly higher percentage concentration than the aqueous extract (Table 1). The effect of 25, 50, 100 and 200 mg/kg body weight of aqueous and ethanolic extracts of *E. chlorantha* stem bark on the brewer's yeast induced hyperpyrexia in rats are shown in Tables 2 and 3 respectively. After the induction of pyrexia, the control rats remained hyperpyretic throughout the duration of the experiment (Tables 2 and 3). The elevated temperature in the two solvent extract groups were significantly reduced ( $P < 0.05$ ) throughout the 120 min experimental period by the reference drug, indomethacin (Tables 2 and 3). The brewer's yeast provoked elevation of body temperature in rats were significantly reduced ( $P < 0.05$ ) throughout the duration of the experiment following the oral administration of aqueous extract of *E. chlorantha* stem bark at the doses of 50, 100 and 200 mg/kg body weight while the 25 mg/kg body weight only significantly reduced the elevated body temperature of the animals by the end of the experimental period. There was no significant change prior to the end of the 120 min experimental period (Table 2).

In contrast, administration of ethanolic extract of *E. chlorantha* stem bark at the doses of 50, 100 and 200 mg/kg body reduced the elevated body temperature in rats only from after 60 min duration and this was sustained throughout the remaining period of the experiment (Table 2). The 25 mg/kg body weight of the ethanolic extract could only effect significant reduction ( $P < 0.05$ ) in

the rats elevated body temperature by the end of the experimental period (Table 3). The 25 mg/kg body weight of the ethanolic extract of the plant stem bark could not reduce the body temperature of the hyperpyretic rats before the 120 min period (Table 3).

## DISCUSSION

Fever may result from infection, one of the sequelae of tissue damage, inflammation, graft rejection, or other disease states. It is produced by certain endogenous substances which include tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ) and prostaglandins (Kluger, 1991). Antipyretics have been shown to suppress fever either by inhibiting prostaglandin synthetase, resulting in the blockade of the synthesis of prostaglandin in the brain or suppressing the rise of interleukin-1 production subsequent to interferon production (Flower and Vane, 1972; Kurokawa et al., 1996).

The significant reduction in the brewer's yeast elevated body temperature in rats by the solvent extracts of *E. chlorantha* stem bark may be attributed to the ability of the plant extracts to inhibit prostaglandin synthetase activity or suppress the rise of interleukin-1 production subsequent to interferon production (Flower and Vane, 1972; Kurokawa et al., 1996). The antipyretic potentials of plant stem bark may also be adduced to the inhibition of the expression of cyclooxygenase type II (COX-2) which in turn reduces or inhibits the synthesis of PGE 2 in the animals (Luo et al., 2005). The antipyretic activities shown by the solvent extracts at 50 - 200 mg/kg body weight were more pronounced after 90-120 min and their potencies were similar to the reference drug, indomethacin.

Alkaloids like boldine have been implicated to have the ability to block and inhibit the synthesis of prostaglandin  $E_2$  (Backhouse et al., 1994) which eventually reduce elevated body temperature in animals. Similarly, flavonoids like baicalin have been shown to exert antipyretic effect by suppressing TNF- (Chang et al., 2007). Therefore, the antipyretic activity of the solvent extracts of *E. chlorantha* stem bark may be associated with the flavonoids and or the alkaloidal components of the plant extracts.

Since similar pattern of antipyretic activity has been observed for the aqueous and ethanolic extract of the stem bark of *E. chlorantha*, it may be inferred that the antipyretic activity of the solvent extracts are the same and may be due to the presence of bioactive agents like flavonoids or alkaloids rather than the quantity of the bioactive principle(s) present in the plant. The result of the present study is quite different from that of Agbaje and Onabanjo (1998) because both ethanolic and aqueous extracts of the plant were investigated and compared, in addition to the use of several dose regimens in this study. Since Agbaje and Onabanjo (1998) used *Klebsiella sp.* to induce pyresis as against brewer's yeast

