

The Journal of Phytopharmacology

(Pharmacognosy and phytomedicine Research)

Research Article

ISSN 2320-480X

JPHYTO 2020; 9(4): 218-223

July- August

Received: 28-04-2020

Accepted: 12-06-2020

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doi: 10.31254/phyto.2020.9401

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Qualitative phytochemical screening and antipyretic activity of methanolic stem bark extract of *Mangifera indica* in wistar rats

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ABSTRACT

Mangifera indica stem bark is traditionally used in management of fever especially in meru community of Kenya though its antipyretic activity is not yet evaluated. The present study aim was to evaluate the phytochemical constituents and antipyretic activity of the methanolic extract of *Mangifera indica*. The standard methods were used to qualitatively analyze the phytochemicals revealing the presence of carbohydrates, tannins, saponins, flavonoids, alkaloids, quinones, cardiac glycosides, terpenoids, phenols, coumarins, steroids and acids. Fever was induced by injecting distilled turpentine in the left dorsal hind paw of the rats. The test groups were treated by administering *Mangifera indica* extract in three dose levels of 50, 100 and 150mg/kg body weight. The rectal temperature was taken at an interval of one hour after treatment with plant extracts and the data obtained was analyzed using ANOVA to give the descriptive statistics and summarized data in terms of means \pm SEM. This was followed by Tukey's post hoc test for comparing the means separation. The data analysis was set at 95% confidence level with statistical significance of $P \leq 0.05$. The data was analyzed and results presented in graphs and tables. The percentage change in rectal temperature of the 50, 100 and 150mg/kg body weight dose levels at 4th hours after administration of the plant extract were 3.13, 3.93 and 4.10% respectively. The result obtained from this research suggest that the methanolic stem bark extract of *Mangifera indica* could be used in management of fever associated with various diseases.

Keywords: *Mangifera indica*, Methanolic, Antipyretic, fever.

INTRODUCTION

Body temperature sometimes can rise above the normal ranges and this condition is referred to as a fever. Fever is a symptom of various diseases. Febrile conditions can alter metabolic function, increase oxygen and fuel demand and lead to lesions developments in the neurologic tissues [1]. Severe cases of febrile conditions are associated with hyperpyrexia where the body temperature rises above 41.5°C [1]. Hyperpyrexia can lead to body heat exhaustion, heat stroke and if not managed, it is associated with death [2]. Febrile illnesses are also associated with teratogenesis [3].

Fever development is a beneficial body mechanism to fight infection but febrile illness management leads to good prognosis. Drugs commonly used in fever management are known to inhibit prostaglandin synthesis which can lead to interference with various body functions. Therefore, there is a need to search for alternative compounds which can manage fever by utilizing different mode of action or by being more specific to receptors leading to minimal side effects associated with conventional drugs. Alternative medicine utilizes various plant materials in management of fever [4, 5].

Mangifera indica belongs to the family Anacardiaceae. It is an evergreen tree and can grow to attain a height of 10 – 45 meters. The Meru community name for this plant is 'Muembe'. The plant originated from Asia but it is now found in many parts of tropics and subtropics [6]. The bark of this plant is used in the Meru community to treat diseases such as pneumonia, toothache, stomachache, cough, chest pain and wound [7]. This study was to evaluate the antipyretic activity of methanolic stem bark extract of *Mangifera indica* in search for alternative antipyretic compounds.

MATERIALS AND METHODS

Experimental animals

Male Wistar albino rats aged 2 – 4 months with a body weight of approximately 115 -120 grams were used in testing the plant extract antipyretic activity. The animals were housed at the animal laboratory, Department of Biochemistry and Biotechnology, Kenyatta University. The study protocol for handling

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the laboratory animals was approved by the ethical committee of Zoological Sciences department, Kenyatta University. The Wistar albino rat were housed in wire meshed cages measuring approximately 30 × 30 × 30cm which were placed on a 0.75m raised surface in the experimental animal house at Kenyatta University. The animal house ambient temperature was maintained at 25 ± 2°C, with a photoperiodicity of 12 hours and humidity range of 35 – 60%. Thirty experimental animals were used in this study and they were housed in separate cages, with each cage labeled with cage numbers (one to six) and having five animals. Wood shavings beddings in the cages were replaced on daily basis. The animals had an access to standard rodent pellets supplied by Unga limited, Kenya and water *ad libitum*. All Wistar albino rats were clinically observed on daily basis for mortality, morbidity and any physical abnormality before the commencement of the study.

