***Original Research Article***

**ANTIPYRETIC ACTIVITY OF *Solanumanomalum*Thonn.ex Schumach ETHANOL LEAF EXTRACT IN RATS**

**ABSTRACT**

*Solanum anomalum* Thonn. ex Schumach, belonging to the family Solanaceae is a medicinal plant used among various cultures especially in Africa. The fruits and leaves have been in use nutritionally and ethnomedically for the treatment of diabetes, gastrointestinal ailments, malaria and various forms fevers among others. This study aims to validate the use of the leaves of *S. anomalum* in the management of fevers. The leaf extract of *S. anomalum* at treatment doses of 70, 140 and 210 mg/kg p.o was investigated for antipyretic activity in rats using various experimental models; amphetamine, dinitrophenol and yeast-induced pyrexia*.* Acetyl salicylic acid (Aspirin) at the dose of 100mg/kgp.oserved as the standard drug, while distilled water was used as negative control in all the models. Data obtained were analysed using one way analysis of variance (ANOVA). Theleaf extract exhibited considerable activity against pyrexia induced by amphetamine, dinitrophenol and yeast. The significant(*p*<0.05–0.001) antipyretic activity of the extract wasdose-dependent and highest from3to5hpost- administrationofextract. The antipyretic effects of this plant may in part be mediated through the chemical constituents of the plant. The findings of this work confirm the ethnomedical use of this plant to treat febrile conditions.

**Keywords:** *Solanum anomalum,* Medicinal plant, antipyretic, fever

1. **INTRODUCTION**

*Solanum anomalum* Thonn. ex Schumach, belonging to the family Solanaceae is a medicinal plant used among various cultures especially in Africa. The fruits and leaves have been in use nutritionally and ethnomedically for the treatment of diabetes, gastrointestinal ailments, infections, pains, inflammations, malaria and various forms fevers among others (Burkhill, 2000). The leaves have been documented to possess hepatoprotective (Etuk *et al.,* 2023; Okokon *et al.,* 2023), nephroprotective (Etuk et al., 2023; Okokon *et al.,* 2024),hypoglycemic and antidiabetic (Okokon *et al.,* 2022), analgesic (Okokon *et al.,* 2020), antidiarrhoeal (Udobang *et al.,* 2023), antioxidant and antiulcer(Okokon *et al.,* 2019a), anticonvulsant and depressant (Okokon *et al.,* 2019b),*in vivo* and *in vitro* antiplasmodial (Okokon *et al.,* 2016; Okokon *et al.,* 2017a), anti-oedema (Okokon *et al.,* 2017b), genotoxic and cytotoxic (Okokon et al., 2023) activities. Moreso, secondary metabolites suchas chemical alkaloids, flavonoids, saponins, tanins as well as active compounds like diosgenin, a diosgenin glycoside (25(R)-diosgenin-3-O-α-L-rhamnopyranosyl-(1→4)-β-D-glucopyranoside, uracil, 5-methyluracil, 1-octacosanol, and octacosane have been identified and isolated from the leaves of the plant (Okokon *et al.*, 2022; Okokon *et al.*, 2016). The antipyretic activity of the leaf extract of *Solanum anomalum* in rats is reported in this study.

1. **MATERIALS AND METHODS**

**2.1 Plants collection**

*Solanum anomalum* fresh leaves were collected from bushes around residential areas in Uruan, Akwa Ibom State, Nigeria in April, 2025. Identification and authentication o the plant was done in the Department of Botany and Ecological Studies, University of Uyo, Uyo, Nigeria by a taxonomist. Hebarium specimen was deposited at Department of Pharmacognosy and Natural Medicine Herbarium, University of Uyo (UUH.75a).

**2.2 Extraction**

Fresh leaves of *S. anomalum* were washed and shade-dried for two weeks. The dry leaves were further reduced to powder using electric grinder. The leaf powder (1.5 kg) was soaked in 50% ethanol (7.5 L) with intermittent agitation for 72 hours at room temperature (28 ±2 ˚C) and thereafter filtered. Using a rotary evaporator (BuchiLab, Switzerland), the liquid filtrate was concentrated and evaporated to dryness in *vacuo* at 40˚C. The extract was stored in a refrigerator at 4˚C, until used for the proposed study.

