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ANTI INFLAMMATORY AND ANALGESIC ACTIVITIES OF SIVA NAMA RASAM IN RODENT MODELS

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ABSTRACT: Siva Nama Rasam (SNR) is a traditional Siddha herbo-mineral formulation used to manage pain and inflammation. The present study evaluated its anti-inflammatory and analgesic activities in rodent models. Anti-inflammatory activity was assessed in Wistar albino rats using carrageenan-induced paw edema, while analgesic activity was evaluated in Swiss albino mice using the hot plate test. Animals were divided into control, standard, and three SNR treatment groups at low, mid, and high doses. In the carrageenan-induced paw edema model, high-dose SNR (18 mg/kg) significantly reduced paw volume, with maximum inhibition of 93.36% at 5 hours ($P < 0.001$), comparable to indomethacin (95.58%). Mid-dose SNR (15 mg/kg) showed 80.09% inhibition ($P < 0.001$), while low-dose (12 mg/kg) achieved 27.88% inhibition. In the hot plate test, high-dose (25 mg/kg) SNR increased reaction time by 71.80% at 120 minutes ($P < 0.001$), mid-dose (21 mg/kg) by 49.29% ($P < 0.001$), and low-dose (17 mg/kg) by 20.33% ($P < 0.01$), compared to control, whereas pentazocine produced 99.04% increase. Results indicate a clear dose-dependent response for both anti-inflammatory and analgesic effects. The herbo-mineral combination in SNR likely contributes to its pharmacological efficacy. These findings support the traditional use of SNR for managing pain and inflammation and provide a scientific basis for further mechanistic and clinical studies.

INTRODUCTION: Inflammation is a biological response of living tissues to injury, characterized by the localized build-up of plasma fluids and blood cells. While it serves as a protective mechanism, the intricate processes and mediators involved in the inflammatory response can also contribute to the onset, persistence, or worsening of various diseases. Consequently, anti-inflammatory drugs play a crucial role in managing and treating these conditions [1].

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Presently available anti-inflammatory medications are often associated with a range of adverse side effects. Therefore, there is a growing interest in exploring effective anti-inflammatory action with minimal side effects. The carrageenan-induced rat paw edema model is a well-established and widely accepted method for assessing the anti-inflammatory potential of therapeutic agents [2].

Pain is a debilitating symptom commonly associated with numerous medical conditions, significantly impacting the quality of life and daily functioning of affected individuals [3]. Pain is commonly triggered by tissue injury, which leads to the release of various chemical mediators that activate nociceptors, initiating the pain sensation. This nociceptive signal is then transmitted to the central nervous system (CNS).

Pain is generally categorized into two types: acute and chronic [4]. Chronic pain is defined by its prolonged duration, often continuing for weeks or months, whereas acute pain appears suddenly and generally subsides within a few hours. Pain significantly interferes with daily functioning and overall well-being; its effective management remains a key priority in healthcare [5].

Inflammation and pain are frequent, nonspecific symptoms associated with a wide range of medical conditions. While non-steroidal anti-inflammatory drugs (NSAIDs) and opioids have traditionally been employed to manage these symptoms, their use is often limited by adverse effects, including gastrointestinal irritation, kidney damage, respiratory suppression, and the risk of dependency [6]. As a result, there has been increasing interest in exploring alternative treatments such as Siddha formulations. Siva Nama Rasam (SNR) is a herbo-mineral formulation composed of purified mineral substances (Sulfur, Mercury, Red orpiment, Borax), purified medicinal herbs (*Aconitum spicatum*, *Piper nigrum*), all processed through trituration used to treat various diseases such as Iraippirumal (Bronchial asthma), Kurainoi (Leprosy), Kunmam (Peptic ulcer), Sanni (Delirium), Moolanoi (Hemorrhoids), Sayam (Tuberculosis), Magotharam (Ascites), Kaakkai *vali* (Epilepsy) and other forms of valippu noi. The formulation is well-regarded for its effectiveness in alleviating pain and treating inflammatory conditions, especially 80 types of vadham, 40 types of pitham and 20 types of kabham as mentioned in siddha literature.