Experimental design

For antipyretic activity testing of the plant extract, thirty Wistar albino rats were used. The six animal cages were labeled as: - normal control, negative control, positive control, experimental A, B and C group. The normal control group rats were peritoneally administered with 0.5ml of dimethyl sulfoxide (DMSO) only. Fever was induced in the negative control, positive control, and experimental group A, B and C rats using distilled turpentine. The positive control group was intraperitoneally administered with aspirin to control the induced fever. The experimental groups A, B and C rats and mice were intraperitoneally administered with 50, 100 and 150mg/Kg of the methanolic *Mangifera indica* stem bark extracts respectively to manage induced fever.

Antipyretic activity

The antipyretic activity of methanolic stem bark extract of *Mangifera indica* was established against turpentine induced pyrexia in rats according to the standard protocol [8, 9]. After overnight fasting, the Wistar albino rats were divided into 6 groups of 5 rats each. The normal control group (Group I) was intraperitoneally administered with 5ml of 10% dimethyl sulfoxide (DMSO). Pyrexia was induced through intraperitoneal administration of 20% distilled turpentine. Group II animals served as a negative control group and were treated with normal saline 2ml/Kg orally after pyrexia induction. The positive controls (Group III) were treated with Aspirin (100mg/Kg body weight) after fever induction using 20% turpentine. The experimental groups (IV, V and VI) were treated with 50, 100 and 150mg/Kg concentration of methanolic stem bark extract of *Mangifera indica* respectively after fever induction by administration of turpentine intraperitoneally (Table 1).

Table 1: Antipyretic activities and treatment evaluation protocol

Animal groups	Treatment
I (Normal control)	10% DMSO (5ml)
II (Negative control)	Turpentine+10% DMSO
III (Positive control)	Turpentine +Aspirin (100mg/kg bw)
IV (Experimental A)	Turpentine + Plant extracts (50mg/kg bw)
V (Experimental B)	Turpentine + Plant extract (100mg/kg bw)
VI (Experimental C)	Turpentine +Plant extract (150mg/kg bw)

Key: bw- body weight; 20% turpentine

The body temperature of the rats was measured by inserting a lubricated digital clinical thermometer into the rectum (about 3cm) of the animal model. The Wistar albino rat body temperature was recorded over the

first hour prior to fever induction and recorded at an interval of 20 minutes. The animals with a rectal temperature increase of at least 0.8°C after fever induction were included in the antipyretic study. The body temperature of each animal in group II – VI was recorded one hour after pyrexia induction. The rectal body temperature of the rat before and after treatment with both conventional antipyretic drug and the methanolic stem bark extract of *Mangifera indica* were compared and the rectal temperature percentage change using the formula described in previous studies [10, 11].

$$\% \text{ change in rectal temperature} = \frac{B - C^n}{B} \times 100$$

Where;

B – Rectal temperature after one hour of fever induction using turpentine

Cⁿ – Rectal temperature after drug administration

Qualitative phytochemical screening

The standard protocols for determining the qualitative presence or absence of phytochemical compounds present in the plant sample were used¹². The phytochemicals tested include: -alkaloids, carbohydrates, flavonoids, anthocyanin and betacyanin, saponins, phenolics, tannins, quinones, coumarins, glycosides, cardiac glycosides, terpenoids and steroids.

Statistical analysis

The values of the parameters used to ascertain the antipyretic activity of the selected plants such as the changes in rectal temperature were analyzed using analysis of variance (ANOVA) to give the descriptive statistics to summarize the data in terms of mean ± SEM. The quantitative data obtained on the change in rectal temperature were collected and recorded in a MS – Excel. The data was subjected to descriptive statistics using version 17.0 of the Minitab statistical software package (Minitab Inc., 2017). The data was then analyzed by Analysis of Variance (ANOVA) and this was followed by Tukey’s post hoc test for comparing the means separation. The data analysis was set at 95% confidence level with statistical significance of P ≤ 0.05. All quantitative and qualitative data was analyzed results were presented in graphs and tables.

