

Comparative Evaluation of Analgesic Activity of Leaves and Fruits Extract of *Coccinia grandis*

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Abstract

Background: Pain is one of the most common clinical symptoms and is generally managed with conventional analgesic drugs; however, their prolonged use may be associated with adverse effects and other therapeutic limitations. Medicinal plants represent an important source of bioactive compounds with potential analgesic activity. *Coccinia grandis* is a traditionally used medicinal plant containing various phytoconstituents that may contribute to its pharmacological effects. Comparative evaluation of different plant parts may help identify the most effective source of analgesic constituents.

Objective: The present study aimed to comparatively evaluate the analgesic activity of leaves and fruits extracts of *Coccinia grandis* and to determine the relative analgesic potential of the two plant parts using established experimental models.

Methods: Fresh leaves and fruits of *Coccinia grandis* were collected, authenticated, shade-dried, and subjected to extraction using a suitable solvent. The obtained extracts were evaluated for preliminary phytochemical constituents. The analgesic activity of the leaf and fruit extracts was investigated in experimental animals using established nociceptive models, including the Eddy's hot plate and tail immersion tests. The effects of different doses of the extracts were compared with a standard analgesic drug. Reaction time was recorded at predetermined intervals following administration, and the analgesic response was evaluated statistically.

Results: Preliminary phytochemical investigation revealed the presence of several bioactive constituents, including flavonoids, alkaloids. Both leaf and fruit extracts demonstrated analgesic activity in the experimental models, as evidenced by an increase in pain-response latency compared with the control group. The leaf extract exhibited comparatively greater analgesic activity than the fruit extract, particularly at the higher tested dose. The observed activity was more pronounced with increasing dose and duration of treatment, supporting a dose-dependent analgesic response.

Conclusion: The present study demonstrates that both leaves and fruits of *Coccinia grandis* possess significant analgesic potential, with the leaf extract showing comparatively superior activity. The findings support the traditional medicinal importance of *Coccinia grandis* and suggest that its leaves may represent a promising source of analgesic phytoconstituents. Further phytochemical, mechanistic, toxicological, and clinical investigations are warranted to establish its therapeutic potential and safety.

Keywords: *Coccinia grandis*; leaves; fruits; analgesic activity; pain; Eddy's hot plate; tail immersion; medicinal plant.

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INTRODUCTION

1.1 Algesia:

An unpleasant sensory and emotional experience connected to, or similar to, existing or potential tissue

damage is called pain. It is regarded as the most common and archaic human experience. Because pain is subjective, it is shaped by the interaction of

nociceptive, cognitive, emotional, and social factors [1]. Acute pain serves as a protective mechanism against secondary injuries, infections, unpleasant stimuli, and dysfunctional homeostasis. Congenital insensitivity patients are unable to prevent harm, which may result in a tendency for self-mutilation. On the other hand, patients frequently seek medical attention primarily due to chronic pain, which is intrinsically uncomfortable. With prevalence rates ranging from 10% to 40%, it presents a significant socioeconomic burden on a global scale, a relatively low recovery rate of only 10% [2]. For clinical treatment, pain alleviation has been a necessary and significant criterion. An important link between basic disorders and secondary consequences is pain. Patients may have incapacity and a bad prognosis as a result of a dynamic and harmful interaction of biological, social, and psychological variables. Insomnia, sadness, anxiety, and poor social interaction are examples of pain-related psychiatric illnesses that might worsen the course of basic diseases. Significant increases in divorce, substance abuse, and suicide rates demonstrate how these pathological declines also have a detrimental effect on social relationships and self-esteem. [3]. The benefits of cancer treatment for survival are also compromised by chronic discomfort. Notably, suffering is not the same as pain. Numerous individual-specific factors influence the consequences of pain. For example, a person in a happy mental state may be more tolerant of pain, and massage can produce pleasant feelings even in the face of temporary discomfort. These illustrations demonstrate how the brain processes pain in a complex way and that it is more than just a biochemical phenomenon [4, 5].

There are many ways to relieve pain, and the foundation of analgesic treatment is the use of drugs. Over the past few years, the clinical use of analgesic medication combinations has significantly increased. Combining two or more medications with distinct modes of action is intended to create a synergistic interaction that will produce an adequate analgesic effect at lower dosages and, thus, lessen the severity and frequency of side effects [5]. Nowadays, a wide range of medication classes effectively supplement opioids or non-steroidal anti-inflammatory medications (NSAIDs) in the treatment of pain. However, we stress that the type of pain that is targeted (acute/chronic, inflammatory, neuropathic, cancer) determines whether a medicine combination is successful. For the clinical treatment of both acute and chronic pain, opioids have therefore often been used in conjunction with NSAIDs. Similarly, patients have been given a combination of NSAIDs and acetaminophen to relieve their discomfort.