Combining traditional medical wisdom with modern scientific validation offers promising opportunities to develop alternative therapeutic approaches that can improve symptom management and broaden treatment options. Although SNR is commonly utilized by Siddha practitioners for the management of pain and inflammation, its pharmacological properties have not been thoroughly investigated through systematic scientific studies. Hence, the present research was designed to evaluate the anti-inflammatory and analgesic potential of SNR using well-established animal models.

MATERIALS AND METHODS:

Choice of the Trial Drug: *Siva Nama Rasam* is a herbo-mineral preparation used in the treatment of "Convulsions, Rheumatism, and Haemorrhoids". This formulation is documented in the classical Siddha text, *Anuboga Vaithiya Navaneedham* [7].

Collection and Authentication of Raw Drugs: The raw drug was bought from Country Medical Shop, and authenticated with the help of a botanist from the "Department of Gunapadam, National Institute of Siddha, Chennai (certified No. NISMB6662024, GUN/AUT/09/24)".

Ingredients for Siva Nama Rasam: The ingredients are depicted in **Table 1.**

TABLE 1: INGREDIENTS OF SIVA NAMA RASAM

S. no.	Ingredients	Botanical name / Chemical name	Quantity
1.	Purified Gandhagam	Sulfur	50g
2.	Purified Rasam	Hydrargyrum	50g
3.	Purified Manosilai	Red orpiment	50g
4.	Purified Venkaaram	Borax	50g
5.	Purified Karu Nabi	*Aconitum spicatum*	50g
6.	Purified Milagu	*Piper nigrum*	50g

Purification of the Drugs:

Purification of Gandhagam (Sulfur): A required amount of ghee was taken and gently heated until it melted. Sulfur was then added to the melted ghee, and the mixture was poured into a vessel containing milk, where it cooled and solidified.

The solid mass was collected, washed with warm water, and allowed to dry naturally. This procedure was repeated 30 times until the sulfur appeared soft and brittle, with reduced odor, decreased oil content, and an increased melting temperature, indicating effective purification [8].

Purification of Rasam (Hydrargyrum): Mercury was triturated with brick powder in a kalvam. After one hour of grinding, turmeric powder was added, and trituration was continued. The treated mercury was then transferred to an earthen vessel and gently heated with a measured quantity of Kuppaimeni

(*Acalypha indica*) leaf extract. The purified mercury was subsequently washed repeatedly with clean water until all visible impurities were removed and the characteristic metallic lustre was restored, indicating completion of the purification process [8].

Purification of Manosilai (Red orpiment): Fifty grams of Manosilai were ground with fresh lemon juice in a stone mortar for three hours until a fine paste was obtained. The completion of purification was confirmed when the material became a smooth, uniformly triturated paste without visible impurities or coarse particles. The paste was then dried under shade and stored for further use [8].

Purification of Venkaaram (Borax): Fifty grams of Venkaaram were heated in an earthen vessel until frothing ceased and the material became light and porous, indicating completion of purification [8].

Purification of Karunabi (*Aconitum spicatum*): *Karunabi* was soaked in cow's urine for three days and exposed to sunlight daily. After the third day, it was dried and collected. Completion of purification was confirmed by the reduction of the characteristic odor, softening of the tubers, and removal of surface impurities [9].

Purification of Milagu (*Piper nigrum*): Pepper was soaked in buttermilk for one and a half hours. After that, it was dried and roasted. Completion of purification was confirmed by the absence of surface impurities, reduction in pungent taste, and the development of a mild aromatic odor after roasting [9].

Preparation of Siva Nama Rasam: *Rasam* (Hydrargyrum) and *Gandhagam* (Sulfur) were ground together until black. The other three ingredients were powdered, sifted, and added. The mixture was ground for 2 hours, then pepper powder was added and ground for 12 more hours. The final product was stored in an airtight container.

Dose: 1-1 ½ *Kundri* (130-195 mg).

Vehicle: Honey.

