



*Full Length Research Paper*

## Antipyretic effect of *Ocimum gratissimum* on brewer's yeast induced fever in wistar rats

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### Abstract

Pyrexia or fever is a disease caused as a result of secondary impact of other diseased states due to the resetting of the hypothalamic set-point. From scientific discovery, antipyretic drugs such as aspirin, NSAIDs, opioids have been developed for use and of which mostly produces side effects including gastrointestinal bleeding, renal, hepatic effect, etc. Therefore, many herbal plants have been found to be having antipyretic effects. *Ocimum gratissimum* is a shrub commonly found in Africa and has been used to treat bacterial fevers locally. This study investigates the antipyretic activity of the methanolic extract of *Ocimum gratissimum* on brewer's yeast induced fever in experimental rats. 30 albino rats weighing 150g-200g were used. They were divided into six groups of five rats each. Group one serve as control (n=5) and was given 1ml of normal saline, group two (n=5) was treated with brewer yeast alone, group three (n=5) was given 100mg/kg of aspirin, while groups four, five and six were treated with 300mg/kg, 200mg/kg and 100mg/kg (n=5) of *Ocimum gratissimum* respectively. A suspension of brewer's yeast was injected subcutaneously to induce fever in all the experimental animals. After 18hrs, the rectal temperature was taken and the animals were administered *Ocimum gratissimum* (100mg/kg, 200mg/kg, 300mg/kg) and aspirin (standard group, 100mg/kg) orally. The body temperature of the rats was measured rectally over a period of 4 hours. *Ocimum gratissimum* (100mg/kg, 200mg/kg and 300mg/kg) significantly reduced yeast induced pyrexia,  $36.88 \pm 0.39^{\circ}\text{C}$ ,  $36.43 \pm 0.26^{\circ}\text{C}$  and  $35.83 \pm 0.46^{\circ}\text{C}$  when compared with the group two (20ml/kg, brewer's yeast) temperature of  $37.80 \pm 0.18^{\circ}\text{C}$  (\*p<0.01, respectively). The group three (aspirin, 100mg/kg) also show significant reduction  $36.55 \pm 0.22$ , p<0.01 compared with group two (20ml/kg, brewer yeast) with temperature  $37.80 \pm 0.18^{\circ}\text{C}$ . Thus, this experiment shows that the antipyretic effect of *ocimum gratssimum* is dose dependent and the effect is as a result of the flavonoid component of the extract. These data therefore suggest that methanolic extract of *Ocimum gratissimum* leaves possesses significant antipyretic activity and its mechanism could be by inhibition of/release inflammatory mediators.

**Keywords:** *Ocimum gratissimum*, brewer's yeast, antipyretics, aspirin, temperature.

### INTRODUCTION

Pyrexia or fever is a disease caused as a secondary impact of infection, malignancy or other diseased states (Sharm et al., 2010; Chattopadhyaya et al., 2005). It is the body's natural function to create an environment where infectious agents or damage to tissue cannot survive (Chattopadhyay et al., 2005). Normal body temp-

erature is regulated by centres in the hypothalamus that ensures balance between heat loss and heat gain. Fever occurs where there is a disturbance of this hypothalamic "thermostat" which therefore leads to the set point of the body temperature being raised. This will cause readjustment to normal set point by temperature regulating system (mechanism such as dilation of superficial blood vessels) which operates to reduce the body temperature (Kelly, 2006). From scientific discovery, antipyretic drugs have been developed to reduce elevated body temperature, of which some mostly inhibit

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COX-2 expression to reduce PGE2 biosynthesis which is mostly produced in increased or elevated temperature (Cheng et al., 2005, Sharma et al., 2010). There are other therapeutic agents that are employed such as NSAIDs, opioid etc. However, on chronic usage, most of these agents have produced several side effects including gastrointestinal, renal, hepatic, central nervous system and dermatological effects (Sharma et al., 2010; Chaudhary, 2001)

Though plants have been used as a source of antipyretic agent from time immemorial to treat fever, due to discovery of chemical antipyretic agents they were neglected. Fortunately, due to various reasons low cost, easy access and reduced side effects, there is therefore revisitation to herbal medicines (Graz et al., 2011). Herbal medicines tend to look primitive and unscientific when compared to synthetic (conventional) drugs, which are thought to be more reliable than those made from plants. Yet, herbal medicine is still the mainstay of about 75-80% of the world population, mainly in the developing countries for primary health care (Kamboj, 2000).

*Ocimum gratissimum* belongs to the family labiatae, commonly known as scent leaf. It is widely distributed in tropical Africa and Asia. In the southern part of Nigeria, the plant is called "*effirin-nia*" by the Yoruba speaking tribe, "*Nchonwu*" in Igbo, while in the northern part of Nigeria; the Hausas call it "*Daidoya*" (Efraim et al., 2001).

It is a perennial plant that is woody at the base. It has an average height of 1-3m high. The leaves are broad and narrowly ovate, usually 5-13cm long and 3-9cm wide. It is a scented shrub with lime-green fuzzy leaves (Orwa et al., 2009).