Ultimately, using these combinations restricts how much medication a patient can be given. Nevertheless, not every combination of opioid and NSAID, opioid and acetaminophen, or NSAID and acetaminophen is clinically effective [6].

1.2 *Coccinia grandis*

Grown all over the Indian subcontinent, *Coccinia grandis*, or ivy gourd, is a member of the Cucurbitaceae family and is consumed as a vegetable. In India, it is usually referred to as kundru. Traditional medicine has utilized ivy as a home treatment for a number of illnesses. One of the main contributors to the therapeutic qualities is *Coccinia grandis* (Voigt). Wound healing, ulcers, jaundice, diabetes, antipyretic analgesics, anti-inflammatory, antitussive, antioxidant, anti-mutagenic, antibacterial, antiprotozoal, hepatoprotective, and expectorants are just a few of the medical uses for the plant parts of *C. grandis*, including roots, leaves, and fruits [26].

The vegetable *Coccinia grandis* belongs to the Cucurbitaceae family and is widely distributed over the Indian subcontinent. It is often known as kundru in India. Ivy has been used as a home remedy for a variety of ailments in traditional medicine. *Coccinia grandis* is one of the key elements of its medicinal properties. The plant parts of *C. grandis*, including its roots, leaves, and fruits, have numerous medical applications, including hepatoprotective, antipyretic, analgesic, anti-inflammatory, antitussive, antioxidant, anti-mutagenic, antibacterial, anti-protozoal, and expectorant. Ayurveda is India's oldest medical system and has been used for more than 5,000 years. Pain and inflammation are typical, non-specific symptoms of many illnesses. It is a defense mechanism that starts tissue mending and gets rid of harmful stimuli. Inflammatory cells are rich in a variety of endogenous mediators, including prostaglandin, which are widely distributed mediators that signal and regulate the cell and tissue response associated with inflammation [27].



**Leaves & Fruits of coccinia grandis****1.3 Plant Profile:**

Kindom	Plantae
Phyllum	Tracheophyta
Class	Magnoliopsida
Order	Cucurbitales
Family	Cucurbitaceae
Genus	<i>Coccinia</i>
Species	<i>grandis</i>
Botanical Name	<i>Coccinia grandis</i> (L.) Voigt

1.4 Scientific (Botanical) Synonyms:

Marathi	Tindora, Tondli
Hindi	Parval, Tindora, Tinda, Kundru
Danish	Skariagenagurk
English	Scarlet
Telagu	Dondakaya
Kannada	Tondekayi
Malayalam	Tendli, ghiloda, kundri, kowai
Chinese	Hong Qua

2 Materials and Methodology:**2.1 Experiment design:****2.1.1 Collection of plant materials (leaves and fruits):**

Fresh Leaves and fruits of *Coccinia grandis* were collected from the Rural area.

2.1.2 Authentication of plant materials (leaves and fruits):

Fresh leaves and fruits of *Coccinia grandis* were authenticated by Botanist.

2.1.3 Drying of plant materials (leaves and fruits):

Drying the plant material to remove the moisture from the plant material through the sunlight and room temperature. Washing the plant material to remove the soil, dirt, dust, from plant materials.

2.1.4 Powder the plant materials (leaves and fruits):

Grinding the plant materials is the process of converting dried plant parts into a fine powder of plant materials using a grinder.

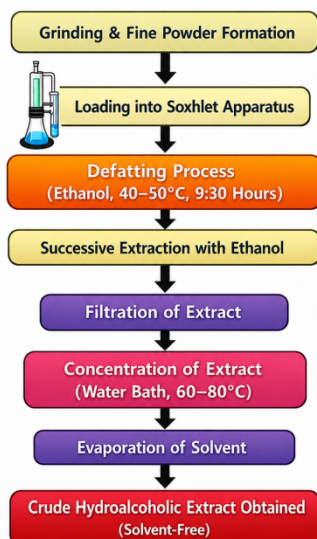
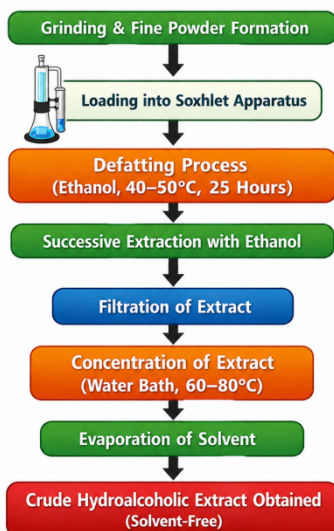
2.1.5 Total Ash value:

A clean and dry silica crucible is first heated in a muffle furnace at 300°C for 15 minutes. The crucible is then cooled in a desiccator for 10–15 minutes and accurately weighed. Next, 3 g of air-dried powdered drug is transferred into the crucible. The crucible containing the powdered drug is placed in a muffle furnace and incinerated at 450–600°C for 1 hour. Heating is continued until white ash is obtained. The crucible is then removed from the muffle furnace and cooled in a desiccator for 10–15 minutes. Finally, the crucible containing the ash is accurately weighed, and the total ash value (% w/w) is calculated using the appropriate formula.

