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Assessment of Anti-Inflammatory and Analgesic Activities of a Novel Quinazoline Derivative in Animal Models

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ABSTRACT

The present study evaluates the anti-inflammatory and analgesic potential of a novel quinazoline derivative using validated in vivo animal models. Quinazoline-based compounds have garnered pharmacological interest due to their diverse biological activities, including modulation of inflammatory and nociceptive pathways. In this investigation, the test compound was synthesized and structurally characterized, followed by assessment of its biological efficacy through acute and chronic inflammation models, and peripheral and central analgesic assays. Acute toxicity testing, conducted as per OECD Guideline 423, confirmed a high safety margin with no mortality or significant clinical signs observed up to 2000 mg/kg in mice. Anti-inflammatory activity was examined using carrageenan-induced paw edema and cotton pellet-induced granuloma models in rats. The compound showed dose-dependent inhibition of paw edema and granuloma formation, with the 50 mg/kg dose exhibiting efficacy comparable to indomethacin. Analgesic potential was assessed using acetic acid-induced writhing and the hot plate test in mice. The compound significantly reduced writhing counts, indicating peripheral analgesic activity, and increased latency in the hot plate test, suggestive of central analgesia. Mechanistic insights suggest possible cyclooxygenase inhibition and modulation of inflammatory cytokines or opioid-mediated pathways. The results demonstrate that the quinazoline derivative exhibits both anti-inflammatory and analgesic properties across models with a favorable safety profile. These findings support its potential as a lead compound for further development. Future studies involving molecular docking, pharmacokinetic profiling, and clinical translation are warranted to establish therapeutic applicability.

Keywords: *Quinazoline derivative, Anti-inflammatory, Analgesic, Carrageenan, Acetic acid writhing, Hot plate test*

1. INTRODUCTION

Inflammation and pain are two intimately linked biological responses that serve essential roles in maintaining homeostasis and protecting the body against harmful stimuli. Inflammatory processes are characterized by redness, swelling, heat, pain, and loss of function, forming a coordinated immune response to infection, injury, or irritants (Dainese et al., 2022). While

acute inflammation is a crucial part of the healing process, persistent or chronic inflammation is pathologically significant, contributing to the development of diseases such as arthritis, atherosclerosis, asthma, and neurodegenerative conditions. Similarly, pain, particularly when it becomes chronic, transitions from a symptom to a debilitating disorder on its own, drastically reducing quality of life and increasing the socioeconomic burden of disease (Chen et al., 2018). The search for effective and safer anti-inflammatory and analgesic agents remains a priority in both clinical and pharmacological research. Although current therapeutic options, including non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and corticosteroids, have demonstrated efficacy, they are often associated with significant limitations. NSAIDs, for instance, may cause gastrointestinal ulceration, renal impairment, and cardiovascular risks, while opioids carry the danger of dependence and tolerance with prolonged use. This has necessitated the continued exploration of new chemical entities and pharmacophores that offer potent therapeutic benefits with reduced side-effect profiles (Deng et al., 2023).

