ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

PRECLINICAL EVALUATION OF ANTIPYRETIC AND ANALGESIC ACTIVITIES OF ETHANOLIC EXTRACT OF WHOLE PLANT OF *OXALIS LATIFOLIA* KUNTH

Basavaraj K Somapur*[1], Bharathi K N[2]

[1]Department of Pharmacology, Visveswarapura Institute of Pharmaceutical Sciences, Bengaluru, Karnataka, India.

[2]Professor, Department of Pharmacology, Visveswarapura Institute of Pharmaceutical Sciences, Bengaluru, Karnataka, India.

Corresponding author E- mail: basavarajksompur@gmail.com

ARTICLE INFO

Key words:

Oxalis Latifolia Kunth, Antipyretic Activity, Analgesic Activity, Ethanolic Extract, Wistar Rats

Access this article online
Website: https://www.jgtps.com/
Quick Response Code:

ABSTRACT

Background: Fever and pain are common clinical manifestations associated with inflammatory disorders. Although synthetic antipyretic and analgesic agents are effective, their prolonged use may lead to adverse effects. Medicinal plants are considered safer alternatives because of their therapeutic potential and lower toxicity profile. **Objective:** The present study was designed to evaluate the antipyretic and analgesic activities of the ethanolic extract of whole plant of *Oxalis latifolia* Kunth using experimental animal models. **Materials and Methods:** The ethanolic extract of *Oxalis latifolia* Kunth was prepared using Soxhlet extraction. Antipyretic activity was evaluated using Brewer's yeast-induced pyrexia in Wistar rats. Analgesic activity was assessed using tail immersion and acetic acid-induced writhing methods. The extract was administered orally at doses of 100 mg/kg and 400 mg/kg body weight. Paracetamol, tramadol, and diclofenac sodium were used as standard drugs. Statistical analysis was performed using one-way ANOVA followed by Dunnett's and Tukey-Kramer multiple comparison tests. **Results:** The ethanolic extract significantly reduced rectal temperature in yeast-induced pyrexia models and exhibited dose-dependent antipyretic activity. In the tail immersion test, the extract significantly increased tail flick latency, indicating centrally mediated analgesic activity. In the acetic acid-induced writhing test, the extract significantly reduced the number of writhes, suggesting peripheral analgesic activity. The 400 mg/kg dose showed greater efficacy and produced results comparable to standard drugs. **Conclusion:** The findings demonstrate that the ethanolic extract of *Oxalis latifolia* Kunth possesses significant antipyretic and analgesic activities, thereby supporting its traditional medicinal use. The activity may be attributed to the presence of flavonoids, alkaloids, tannins, and phenolic compounds.

INTRODUCTION:

Fever and pain are among the most common clinical manifestations associated with infections, inflammation, and tissue injury. Fever is a physiological response produced by pyrogenic substances that stimulate prostaglandin synthesis in the hypothalamus, whereas pain acts as a protective mechanism initiated through nociceptor activation. Conventional drugs such as non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and antipyretic agents are widely used for the management of these conditions. However, prolonged use of these drugs is often

associated with adverse effects including gastrointestinal irritation, renal toxicity, hepatotoxicity, and drug dependence. These limitations have created a growing interest in the development of safer and effective therapeutic agents derived from medicinal plants.

Medicinal plants have been used since ancient times in traditional systems of medicine for the treatment of various diseases. Phytoconstituents such as flavonoids, alkaloids, tannins, saponins, and phenolic compounds are known to possess significant pharmacological activities including antipyretic, analgesic, anti-inflammatory, antioxidant, and antimicrobial properties. Scientific validation of traditionally used medicinal plants is essential for identifying novel bioactive compounds and developing safer herbal medicines.

Oxalis latifolia Kunth, commonly known as broadleaf wood sorrel, is a perennial herb belonging to the family Oxalidaceae. The plant is native to Central and South America and is widely distributed in tropical and subtropical regions. Traditionally, the plant has been used in folk medicine for the treatment of fever, pain, inflammation, microbial infections, diarrhea, diabetes, and skin disorders. Phytochemical investigations have revealed the presence of flavonoids, tannins, alkaloids, saponins, and phenolic compounds, which may contribute to its therapeutic potential. Despite its traditional medicinal importance, limited scientific evidence is available regarding its antipyretic and analgesic activities [1].

Therefore, the present study was undertaken to evaluate the antipyretic and analgesic activities of the ethanolic extract of whole plant of *Oxalis latifolia* Kunth using standard preclinical experimental models. The study aims to provide scientific validation for its traditional medicinal use and explore its potential as a safer herbal alternative for the management of fever and pain.