It has been used locally to treat bacterial fevers such as typhoid fever (Tor-Anyiin et al., 2003). It has also been used to treat bacterial infections such as enteric diseases like diarrhoea, dysentery and gastrointestinal infections, epilepsy, shigellosis, trypanosomiasis, convulsion, pile and anaemia in Nigeria (Idika, 2008, Chukwuka et al., 2011). A survey of literature revealed that there is no scientific study on the antipyretic effects of *Ocimum gratissimum*. This study was designed to evaluate antipyretic activities of methanolic extract of *Ocimum gratissimum* on brewer's yeast-induced fever.

## METHOD

### Drugs and chemicals

Aspirin was purchased from Aspar Pharmaceutical Limited. The solvents and other chemicals of analytical grade were used and obtained from the institute's central store. Brewer's yeast was procured from Lessaffre Red Star bakers.

### Collection of Leaves

The fresh leaves of *Ocimum gratissimum* was purchased from a local market in Nasarawa state. It was identified by the Botany Department of Ahmadu Bello University, Zaria.

### Preparation of Extraction

The leaves were air-dried and were ground into coarse powder. The powder was first weighed and was extracted with absolute methanol using Soxhlet extractor. The extract was concentrated using rota-evaporator. This methanolic extract was further evaporated to dryness to obtain alcoholic extract.

### Animals

30 albino rats weighing between 150-200g of either sex were procured from the Animal House of the University of Jos for this experimental study. They were divided into six groups (n=5). They were acclimatized to laboratory condition seven days before the commencement of the experiment and were allowed free access to standard dry pellet diet and water ad libitum. The experimental protocol was approved by IAEC (Institutional animal ethics committee), for using animals in this experiment. Animals were fasted overnight with free access to water prior to each experiment.

### Animal Grouping

Group 1- control group was given 1ml of water  
Group 2- negative control was treated with 20 ml/kg brewer yeast alone  
Group 3 -standard reference was treated with brewer yeast and with 100mg/kg of Aspirin  
Group 4- was treated with brewer yeast and 100mg/kg of *Ocimum gratissimum*  
Group 5- was treated with brewer yeast and 200mg/kg of *Ocimum gratissimum*  
Group 6- was treated with brewer yeast and 300mg/kg of *Ocimum gratissimum*

### Acute Toxicity Test

Acute toxicity was carried out on the albino rats by up and down method (425 OECD, 2001). The animals were fasted overnight and the extract at different doses was administered orally. The animals were kept under observation continuously for 3 hours for general behav-

**Table 1.** Effect of methanolic extract of *ocimum gratissimum* on brewer's yeast induced pyrexia in rats.

Groups	Treatment	Dose	Initial Rectal temperature (°C)	Rectal temperature after 18hours of yeast injection (°C)				
				0 hour	1 hour	2 hour	3 hour	4 hour
I	Normal Saline	1ml/kg	36.60±0.35	36.58±0.34	36.58±0.34*	36.58±0.33*	36.53±0.31*	36.58±0.33*
II	Brewer's yeast	20ml/kg	36.60±0.30	37.33±0.31	38.20±0.23	37.70±0.22	37.78±0.18	37.80±0.18
III	Aspirin	100 mg/kg	36.38±0.20	37.73±0.51	37.15±0.41	36.80±0.29	36.63±0.26*	36.55±0.22*
IV	<i>Ocimum gratissimum</i>	100mg/kg	36.63±0.34	37.95±0.47	37.88±0.67	37.05±0.46	36.93±0.55	36.88±0.39
V	<i>Ocimum gratissimum</i>	200 mg/kg	35.95±0.65	37.38±0.50	37.55±0.23	36.20±0.34**	36.10±0.37**	36.43±0.26**
VI	<i>Ocimum gratissimum</i>	300mg/kg	35.93±0.38	37.23±0.15	36.48±0.38**	35.53±0.37***	35.75±0.50**	35.83±0.41**

Values are Mean± S.E.M. (n=5) Significance vs. Negative control group: \*P<0.05, \*\*P<0.01, \*\*\*P<0.001.

journal, neurological and autonomic profiles and finally after 24hrs.

### Administration of Drugs

The extract was then dissolved in 0.8% Tween 80 to make a solution of concentration 100mg/ml of *Ocimum gratissimum*. The extract was then given orally to the groups of animals in the appropriate dosages of 100mg/kg-300mg/kg. Aspirin was dissolved in distilled water to make a solution of 75mg/ml and was given orally to the appropriate groups of animals in the correct dosage (100mg/kg).

### Brewer's Yeast Induced Pyrexia

Albino rats were divided into six groups of five rats in each group. Fever was induced by injecting 20ml/Kg (subcutaneous) of 20% suspension of brewer's yeast in normal saline below the nape of the neck (Somezeet et al., 2009). The temperature was measured after 18hours using rectal thermometer. The temperatures were taken at 0, 1, 2, 3 and 4 hours after various substances were administered.

### Statistical Analysis

Results are expressed as mean ± SEM. Statistical analysis of data was performed using ANOVA to study differences among the means.