Ethical Approval: Prior to commencing the preclinical evaluation, ethical clearance was obtained from the Institutional Animal Ethics Committee (IAEC) of the National Institute of Siddha, Chennai. All experimental procedures were conducted in accordance with established ethical guidelines and principles for the humane care and use of laboratory animals. The IAEC approval number for this study is NIS/IAEC-25/R05/06112023/E05 dated 06.11.2023. All experimental procedures were conducted in accordance with Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India guidelines, ensuring humane care and ethical use of laboratory animals. The study adhered to the principles of Replacement, Reduction, and Refinement (3Rs) in animal experimentation.

Anti-Inflammatory Activity of SNR in Wistar Albino Rats:

Selection of Laboratory Animals: Healthy Wistar albino rats of both sexes, weighing 140–160 g and aged 4–5 weeks, were obtained from the Tamil Nadu Veterinary and Animal Sciences University, Madhavaram. Both male and female rats were included in this study to ensure broader biological representation and to improve the generalizability of the experimental findings. A total of 30 rats (15 males and 15 females) were selected for the study on *Siva Nama Rasam*. Veterinary checks were done at purchase and after a 7-day acclimatization period. During acclimatization, rats were housed in polypropylene cages with corn husk bedding, fed a standard rodent diet, and given RO water ad libitum. Temperature (24–28°C), humidity (30–70%), and a 12-hour light/dark cycle were maintained. Each rat was individually identified using picric acid markings. Animals were monitored for health, and any showing infection were excluded. All procedures followed ethical animal welfare guidelines.

Experimental Animal Preparation: Based on the Paget and Barnes (1964) dose conversion table, the experimental dose for rats was determined. The animals were randomly divided into five groups (n = 6 per group) and treated according to the protocol described in **Table 2**. Randomization of animals into experimental groups was performed using a simple randomization method based on identification numbers assigned to each animal.

This approach was adopted to minimize selection bias. Drug administration was carried out according to the assigned group codes. Blinding was not applied during dosing or outcome assessment. No animals were excluded after randomization, and all animals were included in the final analysis.

Dose Calculation:

Animal Dose = Human Dose × Surface Area (for rat 0.018)

By referring to the table of Paget & Barnes, 1964.

Human Dose = 130 mg

Dose I: = 130 x0.018 = 2.34 x 5

= 11.7 mg/kg

Animal Dose = 12 mg/kg. This is the converted equivalent dose from therapeutic human dose and it is considered to be the Low Dose.

Human Dose = 163 mg

Dose I: = 163 x0.018 = 2.934 x 5

= 14.67 mg/kg

= 15mg/kg

Human Dose = 195mg

Dose I: = 195 x0.018 = 3.51 x 5

= 17.55 mg/kg

=18 mg/kg

The human therapeutic dose of Siva Nama Rasam ranges from 130–195 mg/day. Considering an average human body weight of 60 kg, the dose was converted to mg/kg and extrapolated to experimental animals using the Paget and Barnes conversion method. Based on this calculation, the rat dose range was approximately 13–20 mg/kg. Therefore, three dose levels (12 mg/kg, 15 mg/kg, and 18 mg/kg) were selected for the present study.

TABLE 2: EXPERIMENTAL DESIGN FOR ANTI-INFLAMMATORY ACTIVITY OF SNR IN WISTAR ALBINO RATS

S. no.	Groups	Treatment	No. of animals
1.	Group–I (Vehicle Control)	Control (Honey) 10 ml/kg p. o	6 (3M+3F)
2.	Group-II(Standard)	Indomethacin – 10mg/kg p. o	6 (3M+3F)
3.	Group – III (Low dose)	SNR- (12 mg/kg p.o) + honey p. o	6 (3M+3F)
4.	Group – IV (Mid dose)	SNR- (15 mg/kg p.o) + honey p.o	6 (3M+3F)
5.	Group – V (High dose)	SNR- (18 mg/kg p.o) + honey p.o	6 (3M+3F)
		Total animals	30 (15M+15F)

