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Antipyretic activity of methanolic fruit extract of *Xylopia aethiopica* in yeast-induced pyrexia

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Abstract
Xylopia aethiopica fruit singly or in combination with other medicinal herbs have been used in traditional medicine for the treatment of pain, inflammation and fever for many years among the Hausa communities of northern Nigeria. The aim of this study is to investigate the antipyretic effects of the methanolic fruit extract of *Xylopia aethiopica* in Brewer's yeast-induced pyretic rats. Phytochemicals were qualitatively determined using standard procedures while the acute oral toxicity was determined using limit dose test and the invivo antipyretic activity was determined by brewer's yeast induced pyrexia method. The results showed that the LD_{50} of methanol fruit extract of *X. aethiopica* was greater than 5000mg/kg and possessed significant ($p<0.05$) antipyretic effect by causing a decrease in rectal temperature. Treated animals (100 and 400mg/kg) exhibited fever reduction from the 3rd to the 6th hour which was not significantly different ($p>0.05$) from animal treated with the standard drug paracetamol. Phytochemicals present includes tannins, alkaloids, saponins, phenols, flavonoids, steroids and terpenoids. In conclusion, this study provides evidences for the antipyretic effect of fruit extract of *Xylopia aethiopica* which supports its ethno medical use.

Keywords: Antipyretic, Brewer's yeast, *Xylopia aethiopica*, fruit extract

Introduction
Pyrexia (fever) is defined as a complex physiological response characterized by an elevation of body temperature. An elevation in core temperature is triggered by substances known as pyrogens [1]. Pyrogens can be either endogenous or exogenous. Pyrexia may result from infection, tissue damage, inflammation, graft rejection or other disease state. Several studies looking at fever mechanisms show that exogenous pyrogens include bacteria, viruses, protozoans, fungi, alkaloids or lectins [2]. Fever treatment with modern medication may not be accessible or affordable by most rural dwellers and sometimes could cause side effects. This, in recent times has influenced the increased patronage of herbal medicines as they are believed to have no side effect, easily accessible and cheap.

Xylopia aethiopica is a deciduous, ever green tree popularly known as "Ethopian pepper'' and in Northern Nigeria it is called "kymba" in Hausa language. It grows in tropical climate and belongs to annonaceae family. Crushed powdered fruits and seeds are dried and used as pepper substitute and as flavorings to prepare local soups in Nigeria. An infusion of the plant bark is used in the treatment bronchosis and dysentery while its fruit is used traditionally in the management of general body pain, headache, rheumatism and fever. Strong dependence on plants as medicines, calls for continuous ethno pharmacological studies to determine their safety, efficiency and discovery of new active principles from them. The present study was therefore carried out to evaluate acute oral toxicity and in vivo antipyretic activity of the methanolic fruit extract of *Xylopia aethiopica*.

Material and methods
Collection of the plant material and identification
The leaves of *Xylopia aethiopica* were collected from Aliero Local government Area, Kebbi State in March, 2016. And the herbarium specimen were identified and authenticated in the Biological Sciences Department, Kebbi State University of Science and Technology Aleiro Kebbi State, Nigeria.

Preparation of fruits extract
The plant materials were open air dried under the shade and chopped into smaller pieces. The dried fruits were pulverized into moderately coarse powder. The powder plant materials (100g) were macerated in 50% methanol in an air tight aspirator bottle for 72 hour. This was then filtered with the aid of sterile sieving cloth and evaporated using a drying cabinet at $45^{o}_{C.}$ The dried extract collected was weighed, labeled and stored in an air tight bottle container [3].

Phytochemical screening
Qualitative phytochemical screening was done using standard procedures for the presence of secondary metabolites such as alkaloids, tannins, steroids, saponins, cardiac glycosides, phenolics resins, and terpenoids [4].

Experimental animals
Thirty five (35) of Albino rats of both sex about (120g-150g) obtained in March, 2017 were purchased at the Animal House, Usman Danfodio University Sokoto, Sokoto State and transported to the Animal House, Faculty of Science, Kebbi State University of Science and Technology, Aliero. The

animals were fed with standard rodent pillet (Vital Feeds Ltd, Nigeria) and water *ad libitum*. All the animals were kept in well spaced cages and allow to acclimatizing for two week prior to the commencement of the experiment.

Lethal dose determination (LD_{50})

The procedure as described by Dixon [5] was adopted in the evaluation of the oral acute toxicity of the hydromethanolic extract of *Xylopia aethiopica*. Five non pregnant albino rats selected randomly from the acclimatized rats were used for the experiment. The animals were weighed individually, marked and housed individually in cages prior to treatment. The rats to be tested were fasted overnight but allowed free access to water. Fresh prepared methanolic fruit extract of *Xylopia aethiopica* was administered at 5000mg/kg. The same method was adopted until all the five rats were dosed and observed for 48hrs for sign of acute toxicity, morbidity and mortality for the first 48hrs and up to 14days. The behavioural changes and other changes observed in the animals were recorded in animals were recorded according to the Organization for Economic and Cultural Development (OECD), 425guidelines.