**Table 2.** Effect of aqueous extract of *Enantia chlorantha* stem bark on brewer's yeast-induced hyperpyrexia in rats

Treatments	Initial Temp ( <sup>o</sup> C)	Temp ( <sup>o</sup> C) (17 h after induction of fever)	Temp ( <sup>o</sup> C) (60 min after extract)	Temp ( <sup>o</sup> C) (90 min after extract)	Temp ( <sup>o</sup> C) (120 min after extract)
Control (Physiological Saline)	36.94 ± 0.05 <sup>a</sup>	38.36 ± 0.17 <sup>o</sup>	38.20 ± 0.18 <sup>o</sup>	38.26 ± 0.17 <sup>o</sup>	38.14 ± 0.18 <sup>o</sup>
Indomethacin (5 mg/kg body weight)	36.96 ± 0.06 <sup>a</sup>	38.24 ± 0.15 <sup>b</sup>	37.36 ± 0.18 <sup>a</sup>	37.04 ± 0.09 <sup>a</sup>	36.86 ± 0.05 <sup>a</sup>
Extract (25 mg/kg body weight)	37.00 ± 0.04 <sup>a</sup>	38.46 ± 0.13 <sup>b</sup>	37.92 ± 0.22 <sup>b</sup>	37.50 ± 0.19 <sup>b</sup>	37.14 ± 0.17 <sup>a</sup>
Extract (50 mg/kg body weight)	36.56 ± 0.35 <sup>a</sup>	38.00 ± 0.34 <sup>b</sup>	37.28 ± 0.31 <sup>a</sup>	37.26 ± 0.30 <sup>a</sup>	36.84 ± 0.25 <sup>a</sup>
Extract (100 mg/kg body weight)	36.76 ± 0.22 <sup>a</sup>	38.24 ± 0.14 <sup>b</sup>	37.36 ± 0.35 <sup>a</sup>	37.02 ± 0.40 <sup>a</sup>	36.62 ± 0.44 <sup>a</sup>
Extract (200 mg/kg body weight)	36.68 ± 0.21 <sup>a</sup>	38.20 ± 0.22 <sup>b</sup>	37.22 ± 0.34 <sup>a</sup>	36.80 ± 0.38 <sup>a</sup>	36.56 ± 0.37 <sup>a</sup>

Values are means ± SD; n = 5

Values across the same row carrying different superscripts from those of the initial temperature are significantly different (P<0.05).

**Table 3.** Effect of ethanolic extract of *Enantia chlorantha* stem bark on brewer's yeast-induced hyperpyrexia in rats

Treatments	Initial Temp ( <sup>o</sup> C)	Temp ( <sup>o</sup> C) (17 h after induction of fever)	Temp ( <sup>o</sup> C) (60 min after extract)	Temp ( <sup>o</sup> C) (90 min after extract)	Temp ( <sup>o</sup> C) (120 min after extract)
Control (Physiological Saline)	36.94 ± 0.05 <sup>a</sup>	38.36 ± 0.17 <sup>o</sup>	38.20 ± 0.18 <sup>o</sup>	38.26 ± 0.17 <sup>o</sup>	38.14 ± 0.18 <sup>o</sup>
Indomethacin (5 mg/kg body weight)	36.96 ± 0.06 <sup>a</sup>	38.24 ± 0.15 <sup>b</sup>	37.36 ± 0.18 <sup>a</sup>	37.04 ± 0.09 <sup>a</sup>	36.86 ± 0.05 <sup>a</sup>
Extract (25 mg/kg body weight)	36.98 ± 0.07 <sup>a</sup>	38.38 ± 0.15 <sup>b</sup>	38.00 ± 0.19 <sup>b</sup>	37.58 ± 0.14 <sup>b</sup>	37.24 ± 0.09 <sup>a</sup>
Extract (50 mg/kg body weight)	36.84 ± 0.07 <sup>a</sup>	38.26 ± 0.17 <sup>b</sup>	37.74 ± 0.07 <sup>b</sup>	37.30 ± 0.08 <sup>a</sup>	37.04 ± 0.07 <sup>a</sup>
Extract (100 mg/kg body weight)	36.88 ± 0.09 <sup>a</sup>	38.00 ± 0.07 <sup>b</sup>	37.62 ± 0.08 <sup>b</sup>	37.24 ± 0.11 <sup>a</sup>	37.00 ± 0.07 <sup>a</sup>
Extract (200 mg/kg body weight)	36.91 ± 0.12 <sup>a</sup>	38.24 ± 0.17 <sup>b</sup>	37.74 ± 0.12 <sup>b</sup>	37.26 ± 0.05 <sup>a</sup>	37.02 ± 0.05 <sup>a</sup>

Values are means ± SD; n = 5

Values across the same row carrying different superscripts from those of the initial temperature are significantly different (P<0.05).

in this study, it can therefore, be inferred that the antipyretic activity of the plant is not due to its antimicrobial activity (Atata et al., 2003; Adesokan et al., 2007), but solely an antipyretic effect. The fact that antipyretic activity was not observed significantly in the least dose (25 mg/kg body weight) of the two solvent extracts suggests that the dose was not effective in reducing the brewer's yeast elevated body temperature in rats.

In conclusion, the data obtained in this study indicate that the ethanolic and aqueous extracts of *E. chlorantha* stem bark exhibited antipyretic activity at the doses greater than the least dose (25 mg/kg body weight) investigated in this study and that the antipyretic activity of *E. chlorantha* is a 'pure' antipyretic effect and not due to its antimicrobial activity. The antipyretic activities of *E. chlorantha* stem bark supports its use in the management

of fever by traditional medicine practitioners.

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