RESULTS

Antipyretic activities of methanolic stem bark extract of *M. indica*

One hour after the administration of the methanolic stem bark extract of the *M. indica*, there was a significance difference in the rectal temperature of the animal models treated with a conventional antipyretic drug (Aspirin) and varying dosage of the methanolic stem bark extract of *M. indica* (50, 100 and 150Mg/Kg) with a P value = 0.00, P < 0.05. The methanolic stem bark extract dosage of 50mg/Kg antipyretic potential was significantly different in relation to the conventional drug (Aspirin). The percentage change from the initial rectal temperature for the rat model in normal control group, negative control group, positive control, group, experimental groups A, B and C was - 0.16, - 0.26, 0.67, 0.46, 0.61 and 0.82% respectively (Figure 1; Table 2).

Two hours upon the administration of the methanolic stem bark extract of *M. indica*, there was a significance difference in the rectal

temperature change of the animal models in the normal group, negative control group, positive control group and experimental groups A, B and C with a $P = 0.00$, $p < 0.05$ but the rectal temperature change between the positive control group and the experimental test groups A, B and C were not significantly different. (Table 2). The percentage change in rectal temperature change in the normal group, negative control group, positive control group and the experimental groups A, B and C was -0.16, -0.31, 1.75, 1.23, 1.28 and 1.69% respectively (Table 2; Figure 1). The three different dosages of the methanolic stem bark extract of *M. indica* were effective in management of fever after 2 hours (Table 2).

Three hours after the administration of the methanolic stem bark extract of the *M. indica*, there was a significance difference in the rectal temperature among the animals in normal group, negative control group, positive control group and experimental groups A, B and C with a $P = 0.00$, $p < 0.05$ (Table 2). The percentage change in rectal temperature change in the normal group, negative control group, positive control group and the experimental groups A, B and C was -

0.27, -0.16, 3.00, 2.36, 2.45 and 2.87% respectively (Table 2; Figure 1). The rectal temperature in group treated with conventional drug and 50, 100 and 150mg/Kg of the methanolic stem bark extract of *M. indica* had no significance different (Table 2).

Four hours after the administration of the methanolic stem bark extract of *M. indica*, there was a significance difference in the rectal temperature among the animals in normal group, negative control group, positive control group and experimental groups A, B and C with $P = 0.00$, $p < 0.05$ (Table 4.5). The percentage change in rectal temperature change in the normal group, negative control group, positive control group and the experimental groups A, B and C was -0.32, 0.21, 3.91, 3.13, 3.93 and 4.10% respectively (Table 2; Figure 1). The three dosages of 50, 100 and 150mg/Kg did not have any significant different in antipyretic potential with the conventional drug (Aspirin) used in this experiment (Table 2). The phytochemicals present in methanolic stem bark extract of *Mangifera indica* is as indicated in table 3.

Table 2: Antipyretic activities of methanolic stem bark extract of *Mangifera indica*.

Groups	Treatment	1hr	2hr	3hr	4hr
Normal control	DMSO	100.16±0.16 ^{ab} (-0.16)	100.16±0.11 ^a (-0.16)	100.27±0.23 ^a (-0.27)	100.32±0.16 ^a (-0.32)
Negative control	Turpentine+ DMSO	100.26±0.26 ^a (-0.26)	100.31±0.05 ^a (-0.31)	100.15±0.10 ^a (-0.16)	99.79±0.10 ^a (0.21)
Positive control	Turpentine+ Aspirin	99.33±0.13 ^c (0.67)	98.25±0.28 ^b (1.75)	97.01±0.29 ^b (3.00)	96.09±0.22 ^c (3.91)
Experimental A	Turpentine+ <i>M. indica</i> 50mg/kg	99.54±0.05 ^{bc} (0.46)	98.77±0.15 ^b (1.23)	97.64±0.12 ^b (2.36)	96.87±0.14 ^b (3.13)
Experimental B	Turpentine+ <i>M. indica</i> 100mg/kg	99.39±0.10 ^c (0.61)	98.73±0.14 ^b (1.28)	97.55±0.17 ^b (2.45)	96.07±0.24 ^c (3.93)
Experimental C	Turpentine+ <i>M. indica</i> 150mg/kg	99.18±0.05 ^c (0.82)	98.31±0.10 ^b (1.69)	97.13±0.14 ^b (2.87)	95.90±0.11 ^c (4.10)
F value		9.54	35.52	64.97	140.76
P value		0.000	0.000	0.000	0.000

Values are expressed as Mean ± SEM for five animals per group. Statistical comparison were made within a column and values with different superscript are significantly different by one-way ANOVA followed by Turkey's post hoc test ($p < 0.05$). Turpentine =20%; Aspirin = 100 mg/kg body weight and DMSO used as the vehicle.