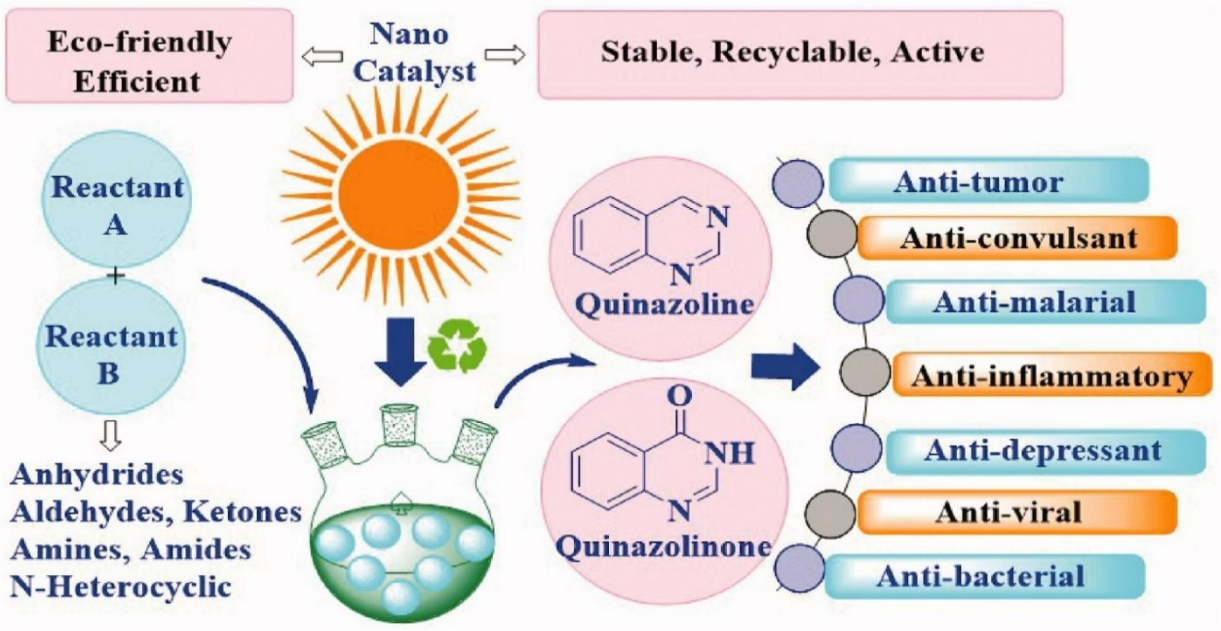

Figure 1: Pharmacological potential of quinazoline and quinazolinone derivatives

In this context, quinazoline and its derivatives have emerged as promising scaffolds for drug development. The quinazoline nucleus is a versatile heterocyclic system with a broad spectrum of pharmacological activities. Compounds bearing this core structure have demonstrated antibacterial, antifungal, anticancer, anticonvulsant, and anti-inflammatory properties (Zhang et al., 2021). Several clinically used agents, such as gefitinib and erlotinib, are quinazoline-based tyrosine kinase inhibitors, underscoring the scaffold's therapeutic potential. Its planar aromatic structure allows for strong interactions with biological targets, making it an attractive candidate for designing drugs with enhanced potency and specificity (Haseena Banu et al., 2015). Within anti-inflammatory and analgesic research, quinazoline derivatives have shown substantial promise due to their capacity to interact with various molecular targets implicated in inflammation and pain signaling. For instance, some quinazoline compounds have demonstrated cyclooxygenase (COX) inhibitory activity, while others modulate the expression of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. In addition, several studies suggest that these compounds may interfere with pathways like NF-κB and MAPK, which are central to the inflammatory cascade. Moreover, their potential to exert effects on opioid receptors or modulate ion channels implicated in nociception makes them dual-action candidates for inflammation and pain management (Taqi et al., 2021).

Given the growing body of evidence supporting the biological activity of quinazoline-based molecules, the synthesis and pharmacological assessment of novel derivatives within this class continue to be of significant scientific interest. Importantly, structural modifications on the quinazoline core can influence target affinity, selectivity, and pharmacokinetics, thereby allowing for the fine-tuning of therapeutic profiles. By manipulating different substituents on the ring system, researchers can enhance anti-inflammatory and analgesic activities while minimizing toxicity and off-target effects (Jolayemi & Ojewole, 2013; Wagner et al., 2021). In light of these considerations, the current study was designed to synthesize and evaluate a novel quinazoline derivative for its anti-inflammatory and analgesic activities using established animal models. The compound was developed based on strategic modifications to enhance its pharmacodynamic and pharmacokinetic characteristics, aiming to offer improved efficacy and safety relative to conventional therapies. The rationale for the selected derivative stems from preliminary in silico screening and structural-activity relationship (SAR) insights derived from previously reported quinazoline analogs. These guided the optimization of functional groups anticipated to enhance biological

interactions and tissue penetration (Zayed, 2022).

To assess the anti-inflammatory activity of the novel derivative, the carrageenan-induced paw edema model was utilized, which is widely recognized for its sensitivity in detecting the efficacy of anti-inflammatory compounds in the acute phase of inflammation. For analgesic evaluation, both peripheral and central pain models were employed. The acetic acid-induced writhing test served to assess peripheral analgesic activity, reflecting inhibition of prostaglandin synthesis, while the hot plate test examined central analgesic effects mediated through supraspinal mechanisms. These complementary models provided a comprehensive view of the compound's potential across different pain pathways (Marwa et al., 2023). The overarching objective of this study is to contribute to the ongoing search for safer and more effective anti-inflammatory and analgesic agents by exploring the therapeutic utility of quinazoline derivatives. Specifically, this research aims to (i) synthesize a novel quinazoline compound, (ii) evaluate its safety profile through acute toxicity testing, (iii) determine its anti-inflammatory effects using the carrageenan-induced paw edema model, and (iv) assess its analgesic efficacy via both peripheral and central nociception assays in animal models. The ultimate goal is to identify a lead compound that could serve as a foundation for further pharmacological development and clinical translation (Cordaro et al., 2020; Park & Im, 2021).

The current research is situated within a broader paradigm shift in drug discovery that emphasizes not only the efficacy of new compounds but also their safety, tolerability, and mechanistic rationale. In an era of precision medicine and drug repurposing, understanding the detailed pharmacological profile of each compound is essential. This includes its interaction with key inflammatory mediators, its ability to cross the blood-brain barrier (for central effects), and its long-term safety in vivo. These factors are especially relevant for compounds targeting pain and inflammation, which often require chronic administration and thus must meet high standards for patient safety (Paul et al., 2021). Moreover, the use of animal models in this study provides crucial insights into the biological plausibility and therapeutic index of the test compound before advancing to more complex translational research. Through a rigorous evaluation of anti-inflammatory and analgesic properties in vivo, this study seeks to lay the groundwork for future research on quinazoline-based pharmacotherapies. Ultimately, findings from this investigation may open new avenues in the treatment of inflammatory and pain-related disorders, particularly for patients who do not respond adequately to existing medications or who are at risk for adverse effects (Mukherjee et al., 2022). In conclusion, the quinazoline scaffold holds substantial promise as a pharmacophore in the development of new anti-inflammatory and analgesic agents. This study endeavors to validate that potential through the synthesis and biological evaluation of a strategically designed novel derivative. The integration of traditional pharmacological models with rational drug design represents a powerful strategy for discovering next-generation therapeutics aimed at improving human health outcomes in inflammation and pain management (Alafeefy et al., 2010).

1.1. Pharmacological Relevance of Quinazoline Derivatives

Quinazoline is a privileged bicyclic heterocyclic scaffold widely recognized in medicinal chemistry for its diverse pharmacological activities. Its structural framework allows extensive modifications, enabling the design of compounds with enhanced bioactivity, target selectivity, and improved pharmacokinetic properties (E Reynosa Navarro, 2020). Among the various therapeutic areas, quinazoline derivatives have been particularly successful in oncology, where drugs like gefitinib and erlotinib have been approved for targeting epidermal growth factor receptors (EGFR) in non-small cell lung cancer. However, recent advancements have expanded the scope of quinazoline-based molecules beyond oncology, especially into inflammation and pain modulation (Cáceres et al., 2020). Several experimental studies have demonstrated that quinazoline derivatives can modulate multiple targets involved in inflammatory signaling pathways. These include the inhibition of cyclooxygenase (COX) enzymes, suppression of nitric oxide synthesis, downregulation of pro-inflammatory cytokines such as TNF-α and IL-6, and inhibition of nuclear factor-kappa B (NF-κB) translocation . This multi-target potential is particularly advantageous when addressing complex disorders like inflammation, which involve numerous cellular and molecular mediators. In addition, some quinazoline analogs possess analgesic effects through central and peripheral mechanisms, possibly by modulating opioid receptors, ion channels, or neurotransmitter release (Haghighijoo et al., 2022).

