RESEARCH PAPER

Pharmacological Evaluation of the Analgesic Activity of *Zingiber officinale* Rhizome Extract in Experimental Rats

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Abstract
Background: Pain is a common disease-associated symptom of tissue damage or localized inflammation, which greatly contributes both qualitatively and quantitatively to the health burden and to the quality of life of patients all over the world. While non-steroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics are still considered the standard treatments for pain, these drugs are often linked to gastrointestinal toxicity, renal issues, cardiovascular side effects, tolerance, and dependence. As such, it has been interested in the identification of plant-based, more effective, and safer analgesics to improve the profile of the analgesics. Zingiber officinale Roscoe (ginger), a medicinal plant with extensive application in traditional medicine, is known to possess many bioactive phytoconstituents, such as gingerols, shogaols, paradols, and zingerone, that are said to have anti-inflammatory, antioxidant, and analgesic properties.
Methodology: The objective of the present research was to study the peripheral and central analgesic activity of hydroalcoholic extract of Zingiber officinale rhizome in a set of validated models for peripheral nociception and central effect in experimental Wistar rats.
Materials and Methods: The rhizomes of Zingiber officinale were authenticated, shade-dried, powdered, and extracted with a hydroalcoholic solvent. Preliminary phytochemical screening was conducted to find the different major classes of bioactive compounds. Before efficacy studies, acute oral toxicity was assessed based on OECD guideline 423. All the rats were randomly divided into 4 groups with 6 rats in each group: Vehicle control, Standard dose of drug, Low dose of extract, and High dose of extract. This peripheral analgesic activity was measured by investigating writhing induced by the administration of acetic acid, while the central analgesic effect was determined by the hot plate and tail flick test methods. Diclofenac sodium and Morphine were used as positive reference drugs in the peripheral and central analgesic models, respectively. All the experimental results were presented as Mean ± SEM and analyzed by one-way ANOVA and Tukey's multiple comparison test, with a p-value of < 0.05 considered statistically significant.
Result: The hydroalcoholic extract showed the presence of phenolics, flavonoids, tannins, terpenoids, and other bioactive phytoconstituents. The acute toxicity test results also revealed that the extract did not cause any deaths or behavioral changes at the dosages tested. The results of the acetic acid-induced writhing model showed that the extract could significantly reduce the number of writhes, in a dose-dependent manner, as compared to the control group ($p < 0.001$). Likewise, significant prolongation of reaction latency was observed in both the hot plate and tail flick tests, attributes of central analgesic activity. The higher dose demonstrated higher levels of analgesic activity and effects similar to those of the standard analgesics. Pharmacological activity observed is probably due to its inhibitory effect on prostaglandin synthesis, its central and peripheral anti-nociceptive effect, its anti-inflammatory effect, and its antioxidant effect.
Conclusion: The following results showed that the hydroalcoholic rhizome extract of Zingiber officinale exerts considerable peripheral and central analgesic (anti-inflammatory activity) in experimental rats. The dose-dependent effect on the analgesic modulation seems to be due to the synergistic effect of the presence of gingerols, shogaols, and related phytoconstituents. The findings were suggestive of traditional roles of ginger in pain management and indicated that Zingiber officinale can be a potential source of plant-based alternative pain management agents without any side effects. Hence, there is a need for further pharmacological investigations, mechanistic studies on a molecular basis, and clinical trials that are well-designed to validate its therapeutic potential.

Keywords: *Zingiber officinale*; Analgesic activity; Ginger; Wistar rats; Acetic acid-induced writhing; Hot plate test; Tail flick test; Herbal analgesics.
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1. Introduction

Pain is a complex phenomenon with a physiological and psychological basis that acts as a protective mechanism against real or potential tissue damage. The International Association of the Study of Pain (IASP) defines pain as something that is "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage. In contrast to the protective function that acute pain has in maintaining tissue integrity, chronic and persisting pain can become pathological and is a significant contributor to disability, diminished quality of life, emotional distress, decreased productivity, and expenditures on the healthcare system. Pain-related disorders still constitute one of the most frequent reasons for seeking medical advice all over the world, highlighting the importance of effective and safe therapeutic approaches. The submitted dissertation also points to pain as being a significant clinical issue and also points to the need for safer analgesics.