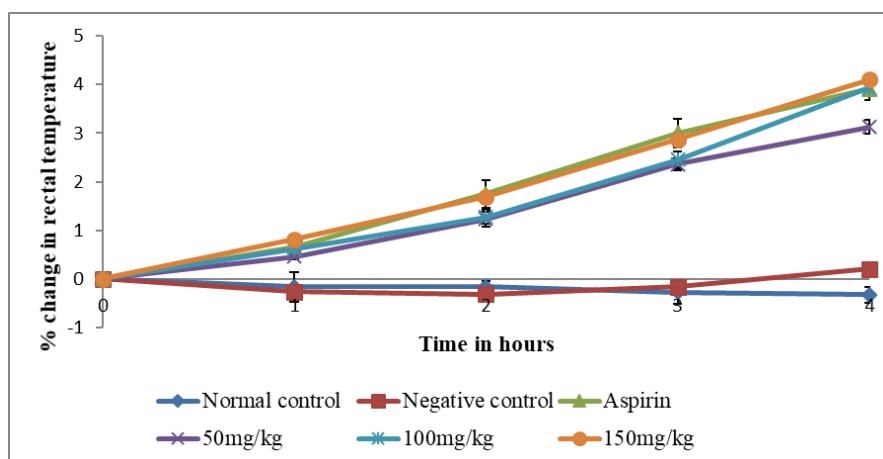


Figure 1: The percent change in rectal temperature after administration of methanolic stem bark extract of *Mangifera indica*

Table 3: Qualitative phytochemical composition of methanolic stem bark extract of *Mangifera indica*

Phytochemicals	MeOH stem bark extract of <i>Mangifera indica</i>
Carbohydrates	+
Tannins	+
Saponins	+
Flavonoids	+
Alkaloids	+
Anthocyanin and betacyanin	-
Quinones	-
Glycosides	-
Cardiac glycosides	+
Terpenoids	++
Triterpenoids	-
Phenols	++
Coumarins	+
Steroids	+
Acids	++

KEY: + = trace, ++ = moderate, +++ = intense, - = not present

DISCUSSION

The aim of the study was to determine the antipyretic activity of the methanolic extract of *Mangifera indica* stem bark. The antipyretic activity was evaluated against distilled turpentine pyrexia induced male Wistar rats. Turpentine commonly used in fever experimental studies is a pyrogen which induces fever by initiating the synthesis and release of the endogenous pyrogens from host phagocytic cells especially the pro-inflammatory cytokines. The release of pyrogens is associated with increased levels of prostaglandins E₂ in the hypothalamus thermoregulatory center which leads to elevated body temperature [13]. Turpentine leads to strong acute phase fever because it is associated with local inflammation in the experimental animals after administration [14]. To induce pyrexia, the experimental rats were injected with 20ml/kg body weight of distilled turpentine after which the animals with rectal temperature change $\geq 0.8^{\circ}\text{C}$ after 1 hour were considered for study [15, 16].

Exogenous and endogenous pyrogens are known to induce fever production. Exogenous pyrogens are product commonly originating from the bacteria cell wall breakdown includes the lipopolysaccharide (LPS). Cytokines are endogenous pyrogens associated with fever production. Cytokines including the interleukins-1, 6 and tumor necrotic factor - α (TNF- α) are fever signaling molecules because they activate the cyclooxygenase - 2 pathways increasing the production of prostaglandin E₂ (PGE₂). Increased prostaglandin E₂ (PGE₂) production is associated with activation of the prostaglandin E₂ hypothalamic receptors [17]. Lipopolysaccharides induces fever by binding to the toll - like receptor 4 (TLR4) commonly found in macrophages, neutrophils and dendritic cells hence stimulating an increased synthesis of prostaglandin E₂. Prostaglandin E₂ which is capable of crossing the blood brain barrier leads to fever initiation [18].

Exogenous pyrogens such as amphetamines, lipopolysaccharides, Sulphur and turpentine are known to induce fever by acting on the immune cells like the macrophages and monocytes leading to release of proinflammatory cytokines like interleukin - 1 (IL-1), interleukin - 6 (IL-6) and tumour necrosis factor α (TNF- α). The proinflammatory cytokines are endogenous pyrogens [18]. Turpentine regulates interaction of IL-1 with IL-1 type receptor 1(IL-1r1) resulting to increased IL-6 production which leads to fever induction [13]. Turpentine is preferred in pyrexia studies since experimental animals do not develop tolerance against turpentine as compared to another pyrogen [19].

