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Apigenin 's Dual Action on Pain and Inflammation: Mechanistic Insights Through NO, COX, and Oxidative Stress Pathways

Vikram H. Potdar[1,2], Ankita P. Kore[2], Asiya S. Bagwan[3], Laxmikant M. Purane[4], Prakash Dilip Jadhav[4] and Atul R. Chopade*[2]

[1]*Department of Pharmacology, Rajarambapu College of Pharmacy, Kasegaon,District – Sangli, Maharashtra, 415404, India*
[2]*Department of Pharmacology, Vasantidevi Patil Institute of Pharmacy, Kodoli. District: Kolhapur, Maharashtra, 416114, India*
[3]*Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Raebareli (NIPER-R), Lucknow (UP)- 226002, India*
[4]*Faculty of Pharmacy, Yashoda ShikshanPrasarak Mandals, Yashoda Technical Campus, Wadhe, Satara (MS) – 415011, India*

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Corresponding Author: **Atul R. Chopade** | E-Mail: **(chopadearv@gmail.com)**

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ABSTRACT

Apigenin, a naturally occurring flavonoid known for its antioxidant and diverse pharmacological properties, was investigated for its potential analgesic and anti-inflammatory effects. The analgesic activity was evaluated using the acetic acid–induced writhing model, whereas anti-inflammatory efficacy was assessed through carrageenan-induced paw edema in Swiss albino mice. Oral administration of apigenin at doses of 25 and 50 mg/kg produced a significant, dose-dependent reduction in writhing responses. Furthermore, the higher dose markedly suppressed carrageenan-induced paw edema, demonstrating notable anti-inflammatory activity.Biochemical analyses revealed that apigenin significantly reduced interleukin-1β (IL-1β) levels while restoring the expression of nuclear factor erythroid 2-related factor 2 (Nrf2), suggesting modulation of inflammatory mediators and oxidative stress–responsive signaling pathways. However, only modest alterations were observed in glutathione (GSH) levels and lipid peroxidation markers. Pharmacological modulation using substance P and L-arginine attenuated the protective effects of apigenin, indicating the possible involvement of nitric oxide and cyclooxygenase-associated signaling pathways in its mechanism of action, the findings demonstrate that apigenin exhibits significant analgesic and anti-inflammatory properties through the regulation of inflammatory cytokines and redox-sensitive molecular pathways, highlighting its therapeutic potential as a natural bioactive compound for the management of pain and inflammatory disorders.

Keywords: *Apigenin, analgesic activity, inflammation, oxidative stress, Nrf2, nitric oxide, cyclooxygenase.*

1. Introduction

Flavonoids constitute a broad class of naturally occurring polyphenolic compounds that are widely distributed in fruits, vegetables, herbs, and medicinal plants. These bioactive compounds are well recognized for their diverse pharmacological properties, including antioxidant, anti-inflammatory, analgesic, antimicrobial, and neuroprotective activities [1]. Due to their significant therapeutic potential and relatively low toxicity, flavonoids have attracted considerable scientific attention as promising candidates for the development of natural and plant-derived therapeutic agents for the management of various human diseases. Among them, apigenin, a dietary flavone abundantly present in parsley, celery, and chamomile, has gained considerable scientific attention due to its favourable safety profile and broad spectrum of biological activities[2]. Previous investigations have shown that apigenin can modulate inflammatory mediators, regulate oxidative stress, and influence signaling pathways associated with chronic inflammatory disorders[4], the analgesic and anti-inflammatory mechanisms of apigenin remain incompletely understood. Most available studies have mainly focused on its antioxidant potential, whereas its direct role in pain modulation and acute inflammatory responses has received comparatively less attention. Experimental animal models remain essential tools for evaluating compounds with potential analgesic and anti-inflammatory activities. The acetic acid–induced writhing assay is widely employed to assess peripheral nociceptive responses, whereas carrageenan-induced paw edema is a well-established experimental model for investigating acute inflammatory reactions [3]. These models provide valuable insights into the mechanisms underlying pain and inflammation, including the release of inflammatory mediators, prostaglandin biosynthesis, cytokine signaling, and oxidative stress pathways, biochemical markers such as interleukin-1β (IL-1β) and nuclear factor erythroid 2-related factor 2 (Nrf2) serve as important indicators for understanding inflammatory and oxidative stress–associated processes. IL-1β is a major pro-inflammatory cytokine involved in the amplification and progression of inflammatory responses [4], while Nrf2 plays a critical role in regulating endogenous antioxidant defense mechanisms and the expression of cytoprotective genes [5]. The evaluation of glutathione (GSH) levels and lipid peroxidation markers provides additional information regarding oxidative tissue damage and antioxidant status during inflammatory conditions.

