

ORIGINAL ARTICLE

Antipyretic activity of *Polyalthia longifolia* Benth. & Hook. F. var. *pendula* (Annonaceae), on lipopolysaccharide-induced fever in rats

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Fever is a complex physiological response triggered by infectious or aseptic stimuli. The present investigation was carried out to study the antipyretic activity of *Polyalthia longifolia* extracts in Wistar rats against Lipopolysaccharide (LPS) -induced pyrexia. *P. longifolia* Benth. & Hook. f. var. *Pendula* (Annonaceae) is an evergreen tropical tree well known for its numerous medicinal properties. Methanol extracts of the leaves, stem bark and root of the plant were tested for their antipyretic activities at doses of 30, 100 and 300 mg kg⁻¹ body weight using LPS-induced antipyretic activity model. All extracts showed significant ($p < 0.001$) dose-dependent antipyretic activity. At 300 mg kg⁻¹, all extracts exhibited activities higher than that of Acetylsalicylic acid (Aspirin) whose percentage inhibition of pyrexia was 86%. The root extract was the most active with a percentage inhibition of 127.5%, followed by the leaf extract (123.0%) and the stem bark extract (99.2%). This study proves *P. longifolia* as an effective antipyretic agent and could be used as an adjunct in the treatment of other ailments.

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INTRODUCTION

Pyrexia is caused in response to infection, tissue damage, inflammation and other diseased conditions. It is the body's natural way of creating an environment where infectious agents cannot survive (Shah and Seth, 2010). Prolonged or high fever however, often increases disease progression by increasing tissue catabolism, dehydration and other existing complaints, as in the case of patients suffering from the human immunodeficiency virus (Veugelers *et al.*, 1997).

Most antipyretic drugs function by inhibiting the expression of cyclooxygenase 2 (COX-2) to reduce the elevated body temperature by inhibiting the biosynthesis of prostaglandin E2 (PGE2) as reported by Shah and Seth, (2010). However, these synthetic

agents irreversibly inhibit COX-2 with high selectivity but are toxic to the hepatic cells, glomeruli, cortex of the brain and heart muscles (Elumalai *et al.*, 2012). Natural COX-2 inhibitors however have been reported to lower selectivity with fewer side effects (Cheng *et al.*, 2005). It is therefore essential to investigate traditionally used antipyretic agents of alternatives to these toxic synthetic antipyretic agents.

P. longifolia var. *pendula* (Annonaceae) is a single-stemmed tree which thrives in the tropics. Various parts of the plant have been used in traditional system of medicine for the treatment of fever, skin diseases, diabetes, hypertension and helminthiasis (Katkar *et al.*, 2010). A number of biologically active compounds have been isolated from the leaves, stem and stem bark of the plant. Such include aporphine and azafluorene alkaloids (Wu *et al.*, 1990), proanthocyanidins (Nair and Chanda, 2006), clerodane-type diterpenoids (Matharanda-Murphy *et al.*, 2005) and sesquiterpene compounds

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(Ogunbimi *et al.*, 2007). These have been studied for various biological activities like anticancer (Chen *et al.*, 2003), antimicrobial (Faiz *et al.*, 2008), anti-inflammatory (Ramakrishna *et al.*, 2000), hypotensive (Saleem *et al.*, 2005), antiulcer (Malairajan *et al.*, 2008), hypoglycaemic (Nair *et al.*, 2007) and antioxidant (Chang *et al.*, 2008). There is however, no scientific evidence supporting the traditional use of *P. longifolia* var. *pendula* as an effective remedy for fever.

The present study therefore aimed at evaluating the antipyretic activities of crude methanol extracts obtained from the root, stem bark and leaves of *P. longifolia* var. *pendula*, using the LPS-induced model in rats. This is to provide evidence for the potential role of *P. longifolia* var. *pendula* as a remedy for fever.

MATERIALS AND METHODS

Collection and preparation of plant materials

The leaves, stem bark and root of *P. longifolia* were collected in Kumasi in the Ashanti Region of Ghana and were authenticated by Mr. G. H. Sam at the Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, KNUST. A voucher specimen (FP/ 097/11) of the plant has been deposited in the Department of Herbal Medicine, KNUST. The various parts were sun dried for two weeks and milled into coarse powder.

Extraction of plant material

Five hundred grams (500 g) of each plant part was weighed and Soxhlet extracted in methanol for 8 hours. The liquid extracts were evaporated into a syrupy mass under reduced pressure using a rotary evaporator at 40°C and vacuum-dried for 24 hours. The crude extracts were kept in a desiccator until required for use. The yields per gram of the extracts were 13.5%, 14.3% and 16.2% for the root, leaf and stem bark respectively.