Four hours after the test period, it was observed that methanolic *Mangifera indica* stem bark extract was associated with antipyretic activity in turpentine fever induced rats. Methanolic stem bark extract of *M. indica* dose level of 150mg/kg body weight had greatest rectal temperature change of 4.10% which was comparable to the rectal temperature change (3.91%) associated with Aspirin. The study finding supports previous studies results which associates various medicinal plants with antipyretic activity in turpentine fever induced laboratory animals. Previous studies on the antipyretic activity of *P. kotschy* methanolic leaves extract indicates substantial antipyretic activity in rats after fever induction using amphetamine and brewer's yeast [19]. Previous studies demonstrated that *Diospyros lotus* organic and crude methanolic fraction extracts is associated with antipyretic activity in mice following brewer's yeast intraperitoneal administration [21].

The Non - steroidal anti-inflammatory drugs (NSAIDs) like aspirin and paracetamol are the common drugs of choice for febrile condition management. Non - steroidal anti-inflammatory drugs antipyretic activity is associated with their capability to block the enzyme cyclooxygenase pathway thereby inhibiting prostaglandins synthesis [22]. They are capable of inhibiting hypothalamus prostaglandin biosynthesis [23]. Inhibition of the enzymes prostaglandin synthase and cyclooxygenase inhibits biosynthesis of PGE₂ in the hypothalamus [24]. Methanolic extract of *Mangifera indica* stem bark antipyretic activity was comparable to that of aspirin in this study, suggesting mimicry of aspirin action of the bioactive components of the extract. Previous studies have established that the DCM stem bark extract of plants like *A. nubica*, *A. Senegal* and *A. nilotica* are associated with high selective COX-2 inhibition properties [25]. Therefore, the antipyretic activities of methanolic extracts of *Mangifera indica* stem bark may be linked to interruption of hypothalamus prostaglandin synthesis resulting from inhibition of both the prostaglandin synthase and/or cyclooxygenase enzymes. However, various alternative mechanisms may be involved in blocking fever.

Methanolic extracts of *Mangifera indica* stem bark after intraperitoneal administration to turpentine fever induced Wistar rats demonstrated a dose dependent response. This is in agreement with dose dependent antipyretic activity response observed in brewer's yeast fever induced Wistar rats associated with alkaloid extract fraction of *H. zeylanica* [26]. *Capparis zeylanica* Linn extract in brewer's yeast fever induced experimental rats also demonstrated a dose dependent antipyretic activity [27]. The dose dependent antipyretic activity of methanolic extract of *Mangifera indica* stem bark could be explained with passive diffusion of the plant active compounds across the cell membrane in the peritoneal cavity

The *Mangifera indica* Methanolic extracts resulted to fever reduction in time and dose - dependent manner. This could be associated with the fact that in low doses leads to insufficient low plasma concentration of the pharmacologically active phytochemicals. Time - dependent antipyretic activity can be explained with time required to transport bioactive phytochemicals across the peritoneum cavity [28]. The dose and time dependent antipyretic activities were also observed in study carried out to evaluate the antipyretic activities of both *Acacia hydaspica* ethyl acetate and methanolic extracts in brewer's yeast fever induced Sprague Dawley rats [29]. The antipyretic activities study of *Carissa edulis* methanolic: dichloromethane root barks extracts also demonstrated dose - dependent pharmacological activity on turpentine-induced pyrexia rats [13]. Similarly, *Kigelia africana* and *acacia hockii* demonstrated dose - dependent antipyretic activities in a study involving turpentine - induced pyrexia rats [30].

The study dosage levels are in consistence to what has been used in previous studies. Ethanolic extract of *Pseudocedrella kotschy* antipyretic activities studies in rats also involved dose levels of 50, 100 and 150mg/kg body weight, while methanolic extract of *Diospyros lotus* was evaluated using dose levels of 50 and 100mg/kg body weight [20, 21].

It was observed that lower doses of methanolic extracts of *M. indica* stem bark at dose levels of 50 and 100mg/kg body weight were less effective compared to higher dose of 150mg/kg body weight. This could be due to inactivation and fast metabolism of pharmacologically active compounds at lower concentrations or active principle(s) insufficient concentration at lower doses.