Therefore, the present study was undertaken to investigate the analgesic and anti-inflammatory effects of apigenin using acetic acid–induced writhing and carrageenan-induced paw edema models in Swiss albino mice. The study further aimed to elucidate the underlying molecular mechanisms through biochemical analyses and pharmacological pathway modulation.

Materials and Methods

2.1 Animal Care and Ethical Approval

Male and female Swiss albino mice weighing between 25 and 30 g were used for the study. The animals were housed under standard laboratory conditions with controlled temperature and humidity, and maintained on a 12 h light–dark cycle. Standard rodent pellet diet and purified water were provided ad libitum throughout the experimental period. Prior to the initiation of the experiments, the animals were acclimatized to the laboratory environment for seven days in order to minimize stress and ensure physiological stability. All experimental procedures were conducted between 09:30 and 17:30 under controlled laboratory conditions. Animal handling and experimental protocols were performed in accordance with the guidelines established by the Committee for the Control and Supervision of Experiments on Animals (CCSEA), Ministry of Environment, Forest and Climate Change, Government of India, to ensure proper animal welfare and ethical compliance. The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) under Approval No. RCP/2024/IAEC/P/04.

2.2 Experimental Materials

The study utilized high-purity reagents and compounds: Apigenin purity 98 % (YUCCA enterprises Mumbai India Pvt. Ltd. CAS no. 520-36-5), acetic acid andcarrageenan (Loba Chemie Pvt Ltd.) and Substance-P (Sigma-Aldrich, USA). Immunological assessments employed IL-1β and Nrf-2 ELISA kits (Krishgen Biosystems, Mumbai). The reference drug indomethacin was sourced from Jagsonpal Pharmaceutical Ltd., while L-Arginine was obtained from Loba Chemie Pvt Ltd. Additional biochemical reagents were procured from certified suppliers at analytical grade quality. Fresh preparations of all solutions were made immediately before experimental use.

2.3 Research Protocol

A total of seventy-two Swiss albino mice of either sex, weighing 20–25 g and approximately 10 weeks of age, were randomly divided into twelve experimental groups comprising six animals per group. Animals initially used in the acetic acid–induced writhing assay were subsequently included in the carrageenan-induced paw edema experiment following an adequate recovery period to minimize physiological stress and experimental interference. Apigenin was administered intraperitoneally at dose levels of 2.5 and 5 mg/kg, while indomethacin (10 mg/kg, i.p.) served as the standard anti-inflammatory drug. All treatment regimens were administered 30 min prior to intraperitoneal injection of acetic acid (0.6% v/v, 10 ml/kg) for the induction of nociceptive responses. To investigate the possible involvement of nitric oxide and cyclooxygenase-associated signaling pathways in the pharmacological effects of apigenin, L-arginine (40 mg/kg, i.p.) and substance P (10 µg/kg, i.p.) were administered 30 min before apigenin treatment. At the end of the inflammatory experiments, the animals were anesthetized using ketamine (50 mg/kg, i.p.), and paw tissue samples were carefully excised for subsequent biochemical analyses and molecular investigations [6].

2.4 Experimental Models and Analytical Methods

a. Pain Response Assessment

The analgesic properties of Apigenin were evaluated using the established acetic acid-induced nociception model and the established protocols (adapted from Koaster et al., 1959), mice received intraperitoneal injections of acetic acid solution (0.6% v/v, 10 ml/kg) to elicit pain responses. The characteristic writhing behavior, manifested as rhythmic abdominal muscle contractions, was quantified over a 30-minute observation period. Treatment compounds were introduced 30 minutes before nociceptive stimulation[7].

b. Inflammation Analysis

To evaluate anti-inflammatory efficacy, we employed the carrageenan-induced edema model, following modified protocols from Winter et al. (1962). The procedure involved subplantar injection of carrageenan solution (1% w/v) into the left hind paw. Edema development was monitored via Vernier caliper measurements at hourly intervals for 5 hours post-injection. Experimental treatments preceded carrageenan administration by 30 minutes[8].

