International Journal of Zoology and Applied Biosciences **ISSN: 2455-9571**
Volume 10, Issue 6, pp: 300-305, 2025
https://doi.org/10.55126/ijzab.2025.v10.i06.035 **http://www.ijzab.com**

Research Article

SCIENTIFIC EVALUATION OF SIDDHA HERBAL DECOCTION MANJAL NOI KUDINEER: INSIGHTS INTO ITS ANTIPYRETIC AND ANTI-INFLAMMATORY MECHANISMS

[1*]Senthil Kumar P, [2]Elansekaran S and [3]Bharath Kumar G

[1]Velumailu Siddha Medical College and Hospital, Sriperumbudur, Kancheepuram, Tamil Nadu, India.
[2]Department of Noi Naadal, National Institute of Siddha, Tambaram, Chennai, Tamil Nadu, India.
[3]The Tamil Nadu Dr MGR medical University, Guindy, Chennai, Tamil Nadu, India.

Article History: Received 22nd September 2025; Accepted 16th November 2025; Published 1st December 2025

ABSTRACT

Manjal noi kudineer (MNK) is a classical Siddha formulation documented in the Siddha Pharmacopoeia of India, traditionally employed for its detoxifying, anti-inflammatory, and antipyretic properties. Despite its long-standing use, systematic pharmacological validation is limited. This study aimed to evaluate the antipyretic and anti-inflammatory potential of MNK in experimental animal models. Female Wistar rats were used to assess antipyretic activity via Brewer's yeast-induced pyrexia, while carrageenan-induced paw edema in Wistar rats was employed for anti-inflammatory evaluation. MNK was administered orally at doses of 50, 250, and 500 mg/kg. Rectal temperature and paw edema were recorded at specified intervals and compared with negative (vehicle) and positive (paracetamol/diclofenac) controls. MNK at 500 mg/kg significantly reduced pyrexia, comparable to paracetamol. Similarly, MNK dose-dependently inhibited paw edema, with the highest dose approaching the efficacy of diclofenac. MNK exhibits significant antipyretic and anti-inflammatory effects in vivo, supporting its traditional therapeutic use and providing a foundation for further pharmacological studies.

Keywords: Manjal Noi Kudineer, Siddha medicine, Antipyretic activity, Anti-inflammatory activity.

INTRODUCTION

Fever and inflammation are among the most frequently encountered clinical manifestations in both traditional and contemporary medical systems. In Siddha medicine, these conditions are primarily attributed to disturbances in the *udal thathukkal* (seven body constituents) and derangements of the three fundamental humours, *Vatham, Pitham* and *Kabam* (Anbarasu 2018; Subramanian 2015). The integrity of these constituents is considered essential for maintaining physiological balance, and their dysfunction is believed to precipitate pathological processes such as *jvaram* (fever) and *sotham* (inflammation) (Kulanthai, 2019). Herbal decoction powders, known as *kudineer choornam*, occupy a central place in Siddha therapeutics for managing febrile and inflammatory disorders (Rajan, 2017). Among them, Manjal Noi Kudineer (MNK) is a classical formulation prescribed for conditions characterized by heat, swelling, and toxin accumulation. The Siddha Pharmacopoeia describes MNK as possessing *jvaranivarthi* (antipyretic), *sothanivarthi* (anti-inflammatory) and *vishahara* (detoxifying) properties owing to the synergistic actions of its botanical ingredients (Siddha Pharmacopoeia Committee, 2008). Despite its long-standing clinical relevance, modern scientific evidence supporting its pharmacological activity remains sparse, highlighting the need for systematic preclinical evaluation (Paramasivam 2020).

From a biomedical perspective, fever is triggered by exogenous and endogenous pyrogens that stimulate immune cells to release pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-6, which subsequently activates cyclooxygenase-2 (COX-2) and elevates prostaglandin E_2 levels in the hypothalamus (Dinarello 2016). Inflammation similarly results from activation of mediators including histamine, serotonin, bradykinin and prostaglandins,