The methanolic extracts of *M. indica* antipyretic effectiveness are less in the first two hours in relation to the effectiveness observed in the third and fourth hours. Antipyretic activities of methanolic extract of *Mangifera indica* at dose levels of 50, 100, and 150mg/kg body weight was 1.23, 1.28 and 1.69% at the end of 2nd hours respectively while at the end of 4th hour it was 3.13, 3.93 and 4.10% respectively. This could be explained by the fact that some of the phytochemicals must undergo some biotransformation before they can be able to achieve some antipyretic activity. The high dose level of 150mg/kg body weight was more effective in rectal temperature reduction after 4 hours. This was a clear indicator that methanolic stem bark extract of *Mangifera indica* contains bioactive compounds which are capable of crossing the brain blood barrier thereby inhibiting biosynthesis of prostaglandins and/or other substances that stimulate production of antipyretic substances such as the glucocorticoids and arginine vasopressin [14, 32]. This is a clear demonstration to suggest that the plants extracts are capable of mimicking the action of the aspirin and can offers a better or equal prostaglandins biosynthesis blockage. This also can demonstrate the effectiveness of the plants extracts to inhibit other fever blockage mechanisms. Sudden rectal temperature decline associated with plants samples treatments suggests some advantage over the conventional drug (aspirin).

Methanolic extracts of *M. indica* qualitative phytochemical analysis is associated with some of the phytochemicals associated with antipyretic potential like alkaloids, flavonoids, phenolics, saponins, steroids and terpenoids. Some of these phytochemicals can be able to prevent prostaglandins and/or increases body antipyretic components through inhibition of the cyclooxygenase enzyme action [33]. Steroids, alkaloids, tannins and terpenoids are associated with inhibition prostaglandin synthase while flavonoids are associated with inhibition of arachidonic acid peroxidation and tumor necrosis factor – α . Tumor necrotic factor – α is associated with stimulation of PGE₂ synthesis which results to fever. Flavonoids antipyretic activity results from suppression of TNF – α [34]. They are also associated with reduction of prostaglandins levels hence inhibiting the peroxidation of arachidonic acid resulting to antipyretic activity [35]. Presence of flavonoids in methanolic extracts of *M. indica* in this study could contribute to the antipyretic activity.

Previous studies have associated alkaloids with some antipyretic activity. Alkaloids isolated from the *Hunteria zeylanica* indicated some antipyretic activity in experimental animals' studies [26]. Alkaloid presence in methanolic extracts *M. indica* may be responsible for antipyretic activity observed in this study.

Saponins isolated from methanolic *Mangifera indica* plant extracts could be responsible for inhibiting prostaglandin biosynthesis. Saponins inhibit both cyclooxygenase and phospholipase A₂ enzymes involved in pyrexia development [30, 36, 37]. Different saponins act synergistically to exhibit antipyretic activity in experimental animals' studies [38]. Previous study involving ethanolic extracts of *Asparagens racemosus* ethanolic extracts linked its antipyretic activity to saponins [39].

Most antipyretics compounds down regulate the activity of the cyclooxygenase enzyme. Others reduce the production of the proinflammatory markers resulting to enhanced anti-inflammatory signals either in injured tissues or hypothalamic antipyretic signals. The methanolic extract *M. indica* indicated some antipyretic activity on the turpentine induced fever in mice. This is a clear indication that the phytochemical compounds found in dichloromethane and methanol extracts of this plant's parts interfere with the activity of the cyclooxygenase and also proinflammatory cytokines like the

interleukins – 1, Interleukin – 6 (II - 6) and the Tumor necrotic factor – α (TNF – α) release hence the antipyretic activity.

CONCLUSION

The result of this study indicates that the methanolic stem bark extract of *Mangifera indica* possesses substantial antipyretic activity. The antipyretic activity of the methanolic stem bark extract of the *Mangifera indica* can be associated with the phytochemical compound's constituents identified in the study.

Conflict of interest

The authors declare no conflict of interest

Authors Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claim relating to the content of this article will be borne by them

Acknowledgement

The authors appreciate the support offered by technical staff like Vivian, Joyce and the whole fraternity of Kenyatta University.