Antipyretic activity

Pretreatment of animals

Rectal temperature (TR) of the animals was determined by inserting a lubricated (glycerin as the lubricant) digital thermometer (external diameter: 3 mm, 0.1°C precision; Model MT-101, N & B Medical, Delhi) 2.8 cm into the rectum of rats. Animals presenting initial rectal temperature between 36 and 37°C were selected. The Animals was selected for the experiment after confirmation of approximate constant rectal temperature for 7 days. After which they were divided into 5 groups of 5 rats each for the antipyretic tests.

Antipyretic activity

The antipyretic activity of the extracts was evaluated based on Brewer's yeast- induced pyrexia in the rats. The Pyrexia was induced by subcutaneous injection of 10 ml/kg of 15% w/v Brewer's yeast suspension below the nape of the neck. After 18 hours of the yeast injection, the different groups were treated with the fruit extracts 100, 200 and 400 mg/kg respectively and standard drug (paracetamol) 150 mg/kg. The rectal temperature was recorded over a period of 6 hours [6].

Statistical analysis

All the results will be expresses as the mean ± S.E.M. The data were analyzed for statistical significance by one-way analysis of variance (ANOVA). Values of $p < 0.05$ were considered statistically significant.

Results

Methanolic extraction of *Xylopia aethiopica* fruits yielded 6.1%. The extract was very sticky, brownish and taste bitter. The preliminary qualitative phytochemical screening of *Xylopia aethiopica* Methanolic fruits extract revealed the presence of some secondary metabolites (Table 1). The methanolic fruits extract of *Xylopia aethiopica* when administered orally at a dose of 5000mg/kg body weight resulted in no mortality. Therefore the LD_{50} is assumed to be greater than 5000mg/kg body weight. However the behavioral signs and symptoms such as restlessness, scratching of mouth part and rapid breathing were reversed one hour after administration of the extract. Rectal temperature of the animals were measured daily for 1 week. Animals presenting initial rectal temperature between 36 and 37°C were selected. The animals were selected for the antipyretic studies. Subcutaneous injection of the pyrogenic dose of yeast produced elevated changes in rectal temperature of the rats which were significantly different ($p<0.05$) from control (Figure 1). The methanolic fruits extracts of *Xylopia aethiopica* (100 and 400mg/kg) caused a time dependent (3rd to 6th hour) decrease in rectal temperature which was comparable with the paracetamol treated groups.

Table 1: Phytochemical analysis of *Xylopia aethiopica* fruits

Phytochemical	Result
Tannins	+
Alkaloids	+
Saponin	+
Glycosides	ND
Phenols	+
Flavonoids	+
Steroids	+
Resins	ND
Terpenoids	+

+ = Present ND = not detected

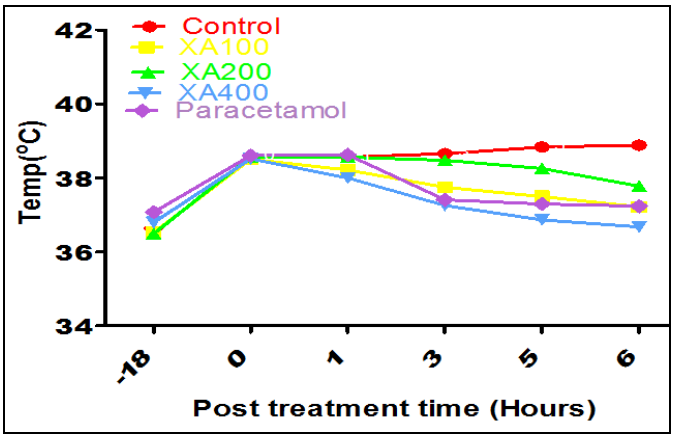

Fig 1: Antipyretic effect of *Xylopia aethiopica* fruit extract in albino rat

Discussion

The control centre of the thermoregulatory system is located in the anterior hypothalamus, which is responsible for the maintenance of the body's thermal homeostasis [7]. Elevation in body temperature (fever or pyrexia) occurs when the concentration of prostaglandin E_2 (PGE_2) increases within parts of the brain. Such an elevation contributes to a considerable alteration in the firing rate of neurons that control the thermoregulation process in the hypothalamus [8]. Drug capable of inhibiting this physiological response (elevation of temperature) are known as antipyretics. The mechanism of action of antipyretic such as paracetamol (acetaminoplan) and other non-steroidal anti-inflammatory drugs is by inhibiting COX-2 expression and thus inhibiting PGE_2 biosynthesis leading to the reduction in elevated body temperature [9]. In the present study, the ability of methanolic fruit extract of *X.*

aethiopica to ameliorate Brewer's yeast-induced elevation of body temperature in albino rats may be attributed to inhibitory effects of some of its secondary metabolites. Alkaloids have been reported to inhibit prostaglandin synthesis [10]. Also steroids, tannins, and flavonoids have been reported to be predominant inhibitors of prostaglandin synthetase and cyclooxygenase or lipoxygenase [11], thus inhibiting pyrexia.

Conclusion

In conclusion, the present study report the potential antipyretic effects of the methanolic fruit extract of *X. aethiopica*. Further studies to isolate the active ingredient and elucidate its mechanism of antipyretic action are recommended.

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