Formula:

$$\text{Ash Value (\%)} = \frac{\text{Weight of Total Ash}}{\text{Weight of sample}} \times 100$$

2.1.6 Extraction of plant material powder (leaves & fruits) by Soxhlet Method:



Extraction process of *coccinia grandis* leaves and fruits

2.1.7 Thin layer chromatographic Profiling of Leaves Extract:

The TLC analysis of the *Coccinia grandis* extract was carried out using **Ethyl acetate: Methanol: Distilled water (12.5:5:2.5)** as the mobile phase. The **same extract** was chromatographed on **twenty five separate TLC** under identical experimental conditions to evaluate the reproducibility of the chromatographic method. The observed **R_f values ranged from 0.71 to 0.90**. The chromatograms showed distinct and well-resolved bands on all plates, indicating successful separation of the phytoconstituents. The close agreement among the R_f values suggests good reproducibility and consistency of the TLC method for the analysis of the extract.

Formula:

$$R_f = \frac{\text{Distance travelled by solute from origin line in cm}}{\text{Distance travelled by solvent from origin line in cm}}$$

2.1.8 Thin layer chromatographic Profiling of Fruits Extract:

The TLC analysis of the *Coccinia grandis* extract was carried out using **Toluene: Ethyl acetate: Formic acid (10:8:2)** as the mobile phase. The **same extract** was chromatographed on **TLC** under identical experimental conditions to evaluate the reproducibility of the chromatographic method. The observed **R_f values ranged from 0.64 to 0.74**. The chromatograms showed distinct and well-resolved

bands on all plates, indicating successful separation of the phytoconstituents. The close agreement among the R_f values suggests good reproducibility and consistency of the TLC method for the analysis of the extract.

Formula:

$$R_f = \frac{\text{Distance travelled by solute from origin line in cm}}{\text{Distance travelled by solvent from origin line in cm}}$$

3. In-vivo studies:

3.1 Eddy hot plate method

This method's basic idea is based on thermal stimulus. When an animal's paw is heated, pain is introduced. The rat will exhibit behaviors like paw licking, leaping, nicking, etc. because it is in discomfort. The apparatus's temperature is kept between 55 and 60°C.

Procedure:

Healthy rats weighing 150–200 g are selected for the study and their body weights are recorded. The test drug is administered by the oral route, followed by a waiting period of 30 minutes to allow adequate absorption of the drug. The Eddy's hot plate apparatus is then set to the required temperature, and each rat is carefully placed on the hot plate. The animal's response, such as paw licking or jumping, is observed, with the reaction generally occurring within 6–10 seconds. The reaction time is recorded at predetermined intervals of 30, 60, 90, 120, 150, and 180 minutes after drug administration. The recorded reaction times are used for the evaluation of analgesic activity.



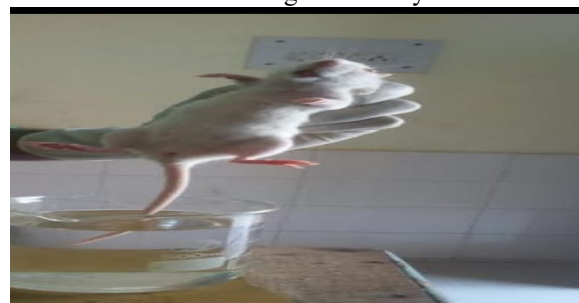
Eddy hot plate

3.2 Tail immersion method:

This technique, which also employs thermal stimulus as a principle and uses hot water as the source of heat, is used to test the analgesic effect in Wistar albino rats via caudal immersion. The animal is housed in a cage with roughly one-third of its tail hung. It is then submerged in water that is between 55 and 60 degrees Celsius until it pulls its tail.

Procedure:

Healthy rats weighing 150–200 g are selected for the study, and their body weights are recorded. A warm water chamber is prepared and maintained at the required temperature. The test drug is administered by the oral route, after which the animal is placed carefully in a restraining cage. Approximately 5 cm of the distal portion of the tail is marked, and the marked portion is immersed in the warm water chamber to perform the tail immersion test. The animal is observed for the withdrawal response, which generally occurs within 6–10 seconds as the rat withdraws its tail from the warm water. The reaction time is recorded at predetermined intervals of 30, 60, 90, 120, 150, and 180 minutes after drug administration. The recorded reaction times are used for the assessment of analgesic activity.