REFERENCES

1. Dinarello CA, Cannon JG, Wolff SM. New Concepts on the Pathogenesis of Fever. Rev of Infect Dis. 1988; 10(1):168-190.
2. Guyton A, Hall JE. A Text of medical physiology. 11th edition Saunders, Elsevier; 1600 John F. Kennedy Blvd., Suite 1800 Philadelphia, Pennsylvania; 2006.
3. Edwards MJ. Review: Hyperthermia and fever during pregnancy. Birth Defects Research Part A: Clin Mol Teratol. 2006; 76(7):507-516.
4. Kokwaro JO. Medicinal plants of East Africa. 2nd ed. East African literature bureau. Nairobi; 1993.
5. Mwonjoria JK, Kariuki HN, Waweru FN, The antinociceptive, antipyretic effects of *Solanum incanum* (Linnaeus) in animal models. Inter J Phytopharmacol. 2011; 2:22-26.
6. Ross I. Medicinal plants of the world, chemical constituents, traditional and modern medicinal uses, Humana press, Totowa, 1999.
7. Stoilova I, Gargova S, Stoyanova A, Ho L. Antimicrobial and antioxidant activity of the polyphenol mangiferin. Herbal Polonica. 2005; 51:37-44.
8. Brito AS. Pyrexia in fighting of diseases caused by micro- organisms. UNICAMP Press, Campinas; 1994.
9. Metowogo K, Agbonon A, Eklu-Gadegbeku K, Aklirikou AK, Gbeassor M. Drugs used in management of fever. Trop J Pharmacol Res. 2008; 7:907.
10. Hardiker W, Suchy FJ. Medical Physiology: A cellular and molecular approach. Updated ed. Editors Boron, W. F., and Boulpaep, E. L. Elsevier Saunders; 2006.
11. Ray D, Sharatchandra KH, Thokchom IS. Antipyretic, anti diarrhoeal, hypoglycemic and hepatoprotective activities of ethyl acetate extract of *Acacia catechu* Wild. in albino rats. Indian J Pharmacol. 2006; 38:408-413.
12. Tjølsen A, Hole K. Animals models of analgesia. J Pain. 1997; 38:347-352.
13. Gitahi SM, Mwangi BM, Njagi JM, Mworio JK, Juma KK, Aliyu U, et al. Antipyretic properties of dichloromethane: methanolic leaf and root bark extract of *Carissa edulis* in rats. Asian J Biomed Pharmaceut Sci. 2015; 5(43):12-20.
14. Leon LR. Molecular biology of thermoregulation invited review: cytokine regulation of fever: studies using gene knockout mice. J Appl Physiol. 2002; 92:2648-2655.
15. Taran SG, Bezuglyi PA, Depeshko IT. Synthesis, structure, and biological activity of α -acyl derivatives of N-Roxamoylphenylhydrazines. Pharmaceut Chem J. 1984; 18:17-20.
16. Grover JK. Experiments in Pharmacy and Pharmacology. CBS Publisher and Distributor. Shahdara Delhi, India. 1990.
17. Dinarello CA. Review: Infection, fever, and exogenous and endogenous pyrogens: some concepts have changed. J Endotoxin Res. 2004; 10(4):201-222.
18. Evans SS, Repasky EA, Fisher DT. Fever and the thermal regulation of immunity: the immune system feels the heat. Nat Rev Immunol. 2015; 15(6):335-349.

