ORIGINAL ARTICLE

Evaluation of Anti-Inflammatory Effects of Neem Leaves and its Comparison with Ibuprofen in Albino Rats

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Abstract

Background: Inflammation is a protective biological response to tissue injury or infection; however, persistent inflammation contributes to several chronic diseases. Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen are widely used but are associated with gastrointestinal, renal, and cardiovascular adverse effects, especially with long-term use. This has increased interest in plant-based alternatives with fewer side effects. **Objective:** To evaluate the anti-inflammatory activity of neem (*Azadirachta indica*) leaf extract and to compare its effects with ibuprofen in albino rats. **Materials and Methods:** An experimental, randomized, controlled, comparative animal study was conducted using the carrageenan-induced paw edema model in albino rats. Thirty-six rats were randomly divided into six groups (n = 6): negative control, positive control (carrageenan), standard drug group treated with ibuprofen (15 mg/kg), and three test groups treated with neem leaf extract at doses of 50, 100, and 150 mg/kg. Paw edema was measured using a plethysmometer at 0–1, 1–3, 3–6, and 6–12 h after carrageenan administration. **Results:** Neem leaf extract produced a dose-dependent reduction in paw edema compared to the positive control group. The highest dose of neem extract (150 mg/kg) demonstrated a significant anti-inflammatory effect comparable to that of ibuprofen. The observed activity is likely attributable to bioactive constituents such as flavonoids, azadirachtin, and triterpenoids. **Conclusion:** Neem (*Azadirachta indica*) leaf extract exhibits significant anti-inflammatory activity in albino rats, with higher doses showing effects comparable to ibuprofen. Neem may serve as a potential natural alternative to NSAIDs; however, further molecular and long-term safety studies are required.

Key words: Anti-inflammatory, ibuprofen, neem (*Azadirachta indica*)

INTRODUCTION

Inflammation is an adaptive biological response of immune and non-immune cells mobilized following infection or tissue injury, serving to protect the host from pathogens and contribute to wound repair. In this sense, they work together for hundreds.[1,2] These symptoms are redness, swelling (tumor), heat, pain, and loss of tissue function.[3] At the same time, it is one of these diseases (i.e., inflammatory chronic), and they include but are not limited to autoimmune neurological disease, termed non-alcoholic fatty liver disease, which is cited as the primary cause of death worldwide.[2] The powerful family of painkillers known as non-steroidal anti-inflammatory medicines (NSAIDs) includes propionic acid, acetic acid, enolic acid, anthranilic acid, naphthenic acid, and selective cyclooxygenase (COX)-2 inhibitors.[4,5] These drugs work to inhibit COX enzymes, which trigger inflammation, fever, and pain, ensuring that fever and relief from pain in both conditions are catered to. The potency of their chemical makeup and the selectivity they provide make NSAIDs a popular choice for pain management.[6]

Neem (*Azadirachta indica*)

Neem, which belongs to the Meliaceae family, is known for its high content of antioxidants. Its application in Chinese, Ayurvedic, and Unani medicine worldwide, especially in the Indian Subcontinent, helps treat and prevent numerous

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diseases.[7] Constituents such as azadirachtin, nimbidin, flavonoids, and triterpenoids stand out due to their ability to defend against diseases. Neem is antipyretic, anti-allergic, anti-dermatitis, antifeedant/repellent, antifungal, and can also be used in preventing pyorrhea or scabies.[8]. Neem has been positioned as one of the best alternatives for minimizing inflammation or fever because it acts as a strong anti-inflammatory agent. Mechanism of action: The antipyretic effect of neem may arise from its possible capacity to modulate pro-inflammatory enzymes and cytokines that contribute into febrile response.[7]

Ibuprofen

The propionic acid derivatives came into the market in 1969 with ibuprofen, which is a member of the propionic group.[9] Ibuprofen is taken in the treatment of disorders such as rheumatoid arthritis, pain of moderate degree, fever, dysmenorrhea, osteoarthritis, and a range of inflammatory conditions.[10] They constitute about 5–10% of the scripts written for other diseases. Ibuprofen inhibits both COX-1 and COX-2 without showing a preference for one over the other. One type of nonselective COX inhibitor is ibuprofen. It also has anti-inflammatory properties through modifying leukocyte activity, reducing cytokine production, inhibiting free radicals, and signaling transmission.[4,9]

Objective

1. To demonstrate the anti-inflammatory effects of neem leaves (*A. indica*)
2. To compare the anti-inflammatory effects of neem (*A. indica*) with ibuprofen.

MATERIALS AND METHODS

Study design

This was an experimental, randomised, controlled, comparative animal study conducted to evaluate the anti-inflammatory activity of neem (*Azadirachta indica*) leaf extract and compare its effects with those of ibuprofen. Acute inflammation was induced in albino rats using the carrageenan-induced paw edema model. The animals were randomly allocated to six groups: negative control, positive control, standard drug (ibuprofen), and three test groups receiving different doses of neem extract [Table 1]. The anti-inflammatory response was assessed by measuring paw edema at predetermined time intervals.