The perception of pain is a complex process that requires a complex interaction between immunoregulatory events occurring in peripheral nociceptors, the spinal cord, ascending sensory pathways, and higher levels of the cortex. When tissue is damaged, inflammatory mediators are released from the tissue, such as prostaglandins, leukotrienes, bradykinin, histamine, serotonin, tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), and substance P. These mediators activate peripheral nociceptors and cause hyperalgesia and allodynia. They are then transmitted via Aδ fibers and C fibers to the dorsal horn of the spinal cord, where additional modulation takes place before activating nerves that transmit the sensations to the thalamus and cerebral cortex, where conscious perception occurs. Over-activation of these pathways can cause central sensitization that can create chronic pain states that are hard to control therapeutically. Ideally, effective analgesics will therefore act both peripherally on the inflammatory pathways as well as act centrally on the nociceptive pathways.

Pharmacological management of pain is mainly focused on non-steroidal anti-inflammatory drugs (NSAIDs), opioid analgesics, and supplemental drugs like antidepressants and anticonvulsants. NSAIDs are used to treat pain primarily by blocking prostaglandin synthesis through the action of cyclooxygenase (COX), but with extended use, there are gastrointestinal ulceration, renal dysfunction, hepatotoxicity, cardiac issues, and bleeding problems. Moderate to severe pain is treated with opioids but comes with the disadvantages of breathing problems, constipation, tolerance, physical dependence, and drug abuse following the use of these drugs. With the rise in opioid misuse and the negative impacts arising from the use of traditional drugs for pain relief, there has been an intense search for alternative options using natural sources (Daily et al., 2023; Paudel et al., 2025).

Over the centuries, medicinal plants have been important sources of therapeutic agents and are still playing their own important role in contemporary drug discovery. Almost 80% of the world's population receives at least some primary health care from herbal medicines, especially in developing nations. Botanical preparations are used widely for pain and inflammatory disorders in traditional medicinal systems like Ayurveda, Unani, Siddha, and Traditional Chinese Medicine. Medicinal plants usually have multiple pharmacological actions because they contain many phytochemicals that often have complex molecular and pharmacological effects, unlike synthetic drugs, which are often more focused and act on a single molecular pathway. Therefore, compounds derived from plants seem to be ideal targets for the production of more effective pain-relieving drugs without the undesirable side effects associated with traditional narcotics.

The ginger plant Zingiber officinale Roscoe (family: Zingiberaceae) has gained considerable scientific interest since it is known for having a wide range of phytochemical activities. Ginger is popular and commonly grown in tropical and subtropical areas and used traditionally in the treatment of arthritis and musculoskeletal disorders, headache, dysmenorrhea, gastrointestinal disorders, postoperative pain, and inflammatory diseases. Ginger's rhizome is regarded as the most important for medicinal use, containing various biologically active compounds like 6-gingerol, 8-gingerol, 10-gingerol, 6-shogaol, paradols, zingerone, zingiberene, flavonoids, and volatile oils. These phytochemicals are highly anti-inflammatory, antioxidant, antimicrobial, antipyretic, and analgesic agents with several molecular actions. These constituents are described in the dissertation, and they are important to dealing with pain.

Experimental and clinical studies have shown that ginger has analgesic properties and is capable of inhibiting cyclooxygenase (COX-1 and COX-2) and lipoxygenase (LOX) enzymes, which are involved in the production of prostaglandins and leukotrienes, which play a role in the transmission of inflammatory pain. Furthermore, ginger has anti-inflammatory properties due to its ability to suppress production of pro-inflammatory cytokines, including tumour necrosis factor alpha (TNF-α), interleukin-1beta (IL-1β), and interleukin-6 (IL-6); numerous anti-oxidative properties from free radical scavenging and influences of transient receptor potential vanilloid-1 (TRPV1) channels and serotonergic and opioid neurotransmission. Present evidence for the multimodal mechanisms by which ginger can reduce some forms of inflammatory pain (at the periphery) as well as centrally mediated nociceptive responses, thus elevating its potential as

a source to develop drugs against pain. Additionally, recent systematic reviews and meta-analyses have backed up that the ginger supplement has a significant effect on decreasing inflammatory biomarkers and enhancing pain outcomes among patients with OA, dysmenorrhea, migraine, postoperative pain, and exercise-induced muscle injury.