**2.3 Animals**

Albino Wistar rats (120-130 g) (male and female) obtained from the University of Uyo animal house were used for the study. They were allowed free access to water and fed with standard animal pellets.The study was approved by the College of Health Sciences Animal Ethics committee, University of Uyo(UU/CHS/AE/25/022).

## 2.4 Evaluation of antipyretic activity of Solanum anomalum leaf extract on D-amphetamine-induced pyrexia

In this study, overnight fasted adult albino rats (male and female) allowed free access to water were used for the experiment. They were grouped based on their weight into groups of 5 rats each. After obtaining their basal temperatures, pyrexia was induced by intrperitoneal injection of amphetamine (5 mg/kg, i.p) to the animals. Pyrexia development was monitored from measurement of the rectal temperatures of the rats 0.5 h post-administration of amphetamine. The leaf extract were administered to the animals at 70, 140 and 210 mg/kg orally in their respective treatment groups, while aspirin (100 mg/kg) and distilled water (10 mL/kg, orally) were administered respectively to the positive and negative control groups of animals. Measurements of rectal temperatures of the animals were carried out at an hour interval for 5 h (Edem *et al*., 2023).

**2.5 Effect of *Solanum anomalum*leaf extract on 2,4-Dinitrophenol (DNP)-induced pyrexia**

The animals used for this experiment were twenty-four hour fasted adult albino rats of both sexes which were allowed free access to water *ad libitum.* They were divided based on their weights into groups of five rats each. After obtaining their basal temperatures, pyrexia was induced by intrperitoneal injection of dinitrophenol (DNP) (10 mg/kg, i.p.) to the animals. Pyrexia development was monitored from measurement of the rectal temperatures of the rats 0.5 h post-administration of dinitrophenol (DNP). Hyperthermia developed within 30 min of DNP administration. The leaf extract were administered to the animals at 70, 140 and 210 mg/kg orally in their respective treatment groups, while aspirin (100 mg/kg) and distilled water (10 mL/kg, orally) were administered respectively to the positive and negative control groups of animals. Measurements of rectal temperatures of the animals were carried out at an hour interval for 5 h (Edem *et al*., 2023).

## 2.6 Effect of Solanum anomalum leaf extract on yeast-induced pyrexia

In this experiment, overnight fasted adult albino rats (male and female) allowed free access to water were used for the study. After obtaining their basal temperatures at zero hour using digital clinical thermometer, pyrexia was induced by subcutaneous injection of 20% W/V aqueous suspension of yeast at a volume of 10 mL/kg (Okokon and Nwafor, 2010; Edem *et al*., 2023). The rectal temperatures of the animals were monitored over time beginning from one hour post yeast injection. Animals with temperature increase of 1˚C were selected and grouped based on their weight into groups of five rats each. The leaf extract were administered to the animals at 70, 140 and 210 mg/kg orally in their respective treatment groups, while aspirin (100 mg/kg) and distilled water (10 mL/kg, orally) were administered respectively to the positive and negative control groups of animals. Measurements of rectal temperatures of the animals were carried out at an hour interval for 5 h (Edem *et al*., 2023).

**2.7 Statistical analysis**

Data collected were analyzed using one way analysis of variance (ANOVA) followed by Tukey’s multiple comparison post-test (Graph pad prism software Inc. La Jolla, CA, USA). Values were expressed as mean ± SEM and significance relative to control were considered at p˂0.05.

1. **RESULTS**

**3.1 Effect of leaf extract of *Solanum anomalum* on D-amphetamine induced pyrexia**

Table 1 shows the effect of the leaf extract on amphetamine - induced pyrexia. The leaf extract (70, 140, 210 mg/kg), exhibited significant (p<0.05 – 0.001) lowering of rectal temperatures of the extract- treated rats relative to control. These temperature lowering effects were intensified from 2- 5 h post treatment with the extract, but were not comparable with that of the standard drug, ASA 100 mg/kg (T[able](#_bookmark5) 1).

**3.2 Effect of ethanol leaf extract of *Solanum anomalum* on 2,4-dinitronitrophenol (DNP)-induced pyrexia in rats**

The leaf extract of *S. anomalum* (70, 140, 210 mg/kg) exerted significant (p<0.05–0.001) reduction of temperature in DNP-induced pyretic rats in a dose-dependent manner when compared to control. The significant (p<0.05–0.001) antipyretic effect when compared to control was sustained from 4 -5h in all the groups treated with the extract. The effect of the standard drug, ASA, 100 mg/kg was more than that of the highest dose (210 mg/kg) of the extract (T[able](#_bookmark4)2).

