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Anti-inflammatory and antipyretic properties of *Corchorus olitorius* aqueous root extract in Wistar rats

Abstract

Background: This study was designed to provide information about the antipyretic and anti-inflammatory effects of *Corchorus olitorius* root.

Methods: Thirty male Wistar rats were divided into six groups of five animals each; the control and reference groups were administered normal saline (10 mL/kg) and indomethacin (5 mg/kg), respectively, whereas the remaining four groups were administered aqueous extract of *C. olitorius* at doses of 25, 50, 100, or 200 mg/kg, respectively. Pyrexia was induced by injecting 10 mL/kg of 20% (w/v) brewer's yeast suspension into the dorsum of rats, whereas inflammation was induced through an injection of 0.1% carrageenan into the right hind paw of each rat and through a subcutaneous implantation of a 30-g sterilized cotton pellet into the groin of each rat.

Results: The results showed that *C. olitorius* root extract ($p<0.05$) decreased the elevated temperature after brewer's yeast injection compared with the 17 h (pre-drug) temperature. In the inflammatory tests, the paw sizes and granuloma weights in the test groups were significantly ($p<0.05$) decreased compared with the control group.

Conclusions: *Corchorus olitorius* root is another good source of phytomedicine that can be used effectively to treat inflammation and pyrexia that accompany some diseases.

Keywords: anti-inflammatory; antipyretic; *Corchorus olitorius*; granuloma; rats.

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Introduction

Pyrexia is also known as fever; it is one of many ways by which the body immune system attempts to neutralize microbial infections [1, 2]. Pyrexia, a pyrogen-induced medical symptom, is linked mainly with elevated body temperature. The elevated temperature is achieved through an increase in the regulatory setpoint in the brain. The increased setpoint triggers increased muscle tone and shivering; this generates more heat, hence causing an elevation of temperature above the normal range of 36.5 °C–37.5 °C. Pyrexia is usually accompanied by some sickness-related behavioral features such as depression, sleepiness, hyperalgesia, anorexia, and a number of disease conditions such as infections, skin inflammation, tissue destruction, cancer, metabolic disorders, malaria, lobar pneumonia, and typhoid [2–4].

Like pyrexia, inflammation is a nonspecific immune response that occurs in reaction to bodily injury. This bodily injury includes cell injury or cell death that is initiated by several factors ranging from microbe infection and chemical injury to environmental pollution [5–7]. The resultant tissue injury causes the release of inflammatory mediators that include cytokines and tumor necrosis factor-α, and interleukin-1 (IL-1) from leukocytes, monocytes, and macrophages [8].

Documented evidence showed that a minimal level of IL-1β evoked fever [9]. Hence ordinarily, inflammation processes can initiate a pyretic cascade. History revealed that inflammation could be beneficial and pathological. Galen considered inflammation as beneficial because it is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing process. Centuries later, Virchow viewed inflammation as inherently pathological [9, 10]. These two historical views are better understood today with the knowledge of acute and chronic inflammation. The former is a defense mechanism aimed at killing

the invading microbes and still facilitating wound repairs, whereas the latter increases the development of degenerative diseases [5, 11]. Laboratory and clinical data showed that inflammatory pathways form a major part of pathogenesis of a number of chronic diseases. In the development of these diseases, the inflammatory process that is usually a self-limiting process becomes continuous and referred to as being chronic [9].

Inflammation and pyrexia are initiated in the body by a sequential cascade of reactions, which once initiated may result into degenerative diseases if not properly checked. The phytochemical constituents that can block or inhibit any of these initiating cascades have the potential to stop, inhibit, or decrease the inflammatory and pyretic process. *Corchorus olitorius* root is believed to be a plant with such phytochemical constituents.