c. Tissue Processing Protocol

Following completion of edema measurements, animals were humanely euthanized under anesthesia via cervical dislocation. Paw tissue specimens were immediately harvested for biochemical marker analysis. Fresh tissue samples (100 mg) underwent mechanical processing in phosphate buffer solution (pH 7.4, 100 ml), followed by centrifugation (3000 rpm, 15 minutes). The resulting supernatant was allocated for multiple biochemical analyses[9].

d. Lipid Peroxidation Analysis

Lipid peroxidation in paw tissue was assessed by measuring thiobarbituric acid reactive substances (TBARS) using a modified method described by [10]. Briefly, 0.1 ml of the tissue homogenate supernatant was mixed with 2 ml of a reagent solution containing thiobarbituric acid (TBA), trichloroacetic acid (TCA), and hydrochloric acid (HCl) in equal proportions. The reaction mixture was then heated in a boiling water bath at 100 °C for 15 min to facilitate color development and subsequently cooled to room temperature. Following incubation, the samples were centrifuged at 1000 rpm for 10 min to obtain a clear supernatant. The absorbance of the supernatant was measured at 535 nm using a spectrophotometer. Quantification of lipid peroxidation products was carried out using 1,1,3,3-tetramethoxypropane (TMP) as the reference standard. The results were expressed as µM/mg tissue weight [10].

2.5 Biochemical Analyses

a. Glutathione Quantification

Reduced glutathione (GSH) levels in tissue samples were estimated using a modified method described by Beutler et al. The assay is based on the reaction between the sulfhydryl groups of GSH and 5,5′-dithiobis-(2-nitrobenzoic acid) (DTNB), resulting in the formation of a yellow-colored chromogen measurable spectrophotometrically. Briefly, 0.5 ml of tissue supernatant was mixed with 2 ml of disodium hydrogen phosphate buffer (0.3 M, pH 8.4), followed by the addition of 0.25 ml of freshly prepared DTNB reagent.

The reaction mixture was allowed to develop color, and the absorbance was subsequently recorded at 412 nm using a spectrophotometer. The concentration of GSH was determined using a standard calibration curve prepared with reduced glutathione standards, and the results were expressed as μM/mg tissue weight [11].

b. Protein Marker Assessment

Quantitative analysis of Nrf-2 and IL-1β employed commercial immunoassay kits (Krishgen Biosystems). Sample preparation and analysis strictly followed manufacturer-specified protocols to ensure measurement accuracy. Kit-specific reagents were prepared and utilized according to the provided guidelines, optimizing target protein detection. Calibration curves were established using kit-supplied standards. Microplate readings at prescribed wavelengths enabled concentration determinations based on standardized parameters[12].

2.6 Data Processing and Statistical Evaluation

All experimental data were expressed as mean ± standard deviation (SD). Statistical analysis was performed using one-way analysis of variance (ANOVA), followed by the Tukey–Kramer multiple comparison test to determine significant differences among the experimental groups. All statistical computations were conducted using GraphPad Prism. A probability value of $p< 0.05$ was considered statistically significant. The adopted statistical approach ensured accurate interpretation of treatment-related effects while minimizing the influence of experimental variability and random error.

2.7 Ligand Structure Preparation

The three-dimensional structure of Apigenin (PubChem CID: 5280443) was retrieved from the PubChem compound database (https://pubchem.ncbi.nlm.nih.gov/) in SDF format. The downloaded structure was subsequently subjected to energy minimization to achieve a geometrically optimized, low-energy conformation, ensuring structural accuracy prior to docking analysis. Force field-based geometry optimization was performed to eliminate steric clashes and relieve unfavorable bond angles and torsions. The refined ligand structure was then converted into the LigandScout-compatible (.lqt) format for downstream molecular docking studies.

2.8 Protein Structure Preparation

The three-dimensional crystal structures of the target proteins were retrieved from the RCSB Protein Data Bank. Two protein targets were selected based on their established involvement in inflammatory signaling pathways: Cyclooxygenase-2 (COX-2; Prostaglandin H Synthase-2) complexed with the selective inhibitor SC-558 (PDB ID: 1CX2), and human Interleukin-1 beta (IL-1β) complexed with a low-molecular-weight antagonist (PDB ID: 8C3U). Prior to molecular docking, the retrieved protein structures were subjected to a standardized preparation protocol. The preparation process included the removal of co-crystallized water molecules and heteroatom groups, addition of polar hydrogen atoms, assignment of Gasteiger partial charges, and energy minimization to eliminate steric strain and optimize structural stability. The prepared protein structures were subsequently imported into PyRx for grid box generation and docking analysis.