**3.3 Effect of ethanol leaf extract of *Solanum anomalum* on yeast-induced pyrexia in rats**

Administration of *Solanum anomalum* leaf extract (70, 140, 210 mg/kg) exhibited significant (p<0.05-0.001) lowering of rectal temperature of rats elevated by yeast administration relative to control. The standard drug, ASA, 100 mg/kg, reduced the temperature significantly (p<0.05) relative to control with its effect higher than that of the highest dose (210 mg/kg) of the extract (T[able](#_bookmark5) 3).

TABLE 1: Antipyretic effect of *Solanum anomalum* leafextract on D-amphetamine-induced pyrexia

|  |  |
| --- | --- |
| Treatment/Dose(mg/kg) |  **TIME INTERVALS (hrs)** |
| Basal Temp | 0 | 0.5 | 1.0 | 2.0 | 3.0 | 4.0 | 5.0 |
| Control | 35.20±0.10 | 36.40±0.12 | 36.50±0.12 | 36.52±0.31 | 36.88±0.56 | 37.12±0.34 | 37.30±0.11 | 37.26±0.40 |
| Extract 70 | 34.33±0.25 | 35.80±0.26 | 35.61±0.14 | 35.53±0.28 | 35.50±0.18a | 35.55±0.43b | 35.58±0.25a | 34.45±0.24a |
| Extract 140 | 35.60±0.22 | 36.64±0.25 | 35.41±0.26 | 35.33±0.15 | 35.31±0.24a | 35.50±0.24a | 35.10±0.23b | 34.84±0.24b |
| Extract 210 | 35.48±0.10 | 36.42±0.10 | 35.38±0.13 | 35.30±0.15 | 34.88±0.43a | 34.61±0.33b | 34.19±0.18b | 34.20±0.16c |
| ASA 100 | 35.15±0.20 | 36.32±0.22 | 35.10±0.20 | 34.91±0.18 | 34.85±0.20a | 34.33±0.32c | 33.90±0.22c | 33.60±0.45c |

Values are expressed as mean ± SEM. Significance relative to control. ap<0.05; bp<0.01; cp<0.001. n = 5.

TABLE 2: Antipyretic effect of *Solanum anomalum* leafextract on Dinitrophenol-induced pyrexia

|  |  |
| --- | --- |
| Treatment/Dose(mg/kg) |  **TIME INTERVALS (hrs)** |
| Basal Temp | 0 | 0.5 | 1.0 | 2.0 | 3.0 | 4.0 | 5.0 |
| Control | 34.10±0.22 | 36.70±0.14 | 36.55±0.36 | 36.35±0.51 | 36.20±0.66 | 36.34±0.34 | 36.10±0.18 | 36.33±0.46 |
| Extract 70 | 34.34±0.18 | 36.55±0.21 | 36.40±0.45 | 36.30±0.25 | 35.90±0.16 | 35.65±0.63 | 34.50±0.26a | 34.01±0.15b |
| Extract 140 | 34.45±0.25 | 36.45±0.56 | 36.34±0.18 | 36.10±0.24 | 35.65±0.43 | 35.16±0.44 | 34.32±0.24a | 33.62±0.26b |
| Extract 210 | 34.50±0.56 | 36.10±0.34 | 35.80±0.53 | 35.72±0.34 | 35.30±0.21 | 34.62±0.16 | 33.55±0.28c | 33.36±0.10c |
| ASA 100 | 34.50±0.2 | 36.00±0.15 | 35.80±0.22 | 35.55±0.19 | 34.10±0.20 | 34.02±0.10a | 33.40±0.12c | 33.10±0.12c |

Values are expressed as mean ± SEM. Significance relative to control. ap<0.05; bp<0.01; cp<0.001. n = 5.