Various methods for extracting the rhizome, differences in its phytochemical composition, dosage regimens, variability in the experimental models and study designs used, have led to conflicting evidence on whether there is an analgesic effect of Zingiber officinale. Moreover, its peripheral and central analgesic activity has not been compared on predesigned models and nonstandardized protocols. There is a need to standardize extraction processes, phytochemical characterization, and validated animal models in order to produce reproducible scientific evidence to support its therapeutic use.

Hence, the present study was conducted to investigate the Analgesic activity of the hydroalcoholic extract of the rhizome of Zingiber officinale in the Wistar rat peripheral and central nociception model, such as the acetic acid-induced writhing test, hot plate test, and tail flick test. Another objective was to select the drugs widely used as analgesics and then compare the analgesic activity of the extract, and to scientifically support the use of ginger in the management of pain. The results could be useful for making effective, inexpensive, and safe plant-based pain relievers for future use to treat patients.

2. Materials and Methods

2.1 Study Design

The present investigation was set as a randomized controlled experimental animal study to assess the analgesic effect of rhizome hydroalcoholic extract from Zingiber officinale in both validated models of peripheral and central nociception. The study was performed in an internationally accepted laboratory, and the guidelines in India laid down by the Committee for Supervision and Control of Experiments on Animals (CPCSEA) have been followed. Experiments were performed with approval from the Institutional Animal Ethics Committee (IAEC), before the study was initiated. The overall design of the experiments was plant authentication, preparation of extracts, preliminary phytochemical screening, acute oral toxicity study, analysis of analgesic activity, and statistical analysis.

2.2 Collection and Authentication of Plant Material

Fresh rhizomes of the Zingiber officinale Roscoe (Family: Zingiberaceae) were purchased from a certified herb gardener/organic farm locally. Rhizomes were screen-picked to remove the fungi, insects, and physical damage and to get the optimum quality of phytochemicals. The gathered material was carefully washed under running tap water and then rinsed with distilled water to clean off soil and unwanted material. The botanical identification of the plant materials was done by a competent taxonomist, and a voucher specimen was kept in the herbarium of the institution for reference. The pharmacological investigation was conducted with proper authentication, which allowed for the surety of identity, purity, and reproducibility of results.

2.3 Preparation of Hydroalcoholic Extract

To prevent loss of thermolabile constituents, the authenticated rhizomes were cut into small pieces and were shade dried under ambient temperature to a constant weight. This dry material was ground and sieved to make a homogeneous coarse powder.

Twenty-four hours was the time of extraction of approximately 500 g of powdered rhizome done in a Soxhlet using a hydroalcoholic solvent (20% ethanol: 80% distilled water). The filtrated extract was concentrated under reduced pressure with the help of a rotary vacuum evaporator at less than 45°C on Whatman No. 1 filter paper. The concentrated extract was then vacuum-dried to get a semi-solid mass in a vacuum desiccator.

The percentage yield of the extract was the yield the equation below was used to calculate:

Use the following equation to calculate the percentage yield (%).

"Percentage Yield (%)"="Weight of dried extract" /"Weight of powdered rhizome" ×100

Dried extract was kept at 4°C in airtight amber bottles until further pharmacological studies.

2.4 Preliminary Phytochemical Screening

The hydroalcoholic extract was subjected to qualitative phytochemical screening for the presence of important secondary metabolites associated with biological activities using conventional phytochemical screening methods. Using the methods reported, the phytochemical constituents of the extract were screened for alkaloids (Dragendorff's test and Mayer's test), flavonoids (Shinoda test), phenolic compounds (Ferric chloride test), tannins (Lead acetate test), terpenoids (Salkowski test), and saponins (Froth test).

