Experimental evaluation of analgesic activity of Naga Parpam: An Siddha formulation

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Abstract:

Background :

Prolonged usage of NSAIDs and corticosteroids was associated with serious side effects. Siddha is an ancient system of medicine, promotes the utilization of herbal anad elemental formulations. Interestingly, certain elements considered toxic in modern medicine, such as Arsenic (As), Cadmium (Cd), Mercury (Hg), Iron (Fe), Silver (Ag), Gold (Au), etc., have been employed in Siddha herbo mineral formulation for the treatment of illness, a practice that dates back to ancient times.

Introduction

Pain is a widely recognized indicator of poor health, the analgesic medications are employed to alleviate it. In Siddha classics, pain is considered a separate disease called *Soolai*. Naga Parpam is one of the herbo metal preparations with analgesic potential but no scientific evaluation there.

Aim:

To evaluate the analgesic activity of *Naga parpam* in experimental rats using Tail immersion method.

Materials and methods :

After obtaining permission from the IAEC, the animals were separated into 5 groups of 6 animals Each Group 1 (control) received ghee orally, and Group 2 (standard) received Pentazocine in dose 10 mg/kg intraperitoneally. The test drug *Naga parpam* was mixed with the adjuvant Ghee and administrated per oral route to three groups (Group 3,4,5), Group 3 (test) received *Naga Parpam* in low dose 6 mg/kg, Group 4 (test) received mid dose 12 mg/kg, Group 5 (test) received high dose – 24 mg/kg).

Statistical analysis :

One-way ANOVA followed by the Dunnett test $P < 0.05$ was considered to be significant.

Results :

The test drug *Naga parpam* has significant analgesic activity in the tail flick method ($P < 0.01$) by increasing the reaction time of the rats.

Conclusion :

The present study indicates that the test drug *Naga parpam* possesses significant central analgesic activity in the tail flick method.

Keywords: Analgesic, Siddha Herbo metal preparation, *Naga parpam*, Tail flick method.

1. INTRODUCTION

Siddha is an ancient and unique traditional system of medicine, it advocates the use of herbal, metal, and mineral preparations. As per the Siddha text medicines are divided into 32 internal medicine and 32 external medicine. Parpam is one among the 32 types of internal medicine [1]. In modern medicine, many of the elements that are toxic to consume have also been used in the Siddha system of Medicine to cure the illness since ancient times.

Naga Parpam (ash of zinc) is a Siddha herbo metallic formulation described by *Kuppusamy mudhaliyar* in *Kannusamy parambarai vaithiyam*. It contains *Nagam* (Zing), *Rasam*(Mercury), (*Utthamani* whole plant *Pergularia daemia* (Forsskal) Chiov. and *Thutthi* leaf juice (*Abutilin indicum*.L). This herbo metallic formulation is indicated for *Moolam*(Hemorrhoids), *Pavuthiram* (Fistula-in-ano), *Ilaippu* (Emaciation), *Thegathil undagum koppulam* (Boils), *Veekam* (Inflammation), *Rattha moolam* (Bleeding piles)**,** *Seezh moolam* (Ulcerated piles), *Rattha pethi* (Bloody motion), *Kirani* (Chronic diarrhea), *Seedha pethi* (Dysentary) [2]. Signs and symptoms of Hemorrhoids correlated with Moolam in Siddha terminology [3].

Ingredients of this Naga Parpam are also individually used in the treatment of *Moolam* . Analgesic drugs reduce the pain sensation without affecting the consciousness by inhibiting prostaglandin synthesis. In modern medicine, NSAIDs (Non-Steroidal Anti-inflammatory Drugs) are frequently prescribed analgesics since they have the dual benefit of relieving pain and inflammation. NSAIDs act acts both analgesic and anti-inflammatory due to blocking the prostaglandin synthesis (PG). Prostaglandins is a mediator for both pain and inflammation. In analgesic activity, NSAIDs inhibit the cycloxygenase (COX) mechanism [4].

As the safety of Zinc ash has been confirmed through long-standing traditional usage, the primary aim of reverse pharmacology is to delve into the mechanism of action and enhance the safety and acceptability of the primary compounds found in natural products. To provide additional validation of its analgesic properties, reverse pharmacological investigations were scheduled to assess the impact of zinc ash and determine whether it operates via the opioid system or not.

2. Materials and methods:

Table no : 1 Ingredients of Naga parpam

S.No	Ingredients	Quantity
1	Nagam (Zinc)	2 *Palam*
2	Vaalai Rasam (Mercury)	½ amount of parpam
3	Utthamani (Pergularia daemia (Forsskal) Chiov.)	Required quantity
4	Thutthi (Abutilon indicum.L)	Required quantity

Identification and authentication of the drug :

Authentication of the herbs:

The medicinal herbs such as *Uthamani* (*Pergularia daemia* (Forsskal) Chiov.) and *thutthi* (Abutilon indicum.L) were Identified and authenticated by the expert in Medicinal plants, NIS, Chennai-47. (**Certificate No: NISMB5902023**)

Authentication of the metals:

Raw drugs Nagam (Zing) and Rasam (Mercury) were identified and authenticated by expert in Gunapdam, NIS, Chennai-47. (**Certificate No: Gun/ Aut/07/23**)

Purification of Ingredients:

The purification process of Nagam

Illupai Nei Ghee of *Madhuca longifolia* was taken in a mud pot and 2 pieces of Navacharam (Ammonium Chloride) were placed on both sides of the mud pot (half of the portion of Navacharam was immersed in Illupai nei in opposite direction). Nagam was melted in moosai under the heat of thuruthi karuvi, and melted Zinc Nagam was poured into a mud pot containing Illupai nei and navacharam. After that wash the Nagam with water. Repeated the same process for 20 times [1].