NOVELTY OF THE WORK

1. The study scientifically validates the traditional use of *Oxalis latifolia* Kunth in the treatment of fever and pain.
2. The ethanolic extract demonstrated both central and peripheral analgesic activities in experimental animal models.
3. The study highlights the dose-dependent pharmacological efficacy of *Oxalis latifolia* Kunth.
4. The findings support the potential development of plant-based alternatives to synthetic antipyretic and analgesic drugs.

MATERIALS AND METHODS

Plant Material

Fresh whole plants of *Oxalis latifolia* Kunth were collected during the months of December to February from Bengaluru Rural, Karnataka, India. The plant material was authenticated by Dr. Rama Rao, Research Officer (Botany), Central Ayurveda Research Institute, Uttarahalli, Bengaluru, Karnataka. A herbarium specimen bearing voucher number Authentication/SMPU/ CARI/BNG/2023-24/2179 was deposited at the Central Ayurveda Research Institute, Uttarahalli, Bengaluru, Karnataka, for future reference.

Chemicals and Reagents

Diclofenac sodium, tramadol, and paracetamol used in the study were procured from KAPL and Biocon Pvt. Ltd. All chemicals and reagents used in the experimental study were of analytical grade and high purity.

Preparation of Plant Extract

The collected whole plants of *Oxalis latifolia Kunth* were shade dried and coarsely powdered. Approximately 100 g of powdered plant material was subjected to Soxhlet extraction using ethanol as the solvent. The extraction process was carried out at a temperature range of 70–75°C for about 7 h until complete extraction was achieved. The extract obtained was concentrated and dried to obtain a semisolid mass. The percentage yield of the ethanolic extract was found to be 5.05% w/v. The prepared extract was stored in an airtight container for further pharmacological studies [2].

Experimental Animals

Female Wistar albino rats weighing 150–200 g were procured from a CPCSEA-approved breeder, Bengaluru, Karnataka (Reg. No. 2138/PO/ReBiBt/S/21/CPCSEA). The animals were housed in the animal house of

Visveswarapura Institute of Pharmaceutical Sciences, Bengaluru, Karnataka. Animals were maintained in polyacrylic cages under standard laboratory conditions with controlled temperature (27 ± 2°C), relative humidity (65 ± 2%), and natural light-dark cycle. Standard pellet diet and water were provided ad libitum throughout the experimental period.

The animals were acclimatized to laboratory conditions for seven days before commencement of the experiment. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) under CPCSEA guidelines (Reg. No. 152/99/CPCSEA).

EXPERIMENTAL MODELS

Antipyretic Activity [3,4]

Antipyretic activity was evaluated using Brewer's yeast-induced pyrexia in Wistar rats. Animals were divided into four groups consisting of six animals each.

- **Group I:** Control group treated with Brewer's yeast suspension (20% w/v, 10 mL/kg, s.c.)
- **Group II:** Ethanolic extract of *Oxalis latifolia* Kunth (100 mg/kg, p.o.) + Brewer's yeast
- **Group III:** Ethanolic extract of *Oxalis latifolia* Kunth (400 mg/kg, p.o.) + Brewer's yeast
- **Group IV:** Standard drug paracetamol (150 mg/kg, p.o.)

Rectal temperature was recorded at regular intervals after administration of treatments.

Tail Immersion Test for Centrally Acting Analgesic Activity [5,6]

The analgesic activity of the ethanolic extract was evaluated using the tail immersion method. Animals were divided into four groups containing six rats each.

- **Group I:** Control group receiving vehicle only
- **Group II:** Ethanolic extract of *Oxalis latifolia* Kunth (100 mg/kg, p.o.)
- **Group III:** Ethanolic extract of *Oxalis latifolia* Kunth (400 mg/kg, p.o.)
- **Group IV:** Standard drug tramadol (10 mg/kg, p.o.)

The tail flick response time was recorded at different time intervals following treatment administration.

Acetic Acid-Induced Writhing Test for Peripheral Analgesic Activity [7,8]

Peripheral analgesic activity was evaluated using acetic acid-induced writhing in rats. Animals were divided into four groups consisting of six animals each.

- **Group I:** Control group treated with acetic acid (3% v/v, 10 mL/kg, i.p.)
- **Group II:** Ethanolic extract of *Oxalis latifolia* Kunth (100 mg/kg, p.o.) + acetic acid
- **Group III:** Ethanolic extract of *Oxalis latifolia* Kunth (400 mg/kg, p.o.) + acetic acid
- **Group IV:** Standard drug diclofenac sodium (10 mg/kg, p.o.)