*Corresponding Author: Senthil Kumar P, Professor, Velumailu Siddha Medical College and Hospital, Sriperumbudur, Kancheepuram, Tamil Nadu, India Email: senthilsamrat.sk@gmail.com

producing vasodilation, edema, and pain (Medzhitov 2008). Although standard allopathic agents such as NSAIDs and paracetamol effectively suppress these pathways, their use is often restricted by adverse effects including gastrointestinal irritation, hepatotoxicity, and renal complications (Hawkey 2017; Watkins 2020). These limitations have intensified global interest in botanicals as safer therapeutic alternatives (Benzie & Wachtel-Galor 2011). Experimental animal models serve as reliable platforms for evaluating such herbal formulations. Brewer's yeast–induced pyrexia is an established model that mimics prostaglandin-mediated fever (Gupta 2019), while carrageenan-induced paw edema is widely used to assess acute inflammatory responses mediated by early- and late-phase mediators (Winter 1962; Vinegar 1976). Hence, the present study aims to investigate the antipyretic and anti-inflammatory efficacy of Manjal Noi Kudineer using these validated in vivo models. By correlating experimental outcomes with Siddha textual claims, the study seeks to provide scientific validation and contribute to evidence-based standardization of MNK

MATERIALS AND METHODS

Animal Selection and Acclimatization

Healthy Wistar albino rats (*Rattus norvegicus*) were selected for the study owing to their stable physiology, well-documented responses to experimental interventions, and widespread use in toxicological and pharmacological research (Turner, 2017; Gupta, 2019). Animals of either sex, aged 8–12 weeks, weighing between 100–120 g for toxicity and anti-inflammatory assessments, and 150–200 g for antipyretic studies, were included in accordance with CPCSEA and OECD recommendations (CPCSEA, 2018; OECD, 2002). All animals were procured from an authorized breeder at TANUVAS, Madhavaram, Chennai, and housed in sanitized polypropylene cages at the animal facility of the respective institution. Each cage was lined with clean corncob bedding, replaced routinely to maintain optimum hygiene and reduce stress-related confounders. Animals were acclimatized for 5–7 days before the initiation of dosing to allow adaptation to the laboratory environment. During this period, the housing room was maintained at a temperature of 25 ± 3 °C, relative humidity of 45–55%, and a controlled 12-hour light–dark cycle, consistent with recommended laboratory animal care guidelines (Flecknell, 2016). Standard pellet chow (Amrut Feeds, Bangalore, India) and RO-purified water were supplied *ad libitum*. Regular health monitoring was performed to evaluate signs of distress, changes in coat texture, locomotor abnormalities, and respiratory patterns (Sharma, 2015). Baseline physiological parameters including body weight, rectal temperature, feed intake, and general behavior were recorded, and only animals exhibiting normal physiological profiles were included. Body weight variations were maintained within ±20% of the group mean for acute and repeated-dose testing (Reynolds, 2018). Animals showing abnormal responses or signs of subclinical illness were excluded to ensure data accuracy and reproducibility.

Preparation of Siddha Drug (Manjal Noi Kudineer)

Manjal Noi Kudineer (MNK) was formulated following classical procedures described in the Siddha Pharmacopoeia of India (Siddha Pharmacopoeia Committee, 2008). The raw herbal drugs were procured from a reputable local raw drug store in November 2024 and authenticated by the Department of Botany (Maruthuva Thavaraiyal), National Institute of Siddha, Tambaram Sanatorium. Authentication numbers were recorded for documentation. The formulation consisted of equal proportions of Keezhanelli (*Phyllanthus niruri Linn.*, whole plant), Karisalai (*Eclipta prostrata Linn.*, whole plant), Peipudal (*Trichosanthes cucumerina Linn.*, whole plant), Venmilagu (*Piper longum Linn.*, white seed), Sombu (*Foeniculum vulgare Mill.*, seed), and Vilvam (*Aegle marmelos L.*, root). Each raw drug underwent initial inspection and purification to remove dust, soil, fungal traces, insect remnants, and other extraneous matter, as recommended by the Siddha Pharmacopoeia (2008). The authenticated materials were thoroughly washed with running tap water and shade-dried under well-ventilated conditions to safeguard thermolabile and volatile phytoconstituents (Yogananth et al., 2024). Once completely dried, the botanicals were coarsely powdered using a stainless-steel mechanical grinder to prevent metallic contamination. The powder was then sieved through a 60-mesh sieve to ensure uniform particle size, which is essential for optimal extraction and bioavailability during decoction preparation (Paramasivam, 2020).