## RESULT

### Acute Toxicity studies

The result of acute toxicity in rats indicated that the

methanolic extract did not produce any significant changes in the behavioural or neurological responses.

### Antipyretic activity

The results of the antipyretic effect of the different doses of the test compound (100mg/kg, 200mg/kg, 300mg/kg), standard (aspirin, 100mg/kg), negative control and control are depicted in Table 1. Aspirin as well as methanolic extract at doses of 200mg/kg, 300mg/kg started showing effective antipyretic activity after 1h of post dosing; while at dose of 100mg/kg the effect was not as significant as that of aspirin, when compared with the control. Comparing all other groups with the negative control, there was significant reduction in the temperature. Antipyretic activity was observed up to 4h after aspirin and test extract administration.

## DISCUSSION

*Ocimum gratissimum*, commonly known as scent leaf, has been found to possess various medicinal properties such as anti-bacterial, anti-nociceptive and anti-hypertensive effects (Prabhu et al., 2009).

This present experiment studied the antipyretic effect of *Ocimum gratissimum* on brewer's yeast induced fever as well as the effectiveness of its antipyretic effect when compared with aspirin.

It was found that *Ocimum gratissimum* exhibited antipyretic effects and these effects increased with dosage (dose-dependent). It was also seen that at higher concentrations (200 and 300mg/kg) *O. gratissimum* was more effective than aspirin (100mg/kg). Also, aspirin has greater antipyretic effects than 100mg/kg of *Ocimum gratissimum*. Though, if a higher dose of aspirin is used, it might have the same effect with the 300mg/kg dose of

the methanolic extract with side effect on the other systems.

Fever is known to be caused by several endogenous pyrogens such as interleukin-1 $\beta$ , interleukin-6, interleukin-8, tumor necrosis factor- $\alpha$ , macrophage protein-1 and prostaglandins. Prostaglandin synthesis may be activated by tumor necrosis factor- $\alpha$  and phospholipase A<sub>2</sub>. Brewer's yeast induces both TNF- $\alpha$  and prostaglandin synthesis (Rititid et al., 2007).

It is currently accepted that prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) is the final fever mediator in the brain, specifically in the preoptic area of the anterior hypothalamus (Li et al., 2008). Antipyretics such as aspirin (acetylsalicylic acid) and other non-steroidal anti-inflammatory drugs (NSAIDs) reduce fever by suppressing peripheral production of interleukin-1 $\beta$ , while consecutively lowering the thermoregulatory set point by blocking central cyclo-oxygenase formation of prostaglandin E<sub>2</sub>. Thus it can be inferred that *Ocimum gratissimum* inhibits the synthesis of prostaglandins. It has been established that there are two pathways leading to the transcription and induction of cyclo-oxygenase (COX)-2. Both pathways are activated by cytokines e.g. IL-1 $\alpha$ , IL-6 and tumor necrosis factor (TNF) which trigger central mechanisms that act via the transcription factors such nuclear factor (NF) $\kappa$ B and signal transducer and activator of transcription (STAT-3) (Inoue et al., 2008).

However, additional studies will be needed to determine if the antipyretic mechanism was due to inhibition of TNF- $\beta$  synthesis or prostaglandin synthesis or both.

Phytochemical analysis from previous studies has shown that *Ocimum gratissimum* contained flavonoids (Omodamiro et al., 2012). Flavonoids belong to the polyphenol family and are found in most plant material. The most important dietary sources are fruits, tea and soybean. Some of the activities attributed to flavonoids include: anti-allergic, anti-cancer, antioxidant, anti-inflammatory and anti-viral (Cushnie and Lamb, 2011). A variety of flavonoids have also been found to inhibit prostaglandin synthase (COX-2) production and transcription (O'Leary et al., 2004; Hämäläinen et al., 2011). Plants such as *Palisota hirsuta* K. Schum. (Commelinaceae) and *Jasminum Trichotomum* contain flavonoids and have been found to possess antipyretic properties (Boakye-Gyasi et al., 2011; Achuta et al., 2011). Hence the presence of flavonoids might account for the antipyretic effect that was observed in *Ocimum gratissimum*.

The efficacy of the antipyretic effect of *Ocimum gratissimum* extract was observed to have increased with increased concentration (dose-dependent manner). This can be said to be due to the increased concentration of the component of the extract exhibiting antipyretic effects. Such trends have been seen in the antipyretic effects of the fruits of *Terminalia Bellirica* Roxb seeds (Sharma et al., 2010) and *Galega purpurea* root (Gomathi et al.,

2011).

## CONCLUSION

In conclusion, the data obtained in this study indicates that the methanolic extracts of *Ocimum gratissimum* leaves exhibited antipyretic properties that were significant from 200 mg/kg to 300 mg/kg of body weight and the inhibition of the synthesis and/or release of inflammatory mediators may be its main mechanism(s) of action. The antipyretic activities of *Ocimum gratissimum* leaves supports its use in the management of fever by traditional medicine practitioners.

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