2.9 Molecular Docking

Molecular docking studies were performed using PyRx, which incorporates the AutoDock Vina algorithm for predicting ligand–protein interactions, binding affinities, and preferred binding conformations within the active sites of target proteins. Grid box parameters were carefully optimized to fully encompass the known active-site residues of each protein target. For each docking simulation, an exhaustiveness value of 8 was applied to ensure reliable conformational sampling. The docking pose exhibiting the lowest binding free energy (kcal/mol) was selected as the most favorable conformation for subsequent interaction analysis. The docked ligand–protein complexes were further visualized and analyzed using Discovery Studio Visualizer to characterize the nature and geometry of molecular interactions. These interactions included hydrogen bonding, hydrophobic contacts, π-alkyl interactions, π-sigma interactions, amide–π stacking, and van der Waals forces, which collectively contribute to ligand-binding stability and biological activity.

3. Results

3.1 Analgesic Effects of Apigenin

Administration of acetic acid successfully induced characteristic writhing behaviors in the experimental mice. Treatment with Apigenin demonstrated dose-dependent analgesic effects, with both 25 mg/kg and 50 mg/kg doses significantly reducing writhing frequency compared to control animals. The standard analgesic indomethacin showed comparable efficacy in suppressing the pain response. Mechanistic studies revealed that pretreatment with either substance P (a COX pathway modulator) or L-arginine (NO pathway precursor) significantly diminished Apigenin's analgesic effects at the 50 mg/kg dose, evidenced by increased writhing behaviors compared to Apigenin treatment alone.

3.2 Anti-inflammatory Activity Assessment

The carrageenan challenge effectively induced measurable paw edema in test subjects. Apigenin treatment (50 mg/kg) demonstrated significant anti-inflammatory activity, reducing paw swelling comparable to the standard anti-inflammatory agent indomethacin. The protective effects of Apigenin were notably attenuated by pretreatment with either substance P or L-arginine, resulting in significantly increased paw thickness measurements compared to animals receiving only Apigenin. These findings suggest the involvement of both COX and NO pathways in Apigenin's anti-inflammatory mechanism.

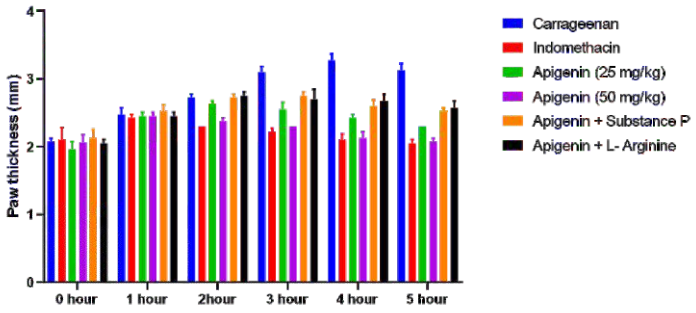

Fig.1: The figure illustrates Apigenin impact on acetic acid-induced writhings. Statistical significance was assessed via two-way ANOVA, followed by Tukey's posthoctest. [a]p <0.05 vs aceticacid, [b]p <0.05 vs indomethacin, [c]p <0.05 vs harmaline(2.5 mg/kg), [d]p< 0.05 vs harmaline (5 mg/kg).

3.3 Effects on Tissue GSH Levels

Carrageenan administration markedly depleted glutathionelevels in paw tissue. Apigenin treatment (50 mg/kg) did not effectively prevented this GSH depletion, maintaining levels similar to carrageenan-only treated animals. The reference drug indomethacin showed similar protective effects on tissue GSH content. The GSH non-preserving effect of Apigenin was significantly similar by pretreatment with either substance P or L-arginine, suggesting that both COX and NO pathways may not contribute to Apigenin's antioxidant mechanisms. These interventions resulted in significantly GSH levels compared to animals treated with Apigenin alone.