The characteristic color change or the formation of precipitate was used to confirm the presence of these phytoconstituents. Zingiber officinale was particularly noted for the identification of phenolic compounds and flavonoids: gingerols and shogaols were believed to be the significant bioactive compounds that account for the analgesic and anti-inflammatory effects found in ginger.

2.5 Experimental Animals

Wistar albino rats of the adult, rat weight 150–250 g, healthy, both males and females, were collected from the institutional animal house. Animals were kept in polypropylene cages in standard lab conditions of 22 ± 2°C, 55–65% relative humidity, and 12 light: 12 dark hours. Food (pellets) and drinking water were provided ad libitum, using a

normal toxicity-free laboratory diet and filtered drinking water, respectively.

Before conducting experiments, animals were acclimatized in a laboratory environment for 7 days. For experimental use of animals, all efforts have been made to reduce animal suffering and minimize the number of animals used as per the recommendations of CPCSEA.

3. Results

3.1 Percentage Yield of Hydroalcoholic Extract

Rhizomes of Zingiber officinale were harvested fresh, and a hydroalcoholic extract was prepared from them to use for pharmacological studies. The process of extraction resulted in the formation of a dark brown semi-solid extract having a distinct aroma and pungent taste. The percentage yield was determined by calculating it from the weight of the powdered rhizome before extraction and that of the dried extract after extraction. The process of hydroalcoholic extraction resulted in a good yield of extract.

Table 1. Percentage Yield of *Zingiber officinale* Hydroalcoholic Extract

Parameter	Observation
Weight of powdered rhizome	500 g
Weight of dried extract	68.45 g
Percentage yield	13.69%
Appearance	Dark brown semisolid
Odor	Characteristic aromatic
Storage condition	4°C

The hydroalcoholic extraction technique resulted in an extraction yield of 13.69%, which is an acceptable extraction yield of bioactive compounds for further pharmacological testing.

3.2 Preliminary Phytochemical Screening

The qualitative phytochemical screening test revealed that there were biologically active secondary metabolites in the hydroalcoholic extract of Zingiber officinale. These phytoconstituents play a role in the analgesic, anti-inflammatory, and antioxidant effects of ginger.

Table 2. Preliminary Phytochemical Screening of Hydroalcoholic Extract

Phytochemical Constituent	Test Performed	Result
Alkaloids	Dragendorff's Test	+
Flavonoids	Shinoda Test	+++
Phenolic compounds	Ferric Chloride Test	+++
Tannins	Lead Acetate Test	++
Terpenoids	Salkowski Test	++
Saponins	Froth Test	+
Glycosides	Keller-Killiani Test	+
Steroids	Liebermann–Burchard Test	+
Gingerols/Shogaols	Phytochemical confirmation	+++

Key:

+++ = Abundantly present

++ = Moderately present = Present– = Absent

Phytochemical analysis indicated a high concentration of phenolics, flavonoids, gingerols, and shogaols, while the presence of alkaloids, glycosides, steroids, tannins, terpenoids, and saponins was noted at moderate to low levels. The preponderance of phenolics is indicative of the pharmacological value of Zingiber officinale since these compounds are well-known for their ability to inhibit inflammatory factors, prevent oxidative stress, and regulate nociceptive pathways.

3.3 Acute Oral Toxicity Study

An acute oral toxicity study of the hydroalcoholic extract was carried out in accordance with the guidelines set by the OECD 423 before starting the painkiller studies. The animals were observed for 14 days after oral administration of the extract.

Table 3. Acute Oral Toxicity Observations

Observation Parameter	Findings
Mortality	None
Behavioral abnormalities	None
Convulsions	Absent
Tremors	Absent

Salivation	Normal
Locomotor activity	Normal
Food intake	Normal
Water intake	Normal
Body weight	Normal increase
Skin/Fur condition	Normal
Toxic symptoms	Not observed

Mortality or any sign of acute toxicity was not observed during the entire experiment period. The animals were active and showed normal activities such as feeding, locomotion, grooming, and weight gain. The findings clearly show that the hydro-alcoholic extract is safe for use at the tested concentrations. On the basis of the toxicity study, 200 mg/kg and 400 mg/kg body weight were selected as the low and high doses, respectively, to determine analgesic activity.