TABLE 3: Antipyretic effect of *Solanum anomalum* leafextract on yeast-induced pyrexia

|  |  |
| --- | --- |
| Treatment/Dose(mg/kg) |  **TIME INTERVALS (hrs)** |
| Basal Temp | 0 | 0.5 | 1.0 | 2.0 | 3.0 | 4.0 | 5.0 |
| Control | 35.20±0.14 | 36.20±0.15 | 36.26±0.34 | 36.80±0.20 | 37.10±0.26 | 37.56±0.11 | 37.82±0.10 | 37.42±0.28 |
| Extract 70 | 35.22±0.24 | 36.50±0.26 | 36.95±0.13 | 36.54±0.15 | 36.34±0.19 | 36.10±0.12 | 36.04±0.44 | 36.00±0.39 |
| Extract 140 | 35.15±0.33 | 36.62±0.17 | 36.75±0.15 | 36.40±0.18 | 36.22±0.08 | 35.94±0.10a | 35.80±0.20b | 35.55±0.25c |
| Extract 210 | 35.80±0.13 | 36.91±0.18 | 36.54±0.43 | 36.32±0.26 | 36.05±0.16a | 35.86±0.24a | 35.54±0.28b | 35.20±0.16c |
| ASA 100 | 35.18±0.20 | 36.44±0.18 | 36.50±0.24 | 36.15±0.46 | 36.00±0.11a | 35.83±0.15c | 35.20±0.16c | 35.00±0.25c |

Values are expressed as mean ± SEM. Significance relative to control. ap<0.05; bp<0.01; cp<0.001. n = 6.

1. **DISCUSSION**

This study investigated the anti-pyretic activity of *S. anomalum* leaf extract using experimental animal models. The extract was observed to exhibit significant activity against pyrexia induced by amphetamine, dinitrophenol and yeast. Hyperthermia induced by amphetamine results from its action on the adrenergic receptors in the brain which evokes the release of biogenic amines from their storage sites in nerve terminals with consequent increase in the level of cAMP and synthesis of prostaglandins from arachidonic acids synthesized in neurons by receptor- mediated hydrolysis of phospholipids (Westfall and Westfall, 2006). Dinitrophenol-induced hyperthermia results from increased level of intracellular calcium and muscle contraction due to uncoupling of oxidative phosphorylation by the drug, which causes stimulation of calcium release from mitochondrial stores as well as prevention of calcium reuptake(Kumar *et al*., [2002).](file:///C%3A%5C%5CUsers%5C%5CGRACE%5C%5CDocuments%5C%5CUTY%20THESIS%202023.doc%22%20%5Cl%20%22_bookmark30)Yeast-induced pyrexia results from yeast-induced stimulation of prostaglandins synthesis in the hypothalamus (Al-Ghamdi, [2001).](file:///C%3A%5C%5CUsers%5C%5CGRACE%5C%5CDocuments%5C%5CUTY%20THESIS%202023.doc%22%20%5Cl%20%22_bookmark8) The lowered rectal temperature observed with the administration of the extract in this study may have resulted from the activities of the extract to cause reduction of brain concentration of prostaglandin E2 especially in the hypothalamus through inhibitory action on COX-2 or by stimulation of synthesis of the body’s own antipyretic substances such as vasopressin and arginine (Chandrasekharan, [2002).](file:///C%3A%5C%5CUsers%5C%5CGRACE%5C%5CDocuments%5C%5CUTY%20THESIS%202023.doc%22%20%5Cl%20%22_bookmark10)The extract could have also caused lowering of the rectal temperature by mediating vasodilatation of superficial blood vessels leading to increased dissipation of heat coupled with resetting of hypothalamic temperature control center (Rang *et al*., [2007).](file:///C%3A%5C%5CUsers%5C%5CGRACE%5C%5CDocuments%5C%5CUTY%20THESIS%202023.doc%22%20%5Cl%20%22_bookmark26) This could have been possible through the activities of its phytochemical constituents. Therefore, the temperature lowering activity of the extract may not be unconnected with the involvement of one or combination of the above-mentioned mechanisms. The phytochemical compounds in this plant may have played a role in the observed antipyretic activities of the leaf extract. This result corroborates those earlier reported on other species such as *Solanum aethiopicum, Solanum viarum* and *Solanum nigrum* ( Tekwem *et al*., 2022; Mandal *et al*., 2019; Zakaria *et al*., 2006)

1. **Conclusion**

 From the results of this study, the leaf extract of *Solanum anomalum* possesses antipyretic activity which is due to the activities of its phytochemical constituents.

**Disclaimer (Artificial intelligence)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, manuscript.

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