Carrageenan-Induced Rat Paw Edema Procedure: The anti-inflammatory activity of the test drug *Siva Nama Rasam* (SNR) was evaluated using the carrageenan-induced paw edema model in Wistar albino rats, following Winter *et al.* (1963). The animals were fasted overnight before the experiment. SNR was administered orally via gastric gavage, suspended in honey as a vehicle. One hour later, 0.1 ml of 1% carrageenan solution was injected into the right hind paw to induce inflammation. Paw volume was measured with a plethysmograph at hourly intervals for five hours. The anti-inflammatory effect was determined by comparing the mean paw volume of the treated groups with that of the control group [10]. The recorded values represent the difference between the initial paw volume and subsequent paw volume measurements. The anti-inflammatory activity was determined by comparing the mean paw volume of the treated groups with that of the control group. The percentage inhibition of paw edema was calculated using the formula:

Percentage inhibition = 100 × Control - Test / Control

Evaluation of Analgesic Activity of SNR in Swiss Albino Mice:

Selection and Housing of Experimental Animals: Healthy swiss albino mice of males, weighing 20 –25 g and aged 4–5 weeks, were obtained from the Tamil Nadu Veterinary and Animal Sciences University, Madhavaram. Only male mice were used in the analgesic experiment to minimize variability associated with hormonal fluctuations during the estrous cycle, which may influence nociceptive responses and pain sensitivity. A total of 30 mice (30 males) were selected for the study on *Siva Nama Rasam*. Veterinary checks were done at purchase and after a 7-day acclimatization period. During acclimatization, mice were housed in

polypropylene cages with corn husk bedding, fed a standard rodent diet, and given RO water *ad libitum*. Temperature (24–28°C), humidity (30–70%), and a 12-hour light/dark cycle were maintained. Each mice was individually identified using picric acid markings. Animals were monitored for health, and any showing infection were excluded. All procedures followed ethical animal welfare guidelines.

Grouping of Test Animals: Based on the Paget and Barnes (1964) dose conversion table, the experimental dose for mice was determined. The animals were randomly divided into five groups (n = 6 per group) and treated according to the protocol described in **Table 3**. Randomization of animals into experimental groups was performed using a simple randomization method based on identification numbers assigned to each animal. Blinding was not implemented during drug administration or outcome measurement. No animals were excluded after randomization, and all animals were included in the final analysis.

Dose Calculation:

Animal dose = human dose x Surface Area (for Mice 0.0026)

By referring to the table of Paget & Barnes, 1964.

Human Dose = 130 mg

Low dose: = 130 x0.0026 = 0.338 x 50 = 16.9 mg/kg

= 17 mg/kg

Animal Dose = 12 mg/kg. This is the converted equivalent dose from therapeutic human dose and it is considered to be the Low Dose.

Human Dose = 163 mg

Mid dose: = 163 x0.0026 = 0.423 x 50 =21.19 mg/kg

= 21 mg/kg

Human Dose = 195mg

High Dose: = 195 x0.0026 = 0.507 x 50

= 25.35 mg/kg

=25 mg/kg

The human therapeutic dose of Siva Nama Rasam ranges from 130–190 mg/day. The experimental dose for mice was calculated using the Paget and Barnes (1964) body surface area conversion method. Based on this calculation, the dose range for mice was approximately 17–25 mg/kg, and three dose levels (17 mg/kg, 21 mg/kg, and 25 mg/kg) were selected for the analgesic study.

TABLE 3: GROUPING AND TREATMENT OF SWISS ALBINO MICE FOR EVALUATING THE ANALGESIC ACTIVITY OF SNR

S. no.	Groups	Treatment	No. of animals
1.	Group–I (Vehicle Control)	Control (Honey) 10 ml/kg p. o	6 Male
2.	Group-II (Standard)	Pentazocine - 5mg/kg i. p	6 Male
3.	Group – III (Low dose)	SNR- (17 mg/kg p.o) + honey p. o	6 Male
4.	Group – IV (Mid dose)	SNR- (21 mg/kg p.o) + honey p. o	6 Male
5.	Group – V (High dose)	SNR- (25 mg/kg p.o) + honey p. o	6 Male
		Total animals	30 Males

Hot Plate Method for Analgesic Activity: The hot plate test was used to assess pain response latency, following Eddy and Leimbach (1953). Mice showing an initial reaction within 15 seconds were included, with a maximum cut-off of 15 seconds to prevent injury. Animals were fasted overnight before the experiment.