Corchorus olitorius, otherwise known as tossa jute plant, is a fiber crop commonly found in Africa and Eastern Asia. The plant produces edible leaves that serve as a traditional vegetable for human consumption [12]. In Nigeria, the mucilaginous soup of jute leaves is a common dish in the western part of the country, but it is also known in the other regions. Locally, it is called "ewedu" in the western part of Nigeria and "fakohoy" by the Songhay of Mali [13, 14]. Various studies showed that the leaf has a protective role against arsenic-induced oxidative stress in tissues [15]. In traditional medicine, local folks use jute leaf for different ailments, including pains, fever, tumors, diabetes, and dysentery [12, 16, 17]. A recent study showed jute leaf to be a potential therapy in the treatment of chronic lead intoxication, thus suggesting that it might probably protect against free radicals that mediate toxic manifestations of heavy metals [18]. The protein isolated from jute seed has been proven able to increase body weight and liver lipids [19]. There is a dearth of information on the medicinal properties of *C. olitorius* root in the literature. This might be because the root of the plant is usually discarded with the stem after removing the edible leaf for food and the seed for replanting. The present study was carried out to fill the observed gap in the literature concerning *C. olitorius* and to investigate the merit behind the ethnopharmacological uses of *C. olitorius* root extract for the treatment of inflammation and pyrexia in rats.

Materials and methods

Animal preparation

Male Wistar rats (150–200 g) obtained from the Department of Biochemistry, University of Ilorin, were used for this study. Rats were fed rat pellet composed and pelletized by Gbemisola Animals Feeds Co. (Ilorin, Nigeria). Animals also had free access to tap water. Both feed and water were made available to the animals before and during the period of experiment. After 7 days of acclimatization, six groups of five rats were formed. The groups and the dosages administered are as follows: saline (10 mL/kg) group, indomethacin (5 mg/kg) group, *C. olitorius* (25 mg/kg) group, *C. olitorius* (50 mg/kg) group, *C. olitorius* (100 mg/kg) group, and *C. olitorius* (200 mg/kg) group. Saline, indomethacin, and the extracts were administered orally to the animals. The Principles of Laboratory Animal Care Guiding Animal Experiment were strictly followed as prescribed by the University of Ilorin research policy.

Plant preparation

Corchorus olitorius plant was collected in Ilorin, Nigeria. The plant was identified at the Forestry Research Institute of Nigeria with an FHI No. 107728. A sample of the plant was kept in the herbarium for later reference. *C. olitorius* roots were harvested from the plants, cleaned, and air dried at room temperature. The air-dried root was reduced to fine powder using mortar and pestle. The powder was 1000 g in weight, and this was stored in a bottle at room temperature before the beginning of the experiment.

Extract preparation

The aqueous extract of *C. olitorius* was prepared by soaking 1000 g *C. olitorius* powder into 10 L distilled water. The formed mixture was kept for 48 h after which it was filtered with a muslin cloth. The filtrate was evaporated over water bath into 27 g crude solid at 40 °C. The extract was subsequently dissolved in normal saline for pharmacological studies.

Antipyrexia test

The antipyretic property of *C. olitorius* root was tested by slightly modifying the method described by Tijani et al. [20]. Rats were weighed and randomized into six groups of five rats per group as described in "Animal preparation". A digital thermometer manufactured by ROMED-Holland (Wilnis, The Netherlands) was used to measure the baseline rectal temperatures. The depth of insertion of the digital thermometer into the anal cavity was 2 cm for all rats, and the temperatures were read at the beep of the thermometer. The obtained steady temperature readings were taken as the pretreatment temperatures. Pyrexia was induced by injecting 10 mL/kg of 20% (w/v) brewer's yeast suspension into the dorsum of rats. After 17 h of brewer's yeast administration, the rectal temperatures were measured again. Rats that showed at least 0.7 °C rise in temperature were used for the test.