Phytochemical screening

The presence of secondary metabolites in the powdered samples was investigated following simple qualitative methods by Trease and Evans, (2009). The plant samples were investigated for saponins, flavonoids, alkaloids, glycosides, phytosterols and terpenoids.

Animals

Sixty five (65) female albino rats (Wistar strain) weighing 140-180 g were used for the experiment. The animals were obtained from the Department of Pharmacology, KNUST. Rats were kept in metal cages and divided into 13 groups of 5 animals each. The animals were acclimatized to experimental conditions for 48 hours prior to the study and kept under standard conditions of room temperature (25°C) and a 12 hour light/darkness cycle. They were starved overnight prior to the experiment while allowing access to drinking water.

Treatment doses

The crude extracts were emulsified in 2% Tween 80 and dissolved in normal saline at doses of 30, 100 and 300 mg kg⁻¹ body weight. The same treatment doses were used for Acetylsalicylic acid (Sigma Aldrich Co., USA) which served as the positive control. Lipopolysaccharide of Gram negative *Escherichia coli* (Sigma Aldrich Co., USA) was prepared at a dose of 50 µg kg⁻¹ body weight (Chomchuen *et al.*, 2010).

Antipyretic activity

The method of Santos and Rao, (1998) was modified and used for the assessment of the antipyretic activity of *P. longifolia*. Basal rectal temperature of each rat was measured using a digital thermometer inserted about 2 cm deep into the rectum. Fever was induced by intramuscular injection of 50 µg kg⁻¹ dose of LPS in the right thigh of each animal. Rectal temperatures were measured and recorded 1 hour after injection. Doses (30, 100 and 300 mg kg⁻¹ body weight) of the extracts were administered orally to the respective groups. Tween 80 in Normal saline was orally administered to the negative control group. Rectal temperatures were taken and recorded hourly for five hours. Changes in rectal temperature expressed as the difference from the basal value were determined.

Statistical analysis of data

The results were analysed using one-way analysis of variance (ANOVA) followed by Dunnett's *multiple comparison* test for all the treated groups. Sigma Plot

11.0 was used for all statistical analyses. Values were expressed as Mean \pm SEM. P values \leq 0.001 were considered statistically significant.

RESULTS

Phytochemical screening

Results from the phytochemical analysis conducted indicated the presence of alkaloids and terpenoids in the powdered materials (Table 1).

Antipyretic activity

All the extracts generally exhibited significant ($p \leq 0001$) dose-dependent antipyretic activities. Animals groups that were administered with 300 mg kg⁻¹ of

Table 1: Phytochemical constituents from the leaves, stem bark and root of *P. longifolia*

Phytochemical constituent	Leaf	Stem bark	Root
Alkaloids	+	+	+
Tannins	-	-	-
Terpenoids	+	+	+
Flavonoids	-	-	-
Saponin Glycosides	-	-	+
Reducing sugars	-	+	+

Table 2: Percentage inhibition of LPS-induced pyrexia of *P. longifolia* at different doses

EXTRACT	Dose (mg kg ⁻¹)	% Inhibition (%)
P. longifolia leaf extract (PLE _{LV})	30	98.1%
	100	97.3%
	300	123.0%
P. longifolia stem bark extract (PLE _{ST})	30	53.0%
	100	93.2%
	300	99.2%
P. longifolia root extract (PLE _{RT})	30	82.8%
	100	78.3%
	300	127.4%
Aspirin	30	26.7%
	100	102.1%
	300	86.1%

the root and stem bark extracts had their temperatures falling below their initial temperatures (Figs. 1 and 2). Percentage inhibition of LPS-induced fever ranged between 53 and 127.4%. At the dose of 300 mg kg⁻¹, all the extracts exhibited activities greater than the standard drug, aspirin (Table 2). At 300 mg kg⁻¹, root extracts showed the highest inhibition of fever (Fig. 3).