3.4 Effect of Zingiber officinale Extract on Acetic Acid-Induced Writhing Test

The extract caused a highly significant decrease in the number of writhes when compared with the control group, demonstrating strong peripheral analgesic activity. The effect was concentration-dependent, as the higher concentration gave a more pronounced writhing inhibition compared with the lower concentration. The greatest inhibition was caused by diclofenac sodium.

Table 4. Effect of Hydroalcoholic Extract on Acetic Acid-Induced Writhing in Rats

Group	Dose	Number of Writhes (Mean ± SEM)	% Inhibition
Control	Vehicle	54.83 ± 2.11	—
Standard (Diclofenac)	10 mg/kg	15.67 ± 1.04***	71.42
Extract Low Dose	200 mg/kg	33.17 ± 1.52***	39.50
Extract High Dose	400 mg/kg	21.50 ± 1.33***	60.79

Values are expressed as Mean ± SEM (n = 6). ***$p < 0.001$ compared with the control group.

The high concentration extract showed a significant reduction in the abdominal pain by about 60.79%, indicating a considerable peripheral analgesic effect which almost equals that of diclofenac sodium. This indicates that there is suppression of prostaglandins, which mediate inflammation in the body; an indication of why Zingiber officinale is used traditionally for treating pain and inflammation.

3.5 Effects of Zingiber officinale Extract on Hot Plate Test

A hot plate test was used to measure the central analgesic effects of the hydroalcoholic extract of Zingiber officinale. Reaction latency (licking or jumping of the paw) was determined prior to and after different doses of the extract and the standard drug. Morphine significantly increased reaction time throughout the experimental period. The hydroalcoholic extract increased the reaction latency in a dose-dependent manner, with the high concentration having a more analgesic effect than the low one.

Table 5. Effect of *Zingiber officinale* Extract on Hot Plate Reaction Time

Group	Dose	0 min	30 min	60 min	90 min	120 min
Control	Vehicle	3.82 ± 0.16	3.94 ± 0.18	3.88 ± 0.14	3.91 ± 0.17	3.85 ± 0.15
Standard (Morphine)	5 mg/kg	3.86 ± 0.17	6.82 ± 0.21***	9.54 ± 0.26***	10.92 ± 0.31***	10.31 ± 0.28***
Extract Low Dose	200 mg/kg	3.80 ± 0.15	5.12 ± 0.20**	6.48 ± 0.24***	7.32 ± 0.22***	6.91 ± 0.20***

Extract High Dose	400 mg/kg	3.84 ± 0.16	5.86 ± 0.23 ***	7.84 ± 0.27 ***	9.18 ± 0.29 ***	8.56 ± 0.25 ***

Values are expressed as **Mean ± SEM (n = 6).**
****p < 0.01; ***p < 0.001** compared with the control group.

There was a marked increase in reaction latency after taking the hydroalcoholic extract. The highest analgesic activity was seen 90 minutes after administration of the extract, which yielded a reaction time of 9.18 ± 0.29 s, close to the reaction time of morphine (10.92 ± 0.31 s). This result suggests that the extract has marked central analgesic activity, probably through activation of opioid receptors and blockage of nociceptive pathways.

3.6 Effect of Zingiber officinale Extract on Tail Flick Test

The tail flick method was also applied to study the central analgesic activity of the hydroalcoholic extract. There was a marked increase in reaction latency after administration of the extract. Like in the hot plate test, analgesic activity is dose-dependent.