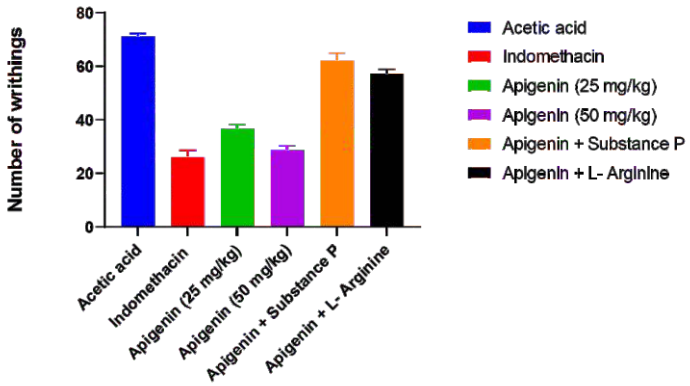

Fig. 2: The figure illustrates Apigenin impact on carrageenan-induced paw edema. Statistical significance was assessed via two-way ANOVA, followed by Tukey's posthoctest. [a]p < 0.05 vs carrageenan, [b]p < 0.05 vs indomethacin, [c]p < 0.05 vs harmaline (5 mg/kg).

3.4 Impact of Apigenin on TBARS Levels in Carrageenan-Induced Paw Inflammation

Carrageenan administration produced a significant rise in TBARS levels in mouse paw tissue, indicating enhanced lipid peroxidation. Treatment with indomethacin markedly suppressed this increase when compared with the carrageenan control group. In contrast, Apigenin (50 mg/kg) showed only minimal protection against carrageenan-induced elevation of TBARS, with levels remaining comparable to those observed in carrageenan-treated animals. The pretreatment with substance P diminished the modulatory effect of Apigenin on TBARS production, resulting in values comparable to the Apigenin-treated group. Similarly, animals receiving L-arginine exhibited TBARS concentrations that did not differ significantly from those observed following Apigenin treatment alone (Fig. 3).

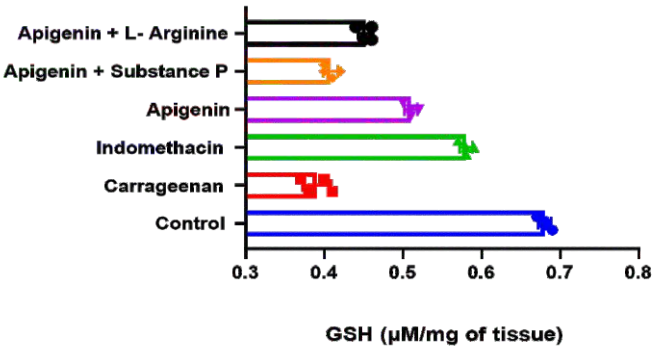

Fig. 3: The figure illustrates Apigenin impact on (A) GSH and (B) TBARS level in carrageenan-treated paw. Statistical significance was assessed via two-way ANOVA, followed by Tukey's post hoc test. [a]p < 0.05 vs control, [b]p < 0.05 vs carrageenan, [c]p < 0.05 vs indomethacin, [d]p< 0.05 vs harmaline (5 mg/kg).

3.5 Effect of Apigenin on Nrf-2 Levels in Carrageenan-Induced Paw Inflammation

Carrageenan administration significantly reduced Nrf-2 expression in paw tissue when compared with the normal control group. Pretreatment with indomethacin effectively prevented this decline and restored Nrf-2 levels toward normal values. Administration of Apigenin (50 mg/kg) also produced a marked elevation in Nrf-2 expression relative to the carrageenan-treated group, indicating activation of antioxidant defense pathways. The prior treatment with substance P weakened the Nrf-2–enhancing effect of Apigenin, resulting in lower Nrf-2 levels than those observed with Apigenin alone. A similar reduction in Nrf-2 expression was noted in animals receiving L-arginine before Apigenin treatment (Fig. 4).