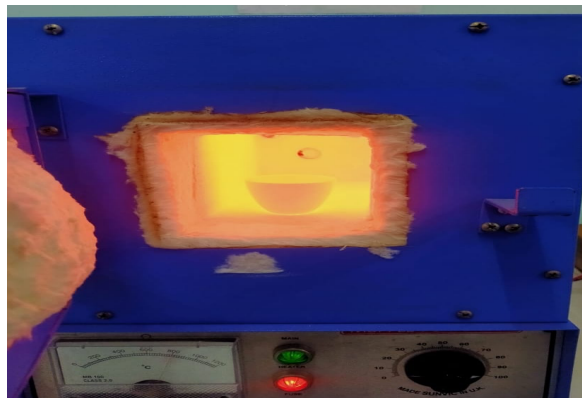
Tail immersion method

4. Result & Discussion:

4.1 Ash Value of *Coccinia grandis* leaves:

To evaluate the quality and purity of the crude medication, the ash value of powdered *Coccinia grandis* leaves was determined. Three grams of powdered dry leaves were precisely weighed and put through the usual ash value determination process for the analysis. The plant material contained inorganic components and naturally existing mineral matter, as shown by the total ash value of 23.66%. The majority of the inorganic residues were soluble in acid and constituted physiological ash components, as shown by the acid-soluble ash value of 0%. The lack of siliceous elements including sand, soil, and other earthy pollutants was shown by the water soluble ash value of 12.00% and the water insoluble ash value of 11.66%. These findings show that there was minimal inorganic adulteration and that the flower powder had good purity. Consequently, *Coccinia grandis* leaves can be identified, authenticated, quality controlled, and standardized for future phytochemical and

pharmacological research using the ash value parameters found in this work.



Muffle Furnance

4.2 Ash Value of *Coccinia grandis* fruits:

To evaluate the purity and quality of the crude medication, the ash value of powdered *Coccinia grandis* fruits was determined. Two grams of powdered dried fruit were precisely weighed and put through the usual ash value determination process for the analysis. The plant material contained inorganic components and naturally occurring mineral matter, as shown by the total ash value of 1%. Three grams of powdered dried fruit were precisely weighed and put through the normal ash value calculation process. It was discovered that the overall ash value was 3%.

4.3 Solubility test of *Coccinia grandis* leaves and fruits

S. No	Drug	Hot ethanol	Hot water	Methanol	Ethanol	Water	Acetone
1	<i>Coccinia grandis</i> (leaves)	Soluble	Soluble	Sparingly Soluble	Sparingly Soluble	insoluble	Insoluble
2	<i>Coccinia grandis</i> (fruits)	Soluble	Soluble	Sparingly Soluble	Sparingly Soluble	Insoluble	Sparingly Soluble

4.4 Phytochemical Screening (leaves extract):

The preliminary phytochemical screening of the leaves and fruits extract revealed the presence of various bioactive constituents, including flavonoids, alkaloids, and terpenoids, which may

contribute to the therapeutic efficacy of the developed formulation.

4.4.1 Phytochemical screening of *Coccinia grandis* leaves extract

S. No	Drug	Parts	Phytochemical Constituents	Chemical tests	Observation	Result
1.	<i>Coccinia grandis</i>	Leaves	Alkaloids	Mayer's test	Dark yellow	++
2.	<i>Coccinia grandis</i>	Leaves	Alkaloids	Dragendorff's test	Yellow	++
3.	<i>Coccinia grandis</i>	Leaves	Alkaloids	Hager's test	Yellow Crystalline	++ +
4.	<i>Coccinia grandis</i>	Leaves	Alkaloids	Wager's test	Dark Brown	++ +
5.	<i>Coccinia grandis</i>	Leaves	Flavonoids	Shinoda test	Crimson red	++ +
6.	<i>Coccinia grandis</i>	Leaves	Flavonoids	Alkaline test	Dark yellow	++
7.	<i>Coccinia grandis</i>	Leaves	Flavonoids	Acidic test	Dark yellow	+
8.	<i>Coccinia grandis</i>	Leaves	Terpenoids	Salkowski test	Absent	-

(+++ = Strongly present, ++ = Moderate present, + = Weekly present, - = Absent)

4.4.2 Phytochemical screening of *Coccinia grandis* fruits extract

S.	Dru	Pa	Phytoc	Chemic	Obser	Re
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No	g	rts	hemica l Constit ients	als tests	vation	sul t
3.	<i>Coc cini a gra ndis</i>	Fr uit s	Alkaloi ds	Mayer's test	Light yello w	++ +
4.	<i>Coc cini a gra ndis</i>	Fr uit s	Alkaloi ds	Dragon roff,s'tes t	Light orang e	++
3.	<i>Coc cini a gra ndis</i>	Fr uit s	Alkaloi ds	Hager's test	Yello w	++ +
4.	<i>Coc cini a gra ndis</i>	Fr uit s	Alkaloi ds	Wager' test	Yello w	+
5.	<i>Coc cini a gra ndis</i>	Fr uit s	Flavan oids	Shinoda test	Dark brown	++
6.	<i>Coc cini a gra ndis</i>	Fr uit s	Flavan oids	Alkaline test:	Light yello w	++ +
7.	<i>Coc cini a gra ndis</i>	Fr uit s	Flavon oids	Acidic test	Light yello w	++
8.	<i>Coc cini a gra ndis</i>	Fr uit s	Terpen oids	Salkows ki test	Green ish	++