Table 6. Effect of *Zingiber officinale* Extract on Tail Flick Latency

Group	**Dose**	**0 min**	**30 min**	**60 min**	**90 min**	**120 min**
Control	Vehicle	2.91 ± 0.14	2.95 ± 0.13	2.93 ± 0.15	2.90 ± 0.16	2.89 ± 0.14
Standard (Morphine)	5 mg/kg	2.94 ± 0.15	5.82 ± 0.19 ***	7.91 ± 0.22 ***	9.84 ± 0.28 ***	9.32 ± 0.26 ***
Extract Low Dose	200 mg/kg	2.93 ± 0.13	4.24 ± 0.18 **	5.86 ± 0.21 ***	6.82 ± 0.23 ***	6.35 ± 0.20 ***
Extract High Dose	400 mg/kg	2.90 ± 0.15	4.92 ± 0.20 ***	6.94 ± 0.24 ***	8.43 ± 0.26 ***	7.88 ± 0.24 ***

Values are expressed as **Mean ± SEM (n = 6).**
****p < 0.01; ***p < 0.001** compared with the control group.

The hydroalcoholic extract caused significant prolongation of the tail withdrawal latency throughout the duration of the experiment. The maximum analgesic effect was observed at 90 minutes, where the high dose of extract gave a latency of 8.43 ± 0.26 seconds, nearly similar to that observed from morphine (9.84 ± 0.28 seconds). These observations provide additional evidence for the contribution of central analgesic mechanisms to the pharmacological effects of Zingiber officinale.

3.7 General Comparison of the Analgesic Effects

The hydroalcoholic extract of Zingiber officinale showed a significant analgesic effect in peripheral and central pain models. The analgesic effect was dose-dependent in all the tests carried out. Although standard drugs (diclofenac sodium and morphine) gave maximum analgesic effects, the high dose of extract was almost equally effective.

Table 7. Summary of Analgesic Activity of *Zingiber officinale* Extract

Experimental Model	**Standard Drug**	**Low Dose (200 mg/kg)**	**High Dose (400 mg/kg)**
Acetic acid writhing	71.42% inhibition	39.50% inhibition	60.79% inhibition
Hot plate test	Maximum latency: 10.92 s	7.32 s	9.18 s
Tail flick test	Maximum latency: 9.84 s	6.82 s	8.43 s

The results showed that the 400 mg/kg hydroalcoholic extract showed significantly more analgesic activity than the 200 mg/kg dose in all experimental models ($p < 0.001$). The significant inhibition of acetic acid-induced writhing and the delayed reaction time observed in the hot plate and tail flick tests suggest involvement of peripheral inflammatory mediators and supraspinal and spinal nociceptive pathways, respectively. Overall results indicated that Zingiber officinale has both peripheral and central analgesic effects, thus it is a prospective plant-source analgesic agent for future research in preclinical and clinical studies.

4. Discussion

4.1 Interpretation of the Analgesic Activity

The present study proved that the hydroalcoholic extract of Zingiber officinale rhizome exhibits remarkable analgesic activity in the experimental Wistar rats. Analgesia against peripheral and central models of nociception was evident, and the activity was not only anti-analgesic but broad. The higher dose (400mg/kg) showed a greater degree of pain response inhibition than the lower dose (200mg/kg), which was of a dose-dependent response. The hAE was proven to be analogous with the standard drugs used (diclofenac sodium and morphine) in both treatments, although not as strong as the former in the high-dose treatment group.

In the present study, the remarkable decrease in acetic acid-induced writhing observed would signify that the extract is highly effective in inhibiting peripheral mechanisms of pain. Acetic acid induces pain through two mechanisms by stimulating the release of endogenous inflammatory mediators such as prostaglandins, bradykinin, serotonin, histamine, and cytokines in the peritoneal cavity. Hence, abdominal writhing inhibition is a strong indication of the inhibitory effect of the extract on the synthesis/release of these inflammatory mediators. From the results observed here, the hydroalcoholic extract could be shown to possess inhibitory activity on prostaglandin biosynthesis, possibly like those of conventional NSAIDs, by inhibiting its production via the cyclooxygenase pathway.

Likewise, the notable increase in reaction latency in the hot plate and tail flick tests justifies the existence of a central analgesic effect. The hot plate is a mainly supraspinally mediated mechanism of analgesia, while the tail flick measures mainly spinally mediated nociceptive reflexes. But enhancement in both modeling indicates that Zingiber officinale may have a multifaceted impact on the central nervous system as a whole in relation to pain transmission. Multimodal Analgesic Effect is beneficial as chronic pain frequently includes peripheral inflammation and central sensitization.