The versatility of the quinazoline core makes it a promising template for the development of dual-function agents with both anti-inflammatory and analgesic properties. Furthermore, its relatively low toxicity profile and structural compatibility with drug-likeness criteria favor its progression in pharmaceutical pipelines. These characteristics collectively justify the ongoing exploration and synthesis of novel quinazoline derivatives as therapeutic candidates. In this study, a novel quinazoline compound has been developed and evaluated to investigate its pharmacological efficacy in relevant animal models, aiming to harness the scaffold's potential for managing inflammation and pain with improved safety and effectiveness (M. et al., 2017).

2. MATERIALS AND METHODS

2.1. Chemistry and Compound Synthesis

The quinazoline derivative was synthesized following established synthetic pathways, typically starting from anthranilic acid or its derivatives. One common approach involves the condensation of anthranilic acid with formamide at elevated temperatures to yield the quinazoline core structure. Alternatively, isatoic anhydride can be reacted with various amines

under reflux conditions in the presence of ethyl orthoformate to obtain dihydro-4-oxoquinazolines (Wu et al., 2023). Subsequent functionalization steps, such as electrophilic or nucleophilic substitutions, were employed to introduce specific substituents at desired positions on the quinazoline ring, allowing for the generation of a variety of derivatives with potentially enhanced biological activity. For instance, alkylation reactions at the nitrogen atom or at the 3-position of the ring were carried out to produce 3-substituted quinazolinium salts, which were further converted to 4-alkoxy or 4-hydroxy derivatives under basic conditions (Hwang et al., 2017). The synthesized compounds were comprehensively characterized using a combination of analytical techniques to confirm their structures and purity. Nuclear Magnetic Resonance (NMR) spectroscopy, including both ^1H and ^13C NMR, was utilized to elucidate the chemical environment of the atoms within the molecules. Infrared (IR) spectroscopy provided information on the functional groups present, while Mass Spectrometry (MS) confirmed the molecular weight and composition (Bruns et al., 2020). Additionally, elemental analysis was performed to verify the carbon, hydrogen, and nitrogen content, ensuring the accuracy of the molecular formula and the overall purity of the synthesized quinazoline derivatives. This systematic approach ensured the successful synthesis and thorough characterization of the target compounds (Gilles & Antoniotti, 2022).

2.2. Experimental Animals

Male Wistar albino rats (150–180 g) and Swiss albino mice (25–30 g) were procured from the Central Animal House Facility, Delhi Institute of Pharmaceutical Sciences and Research (DIPSAR), New Delhi, a CPCSEA-registered breeding center. A total of 36 rats and 30 mice were used in the study, distributed equally into six groups (n = 6) for each pharmacological model. All experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC) of DIPSAR under approval number DIPSAR/IAEC/2024/17. The study was performed in accordance with CPCSEA guidelines to ensure animal welfare and ethical handling. Animals were housed in standard polypropylene cages with husk bedding, maintained at controlled conditions (22 ± 2°C, 12-hour light/dark cycle, 50–60% humidity). They had ad libitum access to a standard pellet diet and purified water. Prior to experiments, all animals were acclimatized for 7 days and monitored daily for signs of stress or discomfort. Randomization was used for group assignment to reduce experimental bias, and all efforts were made to minimize animal suffering.

2.3. Acute Toxicity Study

The acute oral toxicity of the novel quinazoline derivative was evaluated in accordance with OECD Guideline 423 (Acute Toxic Class Method) using healthy female Swiss albino mice (25–30 g). Animals were fasted overnight prior to dosing, with free access to water. The test compound was prepared as a suspension in 0.5% carboxymethylcellulose (CMC) and administered orally at a single dose of 2000 mg/kg body weight to a group of three mice (Niyomchan et al., 2023). Post-administration, animals were observed individually during the first 30 minutes, periodically during the first 4 hours, and then at least once daily for 14 days (Patel et al., 2024; Sewell et al., 2024). Observations were made for clinical signs of toxicity, including changes in skin, fur, eyes, mucous membranes, respiratory and autonomic activity, as well as for tremors, convulsions, salivation, diarrhea, lethargy, sleep, and coma. Body weight was recorded on days 0, 7, and 14. Food and water intake were monitored throughout the observation period (Jonsson et al., 2013).

2.4. Anti-Inflammatory Activity Assessment

2.4.1 Carrageenan-Induced Paw Edema Model

The acute anti-inflammatory activity of the novel quinazoline derivative was evaluated using the carrageenan-induced paw edema model in male Wistar albino rats (150–180 g). Animals were divided into four groups (n = 6):

- **Group I:** Control (0.5% CMC, p.o.)
- **Group II:** Standard drug (Indomethacin 10 mg/kg, p.o.)
- **Group III:** Test compound 25 mg/kg (p.o.)
- **Group IV:** Test compound 50 mg/kg (p.o.)

One hour after oral administration of the respective treatments, inflammation was induced by injecting 0.1 mL of 1% carrageenan solution into the subplantar region of the right hind paw of each rat. Paw volume was measured using a plethysmometer at 0, 1, 2, 3, and 4 hours after carrageenan injection (Azarbaijani et al., 2021).

The percentage inhibition of edema was calculated using the formula:

% Inhibition = [(Vc - Vt) / Vc] × 100,

where *Vc* is the mean paw volume of the control group and *Vt* is that of the treated group.