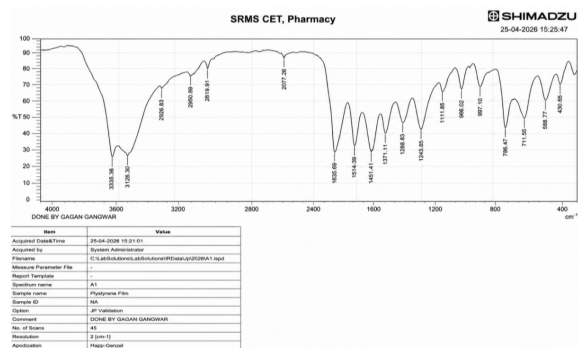
(+++ = Strongly present, ++ = Moderate present, + = Weekly present, - = Absent)

4.5 Fourier Transform Infrared (FTIR):

FTIR, or Fourier-transform infrared spectroscopy, is an analytical technique that uses infrared light to identify materials by measuring their absorption or emission of infrared radiation. When IR radiation passes through a sample, molecules absorb specific frequencies, creating a unique fingerprint spectrum that reveals its chemical composition and structure.

FTIR is used in a wide range of fields, including chemistry, material science, and pharmaceuticals, for tasks like structural analysis, identifying contaminants, and quality control.

4.5.1 FTIR of leaves

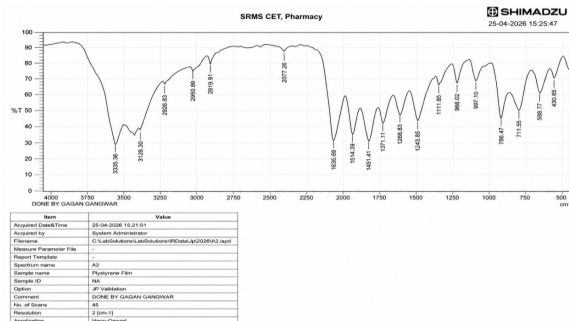


S.No	Peak Range (cm ⁻¹)	Functional Group	Interpretation
1.	3400-3200	O-H	Hydroxy
2.	3350-3200	N-H	Amine
3.	2955-2850	C-H	Aliphatic
4.	1330-1240	C-N	Alkaloids
5.	1260-1050	C-O	Alcohol

FTIR Characteristic peaks and functional groups assignments of *Coccinia grandis* leaves

4.5.2 FTIR of fruits

Comparative Evaluation of Analgesic Activity of Leaves and Fruits Extract of *Coccinia grandis*



S.No	Peak Range (cm ⁻¹)	Functional Group	Interpretation
1.	3400-3300	O-H	Hydroxy
2.	1660-1655	C=O	Carbonyl
3.	1610-1600	C=C	Aromatic
4.	1200-1000	C-O-C	Stretching the glycosidic sugar moiety
5.	1070-1000	C-O	Stretching
6.	3400-3250	O-H	Phenolic stretching
7.	1660-1650	C=O	Conjugated stretching
8.	1610-1550	C=C	Stretchy aromatic
9.	1320-1250	C-O	Phenolic stretching
10.	1150-950	C-O	Stretching

FTIR Characteristic peaks and functional groups assignments of *Coccinia grandis* fruits

5. Experimental Result:

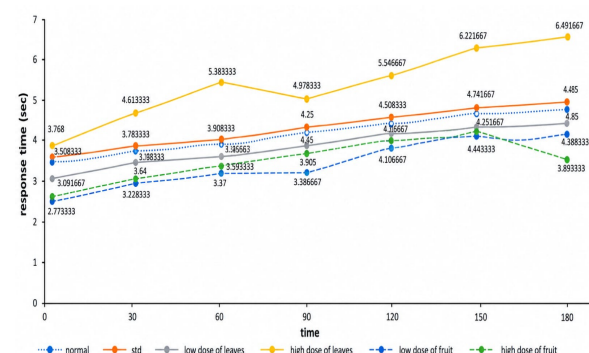
5.1 Tail immersion method:

Statistical evaluation of tail immersion method for analgesic activity of *coccinia grandis* leaves & fruits

Time	Normal	Standard	Low dose of leaves	High dose of leaves	Low dose of fruits	High dose of fruits
Pre	3.508 333	3.508 333	3.09 1667	3.76 8	2.69 1667	2.77 3333
30 min	3.188 3333	3.783 333	3.46 5	4.61 3333	3.22 8333	3.3

n						
60 min	3.186 663	3.908 333	3.64	5.38 3333	3.37	3.59 3333
90 min	4.45	4.25	3.84 6667	4.97 8333	3.38 6667	3.90 5
120 min	4.116 667	4.508 333	4.14 5	5.54 6667	4.10 6667	4.30 6667
150 min	4.251 667	4.471 667	4.25 1667	6.22 1667	4.54	4.44 3333
180 min	4.85	4.485	4.38 8333	6.49 1667	4.61 8333	3.89 3333