Anti-inflammatory test

Carrageenan test: The method of Winter et al. [21] was used to carry out this study. The extract administered groups, *C. olitorius* (25 mg/kg) group, *C. olitorius* (50 mg/kg) group, *C. olitorius* (100 mg/kg) group, and *C. olitorius* (200 mg/kg) group, were given 25, 50, 100, and

200 mg/kg of *C. olitorius* aqueous root extract, respectively. The control and reference groups were also given 10 mL/kg normal saline and 5 mg/kg indomethacin, respectively. An hour after all administrations, edema was induced by injecting 0.1% carrageenan into the right hind paw of each rat under the subplantar aponeurosis. Paw size was measured before and immediately after carrageenan injection and extended to 5 h of post-carrageenan administration. The measurement of paw size was carried out by wrapping a piece of cotton thread around the paw and measuring the circumference on a meter rule.

Cotton pellet granuloma test: A sterilized cotton pellet (30 g) was implanted subcutaneously in the groin of each rat. Animals were subsequently divided into six groups as described above, and each rat was treated for 7 days according to the group it belonged to. On the eighth day, animals were sacrificed with an overdose of ether, and the cotton pellet together with its surrounding granuloma tissues was dissected out carefully and dried at 60 °C to a constant weight. The mean weight of the granuloma tissue was determined for each group, and the percentage inhibition was expressed by comparing with the untreated control.

Statistical analysis

All values were expressed as mean±SE. Statistical significance was determined using ANOVA and Student's t-test values of SPSS 16 version with $p<0.05$ compared with normal saline (10 mL/kg) group.

Table 1 Effect of *C. olitorius* aqueous root extract on carrageenan-induced inflammation in rats.

Group	Paw size, cm	
	3 h	5 h
Saline (10 mL/kg)	3.08±0.07	3.22±0.12
Indomethacin (5 mg/kg)	2.92±0.05[a]	2.82±0.03[a]
C. olitorius (25 mg/kg)	3.06±0.10	2.86±0.10[a]
C. olitorius (50 mg/kg)	2.96±0.17[a]	2.96±0.18[a]
C. olitorius (100 mg/kg)	2.80±0.03[a]	2.66±0.02[a]
C. olitorius (200 mg/kg)	2.70±0.04[a]	2.66±0.05[a]

Each value is the mean±SE of five rats (cm) for the size of edema during 3 and 5 h of study. [a]$p<0.05$ compared with control.

Table 2 Effect of *C. olitorius* aqueous root extract on cotton pellet-induced granuloma formation in rats.

Group	Dry weight granuloma, g
Saline (10 mL/kg)	0.24±0.02
Indomethacin (5 mg/kg)	0.09±0.00[a,b]
C. olitorius (25 mg/kg)	0.20±0.03
C. olitorius (50 mg/kg)	0.14±0.02[a]
C. olitorius (100 mg/kg)	0.16±0.02[a]
C. olitorius (200 mg/kg)	0.18±0.02[a]

Each value is the mean±SE of five rats (g) for the size of granuloma formed during the study. [a]$p<0.05$ compared with control. [b]$p<0.01$ compared with control.

Results

Effect of *C. olitorius* aqueous root extract on carrageenan-induced inflammation

The results of the carrageenan test showed that *C. olitorius* root extract significantly ($p<0.05$) reduced paw edema in all extract-administered groups compared with the control group (Table 1). The groups administered 100 and 200 mg/kg produced the highest inhibition edema.

Effect of *C. olitorius* aqueous root extract on cotton pellet-induced inflammation

In the cotton pellet-induced inflammation test, the results showed that *C. olitorius* aqueous root extract dose-dependently decreased ($p<0.05$) the weight of granuloma tissues compared with the control group (Table 2).

Effect of *C. olitorius* aqueous root extract on brewer's yeast-induced pyrexia

The results of the antipyretic test showed that *C. olitorius* root extract significantly ($p<0.05$) reduced rectal temperature compared with the pre-drug temperature, indomethacin also produced significant ($p<0.05$) reductions in rectal temperature, whereas saline administration did not significantly alter the elevated body temperatures (Figure 1).