The number of writhes produced by each animal was counted for 10 min after administration of acetic acid.

Statistical Analysis

The experimental data were expressed as mean ± standard deviation (SD). Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by Dunnett's and Tukey–Kramer multiple comparison tests. A value of $p < 0.05$ was considered statistically significant.

RESULTS

Antipyretic Effect of *Oxalis latifolia* Kunth on Yeast-Induced Pyrexia

The ethanolic extract of *Oxalis latifolia* Kunth (EOLK) at doses of 100 mg/kg and 400 mg/kg, p.o., significantly reduced rectal temperature in Brewer's yeast-induced pyrexia in rats. The antipyretic activity was found to be dose dependent. The 400 mg/kg dose produced an earlier onset of action and greater reduction in rectal temperature when compared with the 100 mg/kg dose. The effect observed with the higher dose was comparable to the standard drug paracetamol.

Analgesic Effect of *Oxalis latifolia* Kunth on Thermal-Induced Pain

The ethanolic extract of *Oxalis latifolia* Kunth at doses of 100 mg/kg and 400 mg/kg, p.o., significantly increased tail flick latency in the tail immersion test, indicating centrally mediated analgesic activity. The effect was dose dependent, with the 400 mg/kg dose producing earlier onset and greater analgesic activity compared to the 100 mg/kg dose. However, the standard drug tramadol

exhibited greater potency than the plant extract.

Analgesic Effect of *Oxalis latifolia* Kunth on Acetic Acid-Induced Writhing

The ethanolic extract of *Oxalis latifolia* Kunth at doses of 100 mg/kg and 400 mg/kg, p.o., significantly reduced the number of writhes induced by acetic acid in rats when compared with the control group. The analgesic effect was dose dependent, with the 400 mg/kg dose showing greater percentage inhibition of writhing and activity comparable to the standard drug diclofenac sodium.

Table 1. Antipyretic Effect of *Oxalis latifolia* Kunth Extract on Yeast-Induced Pyrexia

Group (n=6)	0 h	1 h	2 h	3 h	4 h
Control	37.7 ± 0.50	37.6 ± 0.56	38.02 ± 0.48	38.11 ± 0.60	37.91 ± 0.77
EOLK 100 mg/kg, p.o.	38.51 ± 0.35	38.22 ± 0.33	38.31 ± 0.46	37.45 ± 0.75**	37.78 ± 0.43**
EOLK 400 mg/kg, p.o.	37.9 ± 0.18	38.1 ± 0.18	37.4 ± 0.23**	37.11 ± 0.25**	36.67 ± 0.18**
Standard Paracetamol 150 mg/kg, p.o.	37.71 ± 0.42	37.37 ± 0.33	37.12 ± 0.34**	36.86 ± 0.21**	36.45 ± 0.11**

Values are expressed as mean ± SD (n=6). Statistical analysis was performed using one-way ANOVA followed by Dunnett's multiple comparison test. **P < 0.01 when compared with 0 h values.

Table 2. Analgesic Effect of *Oxalis latifolia* Kunth Extract on Thermal-Induced Pain

Group	0 min	30 min	60 min	90 min	120 min	150 min
Control	3.5 ± 0.54	3.33 ± 0.21	3.2 ± 0.36	3.6 ± 0.22	3.13 ± 0.08	3.51 ± 0.16
EOLK 100 mg/kg, p.o.	3.52 ± 0.54	3.83 ± 0.23	4.11 ± 0.24*	5.16 ± 0.19***	5.73 ± 0.17***	6.05 ± 0.10***
EOLK 400 mg/kg, p.o.	3.59 ± 0.55	4.81 ± 0.18*	5.01 ± 0.10***	6.05 ± 0.10***aa	6.25 ± 0.13***a	7.25 ± 0.13***aaa
Standard Tramadol 50 mg/kg, p.o.	3.3 ± 0.51	6.01 ± 0.14***	7.5 ± 0.03***	8.1 ± 0.4***aaabbb	8.25 ± 0.08***aaabbb	9.0 ± 0.07***aaabbb

Values are expressed as mean ± SD (n=6). Statistical analysis was performed using one-way ANOVA followed by Tukey–Kramer multiple comparison test. ***P < 0.001, **P < 0.01, *P < 0.05 when compared with control group; aaaP < 0.001, aaP < 0.01, aP < 0.05 when compared with EOLK 100 mg/kg; bbbP < 0.001 when compared with EOLK 400 mg/kg.