19. Soszynski D, Krajewska M. Lack of tolerance between pyrogenic effects of LPS and turpentine in rats, J Thermal Bio. 2002; 27:229-237.
20. Akuodori GC, Essien AD, Essiet GA, Essien David-Oku, Akpan JL, Udoh FV. Evaluation of antipyretic potential of *Pseudocedrela kotschy* Schweint. Harms (Meliaceae). Eur J Med Plants. 2013; 3(1):105-113.
21. Abdur R, Ghias U, Bina S, Siddiqui NM, Haroon K. Antipyretic and antinociceptive activity of *Diospyros lotus* L. in animals. Asian Pac J Trop Biomed. 2014; 4(1):382-386.
22. Blandizzi C, Tuccori M, Colucci R, Fornai M, Antonioli L, Ghisu N. Role of coxibs in the strategies for gastrointestinal protection in patients requiring chronic non-steroidal anti-inflammatory therapy. Pharmacol Res. 2009; 59:90-100.
23. Clark WO, Cumby HR. The antipyretic effect of indomethacin. J Physiol. 1975; 248:625-38.
24. Gege-Adebayo GI, Bassi AS, Igbokwe VU, Shafe MO. Antipyretic effect of *Ocimum gratissimum* on brewer's yeast induced fever in Wistar rats. J Med Sci. 2013; 4(6):247-251.
25. Elgorashi EE, Naokiwada, Warrag IE, Satoh H. Effects of acacia species on adjuvant-induced arthritis in rats. J Nat Remed. 2009; 9(2):185-191.
26. Reanmongkol W, Matsumoto K, Watanabe H, Subhadhirasakul S, Sakai S. Antinociceptive and antipyretic effects of alkaloids extracted from the stem bark of *Hunteria zeylanica*. Bio Pharmaceut Bul J. 1994; 17(10):1345-1350.
27. Amiya RP, Anuj KA, Ashutosh M. A study on antipyretic activity of *Capparis zeylanica* linn. plant methanolic extract. Inter J Pharmaceut Sci Res. 2010; 1(3):169-171.
28. Koech SC, Ouko RO, Michael NM, Ileri MM, Ngugi MP, Njagi NM. Analgesic activity of dichloromethanolic root extract of *Clusia abyssinica* in swiss albino mice. Nat Prod Chem Res. 2017; 5(2):1-4.
29. Afsar T, Khan MR, Razak S, Ullah S, Mirza B. Antipyretic, anti-inflammatory and analgesic activity of *Acacia hydaspica*. BMC Compl Altern Med. 2015; 15(136):2-12.
30. Kamau JK, Nthiga PM, Safari VC, Njagi SM, Mwonjoria JK, Ngugi P, Ngeranwa J JN. Antipyretic properties of methanolic stem bark extract of *Acacia hockii* De wild and *Kigelia Africana* (Lam) Benth in Wistar rats. J Pharmacog Nat Prod. 2016; 2(3):1-6.
31. Leon RL, Kozak W, Rudolph K, Kluger JM. An antipyretic role for Interleukin-10 in LPS fever in mice, Am Physiol Soc, 1999; R81-R89.
32. Nthiga PM, Kamau JK, Safari VZ, Mwonjoria JK, Ngugi MP, Mburu DN. Antipyretic potential of methanolic stem bark extract of *Harrisonia abyssinica* Oliv and *Landolphia buchananii* (Hallier F.) Stapf in Wistar rats. J Appl Pharm. 2016b; 8(3):1-7.
33. Okokon JE, Nwafor PA. Anti-inflammatory, analgesic and antipyretic activities of ethanolic root extract of *Croton zambesicus*. Pakistan J of Pharmaceut Sci. 2010; 23:385-392.
34. Adesokan AA, Yakubu MT, Owoyele BV, Akanji MA, Soladoye AO, Lawal O. Effect of administration of aqueous and ethanol extracts of *Enantia chlorantha* stem bark on brewer's yeast induced pyresis in rats. Afr J of Biochem. 2008; 2(7):165-169.
35. Taiwe GS, Bum EN, Dimo TH, Talla E, Sidiki NWN, Dawe A, et al. Antipyretic and antinociceptive effects of *Nauclea latifolia* roots decoction and possible mechanisms of action. Pharmaceut Biol. 2011; 49(1):15-25.
36. Kumar S, Bajwa BS, Singh K, Kalia AN. Anti-inflammatory activity of herbal plants. Inter J Adv Pharm Biol Chem. 2013; 2:77-88.
37. Ashfaq K, Choudhary AB, Uzair M, Hussain NS, Ghaffari AM, Sarwar W, Manzoor M. Antipyretic, analgesic and anti-inflammatory activities of methanol extract of root bark of *Acacia jacquemontii* Benth (Fabaceae) in experimental animals. Trop J Pharmaceut Res. 2016; 15(9):1859-1863.
38. Zakaria Z, Loo YW, Nurul IAR, Abdul HAA, Sulaiman MR, Gopalan HK. Antinociceptive, Anti-inflammatory and antipyretic properties of the aqueous extract of *Bauhinia purpurea* leaves in experimental animals. Medical Principles and Practice. 2007; 16:443-449.
39. Vasundra DPA, Divya PS. Antipyretic activity of ethanol and aqueous extract of root of *Asparagus racemosus* in yeast induced pyrexia. Asian J Pharmaceut Clin Res. 2013; 6(3):1974-2441.

HOW TO CITE THIS ARTICLE

Gitonga GM, Ngeranwa J, Machochi AK, Kiruki S. Qualitative phytochemical screening and antipyretic activity of methanolic stem bark extract of *Mangifera indica* in wistar rats. J Phytopharmacol 2020; 9(4):218-223.