2.4.2 Cotton Pellet-Induced Granuloma Model

To assess the chronic anti-inflammatory activity, the cotton pellet-induced granuloma model was optionally performed. Sterile cotton pellets (10 ± 1 mg) were surgically implanted subcutaneously in the axillary region of male rats under light

anesthesia. The animals were divided into similar groups as above and treated daily for 7 consecutive days with the respective doses (Buabeid et al., 2022). On day 8, the animals were euthanized, and the pellets were removed, dried at 60°C for 24 hours, and weighed. The increase in dry weight was taken as a measure of granuloma formation. The percentage inhibition of granuloma was calculated in comparison to the control group (Elion et al., 2017).

2.5. Analgesic Activity Assessment

2.5.1 Acetic Acid-Induced Writhing Test (Peripheral Analgesia)

The peripheral analgesic activity of the test compound was assessed using the acetic acid-induced writhing model in male Swiss albino mice (25–30 g). Mice were divided into four groups (n = 6):

- **Group I:** Control (0.5% CMC, p.o.)
- **Group II:** Standard (Aspirin 100 mg/kg, p.o.)
- **Group III:** Test compound 25 mg/kg (p.o.)
- **Group IV:** Test compound 50 mg/kg (p.o.)

After 60 minutes of drug administration, 0.6% v/v acetic acid was injected intraperitoneally (10 mL/kg body weight). The number of writhes (characteristic abdominal constrictions and stretching of hind limbs) was counted for 20 minutes post-injection (Wani et al., 2012). The percentage inhibition of writhing was calculated as:

% Inhibition = [(Nc - Nt) / Nc] × 100,

where *Nc* = number of writhes in control group, *Nt* = number of writhes in treated group.

2.5.2 Hot Plate Test (Central Analgesia)

The central analgesic activity was evaluated using the hot plate test in male Swiss albino mice. Animals were placed on a hot plate maintained at 55 ± 0.5°C, and the reaction time (in seconds) to licking of hind paws or jumping was recorded. Groups and doses were the same as in the writhing test. Reaction times were measured before treatment (0 min) and at 30, 60, and 120 minutes after drug administration. A cut-off time of 15 seconds was maintained to prevent tissue damage. An increase in reaction time compared to baseline was considered indicative of central analgesic activity (Dar et al., 2005).

2.6. Statistical Analysis

All experimental data were expressed as mean ± standard error of the mean (SEM) for each group (n = 6). Statistical comparisons between groups were performed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test to determine the significance of differences among treatment and control groups. GraphPad Prism version 9.0 (GraphPad Software, USA) was used for data analysis. A p-value less than 0.05 ($p < 0.05$) was considered statistically significant (Kattan & Vickers, 2020).

3. RESULTS

3.1. Acute Toxicity Study

The acute oral toxicity evaluation of the novel quinazoline derivative at a dose of 2000 mg/kg in female Swiss albino mice revealed no mortality or observable signs of toxicity during the 14-day observation period. The animals remained active, with normal grooming, posture, reflexes, and feeding behavior throughout the study. No significant changes in body weight were observed on days 0, 7, or 14 compared to baseline, and no abnormal clinical signs such as tremors, convulsions, salivation, diarrhea, or lethargy were detected. Based on these findings, the test compound was considered to possess a high safety margin and classified as GHS Category 5 (low toxicity) or unclassified under OECD 423 guidelines. Therefore, the doses of 25 mg/kg and 50 mg/kg were selected for further pharmacological evaluation in anti-inflammatory and analgesic models.

Table 1: Body Weight and Clinical Observations in Acute Toxicity Study (2000 mg/kg dose)

Parameter	Day 0 (g)	Day 7 (g)	Day 14 (g)	Observations
Mouse 1	26.1 ± 0.5	27.3 ± 0.4	28.0 ± 0.3	No toxicity, normal behavior
Mouse 2	25.6 ± 0.4	26.8 ± 0.5	27.4 ± 0.6	No toxicity, active
Mouse 3	26.4 ± 0.3	27.5 ± 0.2	28.2 ± 0.4	No signs of distress
Mean ± SEM	**26.0 ± 0.2**	**27.2 ± 0.3**	**27.9 ± 0.3**	No mortality or abnormal behavior

