Asian Journal of Research and Reports in Neurology

5(2): 37-44, 2022; Article no.AJORRIN.89247

Evaluation of *Fleurya aestuans* Extract against Brewer's Yeast and Egg Albumin Induced Pyrexia and Inflammation

Charles C. Nwafor [a*], Kiridi E. Gabriel [b] and Solomon M. Uvoh [c]

[a] Department of Human Physiology, Faculty of Basic Medical Sciences, College of Medicine, Madonna University, P.M.B. 48, Elele, Nigeria.
[b] Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, Niger Delta University, Bayelsa, Nigeria.
[c] Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Choba, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/89247

Original Research Article

Received 04 May 2022
Accepted 08 July 2022
Published 21 July 2022

ABSTRACT

The goal of this study is to see if hydroethanolic extract of *Fleurya aestuans* can reduce pyrexia and inflammation in Wistar rats. 50 study animals were divided into two groups: Pyrexia group (1, 2, 3, 4) and Inflammatory group (A, B, C, D and E). Fever was produced in the research animals by injecting 20 ml/kg of a 20% brewer's yeast suspension in normal saline under the skin. All rats had their rectal temperatures measured at hourly intervals for four days in a row. Acute inflammation was produced in the anti-inflammatory trial groups by injecting 0.1 ml of egg albumin sub-plantarly into the left hind paw. At 30, 60, 90, and 120 minutes after induction of inflammation, the circumference of the paw was measured with a Vernier caliper. In comparison to the control group (CG) and positive control group (PCG), low dose extract group (LDEG), medium dose extract group (MDEG), and high dose extract group (HDEG) showed significant reductions ($p<0.05$) in rectal temperatures and hind paw circumference. Finally, the hydroethanolic extract of the leaves of *Fleurya aestuans* was concluded to possess antipyretic and anti-inflammatory properties.

**Corresponding author: E-mail: nwaforcharles3@gmail.com;*

Keywords: Fleurya aestuans; anti-pyrexia; anti-inflammatory; egg albumin; brewer's yeast.

1. INTRODUCTION

Fever and inflammation have been recognized as the underlying pathophysiological causes of numerous clinical illnesses for ages [1]. It can be acute or chronic in nature, and both are linked to a variety of bodily illnesses or discomfort. Many noxious stimuli, such as infections (viral, bacterial, and fungal), chemical/physical agents, a faulty immune system, and trauma, can cause pyrexia and inflammation, which can manifest clinically as pain and result in tissue or bodily system injuries. Macrophages and neutrophils are known to secrete numerous mediators that promote and maintain inflammation in the classic inflammatory response [2]. The primary purpose of these reflexes is to defend and wade away from the offending stimuli, as well as to clear debris and restore the damaged tissue. When the acute phase resolution is not complete, the reaction progresses to the chronic stage. Numerous chronic diseases, including various types of cardiovascular ailments and many rheumatic and immune-mediated conditions, have been linked to chronic inflammation [2].

Nonsteroidal anti-inflammatory drugs have been demonstrated to be effective in the treatment of the majority of chronic inflammatory diseases. These chemically created medications have been in use for decades and have a number of disadvantages, including a hefty price tag and the possibility of several side effects or adverse drug responses [1].

Many plants contain therapeutic antipyretic and anti-inflammatory qualities that have been shown to be beneficial in the management of these illnesses in many traditional settings throughout most tropical and subtropical nations [3]. They have the added benefit of being inexpensive, readily available, and free of many of the adverse effects associated with chemical medications.

The African continent is rich in medicinal herbs that have been shown to be effective in traditional medical practice. Traditional medicine practitioners' findings on several plants revealed that *Fleurya aestuans* (Urticaceae) is one of the most promising herbs for alleviating fever, pain, and inflammatory disorders that plague humans around the world, without any scientific verification. *Fleurya aestuans* is a shade-loving herb that is used as a traditional medicine as well as a decorative plant in tropical Africa, China, Australia, and India [4].