Discussion

Inflammation and pyrexia have always served as indicators of the presence of pathophysiological conditions. These two indicators can sometimes be observed together in certain disease conditions such as parasitic infections and acute infections [22, 23] or separately such as in peptic ulcer (inflammation) and fever (pyrexia) [24, 25]. The inflammatory process and pyrexia have been shown to have a crossing path or meeting point. For instance, inflammatory processes can induce pyrexia through a moderate level of inflammatory marker called IL-1β [9]. In addition to this, pain and pyrexia had also been described as inflammatory symptoms [26]. Our studies showed that *C. olitorius* aqueous root extract could alleviate these two pathophysiological processes not only separately but also concurrently.

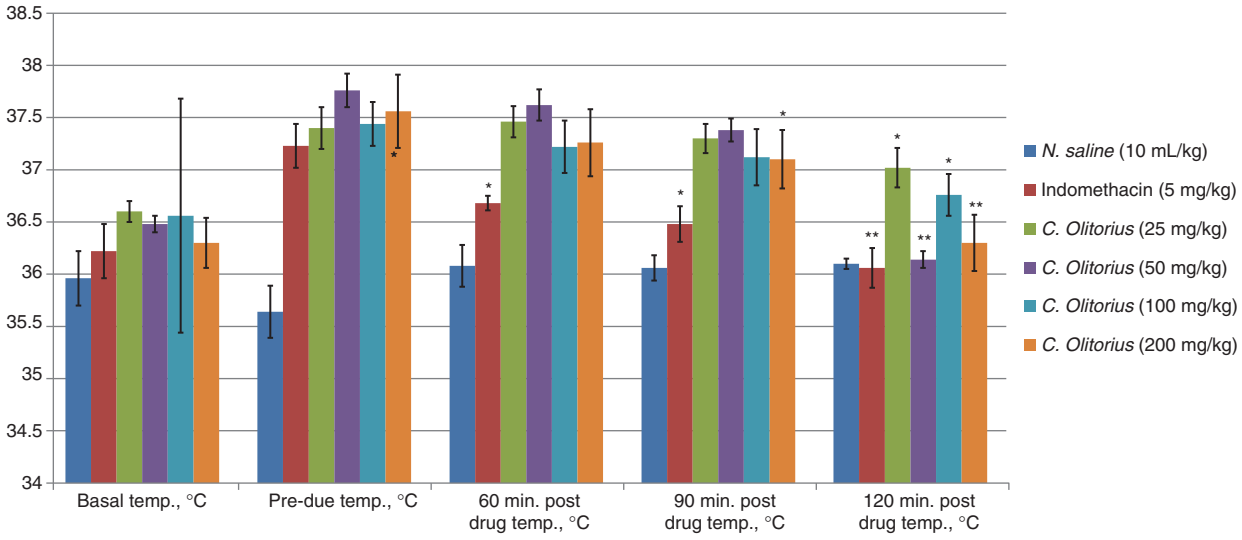

Figure 1 Effect of *C. olitorius* aqueous root extract on brewer's yeast-induced pyrexia in rats.
Each value is the mean±SE of five rats (°C) within 120 min of administration. *p<0.05 compared with control. **p<0.01 compared with control.

In the inflammatory studies, all dosages in the tested groups were able to reduce granuloma formation when compared with the control group, whereas only animals given doses of 50, 100, and 200 mg/kg of *C. olitorius* root extract had significant (p<0.05) reduction in accumulated granuloma compared with the control group. Indomethacin also significantly (p<0.05) decreased accumulated granuloma when compared with the control group. However, when comparing the weight of accumulated granuloma in the indomethacin group with that of the extract administered groups, it was observed that the indomethacin group had the least accumulated granuloma. In this regard, indomethacin at the dose used in this study seemed to be more effective in reducing granuloma formation than the extracts. Surprisingly, we observed that the most effective dosage in the tested groups for treating cotton pellet-induced inflammation was 50 mg/kg because animals in the *C. olitorius* (50 mg/kg) group had the least weight of granuloma, whereas other doses of the extract, except for the *C. olitorius* (25 mg/kg) group, produced significant reductions in granuloma formation compared with the control group. The same trend of observation was observed with the carrageenan-induced edema.