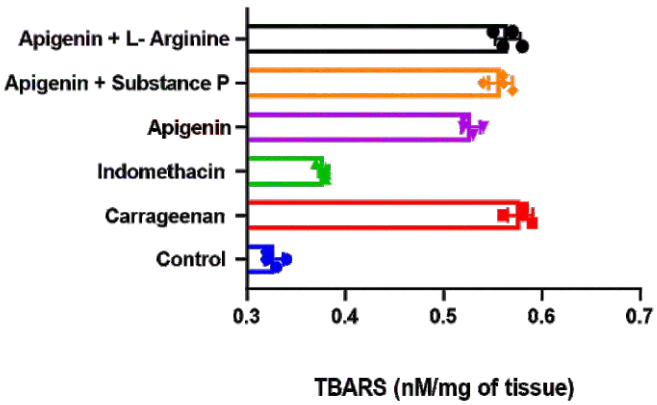

Fig. 4: The figure illustrates Apigenin impact on Nrf-2 level in carrageenan-treated paw. Statistical significance was assessed via two-way ANOVA, followed by Tukey's post hoc test. [a]p < 0.05 vs control, [b]p < 0.05 vs carrageenan, [c]p < 0.05 vs indomethacin, [d]p< 0.05 vs harmaline (5 mg/kg).

3.6 Impact of Apigenin on IL-1β Levels in Carrageenan-Induced PawInflammation

The effect of Apigenin on IL-1β expression in inflamed paw tissue was also investigated. Carrageenan administration produced a marked elevation in IL-1β levels compared with the normal control group. Pretreatment with indomethacin significantly suppressed this increase, indicating effective inhibition of the inflammatory response. Similarly, Apigenin (50 mg/kg) significantly reduced carrageenan-induced IL-1β production. An administration of substance P prior to Apigenin attenuated this protective effect, resulting in comparatively higher IL-1β levels than those observed in the Apigenin-treated group. In animals pretreated with L-arginine, only a mild and statistically non-significant increase in IL-1β concentration was observed relative to the Apigenin group. These findings suggest that higher doses of L-arginine may further interfere with the IL-1β-lowering activity of Apigenin (Fig. 5).

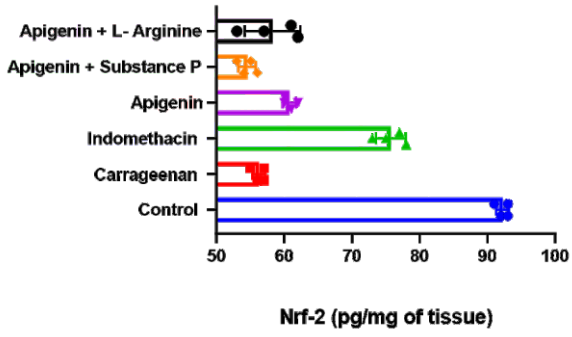

Fig. 5: The figure illustrates Apigenin impact on IL-1β levels in carrageenan-treated paws. Statistical significance was assessed via two-way ANOVA, followed by Tukey's post hoc test. [a]p < 0.05 vs control, [b]p < 0.05 vs carrageenan, [c]p < 0.05 vs indomethacin, [d]p< 0.05 vs harmaline (5 mg/kg).

3.7 Docking Analysis of Apigenin with COX-2 (PDB ID: 1CX2)

Apigenin demonstrated a strong binding affinity toward the COX-2 active site, yielding a binding free energy of −8.6 kcal/mol. Interaction analysis revealed a diverse network of non-covalent contacts stabilizing the ligand within the binding pocket. Specifically, π-alkyl hydrophobic interactions were observed with VAL349 and ALA527, while an amide–π stacking interaction was identified with GLY526, contributing to the planar aromatic stabilization of the flavone scaffold. In addition, an extensive network of van der Waals interactions was established with the surrounding active site residues, including SER353, LEU359, TYR355, VAL116, LEU531, PHE518, VAL523, LEU384, MET522, LEU352, TRP387, TYR385, and SER530. These interactions collectively indicate that Apigenin occupies the COX-2 active site in a manner analogous to known selective inhibitors, suggesting a competitive inhibitory mechanism. The three-dimensional binding pose and corresponding two-dimensional interaction diagram are illustrated in Figure 6.

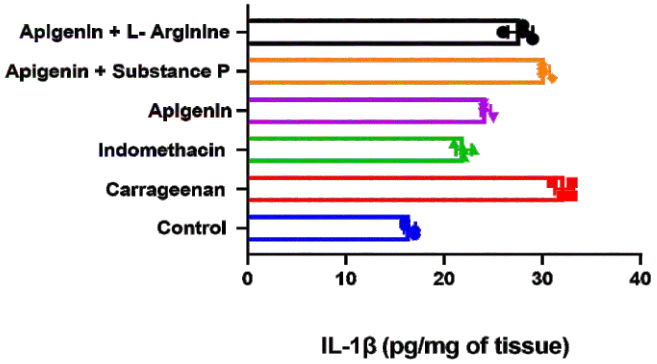

Fig. 6: The figure illustrates Molecular docking interaction of Apigenin with Cyclooxygenase-2 (Prostaglandin Synthase-2) Complexed With A Selective Inhibitor, Sc-558 (PDB ID 1CX2).