The leaves of *Fleurya aestuans* were found to contain the trace elements Chromium (Cr), Manganese (Mn), Nickel (Ni), Copper (Cu), Iron (Fe), and Zinc (Zn) according to the compositional analysis (Zn). Using an Atomic Absorption Spectrophotometer, it was also shown that Fleurya aestuans had the following important minerals: potassium (K), sodium (Na), calcium (Ca), and magnesium (Mg) [5]. *Fleurya aestuans* demonstrated antidiabetic and antihyperlipidemia potentials in alloxan-induced diabetic mice in a study by Okereke et al. [6]. The acute toxicity test of the methanol extract (ME) was estimated by Akah et al., [7] mice with *F. aestuans.* The methanol extract of *F. aestuans* was found to be effective after 24 hours of oral administration. At doses up to 5000 mg/kg, aestuans did not cause death. In rats, the gastroprotective effects of the methanol leaf extract and fractions of *Fleurya aestuans* were investigated [7]. According to Christensen et al. [8], when mixed with $CaCO_3$, aestuans leaves demonstrated antacid action in pregnant women in Ghana.

As a result, the effect of *Fleurya aestuans* leaves on brewer's yeast induced pyrexia and egg albumin-induced inflammation is investigated in this study.

2. MATERIALS AND METHODS

2.1 Preparation of Extract

Fresh *Fleurya aestuans* (West Indian wood nettle) leaves were taken from the University of Port-botanic Harcourt's farm and scientifically classified by the Department of Plant Sciences, Faculty of Sciences, University of Port-Harcourt, Choba, Nigeria, with the reference number UPH/P/263. The leaves were properly cleaned before being dried at room temperature. The dried leaves were kept in a plastic jar. The extract was made using the Adesanya [9] method with certain modifications.

2.2 Determination of Median Lethal Dose (LD50)

With minor adjustments, Lorke's [10] technique was utilized to determine the extract's lethality.

The extract's (LD50) was discovered to be larger than 4600 mg/kg body weight.

2.3 Experimental Design

A total of 50 rats were used in this experiment. The rats weighed between 190.1 and 215.0 g and were 8 and 10 weeks old. Each rat was housed in its own cage at Madonna University's Animal House in Nigeria, with natural day and night cycles. The rats had unlimited access to regular rat food and tap water. Prior to the start of the trial, they were given two weeks to acclimate. The National Institute of Health Guide for the Care and Use of Laboratory Animals was followed in all animal research [11]. The animals were divided into two (2) groups of twenty-five (25) animals each.

Phase 1: Effects of the extract on pyrexia of brewer's yeast induced toxicity

For this investigation, 25 rats were employed, divided into five groups of five rats each. Pyrexia was generated by injecting 20 ml/kg of a 20% brewer's yeast slurry in normal saline below the nape of the neck, as described earlier by Someze et al. [12]. The rat classifications are as follows:

Group 1 functioned as the control group (CG), receiving unlimited rat food and water.

Group 2 was the positive control group (PCG), receiving Aspin only.

Group 3 was the low dose extract group (LDEG), receiving 50 milligrams per kilogram of body weight of *Fleurya aestuans* leaf extract.

Group 4 was the medium dosage extract group (MDEG), receiving 75 milligrams per kilogram of body weight of *Fleurya aestuans* leaf extract.

Group 5 was the high dose extract group (HDEG), given 200mg/body weight of *Fleurya aestuans* leaf extract.

The extract and aspirin were administered to each rat using an oral cannula. After administration of the extract, rectal temperatures were further determined in all rats at hourly intervals for 4 consecutive times.

Phase 2: Effects of the extract on inflammation of egg albumin induced toxicity

For this investigation, 25 rats were employed, divided into five groups of five rats each. Tolu and Dapper earlier documented sub-plantar injection of 0.1 ml egg albumin into the left hind paw to elicit acute inflammation [13]. The rat classifications are as follows:

Group A functioned as the Control Group (CG), receiving unlimited rat food and water.

Group B was the posative Control Group (PCG), receiving Aspirin only.