In the acute inflammatory study, which was represented by carrageenan-induced edema, the extracts produced anti-inflammatory effects at the early (3 h) and late (5 h) phases of the test by decreasing the change in paw circumference compared with the control group. The indomethacin group also significantly reduced the inflammation produced by carrageenan injection compared with the control group. However, unlike in the cotton pellet-induced granuloma formation, the 100 and 200 mg/kg doses of *C. olitorius* root extract seemed to be more effective compared with indomethacin. The trend of observations in this study has shown that *C. olitorius* root has the potential to serve as a drug for the treatment of inflammation.

The results obtained from pyrexia studies followed a similar trend to what was observed in the anti-inflammatory studies. At 60 min, the standard drug (indomethacin) significantly decreased the elevated pre-drug temperature (17 h after brewer's yeast injection) of the animals in the group. The extracts could not produce a decrease in rectal temperatures compared with the pre-drug temperatures; however, at 90 min, there was a significant (p<0.05) decrease in the elevated temperatures in both the indomethacin and *C. olitorius* (200 mg/kg) groups. Furthermore, all doses of extract and indomethacin significantly (p<0.05) reduced the elevated temperature after 120 min of their administration compared with the pre-drug (control) temperature. The trend of the results shows that the root extract has antipyretic activities that may not be immediate but is observable from 90 min after the administration of a minimal dose of 200 mg/kg. It is important to note that the saline-administered group had elevated pre-drug temperature, which remained relatively high and failed to return to the baseline temperature throughout the period of the experiment. Hence, the reductions in elevated pre-drug temperatures observed in the extract- and indomethacin-administered groups did not occur by chance but were actually due to the

antipyretic effects of *C. olitorius* root extract and indomethacin, respectively.

It is not uncommon to find a plant that exhibits both antipyretic and anti-inflammatory activities as observed in this study. Plants with such activities include but are not limited to plants such as *Acalypha wilkesiana* [27], *Faidherbia albida* [20], *Aleurites moluccana* [28], and *Hygrophila spinosa* [29]. Tijani et al. [20] also reported that *F. albida* possesses phytochemical constituents such as tannins and alkaloids that make the plant a potent antipyretic, anti-inflammatory, and antidiarrheal. It is important to note that the mechanism of action of *C. olitorius* root was not investigated in the present study. However, its mode of action might follow one of the four general mechanisms of actions of phytomedicines in the inflammatory process. These four general mechanisms of actions of phytomedicines are classified as follows: immunoprotective/immunomodulatory properties; inhibition of nuclear factor-κB, nitric oxide, cyclo-oxygenase, and reactive oxygen species generation; inhibition of enzymes (tyrosine); and prevention of the entry of microorganisms (membrane-stabilizing properties) [9].

In a recent study of *C. olitorius* root of Nigerian origin, phytochemical analysis showed that the root of the plant is endowed with alkaloids, saponins, cardenolides, β-carotene, and various nutritional components [14]. Numerous studies have indicated that alkaloids and saponins in plants are responsible for the antimicrobial, analgesic, anti-inflammatory, antipyretic, antiulcer, and antioxidant activities of plants [14, 20, 26, 27, 30]. The observed effects of *C. olitorius* may not therefore be unconnected with its alkaloid and saponin contents. It is hereby recommended that more investigation be carried out to determine the active ingredients and exact mechanism of action of *C. olitorius* root. In conclusion, this study has shown that the usually discarded *C. olitorius* root by the local folks is a good source of phytomedicine for the treatment of inflammation and pyrexia.

Conflict of interest statement

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