The acute oral toxicity study also yielded good safety data, contributing to this extract's therapeutic promise. 24 hours of observation did not lead to any mortality, behavioral abnormalities, or toxic manifestations, which shows the relatively safe use of the hydroalcoholic extract at the tested doses. The results obtained are in agreement with the traditional application of ginger as a medicinal herb and its wide tradition of low toxicity in experimental and clinical use.

4.2 Possible Mechanisms Underlying the Analgesic Activity

It is likely that the synergistic action of various bioactive phytoconstituents in the rhizome of Zingiber officinale accounts for their analgesic activity. Preliminary phytochemical analysis revealed the presence of phenolic compounds, flavonoids, terpenoids, tannins, saponins, and other secondary metabolites, which have been reported with anti-inflammatory and anti-oxidant activity.

Of these constituents, 6-gingerol, 8-gingerol, 10-gingerol, 6-shogaol, paradols, and zingerone are regarded as the main pharmacologically active molecules that exercise the pharmacological activity of ginger or may contribute towards this activity. These compounds inhibit cyclooxygenase (COX-1 and COX-2) and Lipoxygenase (5-LOX) enzymes that help prevent the production of prostaglandins and leukotrienes that contribute to inflammatory pain.

One of the other mechanisms is suppression of pro-inflammatory cytokines like TNF alpha, IL-1, and IL-6. These cytokines are important for peripheral sensitization, causing chronic inflammatory pain. Ginger inhibits the production of cytokines, which help to decrease inflammatory edema and activation of nociceptors.

Persistent pain has also been linked with oxidative stress. ROS activate nociceptive neurons and potentiate inflammatory pathways. Ginger is rich in anti-oxidant properties and inhibits lipid peroxidation and increases the activity of endogenous antioxidant enzymes like superoxide dismutase, catalase, and glutathione peroxidase. Thus, the antioxidant activity will likely make a significant contribution to the reported analgesic activity.

Additionally, pharmacological studies of ginger have recently revealed some modulation of transient receptor potential vanilloid-1 (TRPV1) receptors and effects on serotonergic and adrenergic/endogenous opioid pathways connected to pain processes. These multimodal mechanisms could be responsible for the effectiveness obtained by the hydroalcoholic extract in both the peripheral and central analgesic models.

4.3 Comparison with Previous Studies

Results of the present investigation are in close concordance with previously published experimental and clinical investigations of Zingiber officinale, taking into consideration its analgesic activity. Paudel et al. (2025) performed a thorough systematic review and meta-analysis, revealing that ginger supplementation significantly diminished

inflammatory biomarkers, including C-Reactive Protein (CRP), Tumor necrosis factor alpha (TNF-α), and Interleukin-6 (IL-6), and was advantageous for pain response of different inflammatory disorders. The results of their investigations are very supportive of the anti-inflammatory and analgesic effects of action, which are found in the present investigation.

Boarescu et al (2023) found that ginger root capsule extract has significant anti-inflammatory effects in experimental rats and enhances pain threshold when the rats were given carrageenan as inflammation. Furthermore, the synergistic effect between ginger extract and diclofenac sodium demonstrated a greater analgesic effect compared to diclofenac alone, implying a synergistic effect to occur between the constituents of ginger extract and conventionally used NSAIDs. The analgesic activity that was found in the present study is comparable with these findings.

Likewise, Zingiber officinale's synergistic effects with Curcuma longa on enhancing the analgesic and anti-inflammatory effects were observed by Ilyas et al. (2024). Their work has shown that the combined action of various inflammatory pathways yielded better analgesics than individual plant extracts.

Ginger has also proved beneficial in clinical investigations for osteoarthritis, dysmenorrhea, migraine, postoperative pain, and muscle soreness when exercising. In a systematic review and meta-analysis, Daily et al. (2023) found that ginger substantially decreases pain levels without causing severe side effects. The present results corroborate these clinical observations.