For experimental administration, the powdered MNK was suspended uniformly in distilled water or propylene glycol and mixed using a vortex shaker to achieve a homogeneous dosing medium, ensuring consistent oral delivery (Sahoo, 2010). The therapeutic human dose of MNK (60 mL) was converted to the corresponding animal dose using the body surface area scaling method as per the Paget and Barnes conversion table

Assessment of Antipyretic Activity

The antipyretic potential of MNK was evaluated using the Brewer's yeast induced pyrexia method, a validated model for testing antipyretic agents due to its ability to raise body temperature via endogenous pyrogenic mediators (Mazumder 2011; Winter 1972). Thirty female Wistar rats were randomly divided into five groups (n = 6). Baseline rectal temperatures were recorded using a lubricated digital telethermometer. Pyrexia was induced by subcutaneous injection of 20% Brewer's yeast suspension at 10 mL/kg, and animals were monitored for 18 hours. Only those exhibiting an elevation of ≥1 °C were included (Singh 2014). MNK was administered orally at 50, 250, and 500 mg/kg. The negative control group received propylene glycol (10 mL/kg), while the standard reference group received paracetamol (150 mg/kg), a widely accepted antipyretic agent (Watkins 2020). Rectal temperatures were

measured at 1, 2, 3, 4, and 5 hours post-treatment. The percentage reduction in temperature relative to control groups was used to determine antipyretic efficacy.

Evaluation of Anti-inflammatory Activity

Anti-inflammatory activity was assessed using the carrageenan-induced paw edema model, known for its biphasic inflammatory response involving early-phase mediators (histamine, serotonin) and late-phase mediators (bradykinin, prostaglandins) (Winter 1962; Vinegar 1976; Medzhitov 2008). Thirty Wistar rats (3 males and 3 females per group) were grouped into five treatment sets. Groups II–IV received MNK at 50, 250, and 500 mg/kg, respectively. Group I served as the normal control (distilled water), and Group V received diclofenac sodium (10 mg/kg), a standard anti-inflammatory reference drug (Hawkey 2017). Inflammation was induced by intraplantar injection of 50 µL of 3% carrageenan into the right hind paw using aseptic technique. Paw thickness was recorded using a calibrated digital micrometer at baseline and at 0.5, 1, 2, and 4 hours post-injection following established protocols (Barber 2014). Edema volume was calculated as the difference between post-induction and baseline thickness. Comparative evaluation allowed determination of MNK's dose-dependent anti-inflammatory effect

RESULTS AND DISCUSSION

The antipyretic evaluation showed that Brewer's yeast successfully induced a uniform rise in rectal temperature in all animals. The disease control group exhibited the highest temperature values during the early hours, with the maximum recorded at the first hour (38.72 ± 0.24 °C). In contrast, treatment with Manjal Noi Kudineer (MNK) produced a progressive, dose-dependent reduction in rectal temperature. The 50 mg/kg group demonstrated only a mild decline, with its lowest value recorded at the fifth hour (36.64 ± 0.26 °C). A more pronounced reduction was observed in the 250 mg/kg group, where temperature decreased steadily, reaching a minimum of 36.48 ± 0.28 °C at the fifth hour. The strongest antipyretic effect was noted in the 500 mg/kg group, which achieved a temperature of 36.45 ± 0.23 °C at the fifth hour, approaching the standard paracetamol group's minimum value of 36.42 ± 0.24 °C. Collectively, the maximum rectal temperature among all groups occurred in the disease control at the first hour, while the lowest temperatures were recorded in the paracetamol and MNK 500 mg/kg groups toward the end of the study (Table 1 and Figure 1).

Table 1. Effect of MNK on Brewer's Yeast–Induced Pyrexia.

Group	Initial Temp (°C)	1 h	2 h	3 h	4 h	5 h
Disease Control	37.02 ± 0.32	38.72 ± 0.24	38.68 ± 0.21	38.42 ± 0.24	37.68 ± 0.31	37.21 ± 0.34
MNK 50 mg/kg	36.74 ± 0.34	37.68 ± 0.31	37.64 ± 0.28	36.70 ± 0.24	36.68 ± 0.25	36.64 ± 0.26
MNK 250 mg/kg	36.52 ± 0.37	37.53 ± 0.32	37.58 ± 0.23	36.63 ± 0.26	36.52 ± 0.25	36.48 ± 0.28
MNK 500 mg/kg	36.68 ± 0.36	37.38 ± 0.28	37.42 ± 0.27	36.58 ± 0.24	36.50 ± 0.26	36.45 ± 0.23
Paracetamol	36.32 ± 0.38	37.23 ± 0.39	36.82 ± 0.24	36.54 ± 0.22	36.48 ± 0.26	36.42 ± 0.24