3.8 Docking Analysis of Apigenin with IL-1β (PDB ID: 8C3U)

Apigenin also exhibited favorable binding toward human IL-1β, with a calculated binding free energy of −6.1 kcal/mol. The interaction profile revealed that Apigenin engages the IL-1β binding pocket through a combination of hydrophobic and electrostatic contacts. π-Alkyl interactions were identified with VAL41, while a π-sigma interaction was observed with GLU64, indicating partial involvement of the aromatic ring system in non-classical electrostatic contacts. Additional van der Waals interactions were recorded with SER43, LEU62, VAL41, and LYS65, further stabilizing the ligand within the binding interface. These findings suggest that Apigenin may interfere with IL-1β receptor recognition or antagonist binding, thereby potentially attenuating downstream pro-inflammatory signaling cascades. The corresponding binding pose and interaction map are presented in the figure 7.

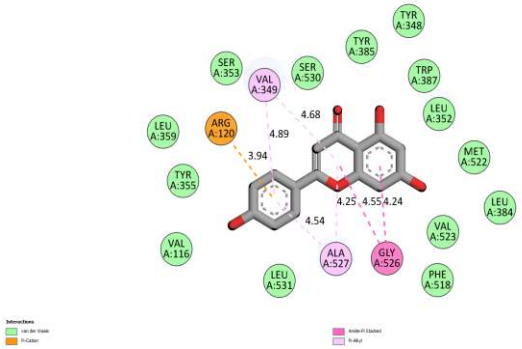

Fig. 7: The figure illustrates Molecular docking interaction of Apigenin with the human IL-1beta Crystal Structure of human IL-1beta in complex with a low molecular weight antagonist (PDB ID 8C3U9).

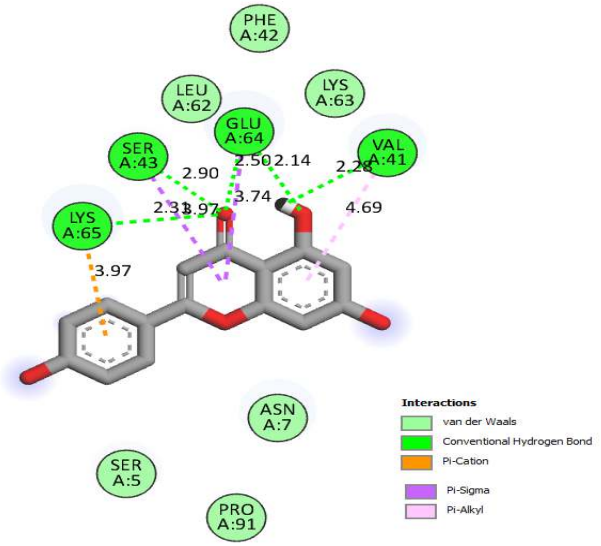

Fig. 8

4. Discussion

The present study demonstrated that apigenin possesses significant analgesic and anti-inflammatory activity in experimental models of pain and inflammation. The observed pharmacological effects appear to involve modulation of inflammatory mediators, oxidative stress–related pathways, and signaling systems associated with nitric oxide and cyclooxygenase activity. In the acetic acid–induced writhing model, apigenin produced a dose-dependent reduction in nociceptive behavior, indicating peripheral analgesic activity. This model is particularly sensitive to compounds capable of suppressing prostaglandin synthesis and inflammatory mediator release. Earlier reports have shown that flavonoids, including apigenin, can inhibit cyclooxygenase-mediated inflammatory responses and reduce peripheral sensitization[7]. The attenuation of apigenin's analgesic effect by substance P and L-arginine suggests the involvement of neuro-inflammatory signaling and nitric oxide pathways in its mechanism of action. Nitric oxide is known to contribute to inflammatory hyperalgesia and peripheral sensitization, while flavonoids have been reported to suppress inducible nitric oxide synthase (iNOS) expression and nitric oxide production[4]. The carrageenan-induced paw edema model further confirmed the anti-inflammatory potential of apigenin. Carrageenan administration induces acute inflammatory edema through the sequential release of histamine, serotonin, prostaglandins, cytokines, and nitric oxide. Treatment with apigenin significantly reduced paw swelling, indicating suppression of inflammatory progression. The reversal of this effect following L-arginine pretreatment further supports the participation of nitric oxide–dependent inflammatory signaling pathways[13]. Previous investigations have similarly reported that apigenin inhibits inflammatory cytokines and suppresses COX-2 expression through regulation of NF-κB signaling pathways[14]. Biochemical findings also supported the anti-inflammatory activity of apigenin. The compound significantly reduced IL-1β levels in inflamed tissue, suggesting inhibition of pro-inflammatory cytokine production. Simultaneously, restoration of Nrf2 expression indicated activation of endogenous antioxidant defense mechanisms. Nrf2 plays an important role in regulating cellular antioxidant responses and suppressing oxidative stress–mediated inflammatory signaling[15].