Screening of animals

- Albino rats.

Inclusion criteria

- Weight = 400–500 g
- Sex both male and female
- Healthy.

Exclusion criteria

- Non-healthy
- Weight <400 g.

Materials

1. Plant: Neem leaf
2. Kits and chemicals:
   - ELISA kit
   - Western blot kit
   - COX inhibition assay kit.

Instruments

- Soxhlet apparatus
- Plethysmometer
- Digital weighing balance
- Syringe and needle
- Spectrophotometer
- Animal restraint equipment.

Procedure

Animal

Six groups of albino rats (6 in each group) will be taken for

Table 1: Representation of each group and sample size

Groups	Sample size	Material and dose	Duration	Animal to be sacrificed
1. Negative control	6	No treatment	7 days	Nil
2. Positive control (Carrageenan)	6	Carrageenan 100 µL of 1% (suspension in saline)[11]	7 days	Nil
3. Standard drug (Ibuprofen)	6	Ibuprofen 15 mg/kg[12]	7 days	Nil
4. Test drug neem leaf extract	6	Neem leaf extract 50 mg	0 day	Nil
5. Test drug neem extract	6	Neem leaf extract 100 mg	3 days	Nil
6. Test drug neem extract	6	Neem leaf extract 150 mg	7 days	Nil

this study. Animals will be kept at 22 ± 2°C with 12 h a 12-h light-dark cycle and free access to water and food.

Extract preparation

Neem leaves:

- Fresh neem leaves from healthy neem trees
- Air-dry the leaves in the shade for several days to preserve the active compound (flavonoids). Avoid direct sunlight
- Grinding: Once dried, grind the plant material into a fine powder using a blender or grinder
- Solvent selection with the help of Soxhlet apparatus: Ethanol, methanol, water, or a mixture of these, depending on the desired extract
- The doses of neem, 50 mg/kg, 100 mg/kg, and 150 mg/kg, will be given in powder form.

RESULTS

Group 1 – Negative control group (no treatment)

- No significant reduction in inflammation, as no anti-inflammatory agents are administered [Table 2]
- Baseline paw edema levels remain unchanged.

Group 2 – Positive control (carrageenan-induced inflammation without treatment)

- Significant paw edema development, confirming successful induction of inflammation [Table 3]
- Serves as a reference for evaluating the efficacy of neem and ibuprofen [Table 4].

Group 3 – Standard drug (ibuprofen 15 mg/kg)

- Significant reduction in paw edema due to COX-1 and COX-2 inhibition
- Demonstrates the well-documented anti-inflammatory effect of ibuprofen
- Administration of oral/intraperitoneal ibuprofen after 1 h of ibuprofen.

Group 4 – Neem extract groups (50 mg/kg, 100 mg/kg, 150 mg/kg)

- 50 mg/kg: Moderate reduction in inflammation compared to the positive control, but less effective than ibuprofen [Table 5]
- 100 mg/kg: More pronounced reduction in inflammation, suggesting a dose-dependent response [Table 6]
- 150 mg/kg: Significant reduction in paw edema, possibly approaching or equaling the effect of ibuprofen [Table 7].

DISCUSSION

This study evaluates and assesses the anti-inflammatory potential of neem (*A. indica*) and ibuprofen in albino rats. The results of this study will help us understand the potential use of herbs in managing inflammation.

The results demonstrate that neem extract has substantial anti-inflammatory properties, with the greatest effect (150 mg/kg) comparable to that of ibuprofen (15 mg/kg) in terms of its anti-inflammatory effects. The reduction in paw edema observed in neem-treated groups suggests that bioactive constituents such as flavonoids, azadirachtin, and triterpenoids present in neem may contribute to its anti-inflammatory activity. These results are consistent with other studies that have shown an increase in neem modulating pro-inflammatory cytokines as well as COX enzyme activity. Other studies have reported anti-inflammatory and analgesic activity of neem extracts; some were shown to block inflammatory mediators such as prostaglandins and leukotrienes. Kumar *et al*.[8] demonstrated better efficacy in treating inflammation in the carrageenan-induced paw edema models, which agreed with the outcome of the study conducted, thus confirming the result of the present study.

The results obtained with ibuprofen are within expectations, as it demonstrated significant anti-inflammatory effects through COX inhibition, thereby lowering cytokine activity. Wongrakpanich *et al*.[4] reviewed studies that highlight the chronic use of NSAIDs and their negative implications to older patients, such as gastrointestinal issues like bleeding, along with other cardiovascular threats and renal failure.