Fig 1: Effect of MNK on Brewer's Yeast–Induced Pyrexia

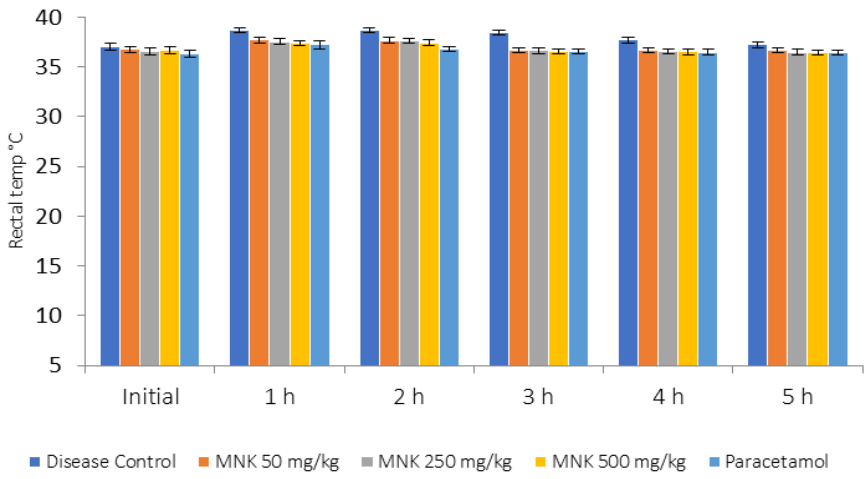
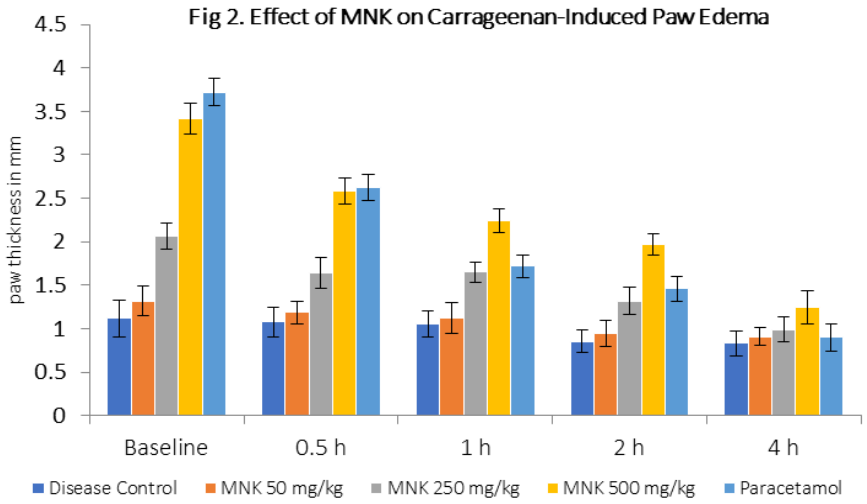


Table 2. Effect of MNK on Carrageenan-Induced Paw Edema.

Group	Baseline (mm)	0.5 h	1 h	2 h	4 h
Disease Control	1.12 ± 0.21	1.32 ± 0.17	2.06 ± 0.15	3.42 ± 0.13	3.72 ± 0.14
MNK 50 mg/kg	1.08 ± 0.17	1.19 ± 0.13	1.64 ± 0.18	2.58 ± 0.15	2.62 ± 0.10
MNK 250 mg/kg	1.06 ± 0.15	1.12 ± 0.18	1.65 ± 0.12	2.24 ± 0.16	1.72 ± 0.14
MNK 500 mg/kg	0.85 ± 0.18	0.95 ± 0.15	1.32 ± 0.14	1.97 ± 0.12	1.46 ± 0.19
Diclofenac	0.83 ± 0.16	0.91 ± 0.15	0.99 ± 0.13	1.24 ± 0.14	0.90 ± 0.16