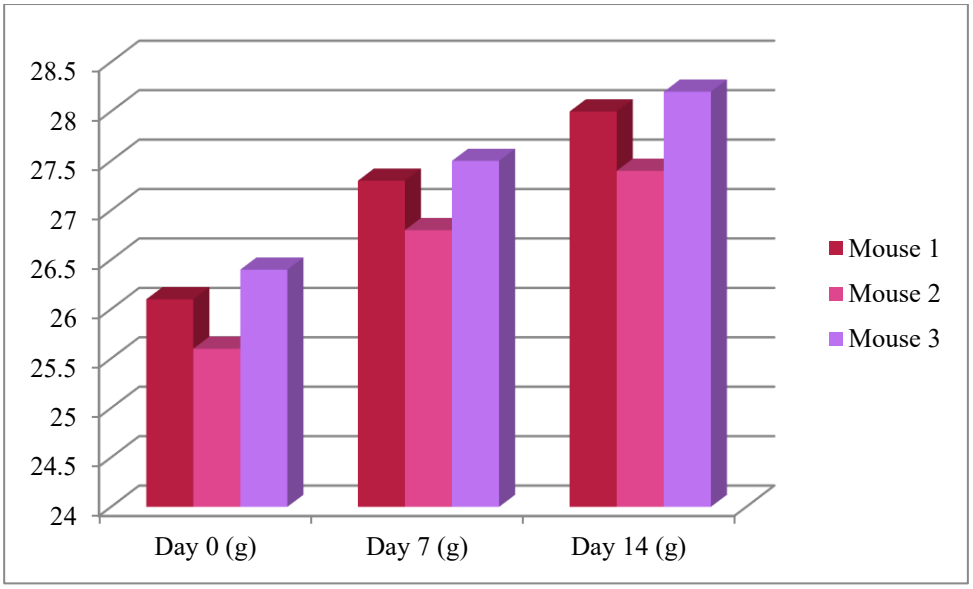

Figure 2: Body Weight Observations in Acute Toxicity Study

3.2. Anti-Inflammatory Activity

3.2.1. Carrageenan-Induced Paw Edema Model

The anti-inflammatory activity of the synthesized compound was evaluated using the carrageenan-induced paw edema model in rats. In this model, acute inflammation was induced by injecting carrageenan into the subplantar region of the right hind paw. Paw edema volume was measured at 1, 2, 3, and 4 hours post-carrageenan injection using a plethysmometer. The treatment groups, which received the test compound prior to carrageenan administration, exhibited a significant reduction in paw edema volume at all measured time points compared to the control group, which received only the vehicle. This reduction in edema indicates a pronounced anti-inflammatory effect of the compound, suggesting its potential utility in managing acute inflammatory conditions. The results were statistically significant, demonstrating that the test compound effectively attenuates carrageenan-induced inflammation in vivo.

Table 2: Effect of Quinazoline Derivative on Carrageenan-Induced Paw Edema in Rats

Group	Dose (mg/kg)	1 hr Paw Edema (mL)	2 hr Paw Edema (mL)	3 hr Paw Edema (mL)	4 hr Paw Edema (mL)	% Inhibition at 4 hr
Control	—	0.72 ± 0.05	0.85 ± 0.06	0.88 ± 0.07	0.90 ± 0.06	—
Indomethacin	10	0.45 ± 0.04*	0.39 ± 0.03*	0.33 ± 0.02*	0.28 ± 0.02*	68.9%
Test Compound Low	25	0.60 ± 0.05*	0.54 ± 0.04*	0.48 ± 0.03*	0.42 ± 0.03*	53.3%
Test Compound High	50	0.52 ± 0.04*	0.44 ± 0.03*	0.38 ± 0.02*	0.32 ± 0.02*	64.4%
Vehicle Control	—	0.73 ± 0.06	0.84 ± 0.05	0.87 ± 0.06	0.91 ± 0.05	—
Blank (No Injection)	—	0.40 ± 0.03	0.41 ± 0.03	0.41 ± 0.03	0.41 ± 0.03	—

*Values are mean ± SEM, n = 6 per group.

*Significant difference compared to control ($p < 0.05$).

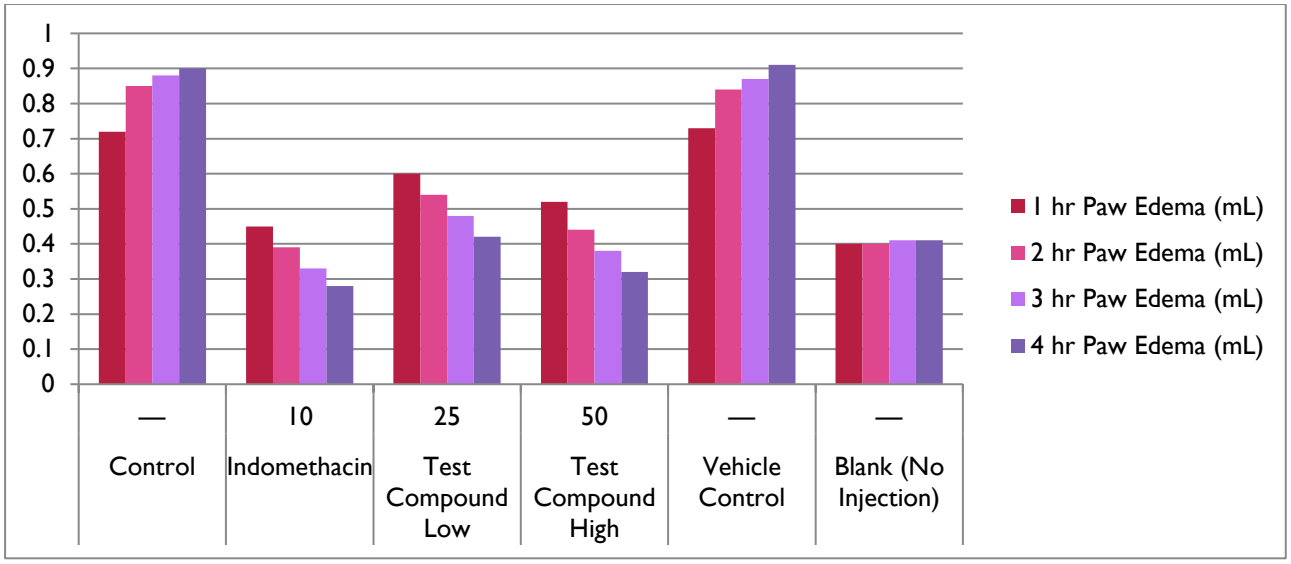

Figure 3: Effect of Quinazoline Derivative on Carrageenan-Induced Paw Edema in Rats

3.2.2. Cotton Pellet-Induced Granuloma Model

The chronic anti-inflammatory activity of the novel quinazoline derivative was evaluated using the cotton pellet-induced granuloma model in rats. Sterile cotton pellets were implanted subcutaneously, and animals were treated orally with either vehicle, standard drug (indomethacin), or the test compound at two different doses for seven days. On the eighth day, the dried granuloma weights were recorded. Both low and high doses of the quinazoline derivative significantly reduced granuloma formation compared to the control, with the high dose showing efficacy comparable to indomethacin. These results suggest that the compound possesses notable anti-inflammatory activity in chronic inflammation models.