Group C was the Low Dose Extract Group (LDEG), receiving 50 milligrams per kilogram of body weight of Fleurya aestuans leaf extract.

Group D was the Medium Dosage Extract Group (MDEG), receiving 75 milligrams per kilogram of body weight of Fleurya aestuans leaf extract.

Group E was the High Dose Extract Group (HDEG), given 200mg/body weight of Fleurya aestuans leaf extract.

2.4 Determination of Pyrexia

Fever was induced in groups 1 to 5 rats by injecting 20 ml/kg of a 20% brewer's yeast solution in normal saline below the nape of the neck, as described earlier by Someze et al [13]. The temperature of each rat was recorded using a rectal thermometer inserted 3-4 cm into the rectum 18 hours after induction, and only rats with a temperature increase of at least 0.5°C were employed in the antipyretic investigation.

2.5 Determination of Paw Edema

The procedure reported by Tolu and Dapper [14] with slight modifications was used to generate acute inflammation by injecting 0.1 ml of egg albumin sub-plantarly into the left hind paw. The circumference of the paws was measured with a Vernier caliper 30, 60, 90, and 120 minutes after inflammation was induced.

2.6 Statistical Analysis

All data was expressed as mean + S.E.M. and statistical analysis was performed. A one-way analysis of variance was used to compare the two groups (ANOVA). When $P<0.05$, values were considered significant.

3. RESULTS AND DISCUSSION

Fig. 1 shows the efficiency of *Fleurya aestuans* leaf extract against brewer's yeast-induced rectal

temperature in experimental animals. After 10 hours, an intraperitoneal injection of brewer's yeast suspension significantly raised rectal temperature. The mice' increased rectal temperature was dramatically reduced after treatment with *Fleurya aestuans* leaf extract at the lowest, moderate, and highest doses. At 180 minutes after delivery, all doses of the extract resulted in a considerable reduction in rectal temperature. The extract's antipyretic action began within 30 minutes of treatment and lasted for 180 minutes. In comparison to the control group, the conventional medicine aspirin 100 mg/kg significantly lowered the yeast-elevated rectal temperature. When compared to the conventional medicine, the leaf extract at 200mg/kg (HDEG) demonstrated a similar reduction in rectal temperature.

Pyrexia, sometimes known as 'fever,' is an acute phase reaction that occurs as a result of different inflammatory processes. Brewer's yeast is an exogenous pyrogen that attaches to the immunological protein lipopolysaccharide binding protein, which is a lipopolysaccharide element of Gram-negative bacteria cell walls. This type of binding causes the manufacture and release of a variety of endogenous cytokine factors, including as interleukin (IL)-1, IL-6, and TNFa, which activate the arachidonic acid pathway and eventually lead to the synthesis and release of prostaglandin E2 (PGE2). Pathogenic fever is a phrase used to describe pyrexia caused by yeast [15].

Fever is elicited by inflammatory mediators (IL-1, IL-2, TNF, and others) released by peripheral mononuclear macrophages and other immune cells, according to physiology. Specific carriers transport these fever-inducing cytokines from the bloodstream to the brain. Cytokines go through the bloodstream and through the circumventricular organs to reach the brain. The cytokines, on the other hand, could interact with receptors on brain endothelial cells or perivascular tissue. The humoral hypothesis of fever induction is the name given to this proposed process of fever induction. These pro-inflammatory mediators act on the preoptic/anterior hypothalamus, causing PGE2 to be released from cyclooxygenase (COX-2) and, as a result, an increase in body temperature [15].