In the anti-inflammatory study, carrageenan produced a marked swelling response, with the disease control group showing the maximum paw thickness at the fourth hour (3.72 ± 0.14 mm). MNK produced notable dose-dependent inhibition of edema. The 50 mg/kg group showed moderate reduction, while the 250 mg/kg group exhibited clearer suppression, particularly evident at the fourth hour (1.72 ± 0.14 mm). The 500 mg/kg group showed the greatest reduction in inflammation, reaching a minimum edema value of 1.46 ± 0.19 mm at the fourth hour. Diclofenac produced the strongest inhibition, with the lowest edema recorded at 0.90 ± 0.16 mm. Thus, the maximum swelling was seen in the disease control, while the minimum occurred in the diclofenac and high-dose MNK groups (Table 2 and Figure 2).

The present study investigated the antipyretic and anti-inflammatory potential of Manjal Noi Kudineer (MNK), a classical Siddha formulation, using validated experimental models. The antipyretic assessment employed the Brewer's yeast–induced pyrexia model, which is widely recognized for simulating fever mediated by endogenous pyrogens and prostaglandin E_2 synthesis in the hypothalamus (Winter, 1972; Mazumder, 2011). In this model, the disease control group exhibited the highest rectal temperature (38.72 ± 0.24 °C at 1 hour), confirming successful induction of pyrexia. MNK demonstrated a dose-dependent reduction in temperature, with the 500 mg/kg group achieving a minimum temperature of 36.45 ± 0.23 °C, closely comparable to the standard paracetamol group (36.42 ± 0.24 °C). The observed antipyretic activity may be attributed to the presence of bioactive phytoconstituents such as curcuminoids, flavonoids, and alkaloids, which are known to modulate cytokine release and inhibit cyclooxygenase-mediated prostaglandin synthesis (Aggarwal, 2007; Dinarello, 2016). This finding supports the traditional Siddha claim of MNK as a jvaranivarthi (antipyretic) formulation and indicates its potential to regulate pyrogenic pathways without causing overt toxicity. The anti-inflammatory evaluation utilized the carrageenan-induced paw edema model, a standard assay for acute inflammation that exhibits a biphasic mediator profile involving early-phase histamine and serotonin release, followed by late-phase prostaglandin and bradykinin activity (Winter, 1962; Vinegar, 1976). The disease control group displayed maximal paw swelling at 4 hours (3.72 ± 0.14 mm), whereas MNK treatment resulted in significant, dose-dependent suppression of edema. The 500 mg/kg dose produced the most pronounced effect (1.46 ± 0.19 mm), approaching the reduction observed with diclofenac (0.90 ± 0.16 mm). The anti-inflammatory effects of MNK may arise from the synergistic action of its herbal constituents, which are rich in polyphenols and terpenoids capable of inhibiting NF-κB activation, reducing nitric oxide

production, and modulating COX enzyme activity (Gupta, 2013; Patwardhan, 2015). The observed dose-response relationship reinforces the concept that higher concentrations of bioactive compounds result in more potent pharmacological effects. Importantly, no abnormal behaviors or physiological disturbances were observed in the animals throughout the study, indicating that MNK is well-tolerated, consistent with its long-standing traditional use in Siddha medicine (Sharma, 2015). These findings suggest that MNK exerts both antipyretic and anti-inflammatory activities through multi-targeted modulation of immune and inflammatory mediators.

CONCLUSION

The present study demonstrates that Manjal Noi Kudineer (MNK) possesses significant antipyretic and anti-inflammatory activities, supporting its traditional use in Siddha medicine. MNK produced dose-dependent reductions in rectal temperature in the Brewer's yeast–induced pyrexia model, with the highest dose showing efficacy comparable to paracetamol. Similarly, MNK significantly suppressed carrageenan-induced paw edema, particularly at 500 mg/kg, approaching the effects of diclofenac. These results indicate that MNK exerts its therapeutic effects through modulation of pyrogenic and inflammatory mediators while maintaining a favorable safety profile. Further mechanistic and clinical studies are warranted to establish its pharmacological relevance and therapeutic potential.

ACKNOWLEDGMENT

The authors express sincere thanks to the head of the Velumailu Siddha Medical College and Hospital, Sriperumbudur, Kancheepuram, Tamil Nadu, India for the facilities provided to carry out this research work.

CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

FUNDING

This study received no specific funding from public, commercial, or not-for-profit funding agencies.

AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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