5.1.1 Pharmacological Comparison between Leaves and Fruits on Tail immersion method



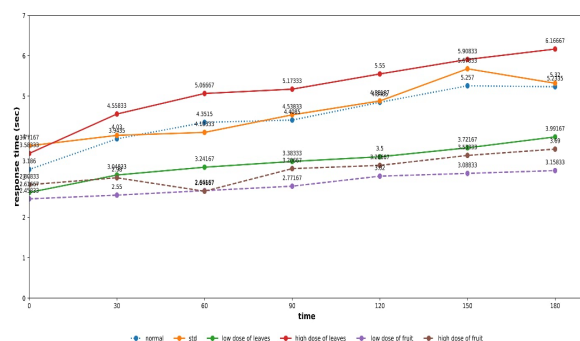
5.2 Eddy hot plate method:

Statistical evaluation of eddy hot plate method for analgesic activity of *coccinia grandis* leaves & fruits

Time	Normal	Standard	Low dose of leaves	High dose of leaves	Low dose of fruits	High dose of fruits
Pre	3.18 6	3.771 667	2.45 833	3.58 333	2.45 833	2.61 667
30 min	3.94 35	4.03	2.98	4.55 833	2.55	3.04 833
60 min	4.35 15	4.103 333	3.24 167	5.06 667	2.64 667	2.64 667
90 min	4.40 85	4.538 33	3.38 333	5.17 333	2.77 167	3.20 667
120 min	4.84 85	4.881 667	3.5	5.55	3.02	3.28 667

n						
150						
mi	5.25	5.678	3.71	5.90	3.08	3.53
n	7	333	67	833	833	333
180						
mi	5.23		3.99	6.16	3.15	
n	35	5.32	167	667	833	3.69

5.2.1 Pharmacological Comparison between Leaves and Fruits on Eddy hot plate method



Major finding

A comparison showed that the extract from the **leaves had a more potent analgesic effect than the extract from the fruits**. The higher concentration of bioactive components in the leaves, such as flavonoids, alkaloids, and triterpenoids, which are known to affect pain perception by modifying nociceptive pathways, may be the cause of this variation in activity.

Eddy hot plate immersion

Tail

Plant part	Low dose	High dose	Low dose	High dose
Leaves	4.43	6.45	5.1	5.73
Fruits	3.02	5.15	2.54	3.08

Novelty of Research

The current study presents a comparative method for assessing the analgesic potential of several *Coccinia grandis* parts, particularly its leaves and fruits, which have not been thoroughly investigated in previous studies. The overall pharmacological characteristics of the plant have been the main focus of earlier research, but direct comparisons of the effectiveness

of the plant's different portions under comparable experimental conditions have received less attention.

This topic has not yet been the subject of a comparison study, and there are few review or research publications that concentrate on its comparative assessment. In order to fill this research vacuum, the current study was conducted.

Additionally, by offering experimental support for the use of *Coccinia grandis* in pain therapy, this study helps close the gap between conventional medical claims and scientific confirmation. The discovery that leaf extract has a stronger analgesic effect creates new opportunities for phytochemical and medication development research. It reveals that the leaves have a greater analgesic capability than the fruits, which has not been conclusively shown in earlier research.

The comparative design, methodological consistency, and contribution to the identification of particular plant parts with increased therapeutic potential which may aid in the creation of safer, plant-based analgesic agents are what make this research novel overall.

Future Scope of this study

Additionally, to increase stability, bioavailability, and patient compliance, formulation development of *Coccinia grandis*-based analgesic products, such as tablets, capsules, or herbal preparations, can be investigated.

The active ingredients of **Zingiber officinale** and *Coccinia grandis* leaves can be combined to create a formulation in the future. This combination may effectively relieve pain and have synergistic analgesic effects. To separate bioactive molecules and assess the formulation's safety and effectiveness, more research is needed.

In the future, bioactive chemicals can be identified and quantified using sophisticated analytical techniques like **Gas chromatography**, **HPLC**, and **HPTLC**, which could aid in the creation of more potent pain relief formulations. In the future, the analgesic properties of *Coccinia grandis* leaves may be compared to those of other medicinal plants.

Its analgesic effectiveness may also be improved and its application in pain management expanded by comparative research with other medicinal plants and combination formulations.

Discussion

Eddy's hot plate and tail immersion methods demonstrated the analgesic potential of *Coccinia grandis* leaf and fruit extracts through centrally mediated mechanisms. Both extracts significantly increased reaction time, indicating pain-relieving activity. The leaf extract showed greater analgesic efficacy than the fruit extract, possibly due to its higher concentration of bioactive constituents such as flavonoids, alkaloids, and triterpenoids. A dose-dependent increase in activity was observed, with 400 mg/kg producing a greater effect than 200 mg/kg. Although the extracts were less effective than the standard drug, the findings support the traditional use of *Coccinia grandis* for pain management and suggest its potential as a natural analgesic agent.