Table 3. Analgesic Effect of *Oxalis latifolia* Kunth on Acetic Acid-Induced Writhing

Group	Mean Writhing Score in 10 min	Percentage Inhibition
Control	40.33 ± 0.4	-
EOLK 100 mg/kg, p.o.	33.83 ± 0.8**	16%
EOLK 400 mg/kg, p.o.	22.16 ± 0.7**aa	45%
Standard Diclofenac Sodium 10 mg/kg, p.o.	13.16 ± 0.98**aabb	67%

Values are expressed as mean ± SD (n=6). Statistical analysis was performed using one-way ANOVA followed by Tukey–Kramer multiple comparison test. **P < 0.01 when compared with control group; aaP < 0.01 when compared with EOLK 100 mg/kg; bbP < 0.01 when compared with EOLK 400 mg/kg.

DISCUSSION

The present study evaluated the antipyretic and analgesic activities of the ethanolic extract of *Oxalis latifolia* Kunth using standard experimental animal models. The findings demonstrated that the extract possesses significant pharmacological activity in a dose-dependent manner, thereby supporting the traditional medicinal use ofthe plant in the management of fever and pain.

In the Brewer's yeast-induced pyrexia model, the ethanolic extract of *Oxalis latifolia* Kunth at doses of 100 mg/kg and 400 mg/kg, p.o., significantly reduced rectal temperature in

experimental animals. The higher dose (400 mg/kg) produced an earlier onset and greater reduction in temperature, showing activity comparable to the standard drug paracetamol. Brewer's yeast-induced pyrexia is a widely accepted experimental model for evaluating antipyretic agents because fever induced by yeast is associated with the release of endogenous pyrogens such as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), which stimulate prostaglandin E2 (PGE2) synthesis in the hypothalamus [9–11]. The reduction in rectal temperature observed in this study suggests that the extract may inhibit prostaglandin synthesis or suppress the release of pyrogenic cytokines. The antipyretic activity may be attributed to the presence of flavonoids, alkaloids, and phenolic compounds present in the plant extract, which are known to possess anti-inflammatory and antipyretic properties. Similar findings have been reported in medicinal plants such as *Nauclea latifolia* and *Bersama abyssinica* [9–11].

The analgesic activity of the ethanolic extract was evaluated using tail immersion and acetic acid-induced writhing methods. In the tail immersion test, the extract significantly increased tail flick latency, indicating centrally mediated analgesic activity. The effect was more pronounced at the dose of 400 mg/kg, although the standard drug tramadol exhibited greater potency. Thermal nociceptive stimuli activate pain receptors such as transient receptor potential vanilloid-1 (TRPV1) channels, leading to depolarization and transmission of pain impulses. Tramadol exerts its analgesic action primarily through μ-opioid receptor agonism and inhibition of neurotransmitter reuptake. The increase in tail flick latency observed with the extract suggests possible involvement of central pain inhibitory pathways and opioid receptor modulation. Flavonoids and phenolic compounds present in the extract may contribute to this activity through antioxidant and neuroprotective mechanisms, as reported for medicinal plants such as *Ginkgo biloba* and *Sida tiagii* [12,13].

Further evidence of analgesic activity was observed in the acetic acid-induced writhing test, where the extract significantly reduced the number of writhes in a dose-dependent manner. Acetic acid-induced writhing is commonly associated with the release of inflammatory mediators such as prostaglandins, bradykinin, and substance P, which stimulate peripheral nociceptors. Diclofenac sodium, the standard drug used in this study, acts by inhibiting cyclooxygenase (COX) enzymes and reducing prostaglandin synthesis. The significant reduction in writhing response produced by the extract suggests that *Oxalis latifolia* Kunth may exert peripheral analgesic activity through inhibition of inflammatory mediators and prostaglandin synthesis. Similar mechanisms have been reported for flavonoid-rich medicinal plants including *Cnicus arvensis* [13].

The pharmacological activities observed in the present study may therefore be attributed to the presence of bioactive phytoconstituents such as flavonoids, alkaloids, tannins, and phenolic compounds in *Oxalis latifolia* Kunth.

Although the present study demonstrated promising antipyretic and analgesic activities, certain limitations should be considered. The study was restricted to preclinical experimental models, and the active phytoconstituents responsible for the observed effects were not isolated or characterized. Therefore, further studies involving phytochemical isolation, molecular mechanism evaluation, toxicity profiling, and clinical investigations are required to establish the therapeutic potential and safety of *Oxalis latifolia* Kunth in humans.