The test formulation SNR was given orally *via* gastric gavage, while the standard drug was administered intraperitoneally. Each mouse was placed on a hot plate at 55°C inside a Plexiglas cylinder, and the time until the first sign of discomfort (paw licking, shaking, or jumping) was recorded. Only the first response was considered as latency. Measurements were taken at baseline (0 min) and at 30, 60, 90, and 120 minutes after drug administration [11].

% Protection = (Test Mean – Control Mean) / Test Mean × 100

RESULTS:

Anti-inflammatory Activity: The outcomes of the carrageenan-induced rat paw edema study are summarized in **Tables 4** and **5** and illustrated in **Fig. 1** and **2.**

TABLE 4: RESULTS OF ANTI-INFLAMMATORY ACTIVITY OF SNR

Groups	Paw volume (mL)					
	0 Min	1 hr	2 hr	3 hr	4 hr	5 hr
Control	1.42±0.12	1.59±0.10	1.79±0.14	2.08±0.18	2.17±0.17	2.26±0.20
Standard	1.43±0.11	1.39±0.12*	1.06±0.08**	0.78±0.04***	0.37±0.02***	0.10±0.01***
Low Dose	1.45±0.10	1.56±0.15	1.76±0.12	2.02±0.13	1.85±0.15*	1.63±0.13**
Mid Dose	1.43±0.13	1.51±0.11	1.48±0.14*	1.16±0.09**	0.92±0.06***	0.45±0.03***
High Dose	1.43±0.12	1.40±0.10*	1.12±0.07**	0.82±0.04***	0.41±0.03***	0.15±0.01***

**Values are expressed as mean ± SEM (n = 6); *P < 0.05, **P < 0.01, ***P < 0.001 compared to the control group.

The anti-inflammatory activity of Siva Nama Rasam was evaluated using the carrageenan-induced paw edema model, and the results are presented in **Table 4**. The control group exhibited a progressive increase in paw volume from 1.42 ± 0.12 mL at 0 h to 2.26 ± 0.20 mL at 5 h, indicating the development of acute inflammation. In contrast, the standard group (Indomethacin, 10 mg/kg) showed a significant reduction in paw volume compared to the control at all time points, with values decreasing from 1.43 ± 0.11 mL at baseline to 0.10 ± 0.01mL at 5 h (P < 0.001). The low-dose group (12 mg/kg) exhibited a moderate anti-inflammatory effect, with paw volume reaching 1.63 ± 0.13 mL at 5 h, while the mid-dose group (15 mg/kg) showed a greater reduction, with paw volume decreasing to 0.45 ± 0.03 mL at 5 h (P < 0.01). The high-dose group (18 mg/kg) demonstrated a marked anti-inflammatory effect, with paw volume reduced to 0.15 ± 0.01 mL at 5 h (P < 0.001), approaching the effect of the standard drug.