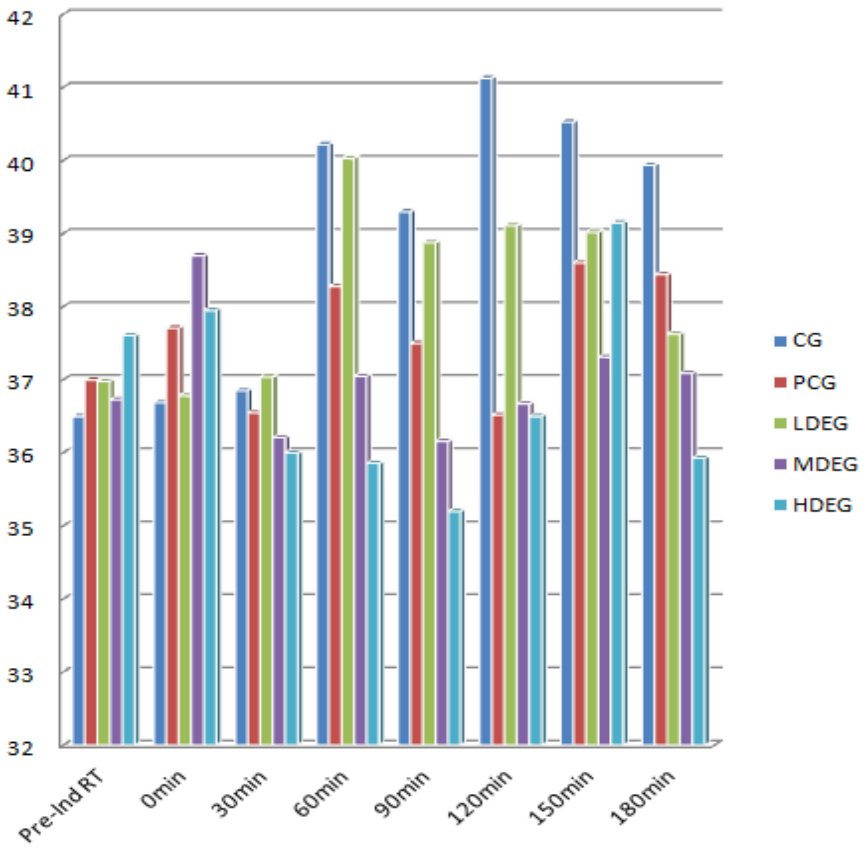


Fig. 1. Values of extract against Brewer's yeast induced pyrexia toxicity

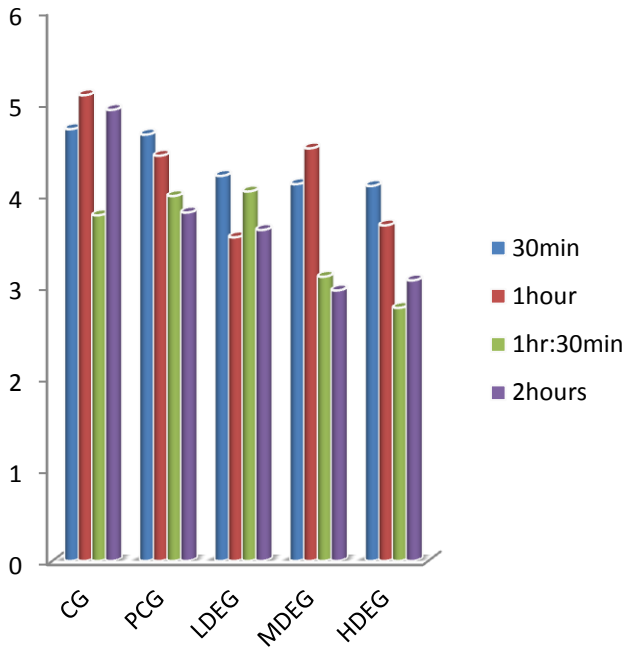
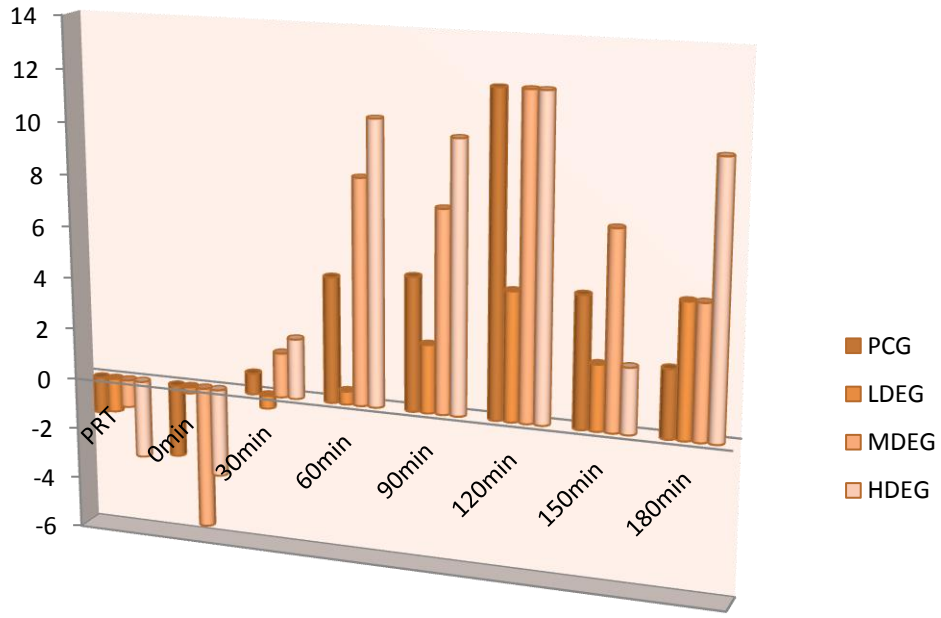
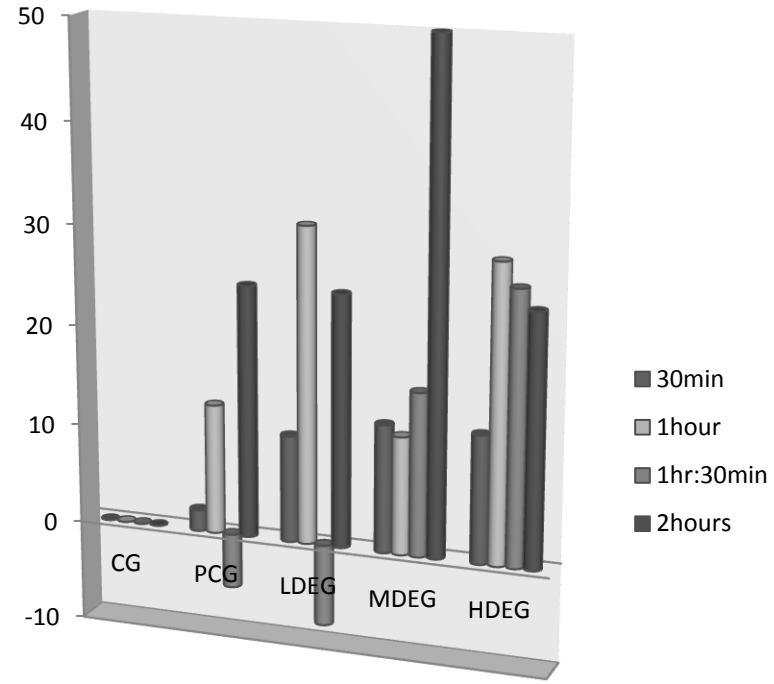


Fig. 2. Values of extract on the hind paw circumference of study animals



	PRT	0min	30min	60min	90min	120min	150min	180min
PCG	-1.4	-2.8	0.8	4.8	5.1	12.2	5	2.6
LDEG	-1.3	-0.24	-0.5	0.5	2.6	4.9	2.5	5.1
MDEG	-1.06	-5.5	1.7	8.6	7.7	12.2	7.5	5.1
HDEG	-3	-3.4	2.3	10.8	10.3	12.2	2.5	10.3

Fig. 3. % Difference of pre and post-induction rectal temperature (°C) of study animals



	CG	PCG	LDEG	MDEG	HDEG
30min	0	2.1	10.6	12.7	12.7
1hour	0	12.9	31.3	11.7	29.4
1hr:30min	0	-5.4	-8.1	16.2	27
2hours	0	25	25	50	25

Fig. 4. % Difference of hind paw circumference of study animals.