CONCLUSION

The present study demonstrated that the ethanolic extract of *Oxalis latifolia* Kunth possesses significant antipyretic and analgesic activities in experimental animal models. The extract produced dose-dependent pharmacological effects, with the 400 mg/kg dose showing greater efficacy,when compared with the 100 mg/kg dose and activity comparable to standard drugs.

The observed pharmacological activities may be attributed to the presence of bioactive phytoconstituents such as flavonoids, alkaloids, tannins, and phenolic compounds,

which are known to modulate inflammatory mediators and pain pathways. The findings of the study scientifically support the traditional use of *Oxalis latifolia* Kunth in the management of fever and pain.

Although the results are promising, further studies are required to isolate and characterize the active constituents responsible for the pharmacological effects, evaluate their molecular mechanisms, and establish the safety profile through detailed toxicological and clinical investigations. The present study suggests that *Oxalis latifolia* Kunth may serve as a potential source for the development of safer plant-based antipyretic and analgesic agents.

Acknowledgement

The authors are thankful to Visveswarapura Institute of Pharmaceutical Sciences, Bengaluru, Karnataka, for providing laboratory facilities and institutional support for carrying out the research work.

Contribution of Authors

Basavaraj K Somapur conducted the experimental work, data collection, statistical analysis, and manuscript preparation. Dr. Bharathi K N supervised the research work, reviewed the manuscript, and provided scientific guidance throughout the study.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this manuscript.

REFERENCES

1. Krishnan G, Murugesh P. Phytochemical analysis, anti microbial and anti-oxidant potential of *Oxalis latifolia Kunth*. Phytochem Anal. 2019 May;7:88-93.
2. Redfern J, Kinninmonth M, et al., Using soxhlet ethanol extraction to produce and test plant material for their antimicrobial properties. Journal of microbiology & biology education. 2014 May;15(1):45-6.
3. Ashok BK, Ravishankar B, et al. Antipyretic activity of Guduchi Ghrita formulations in albino rats. Ayu. 2010;31(3):367-70.
4. Subedi NK, Rahman SM, Akbar MA. Analgesic and antipyretic activities of methanol extract and its fraction from the root of Schoenoplectus grossus. Evid Based Complement Alternat Med. 2016;2016:3820704.
5. Fan SH, Ali NA, Basri DF. Evaluation of analgesic activity of the methanol extract from the galls of Quercus infectoria (Olivier) in rats. Evid Based Complement Alternat Med. 2014:2014:976764.
6. Udell ME, Ni J, Garcia Martinez A, et al. Tail Timer: A device for automating data collection in the rodent tail immersion assay. Plos one. 2021; 16(8):0256264
7. Gutiérrez-Cuevas J, Santos A, et al., Pathophysiological molecular mech-anisms of obesity: a link between MAFLD and NASH with cardiovascular diseases. International Journal of molecular sciences. 2021; 22(21): 11629.
8. Srivastava S, Singh P, et al. Anti-inflammatory, analgesic and antipyretic activities of aerial parts of Costus speciosus Koen. Indian J Pharm Sci. 2013;75(1):83.
9. Kumar V, Monika K, et al. Pharmacological evaluation of analgesic, anti-pyretic and anti-inflammatory activities of ethanolic root extract of Amaranthus caudatus. Journal of Drug Delivery and Therapeutics. 2023;13(1):11-16.
10. Botting RM. Mechanism of action of acetaminophen: is there a cyclooxygenase 3. Clin Infect Dis. 2000;31(5):S202-10.
11. Savva B (2023) The Mechanism of Antipyretic Drugs Regulation and its Importance. J Appl Pharm. 2023;15:394.
12. Anderson BJ. Paracetamol (Acetaminophen): mechanisms of action. Paediatr Anaesth. 2008;18(10):915-21.
13. Biddlestone L, Corbett AD, Dolan S et al. Oral administration of Ginkgo biloba extract, EGb- 761 inhibits thermal hyperalgesia in rodent models of inflammatory and post-surgical pain. Br J Pharmacol. 2007;151(2):285-91.
14. Ali A, Nasir A, Shah SW, Khalil AA, Ahn MJ, Shah SM et al. Evaluation of antinociceptive activity of Ilex dipyrena Wall. in mice. BMC Complement Altern Med. 2021;21(1):18.