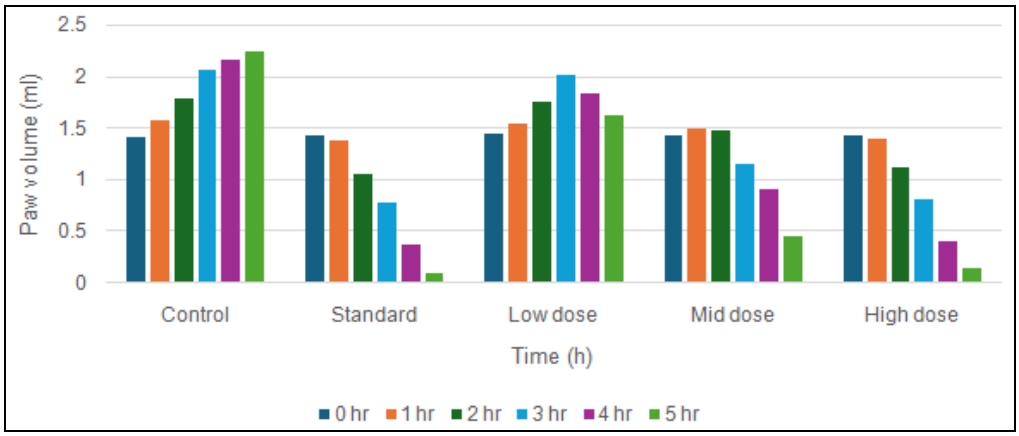

FIG. 1: RESULTS OF ANTI-INFLAMMATORY ACTIVITY OF SNR

TABLE 5: PERCENTAGE INHIBITION OF ANTI-INFLAMMATORY ACTIVITY OF SNR

Groups	Percentage Protection (%)				
	1 hr	2 hr	3 hr	4 hr	5 hr
Standard	12.58	40.78	62.50	82.95	95.58
Low Dose	1.87	1.68	2.88	14.75	27.88
Mid Dose	5.03	17.32	44.23	57.60	80.09
High Dose	11.95	62.57	60.58	81.11	93.36

The percentage inhibition of paw edema is presented in **Table 5**. The standard group exhibited the highest inhibition, reaching 95.58% at 5 h. The low-dose group showed a gradual increase in percentage inhibition from 1.87% at 1 h to 27.88% at 5 h, indicating a mild anti-inflammatory effect. The mid-dose group demonstrated improved inhibition, reaching 80.09% at 5 h, while the high-dose group showed a maximum inhibition of 93.36% at 5 h, comparable to the standard drug, indicating a dose-dependent anti-inflammatory activity of SNR.

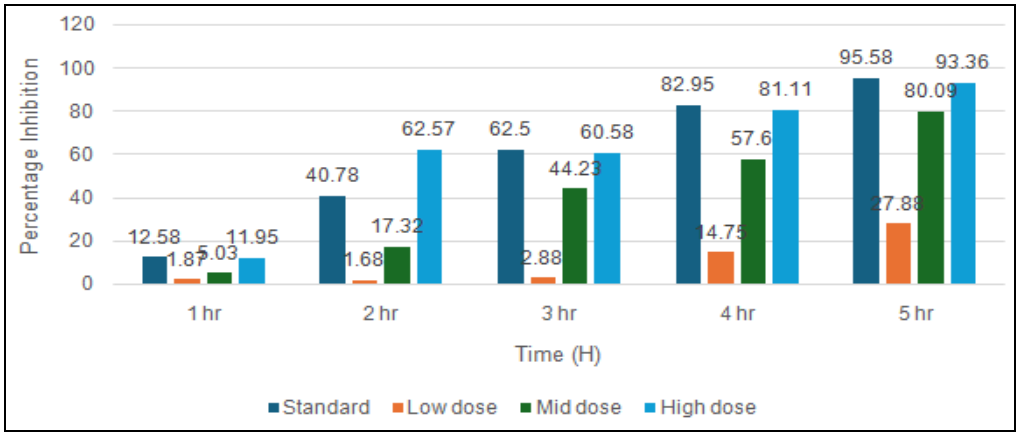

FIG. 2: PERCENTAGE INHIBITION OF ANTI-INFLAMMATORY ACTIVITY OF SNR

Statistical Analysis: Data are expressed as mean ± SEM. Statistical analysis was performed using two-way repeated measures ANOVA, followed by Dunnett's post hoc test for multiple comparisons, using GraphPad Prism (version X). In this analysis, treatment and time were considered as factors. Multiple comparisons across time points were adjusted using Dunnett's correction. A value of *P < 0.05 was considered statistically significant.

Analgesic Activity: The findings of the analgesic activity assessed through Eddy's hot plate method are summarized in **Table 6** and illustrated in **Fig. 3.**

TABLE 6: RESULTS OF ANALGESIC ACTIVITY OF SNR

Groups	Mean Reaction Time (sec)				
	0 min (Initial)	30 min	60 min	90 min	120 min
Control	4.24±0.26	4.36±0.34	4.41±0.32	4.33±0.22	4.26±0.24
Standard	4.16±0.37	7.92±0.57***	8.16±0.44***	8.24±0.43***	8.28±0.59***
Low Dose	4.28±0.28	4.92±0.30	5.07±0.26*	5.82±0.47**	5.15±0.46**
Mid Dose	4.20±0.39	5.14±0.48*	5.96±0.39**	6.22±0.50***	6.27±0.32***
High Dose	4.22±0.33	6.05±0.51***	6.76±0.46***	7.04±0.61***	7.25±0.44***

The analgesic activity of Siva Nama Rasam was evaluated using the hot plate method, and the results are presented in **Table 6.** The control group showed minimal variation in reaction time throughout the study, indicating no analgesic effect.