The attenuation of these protective effects by substance P and L-arginine suggests possible interaction between Nrf2 activation and COX/NO-mediated pathways. Although apigenin influenced inflammatory signaling markers, its effects on GSH and TBARS levels were comparatively limited. These findings indicate that the anti-inflammatory activity of apigenin may depend more strongly on modulation of signaling pathways and inflammatory mediators than on direct antioxidant scavenging alone. Molecular docking studies further supported the *in vivo* findings. Apigenin exhibited favorable binding affinity toward COX-2, interacting with key residues involved in stabilization of the active site. Similar interactions were observed with IL-1β, suggesting possible interference with cytokine-associated inflammatory signaling. Such multi-target interactions are commonly observed with flavonoids and other polyphenolic compounds possessing broad anti-inflammatory activity[16], the findings indicate that apigenin exerts analgesic and anti-inflammatory effects through coordinated modulation of cyclooxygenase activity, nitric oxide signaling, inflammatory cytokines, and oxidative stress–responsive pathways.

Table 1: In Silico BBB permeability and drug likeliness predictions of APIGENIN byhttps://molsoft.com/.

Molecule	MW	#H-bond acceptors	#H-bond donors	MolPSA	MolVol	Number of stereo centers	pKa of most Basic/Acidic group	Drug likeliness score	BBB score
Apigenin	270.05	5	3	73.57 A^2	260.14 A^3	0	< 0. / 6.70	0.39	2.97

Table 2: Summarized details of physicochemical properties of Apigenin (4′,5,7-trihydroxyflavone)

Parameters	Description
Chemical name	5,7-dihydroxy-2-(4-hydroxyphenyl)chromen-4-one
Chemical Formula	$C_{15}H_{10}O_5$
Exact Mass	270.05282342 Da
Molecular Weight [g/mol]	270.24 g/mol
XLogP3	1.7
Topological Polar Surface Area	87 $Å^2$
m/z:	270.0528 (monoisotopic mass)
Elemental Analysis	Carbon (C): 66.67%; Hydrogen (H): 3.73%; Oxygen (O): 29.60%
Boiling Point	Approximately 333.35°C (606.5 K)
Melting Point	347.5 °C
Log P	3.02
Carcinogenicity and Mutagenicity Risk (CMR)	No significant evidence in literature suggesting carcinogenic or mutagenic properties

Conclusion

The present investigation demonstrates that apigenin exhibits significant analgesic and anti-inflammatory effects in experimental models of pain and inflammation. The observed pharmacological actions appear to involve suppression of cyclooxygenase and nitric oxide signaling pathways, reduction of IL-1β expression, and enhancement of Nrf2-mediated cellular defense mechanisms. Molecular docking findings further support the interaction of apigenin with inflammatory targets such as COX-2 and IL-1β, these findings highlight the therapeutic potential of apigenin as a multi-target phytoconstituent for the management of inflammatory and nociceptive disorders. The preclinical and translational studies are warranted to establish its clinical applicability.

Acknowledgment

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Author Contributions

All authors contributed to the conception, design, execution, and interpretation of the study. They collectively participated in data acquisition, analysis, and manuscript preparation, and approved the final version for submission.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process

During the preparation of this manuscript, the authors used AI-assisted tools (ChatGPT and Grammarly) to improve the language and clarity of the text. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Declarations of Competing Interest

The authors declare no competing interests, either financial or non-financial.

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