The findings from the current investigation, when compared with the earlier studies, indicate that Zingiber officinale is a reliable source of analgesic activity with several complementary pharmacological actions.

4.4 Clinical Implications

The fact is that chronic pain disorders are growing more common, and the negative side effects of long-term prescribed NSAIDs and opioids have brought about a greater focus on more effective and safer drugs trying to mimic the effects of these medications. Based on the present results, Zingiber officinale is a potential phytopharmaceutical agent for the treatment of inflammatory and nociceptive pain.

The multiple molecular targets through which ginger works, without any high degree of toxicity, suggest that it could offer special advantages as an adjunctive agent to standard analgesics. Combination therapy may mean that fewer NSAIDs or opioids are needed to provide pain relief or that the quantity can be decreased, which would minimize adverse reactions from the drugs and also provide effective pain relief.

In addition, the easy accessibility, low cost, and evident acceptance of ginger in traditional medicine extend its potential for clinical application, especially in underserved health care environments where access to sophisticated and costly analgesics may be restricted.

4.5 Limitations of the Study

The present investigation has some shortcomings, though, demonstrating the encouraging pharmacological activity. The study only compared the acute analgesic activity in experimental animal models and thus could not fully compare chronic pain with human patients. There was no biochemical or molecular confirmation for the molecular mechanism, but rather derived from previous literature.

Total amounts of individual bioactive components like gingerols and shogaols were not determined in the study by chromatographic methods, nor were inflammatory biomarkers or oxidative stress parameters measured. In addition, pharmacokinetic characterization, receptor binding, histopathological analysis, and chronic toxicity studies were not evaluated in the current study.

Several future studies combining advanced molecular techniques, under standardized conditions of phytochemical characterization, chronic pain models, and randomized clinical needs to be conducted to elucidate the exact therapeutic potential of Zingiber officinale as an effective pain-killer agent in the clinical context.

5. Conclusion

The present study showed that the hydroalcoholic extract of Zingiber officinale rhizome has proven to have considerable analgesic activity on experimental Wistar rats. Both peripheral and central nociceptive evaluation models revealed that the extract was effective in reducing pain responses in a dose-dependent manner. The extract resulted in significantly more inhibition of abdominal constrictions in the acetic acid-induced writhing test and significantly more latency time in the hot plate and tail flick test, suggesting that it has anti-inflammatory and central analgesic activity. The higher dose (400 mg/kg) consistently resulted in higher analgesic effects than the lower dose (200 mg/kg) and similarly had effects close to those of standard analgesic drugs.

The pharmacological activity observed can be explained by the presence of bioactive phytoconstituents, among which are gingerols, shogaols, paradols, flavonoids, and phenolic compounds, which are known for their ability to inhibit both the cyclooxygenase and the lipoxygenase pathways, have anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines, and exhibit an antioxidant effect through their modulation of nociceptive signal transduction pathways. The multimodal mechanism of action exhibited by Zingiber officinale offers an added benefit over the conventional analgesics, which are believed to act on a single pathway.

The acute oral toxicity study also revealed that the hydroalcoholic extract was safe to use at all tested doses since no mortality and behavioural abnormalities were observed during the course of the experimental procedure. This good safety profile explains the ancient medicinal practice of ginger consumption, and also points to its potential long-term application in medicine.

The results of this study confirm the previously reported experimental and clinical research findings, which showed the analgesic, anti-inflammatory, and antioxidant activity of Zingiber officinale. Thus, the present study contributes further scientific evidence in favour of the traditional use of ginger for painful inflammatory diseases and lends credibility to its pharmacological potential in standardized experimental animal models.

The overall conclusion that may be inferred from the hydroalcoholic extract of Zingiber officinale is that it can serve as a valuable natural source of analgesic compounds with both peripheral and central actions. Given its effectiveness, safety, ease of access, and low cost, ginger could be useful as a complementary or alternative therapy for pain medication. The application of this herb could, however, be recommended once more investigations are completed on phytochemical standardization, molecular mechanism studies, pharmacokinetic evaluation, and chronic toxicity assessment, based on large-scale, randomized clinical trials.