The standard group (Pentazocine, 5 mg/kg i.p.) exhibited a significant increase in reaction time from 4.16 ± 0.29 s at baseline to 8.28 ± 0.51 s at 120 min ($P < 0.001$). The low-dose group (17 mg/kg) showed a mild increase in reaction time, reaching 5.15 ± 0.38 s at 120 min, while the mid-dose group (21 mg/kg) demonstrated a moderate increase to 6.27 ± 0.42 s at 120 min ($P < 0.01$).

The high-dose group (25 mg/kg) showed a significant analgesic effect, with reaction time increasing to 7.25 ± 0.44 s at 120 min ($P < 0.001$), comparable to the standard drug.

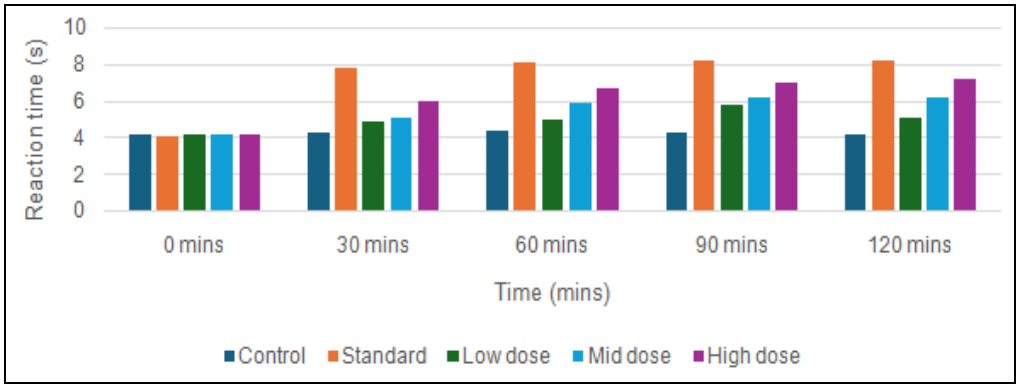

FIG. 3: RESULTS OF ANALGESIC ACTIVITY OF SNR

The percentage increase in reaction time is presented in **Table 7**. The standard group exhibited the highest increase, reaching 99.03% at 120 min. The low-dose group showed a gradual increase in analgesic response, whereas the mid-dose group demonstrated a moderate increase, reaching 49.28% at 120 min. The high-dose group showed a marked increase in reaction time, reaching 71.80% at 120 min, indicating a strong analgesic effect.

TABLE 7: RESULTS OF ANALGESIC ACTIVITY IN SNR (INCREASE IN REACTION TIME)

Groups	% Increase in Reaction Time			
	30 min	60 min	90 min	120 min
Control	2.83	4.01	2.12	0.47
Standard	90.38	96.15	98.07	99.04
Low Dose	14.95	18.46	35.98	20.33
Mid Dose	22.38	41.90	48.09	49.29
High Dose	43.36	60.20	66.82	71.80

Statistical Analysis: Data are expressed as mean ± SEM. Statistical analysis was performed using two-way repeated measures ANOVA, followed by Dunnett's post hoc test for multiple comparisons, using GraphPad Prism (version X). In this analysis, treatment and time were considered as factors. Multiple comparisons across time points were adjusted using Dunnett's correction. A value of *P < 0.05 was considered statistically significant.