Conclusion

The present study demonstrated that *Coccinia grandis* leaf extract possesses greater analgesic potential than the fruit extract. The higher activity of the leaf extract may be attributed to its richer concentration of bioactive phytoconstituents, including flavonoids, alkaloids, and phenolic compounds, which may act through central and peripheral analgesic pathways. In both Eddy's hot plate and tail immersion tests, the leaf extract produced a greater increase in reaction time compared with the fruit extract, indicating superior pain-relieving activity. These findings provide scientific support for the traditional use of *Coccinia grandis* leaves in pain management and highlight their potential for further pharmacological investigation and analgesic drug development.

References

1. Raja, S. N. et al. The revised International Association for the Study of Pain definition of pain, concepts, challenges, and compromises, *Pain* 161, 1976–1982 (2020).
2. Basbaum, A. I, Bautista, D. M, Scherrer, G. & Julius, D. Cellular and molecular mechanisms of pain, *Cell* 139, 267–284 (2009).
3. Julius, D. & Basbaum, A. I. Molecular mechanisms of nociception, *Nature* 413, 203–210 (2001).
4. Yang, D. et al. Nociceptor neurons direct goblet cells via a CGRP-RAMP1 axis to drive mucus production and gut barrier protection, *Cell* 185, 4190–4205, e4125 (2022).
5. Goodwin, G. & McMahon, S. B. The physiological function of different voltage-gated sodium channels in pain, *Nat. Rev. Neurosci.* 22, 263–274 (2021).

6. Steglitz, J, Buscemi, J. & Ferguson, M. J. The future of pain research, education, and treatment, a summary of the IOM report "Relieving pain in America, a blueprint for transforming prevention, care, education, and research". *Transl. Behav. Med* 2, 6–8 (2012).
7. Dahlhamer, J. et al. Prevalence of chronic pain and high-impact chronic pain among adults United States, 2016, *MMWR Morb. Mortal. Wkly Rep.* 67, 1001–1006 (2018).
8. Fayaz, A, Croft, P, Langford, R. M, Donaldson, L. J. & Jones, G. T. Prevalence of chronic pain in the UK, a systematic review and meta-analysis of population studies, *BMJ Open* 6, e010364 (2016).
9. Goldberg, D. S. & McGee, S. J. Pain as a global public health priority, *BMC Public Health* 11, 770 (2011).
10. Morasco, B. J. et al. Systematic review of prevalence, correlates, and treatment outcomes for chronic non-cancer pain in patients with comorbid substance use disorder, *Pain* 152, 488–497 (2011).
11. Jensen TS, Finnerup NB, Allodynia and hyperalgesia in neuropathic pain, clinical manifestations and mechanisms, *Lancet Neurology*, 2014;13:924–935.
12. Yam MF, Loh YC, Tan CS, et al. General pathways of pain sensation and the major neurotransmitters involved in pain regulation, *International Journal of Molecular Sciences*, 2018;19(8):2164, doi:10.3390/ijms19082164.
13. Fillingim RB, Individual differences in pain, understanding the mosaic that makes pain personal, *Pain*, 2017;158(Suppl 1):S11–S18, doi:10.1097/j.pain.0000000000000775.
14. Gatchel RJ, Peng YB, Peters ML, Fuchs PN, Turk DC, The biopsychosocial approach to chronic pain, scientific advances and future directions. *Psychological Bulletin.* 2007;133(4):581–624. doi:10.1037/0033-2909.133.4.581.
15. Woolf CJ. Central sensitization, implications for the diagnosis and treatment of pain, *Pain*, 2011;152(3 Suppl),S2–S15, doi:10.1016/j.pain.2010.09.030.
16. Hadjiat Y, Arendt-Nielsen L, Digital health in pain assessment, diagnosis, and management: overview and perspectives, *Frontiers in Pain Research*, 2023;4:1097379, doi:10.3389/fpain.2023.1097379.
17. Gatchel RJ, McGeary DD, McGeary CA, Lippe B, Interdisciplinary chronic pain management, past, present, and future, *American Psychologist*, 2014;69(2):119–130. doi:10.1037/a0035514.
18. Kamper SJ, Apeldoorn AT, Chiarotto A, et al. Multidisciplinary biopsychosocial rehabilitation for