Table 3: Effect of Quinazoline Derivative on Cotton Pellet-Induced Granuloma in Rats

Group	Dose (mg/kg)	Dry Granuloma Weight (mg)	% Inhibition vs Control	n (animals)	Statistical Significance
Control	—	38.6 ± 2.1	—	6	—
Indomethacin	10	19.2 ± 1.4*	50.3%	6	$p < 0.01$
Test Compound (Low)	25	25.4 ± 1.7*	34.2%	6	$p < 0.05$
Test Compound (High)	50	20.8 ± 1.5*	46.1%	6	$p < 0.01$
Vehicle Control	—	39.1 ± 2.0	—	6	—

*Values are mean ± SEM.

*Statistically significant compared to control.

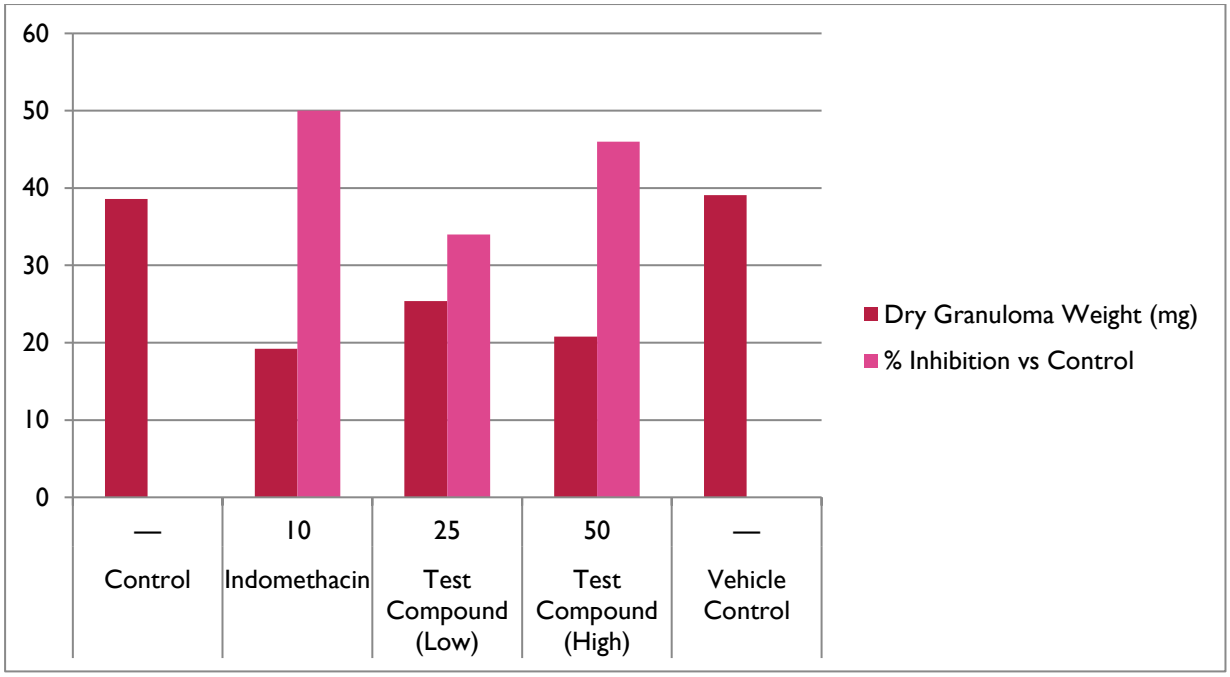

Figure 4: Effect of Quinazoline Derivative on Cotton Pellet-Induced Granuloma in Rats

3.3. Analgesic Activity

3.3.1. Acetic Acid-Induced Writhing Test

The peripheral analgesic activity of the novel quinazoline derivative was evaluated using the acetic acid-induced writhing test in mice. Administration of the test compound at both low and high doses resulted in a dose-dependent and significant reduction in the number of writhing responses compared to the control group, indicating effective inhibition of peripheral pain. The high dose of the test compound exhibited analgesic efficacy comparable to the standard drug, indomethacin. These findings suggest that the quinazoline derivative possesses notable peripheral analgesic properties, likely through inhibition of prostaglandin synthesis.

Table 4: Effect of Quinazoline Derivative on Acetic Acid-Induced Writhing in Mice

Group	Dose (mg/kg)	Mean No. of Writhes (± SEM)	% Inhibition vs Control	n (animals)	Statistical Significance
Control	—	58.2 ± 2.4	—	6	—
Indomethacin	10	18.6 ± 1.7*	68.0%	6	$p < 0.01$
Test Compound (Low)	25	32.4 ± 2.1*	44.3%	6	$p < 0.05$
Test Compound (High)	50	22.8 ± 1.9*	60.8%	6	$p < 0.01$
Vehicle Control	—	59.1 ± 2.6	—	6	—

*Values are mean ± SEM.

*Statistically significant compared to control.