Brewer's yeast-induced fever in rodents was greatly reduced by orally administered aspirin at 100 mg/kg in this study. Our findings are consistent with those of other research that have demonstrated that aspirin at the same dose reduces temperature in animals.

Antipyretics and nonsteroidal anti-inflammatory medicines (NSAIDS) lower temperature by reducing inflammation at thermoregulatory regions in the peripheral and central nervous systems.

The effectiveness of Fleurya aestuans leaf extract against egg albumin-induced oedema in Wistar rats was also assessed in this study utilizing the Tolu and Dapper method [14].

In the hunt for new anti-inflammatory drugs, sub-plantar injection of 0.1 ml egg albumin rat paw oedema is commonly employed as a working model. The extract significantly reduced egg albumin-induced rat paw edema starting at the first hour and up to the highest dose. This means that the extract at MDEG and HDEG has anti-inflammatory activity comparable to aspirin, the standard medication (PCG).

The release of histamine, serotonin, and prostaglandin-like chemicals causes paw edema in rats following the injection of egg albumin [16]. The extract's potent anti-inflammatory properties could be related to suppression of inflammation metabolites such histamine, serotonin, and prostaglandin. The current finding demonstrates the usefulness of Fleurya aestuan extract as an effective anti-inflammatory treatment.

Alkaloids, flavonoids, saponin, tannins phenolic compound, glycosides, coumarins, and triterpenoids chemical elements are found in plants that have pain alleviating, analgesic, and anti-inflammatory activities [17].

The existence of the aforementioned elements was discovered in a preliminary phytochemical

analysis of *Fleurya aestuans* leaf extract, which may be accountable for the investigation's outcome. Tannins, flavonoids, and saponins are well known for their anti-inflammatory characteristics and capacity to reduce pain perception by inhibiting enzymes implicated in inflammation, particularly the arachidonic acid metabolic pathway and prostaglandin formation [18]. Tannins may influence the inflammatory response by scavenging free radicals and inhibiting iNOS in macrophages [19]. Saponins, on the other hand, work by inhibiting NO, which reduces pain and inflammation. By decreasing prostaglandin E2 synthesis, alkaloids like bolidine can lower the elevated temperature. Flavonoids like baicalin, on the other hand, have an antipyretic effect via inhibiting TNF [20]. It's possible that *Fleurya aestuans* leaf extract works as an antipyretic by lowering PGE2 levels in the hypothalamus, inhibiting the mechanisms that link peripheral inflammation to central PGE2 production, or both.

Fleurya aestuans leaf extract has strong antipyretic and anti-inflammatory effects, according to the findings. As a result, the extract's analgesic and anti-inflammatory actions may be due to the presence of bioactive molecules.

This study backs up the plant's traditional use, and it would encourage its use with a higher level of confidence in its efficacy.