- chronic low back pain, Cochrane systematic review and meta-analysis, *BMJ*, 2015;350:h444, doi:10.1136/bmj.h444.
19. Machado GC, Abdel-Shaheed C, Underwood M, Day RO, Non-steroidal anti-inflammatory drugs (NSAIDs) for musculoskeletal pain, *BMJ*, 2021;372:n104, doi:10.1136/bmj.n104.
20. Robb CT, Goepp M, Rossi AG, Yao C, Non-steroidal anti-inflammatory drugs, prostaglandins, and COVID-19, *British Journal of Pharmacology*, 2020;177(21):4899–4920, doi:10.1111/bph.15206.
21. Huo L, Liu G, Deng B, et al. Effect of use of NSAIDs or steroids during the acute phase of pain on the incidence of chronic pain, a systematic review and meta-analysis of randomised trials, *Inflammopharmacolog*, 2024;32(2):1039–1058, doi:10.1007/s10787-023-01405-8.
22. Paul AK, Smith CM, Rahmatullah M, et al. Opioid analgesia and opioid-induced adverse effects: a review, *Pharmaceuticals*, 2021;14(11):1091, doi:10.3390/ph14111091.
23. Hamre HJ, Glockmann A, von Ammon K, Riley DS, Efficacy of homeopathic treatment, systematic review of meta-analyses of randomised placebo-controlled homeopathy trials for any indication, *Systematic Reviews*, 2023;12:191, doi:10.1186/s13643-023-02313-2.
24. Mathie RT, Ramparsad N, Legg LA, et al. Randomised, double-blind, placebo-controlled trials of non-individualised homeopathic treatment, systematic review and meta-analysis, *Systematic Reviews*, 2017;6:63, doi:10.1186/s13643-017-0445-3.
25. Khan TS, Shaikh S, Nazar SM, et al. Unani medicine for inflammation, a review, *International Journal of Unani and Integrative Medicine*, 2024;8(2):92–95, doi:10.33545/2616454X.2024.v8.i2b.284.
26. Sutradhar, B. K, Islam, M. J, Shoyeb, M. A, Khaleque, H. N, Sintaha, M, Noor, F. A, & Rahmatullah, M. (2011), An evaluation of antihyperglycemic and antinociceptive effects of crude methanol extract of *Cocciniagrandis* (L.) J. Voigt, (Cucurbitaceae) leaves in Swiss albino mice, *Advances in Natural and Applied Sciences*, 5(1), 1-5.
27. Nagare, S, Deokar, G. S, Nagare, R, & Phad, N. (2015). Review on *Cocciniagrandis* (L.) voigt (Ivy Gourd), *World journal of pharmaceutical research*, 4(10), 728-743.
28. Pekamwar, S. S, Kalyankar, T. M., & Kokate, S. S. (2013), Pharmacological activities of *Cocciniagrandis*, *J Appl Pharm Sci*, 3(05), 114-119.
29. Ramachandran, A, Prasath, R, & Anand, A, (2014), The medical uses of *Cocciniagrandis* L, Voigt, a review, *Int J Pharmacogn*, 1, 681-690.
30. Varuna, V. (2018), *Cocciniagrandis* (L) Voigt-review, *World J. Pharm. Res*, 7(12), 188-200.
31. Beera, A. M, Nori, L. P, & Seethamraju, S. M. (2022), Nutritional and Therapeutic Potential of *Coccinia Grandis* (L) Voigt, a Wonder Vegetable, *Pharma Times*, 54(07), 7.
32. Putra, I. M. W. A, Fakhrudin, N, Nurrochmad, A, & Wahyuono, S. (2021), Antidiabetic activity of *Cocciniagrandis* (L.) Voigt, Bioactive constituents, mechanisms of action, and synergistic effects, *Journal of applied pharmaceutical science*, 12(1), 041-054.
33. Shifali, T, Hemlata, K., & Gitika, C. (2021), *Cocciniaindica* (Kundru), A magical herb with antidiabetic potential, *International Journal of Ayurveda and Pharma Research*, 19-26.
34. Rao, K. N. V. Updated Review on Pharmacognosy, Phytochemistry & Pharmacological Studies of *CocciniaIndica*.
35. Hasan, M. F, & Sikdar, B, (2016). Screening of antimicrobial, cytotoxic and pesticidal activities of *Cocciniagrandis* (L.) Voigt, *J Microbiol Biotech Food Sci*, 5(6), 584-588.
36. Hossain, M. S, Jahan, I, Islam, M, Nayeem, J, Anzum, T. S, Afrin, N. A, & Hasan, M. K. (2024), *Cocciniagrandis*, Phytochemistry, pharmacology and health benefits, *Clinical Traditional Medicine and Pharmacology*, 5(2), 200150.
37. Meenatchi, P, Purushothaman, A., & Maneemegalai, S, (2017), Antioxidant, antiglycation and insulinotrophic properties of *Cocciniagrandis* (L.) in vitro, Possible role in prevention of diabetic complications, *Journal of Traditional and Complementary Medicine*, 7(1), 54-64.
38. Raje, V. N, Yadav, A. V, & Shelar, P. A. (2013), *Cocciniaindica* A Phytopharmacological Review, *Research Journal of Pharmacognosy and Phytochemistry*, 5(1), 9-14.