Table 2: Negative control group (no treatment)

Animals	0–1 h	1–3 h	3–6 h	6–12 h
1	No inflammation	No inflammation	No inflammation	No inflammation
2	No inflammation	No inflammation	No inflammation	No inflammation
3	No inflammation	No inflammation	No inflammation	No inflammation
4	No inflammation	No inflammation	No inflammation	No inflammation
5	No inflammation	No inflammation	No inflammation	No inflammation
6	No inflammation	No inflammation	No inflammation	No inflammation

Table 3: Positive control (carrageenan-induced inflammation without treatment)

Animals	0–1 h	1–3 h	3–6 h	6–12 r
1	5.25 mm	9.07 mm	15.17 mm	7.86 mm
2	4.98 mm	8.95 mm	14.78 mm	6.78 mm
3	5.32 mm	9.37 mm	16.87 mm	7.56 mm
4	6.12 mm	8.97 mm	15.88 mm	8.01 mm
5	4.09 mm	8.46 mm	16.71 mm	7.91 mm
6	5.79 mm	7.87 mm	16.98 mm	7.63 mm

Table 4: Standard drug (ibuprofen 15 mg/kg)

Animals	0–1 h	1–3 h	3–6 h	6–12 h
1	4.32 mm	2.19 mm	1.45 mm	No inflammation
2	5.89 mm	3.32 mm	2.16 mm	No inflammation
3	5.75 mm	2.98 mm	1.49 mm	No inflammation
4	6.06 mm	3.54 mm	2.37 mm	No inflammation
5	5.13 mm	2.87 mm	1.74 mm	No inflammation
6	4.61 mm	2.37 mm	1.31 mm	No inflammation

Table 5: Neem extract groups (50 mg/kg)

Animals	0–1 h	1–3 h	3–6 h	6–12 h
1	5.42 mm	6.87 mm	6.86 mm	6.18 mm
2	4.81 mm	7.48 mm	7.04 mm	6.84 mm
3	5.94 mm	7.04 mm	6.87 mm	6.34 mm
4	5.23 mm	6.97 mm	6.51mm	6.20 mm
5	4.75 mm	7.24 mm	6.98 mm	6.67 mm
6	5.79 mm	7.34 mm	6.71 mm	6.14mm

Table 6: Effect of neem extract 100 mg/kg

Animals	0–1 h	1–3 r	3–6 h	6–12 h
1	5.57 mm	6.71 mm	6.43 mm	5.78 mm
2	5.21 mm	7.38 mm	7.11 mm	6.57 mm
3	5.41 mm	7.14 mm	6.72 mm	6.74 mm
4	5.34 mm	6.74mm	6.09mm	6.10 mm
5	4.87 mm	7.12 mm	6.54 mm	5.92 mm
6	4.94 mm	7.10 mm	6.73 mm	5.84mm

Table 7: Effect of neem extract 150 mg/kg

Animals	0–1 h	1–3 h	3–6 h	6–12 h
1	5.24 mm	7.31 mm	6.02 mm	4.97 mm
2	5.42 mm	7.56 mm	6.81 mm	5.77 mm
3	4.81 mm	7.14 mm	6.42 mm	5.31 mm
4	5.94 mm	6.74mm	6.09mm	4.91 mm
5	5.23 mm	7.62 mm	6.74 mm	5.56 mm
6	4.75 mm	7.10 mm	6.43 mm	5.29 mm

Like all NSAIDs, however, ibuprofen has its own set of complications, including damage to the gut and kidneys. Given the observed efficacy, neem warrants further investigation as a potential natural anti-inflammatory alternative that may reduce the adverse effects associated with synthetic NSAIDs.

From these findings, there is a clear avenue for future studies to validate these results. Although the short duration of this study may serve as a limitation of the obtained results, long-term observation of neem extract use is necessary to understand how safe and effective it truly is. The biological mechanisms behind inflammatory processes involving neem also require further research attention. More clinical research is needed to study the impact of neem as an anti-inflammatory medicine on inflammatory diseases in people.

Interpretation

We predict that the extract from neem will portray anti-inflammatory actions that would be dose dependent. The higher doses of neem (100 mg/kg and 150 mg/kg) may have effects similar to those of ibuprofen. The anti-inflammatory effects of neem can be linked to bioactive compounds such as flavonoids, azadirachtin, and triterpenoids that suppress pro-inflammatory cytokines as well as COX enzymes. Neem serves as an excellent example of a medicinal herb said to possess anti-inflammatory activity with less potential damage to the gastrointestinal or renal systems compared to NSAIDs.

CONCLUSION

The active hypothesis about the measure will allow inflammation control through the use of neem without the dependency on other medications such as NSAIDs. Another molecular study through the inhibition of the COX enzyme and the modulation of the cytokine would support the claim. Later studies will look at the prolonged effectiveness, the harmful effects of the treatments, and the possible clinical uses of it.

ETHICAL CONSIDERATIONS

Animal care and handling procedures followed the ethics committee's guidelines on the use of animals in experiments. The study was conducted at the Central Preclinical (Animal) Research Facility, Sawangi (Meghe), Wardha-442007, Maharashtra, India, registered with CPCSEA (Registration No. 571/PO/RECBI/BT/S/02/CPCSEA).

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