DISCUSSION: The present study demonstrates that Siva Nama Rasam (SNR) exhibits significant anti-inflammatory and analgesic effects in a dose-dependent manner, with higher doses producing enhanced pharmacological responses. These effects suggest that SNR may modulate multiple biological pathways involved in inflammation and pain perception, thereby offering dual therapeutic benefits. It should be noted that the reported paw volumes for the standard and high-dose groups represent the mean change from baseline (Δ paw volume) rather than absolute volumes, and slight reductions below baseline reflect the resolution of edema and measurement variability, indicating strong anti-inflammatory activity rather than physiologically implausible decreases. The sustained pharmacological action observed indicates its potential utility in the management of inflammatory and painful conditions. The herbo-mineral nature of SNR, involving synergistic interactions between its purified mineral and herbal components, likely contributes to its overall efficacy, which is a characteristic feature of traditional Siddha formulations. These findings are supported by previous investigations that have reported the pharmaceutical standardization and safety evaluation of Siva Nama Rasam (SNR). Comprehensive studies have demonstrated acceptable physicochemical parameters and reproducible HPTLC fingerprint profiles. In addition, heavy metal analysis in these reports indicated the absence of toxic levels of arsenic, cadmium, and mercury, with lead levels within permissible limits (12). Advanced analytical techniques such as X-ray diffraction (XRD) and Fourier transform infrared spectroscopy (FTIR) have also been employed in earlier studies to characterize the chemical and structural properties of the formulation, revealing defined crystalline phases and functional groups (13). However, these findings are derived from previously published studies, and such characterization and safety analyses were not performed as part of the present investigation. The current study was primarily focused on evaluating the anti-inflammatory and analgesic activities of SNR.

The anti-inflammatory and analgesic potential of SNR aligns with earlier studies on natural products and plant-based formulations. Honey has been reported to exhibit anti-inflammatory and analgesic properties by inhibiting pro-inflammatory mediators such as prostaglandins, nitric oxide, TNF-α, and IL-6, and by suppressing enzymes including COX-2 and iNOS. These effects have been demonstrated in carrageenan-induced paw edema as well as nociceptive models such as hot-plate and formalin-induced paw-licking tests [14, 15]. In the present study, honey was used as the vehicle for oral administration of the test formulation. To minimize the influence of its inherent biological activity, the control group received the same volume of honey alone. Nevertheless, the potential pharmacological activity of honey may represent a

minor limitation of the study and should be considered while interpreting the results. Gandhaga Chooranam significantly inhibited paw edema in Wistar albino rats in a dose-dependent manner, with even low doses outperforming diclofenac in early and late phases of inflammation [16]. Aconitum, as evaluated by Chouhan *et al.*, showed marked reduction of carrageenan-induced paw edema, comparable to indomethacin, by modulating both early (histamine, serotonin, kinins) and late (prostaglandins) phases of inflammation [17]. Similarly, Piper nigrum and its active compound piperine inhibited paw edema at doses of 5–15 mg/kg and demonstrated significant analgesic effects across tail immersion, hot-plate, analgesy-meter, and acetic acid-induced writhing tests, confirming their antinociceptive and anti-inflammatory properties [18].

Collectively, these studies highlight the efficacy of SNR and other plant and bee derived formulations in controlling acute inflammation and pain. The dose-dependent effects, modulation of multiple inflammatory mediators, and dual anti-inflammatory and analgesic activities provide scientific support for the traditional use of SNR.

However, certain limitations of the present study should be considered. The anti-inflammatory activity was evaluated using an acute inflammation model (carrageenan-induced paw edema), which may not fully represent chronic inflammatory conditions. Similarly, analgesic activity was assessed using a single central nociceptive model (hot plate method), and peripheral mechanisms were not evaluated. Although both sexes were included in the rat model, sex-based differences were not analyzed separately. Furthermore, the study did not include mechanistic or biochemical evaluations such as cytokine profiling (e.g., TNF-α, IL-6), cyclooxygenase or lipoxygenase pathway analysis, or oxidative stress markers, which could provide deeper insight into the mechanism of action. Therefore, further studies incorporating chronic models, multiple pain models, and detailed biochemical investigations are warranted to validate and extend these findings.

CONCLUSION: In conclusion, Siva Nama Rasam (SNR) demonstrated significant anti-inflammatory and analgesic activities in the experimental models used, with dose-dependent effects. However, these findings are limited to the acute inflammation and central analgesic models employed, and direct comparisons with standard drugs should be interpreted cautiously. Further studies are required to elucidate the mechanism of action, assess safety, and evaluate its efficacy in long-term and chronic conditions.

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