DISCUSSION

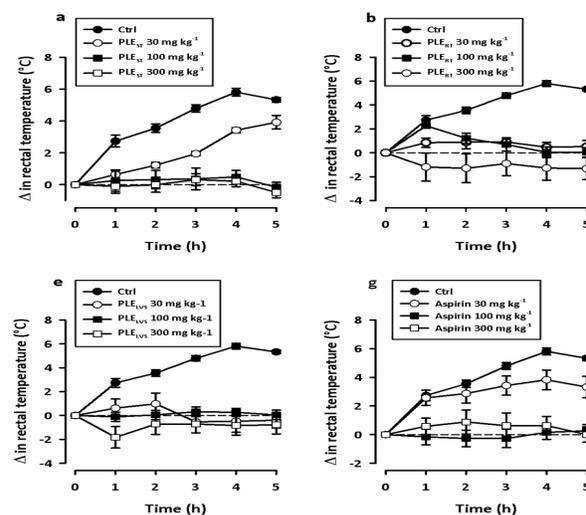


Figure 1: Change in rectal temperature (°C) against time (h) graphs of the stem bark (a), root (b), leaves (e) and aspirin (g)

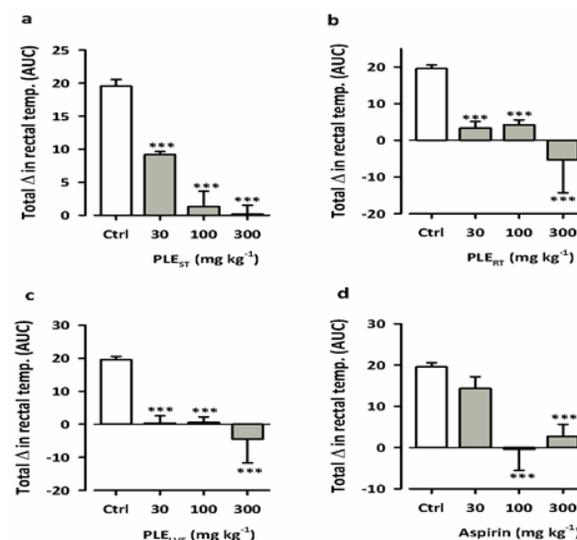


Figure 2: Total change rectal temperature expressed as area under the curve of the stem bark (a), root (b), leaves (c), and aspirin (d)

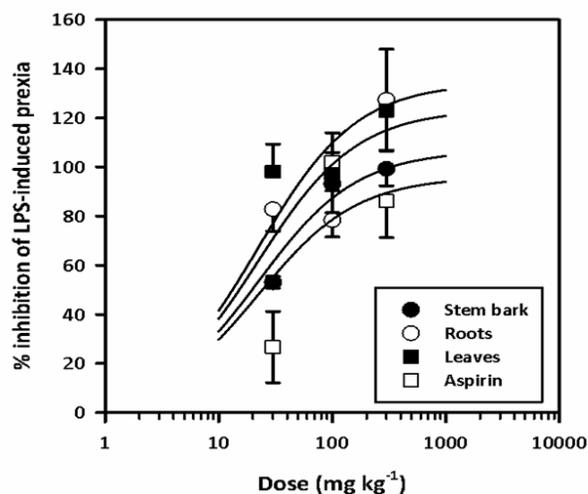


Figure 3: Percentage inhibition of LPS-induced pyrexia against dose concentration (mg/kg)

The present study was performed to determine the antipyretic activities of the leaves, stem bark and roots of *Polyalthia longifolia* var. *pendula* using the LPS-induced fever model in rats. Results from the phytochemical analysis conducted indicated the presence of alkaloids and terpenoids in all the three plant parts. From previous studies, other plants containing such constituents have been associated with antipyretic activities.

Deepa *et al.*, (2009) investigated the antipyretic activity of *Vernonia cinerea* which was known to contain alkaloids, saponins and terpenoids to be its major constituents. *Andropogonis paniculata* and *Adhatoda vasica*, reported to contain andrographolide, a diterpene and vasicine, an alkaloid respectively have also been reported to possess antipyretic activities against yeast-induced fever in rats (Chandra *et al.*, 2010). Rosmarinic acid from *Rosmarinus officinalis* has also been reported to inhibit prostaglandin synthesis (Shah and Seth, 2010).

The antipyretics in common use today include acetaminophen, aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs). The principal action of antipyretics rest in their ability to inhibit the enzyme cyclooxygenase (COX) and interrupt the syn-

thesis of inflammatory prostaglandins (Jongchanapong *et al.*, 2010). They also suppress the production of pyrogenic cytokines such as TNF- α and IL- β (Aronoff and Nelson, 2001).

P. longifolia var. *Pendula* may therefore follow a similar mechanism of action to exhibit such high activity. The presence of the phytoconstituents investigated may partly be attributed to such high activities.

CONCLUSION

The leaves, stem bark and root extracts of *P. longifolia* var. *Pendula* possess high antipyretic activities comparable to aspirin. This may provide in part, scientific evidence for its use as a traditional remedy for fever. Further bioactivity guided fractionation of the extracts to determine specific compounds responsible for such high activities is ongoing our laboratories.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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