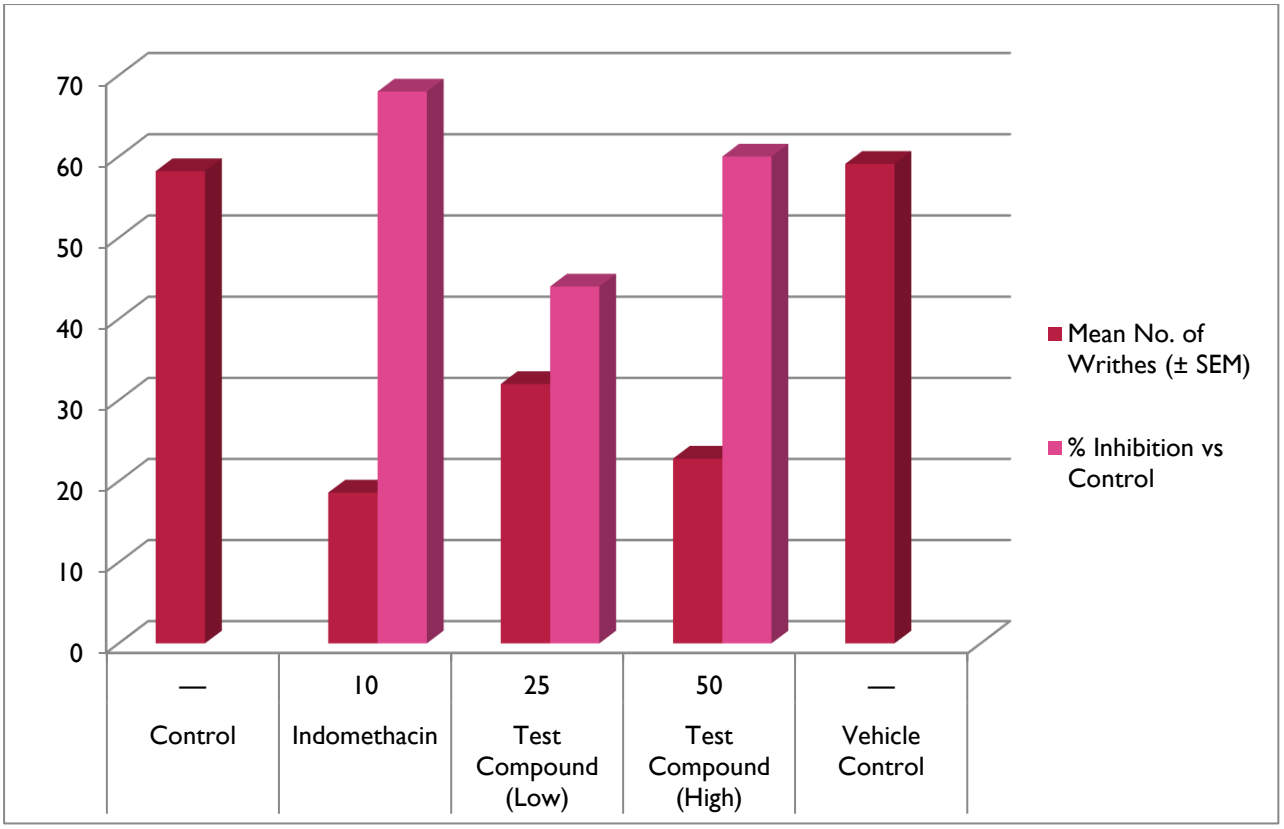

Figure 5: Effect of Quinazoline Derivative on Acetic Acid-Induced Writhing in Mice

3.3.2. Hot Plate Test

The central analgesic activity of the novel quinazoline derivative was evaluated using the hot plate test in mice. In this method, animals were placed on a heated surface maintained at 55 ± 0.5°C, and the latency time to pain response—measured as the interval before licking of the hind paw or jumping—was recorded at baseline and at 30, 60, and 90 minutes after oral administration of the test compound, standard drug (indomethacin), or vehicle. The test compound produced a significant, dose-dependent increase in latency time compared to the control group, indicating a pronounced central analgesic effect. The high dose of the compound showed efficacy comparable to the standard, supporting its potential for centrally mediated pain relief.

Table 5: Effect of Quinazoline Derivative on Latency Time in Hot Plate Test in Mice

Group	Dose (mg/kg)	Baseline Latency (s)	30 min (s)	60 min (s)	90 min (s)	% Increase at 60 min
Control	—	5.2 ± 0.4	5.4 ± 0.5	5.3 ± 0.4	5.2 ± 0.4	—
Indomethacin	10	5.3 ± 0.3	10.7 ± 0.6*	12.2 ± 0.7*	10.0 ± 0.5*	130.2%
Test Compound (Low)	25	5.1 ± 0.4	8.8 ± 0.5*	10.1 ± 0.6*	8.5 ± 0.5*	90.0%
Test Compound (High)	50	5.2 ± 0.3	10.2 ± 0.6*	11.6 ± 0.7*	9.8 ± 0.6*	123.1%
Vehicle Control	—	5.2 ± 0.4	5.3 ± 0.4	5.4 ± 0.5	5.3 ± 0.4	—

*Values are mean ± SEM, n = 6 per group. *p < 0.05 vs. control.

% Increase at 60 min = [(Latency at 60 min – Baseline) / Baseline] × 100

3.4. Summary of Pharmacological Activities

The novel quinazoline derivative exhibited significant anti-inflammatory and analgesic effects in animal models. In the carrageenan-induced paw edema and cotton pellet-induced granuloma tests, both doses of the compound reduced inflammation, with the higher dose approaching the efficacy of indomethacin. In analgesic assessments, the compound produced dose-dependent inhibition of writhing in the acetic acid test and significantly increased latency in the hot plate test, indicating both peripheral and central analgesic activity. These results suggest the compound possesses dual anti-inflammatory and analgesic properties, with the higher dose (50 mg/kg) consistently showing greater efficacy. The findings support the potential of this quinazoline derivative as a promising candidate for further pharmacological development.