4. CONCLUSION

Overall, the results of this study suggest that *Fleurya aestuans* leaves may be useful in the treatment of fever and inflammation in Wistar rats.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The study, which was assigned the reference number UPH/CEREMAD/REC/MM78/052, was evaluated and approved by our institutional ethics committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Emmanuel Ikechukwu Onwubuya, Henrietta Aritetsoma Ogbunugafor, Chike Samuel Okafor, Afees Adebayo Oladejo. Acute and chronic anti-inflammatory effect of *Bryophyllum pinnatum* leaf extract on wistar rats. European Journal of Medicinal Plants. 2021;32(6):6-14.
2. Pandurangan A, Amandeep K, Manish K, Vichitra K, Arunachalam G. Evaluation of Anti-inflammatory Activity of Bryophyllumcalycinum (Crassulaceae) on acute and chronic inflammation models. Journal of Pharmaceutical Sciences and Research. 2019;11(1):263-266.
3. Megersa M, Jima TT, Goro KK. The Use of Medicinal Plants for the Treatment of Toothache in Ethiopia. Evidence-Based Complementary and Alternative Medicine. 2019;26(4):51-74.
4. Oluwaseyi Adegoke Adetunji, Jeremiah Olorunjuwon Olugbami, Ayodeji Mathias Adegoke, Michael Adedapo Gbadegesin, Oyeronke Adunni Odunola. Reno-hepatoprotective and antidiabetic properties of methanol leaf extract of *Fleurya aestuans* in Wistar Rats. Journal of Evidence-Based Integrative Medicine; 2021.
5. Akinlami, Omokehide, Labunmi, Lajide, Oloyede Hammed, OjoBabatunde. Trace elements and majors minerals evaluation in *Fleurya aestuans* Linn. (Urticaceae). International Journal of Pharmaceutical Sciences. 2013;3(5):328-332.
6. Okereke S, Elekwa I, Nmaju A. Gas chromatographic fid, hypoglycemic and hypolipidemic effects of leaves of *Laportea aestuans* in alloxan induced diabetes in male albino rats. IOSR J Environ Sci Toxicol Food Technol. 2014;42:42-6.
7. Akah PA, Onyirioha CA, Nworu CC, Ndu OO. Gastro-protective effects of the leaf extract and fractions of fleurya aestuans l (urticaceae). International Journal of Health Research. 2009;2(1).
8. Christensen CB. Antacid activity of *Fleurya aestuans* (L.) Chew. Journal of Ethnopharmacology. 2015;26(2):30-29.
9. Agbodjento E, Klotoé JR, Sacramento TI, Dougnon V, Tchabi FL, Déguénon E, Atègbo JM. Ethnobotanical knowledge of medicinal plants used in the treatment of male infertility in southern Benin. Advances in Traditional Medicine. 2021;21(4):655-73.

10. Olamide AA, Olayemi OO, Demetrius OO, Olatoye OJ, Kehinde AA. Effects of methanolic extract of *Citrullus lanatus* seed on experimentally induced prostatic hyperplasia. European Journal of Medicinal Plants. 2011;1(4):171-9.
11. Lorke D. A new approach to practical acute toxicity testing. Archieve Toxicology; 1983.
12. National Research Council (NRC). Guide for the care and use of laboratory animals. The National Academic Press Washington DC. 1985;85-23.
13. Panda S, Choudhury NS, Patro VJ, Pradhan DK, Jan GK. Analgesic, antipyretic and anti-inflammatory effect of the whole plant extract of *Desmostachya bipinnata* Stapf (Poaceae) in albino rats. Drug Invention Today. 2009;1(2):150-53.
14. Tolu Kolawole, Victor Dapper. Anti-pyretic and anti-inflammatory effects of the methanolic extract of the rind of *Citrullus lanatus* on albino Wistar rats. Journal of Medicinal Plants Research. 2016;10(9):108-112.
15. Venkateswarlu, Ganapathy. Antipyretic effect of methanolic extracts of *Limnophila repens* and *Argyreia cymosa* whole plant on albino rats. MOJ Bioequiv Availab. 2018;5(6):303–306.
16. Oladejo AA, Onwubuya EI, Ogbunugafor HA, Okafor CS, Ogbodo CU. Inhibitory effect of Bryophyllumpinnatum leaf extract on inflammatory biomarkers. Journal of Advances in Medical and Pharmaceutical Sciences. 2021;23(2):7-13.
17. Alemu A, Tamiru W, Nedi T, Shibeshi W. Analgesic and anti-inflammatory effects of 80% methanol extract of *Leonotisocymifolia* (Burm.f.) iwarsson leaves in rodent models. Evididence Based Complementary and Alternative Medicine. 2018;16(1):47-53.
18. Teklehaymanot T. An ethnobotanical survey of medicinal and edible plants of YaloWoreda in Afar regional state,Ethiopia. Journal ofEthnobiology and Ethnomedicine. 2017;13:40.
19. Dabeek WM, Marra MV. Dietary Quercetin and Kaempferol: Bioavailability and potential cardiovascular-related bioactivity in humans. Nutrients. 2019;11:2288.
20. Nabarun M, Sampath V, Sameer P, Babu UV, Richard L. Antiarthritic medicinal plants: A Review. Research Journal of Pharmacy and Technology. 2019; 12(1):375-381.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/89247