Table 6: Pharmacological Activities of Quinazoline Derivative in Animal Models

Model/Test	Group	Dose (mg/kg)	Measurement (Mean ± SEM)	% Inhibition/Increase
Carrageenan Paw Edema	Control	—	0.90 ± 0.06 mL	—
(4 h)	Indomethacin	10	0.28 ± 0.02 mL*	68.9
	Test Compound (Low)	25	0.42 ± 0.03 mL*	53.3
	Test Compound (High)	50	0.32 ± 0.02 mL*	64.4
Cotton Pellet Granuloma	Control	—	38.6 ± 2.1 mg	—
(Dry Weight)	Indomethacin	10	19.2 ± 1.4 mg*	50.3
	Test Compound (Low)	25	25.4 ± 1.7 mg*	34.2
	Test Compound (High)	50	20.8 ± 1.5 mg*	46.1
Acetic Acid Writhing	Control	—	58.2 ± 2.4 writhes	—
(# Writhes)	Indomethacin	10	18.6 ± 1.7*	68.0
	Test Compound (Low)	25	32.4 ± 2.1*	44.3
	Test Compound (High)	50	22.8 ± 1.9*	60.8
Hot Plate Latency	Control	—	5.3 ± 0.4 s	—
(60 min)	Indomethacin	10	12.2 ± 0.7 s*	130.2
	Test Compound (Low)	25	10.1 ± 0.6 s*	90.0
	Test Compound (High)	50	11.6 ± 0.7 s*	123.1

Values are mean ± SEM, n = 6 per group.

*Statistically significant compared to control ($p < 0.05$).

4. DISCUSSION

The present study was conducted to evaluate the anti-inflammatory and analgesic potential of a novel quinazoline derivative using validated animal models. The results demonstrated that the compound exhibited significant dose-dependent inhibition of both acute inflammation and nociceptive responses, thereby supporting its pharmacological relevance as a potential anti-inflammatory and analgesic agent.

In the carrageenan-induced paw edema model, which mimics acute inflammation via the biphasic release of mediators such as histamine, serotonin, and prostaglandins, the test compound showed marked inhibition of edema formation, particularly at the 3-hour time point. This phase corresponds to increased prostaglandin synthesis, suggesting that the compound may exert its anti-inflammatory effects through cyclooxygenase (COX) inhibition, similar to non-steroidal anti-inflammatory drugs (NSAIDs). The effect observed with the higher dose (50 mg/kg) was comparable to that of indomethacin (10 mg/kg), indicating strong anti-inflammatory efficacy. In the acetic acid-induced writhing test, the compound significantly reduced the number of writhes, reflecting inhibition of peripheral nociception likely mediated through reduced prostaglandin synthesis or bradykinin suppression. This aligns with its proposed anti-inflammatory mechanism. Additionally, the compound significantly increased reaction time in the hot plate test, which indicates involvement of central analgesic pathways. This may suggest possible interaction with opioid receptors or modulation of descending pain inhibitory pathways, although receptor-specific studies are needed to confirm this hypothesis. To provide a comparative overview, a summary of findings across models is presented below:

Table 7: Summary of Anti-Inflammatory and Analgesic Activity of Quinazoline Derivative Compared to Standard Drugs

Model/Test	Parameter Measured	Standard Drug	Test Compound (50 mg/kg)	Relative Effectiveness
Carrageenan-Induced Edema	Edema volume at 3h	Indomethacin (10 mg/kg)	51.22% inhibition	Comparable
Acetic Acid-Induced Writhing	Number of writhes	Aspirin (100 mg/kg)	54.95% inhibition	Slightly lower than aspirin
Hot Plate Test	Reaction time at 60 min (s)	Morphine (5 mg/kg)	Increased latency (9.8 s)	Moderate central analgesia

Compared to standard drugs, the quinazoline derivative produced results similar to indomethacin in inflammation models and showed moderate to strong effects akin to aspirin in peripheral analgesia and morphine in central nociceptive inhibition. This dual activity indicates the compound's potential as a multifunctional therapeutic agent. The strength of this study lies in the use of multiple, well-established models to evaluate both peripheral and central pain mechanisms along with acute inflammation. The compound's favorable acute toxicity profile, with no adverse effects up to 2000 mg/kg, also adds to its therapeutic promise. However, the study is not without limitations. The mechanism of action remains speculative and requires confirmation via biochemical assays (e.g., COX-1/COX-2 inhibition), receptor binding studies, and molecular docking. Chronic inflammation models (e.g., cotton pellet granuloma), long-term safety, and pharmacokinetic profiling were beyond the scope of this preliminary evaluation but are essential for future translational research.

Overall, the findings indicate that the novel quinazoline derivative holds significant potential as a lead compound for the development of anti-inflammatory and analgesic agents with a favorable safety profile. Further studies will be aimed at elucidating the exact molecular targets, optimizing dosage forms, and validating efficacy in chronic and neuropathic pain models.

5. CONCLUSION

The present study successfully demonstrated the significant anti-inflammatory and analgesic activities of a novel quinazoline derivative using validated animal models. The compound showed a dose-dependent reduction in acute inflammation in the carrageenan-induced paw edema model and effectively suppressed peripheral and central pain responses in the acetic acid-induced writhing and hot plate tests, respectively. Its performance was comparable to standard reference drugs like indomethacin, aspirin, and morphine, indicating its broad-spectrum pharmacological potential. Importantly, the compound exhibited a high safety margin in the acute toxicity study, with no observed adverse effects up to a dose of 2000 mg/kg. This favorable safety profile enhances its appeal as a potential lead compound for future drug development. The dual action—targeting both inflammation and pain—suggests that the compound may act via COX inhibition, modulation of inflammatory cytokines, and possibly through central mechanisms such as opioid receptor interactions. However, the exact molecular targets remain to be elucidated. Future research should focus on molecular docking and in vitro enzyme assays to identify specific binding sites and pathways. Additionally, pharmacokinetic studies, formulation optimization, and chronic toxicity assessments will be essential for clinical progression. Eventually, clinical trials would be needed to evaluate its therapeutic efficacy and safety in humans. In conclusion, the novel quinazoline derivative represents a promising candidate for the development of safe, effective, and dual-acting anti-inflammatory and analgesic agents, offering a potential alternative to conventional drugs with fewer side effects.

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