The purification process of *Uthamani* :

The bundle of the *Pergularia deamia* plant was gently rinsed using cold running water to eliminate any soil, insects, dust, or other foreign substances.

The purification process of *Thutthi* (*Abutilon indicum*.L)

Prior to Juicing, Abutilon Indicum leaves were gently rinsed with cold running water to eliminate any soil, dust, insects, or other foreign particles. Afterward, the leaves were thoroughly dried using an absorbent towel.

Method of preparation :

Purified *Nagam* is taken and put into *ulai* stirred with the whole plant of *Pergularia daemia* (utthamani) until it becomes parpam. The calcified *Nagam* and half the amount of vaalai rasam (Mercury) is ground with *Pergularia daemia* (utthamani) leaf juice for 6 hours and made into villai. It is allowed to dry in sunlight. The villai is covered with *Abutilon indicum'*s (Thutthi) leaf paste and it was subjected to calcination (Parpam) process with cow dung cakes. The process is repeated two more times. Finally, the Test drug Naga Parpam was collected with the help of *Surandi* and stored in an air-tight clean glass container.

Drug dosage: 130mg twice a day

Adjuvant: Ghee / Butter

Evaluation of Analgesic activity by Tail immersion method in Wistar albino rats:

The analgesic activity of Naga Parpam in Wistar albino rats was studied by the Tail immersion method.

Procurement and rearing of experimental animals:

Healthy wistar albino rats weighing between 200-250 grams, comprising both males and females, were acquired from Tamilnadu veterinary and Animal sciences University, (TANUVAS) Madhavaram milk colony. This procurement was conducted with the approval of the IAEC (Institutional Animal Ethics Committee), and the Specific IAEC certificate number for this study is **NIS/IAEC-22/R02/16112021/20**.

Upon procurement, the rats were securely housed in plastic cages, and the room temperature was maintained within the range of 24-28^{o}C. Both male and female rats were individually accommodated, ensuring free access to food and water libitum. They were provided with a standard diet and were housed in cycle throughout the duration of the study. Before commencing the actual experiment, the rats underwent a 7-day acclimatization period. During this period, close monitoring was performed to identify any signs or infection, and rats exhibited such signs were excluded from the study. All animal-related procedures were carried out in strict accordance with relevant legislation and guidelines pertaining to animal welfare.

Tail immersion Method

The lower 5 cm portion of the Wistar albino rat's tail was immersed in a cup of freshly filed water at 55^{o}C. The basal reaction time was recorded using a stopwatch. Healthy rats that reacted within 4 sec were chosen for this study. An equal number of male and female animals were taken in each group. Following the each assessment, the tail is

meticulously dried. The reaction time is determined before and periodically 60, 90, and 120 minutes after drug administration. Different groups of animals were subjected to the same procedure mentioned above [6]

Animal grouping and interventions:

Table no : 2, Animal grouping and interventions

S.No	Groups	Treatment	No. of animals with sex
1	Group I	Vehicle control - Ghee 10 ml/kg p.o	3 Male + 3 Female
2	Group II	Standard drug - Pentozocine 5 mg / kg	3 Male + 3 Female
3	Group III	Naga Parpam - 6 mg /kg p.o + Ghee	3 Male + 3 Female
4	Group IV	Naga Parpam - 12 mg /kg p.o + Ghee	3 Male + 3 Female
5	Group V	Naga Parpam - 24 mg /kg p.o + Ghee	3 Male + 3 Female

Statistical analysis :

All data in analgesic activity were expressed as mean ± SEM and analyzed using ANOVA followed by Dunnett's test, comparing were made between Group I (Control) vs Group II(Standard drug), III (Dose I), IV (Dose II) , V (Dose III) P**<0.01, *p<0.05.

3. Results:

Reaction Time in Seconds

Table no : 3 Analgesic activity in Tail immersion method

Reaction time in Seconds					
S.No	**Groups**	**0 Mins**	**60 Mins**	**90 Mins**	**120 Mins**
1	Group I (Control)	3.81 ± 0.46	3.17 ± 0.67	2.83 ±0.93	3.68 ±0.99
2	Group II (Standard)	4.86 ± 0.31	5.21 ± 0.94*	7.23 ± 0.35*	8.93±0.25**
3	Group III (Dose I)	3.71 ± 0.6	4.4 ± 0.7	4.91 ± 0.48*	6.41 ± 0.64*
4	Group IV (Dose II)	3.71 ± 0.83	4.43 ± 0.94	5.03 ± 0.65*	6.93 ± 0.67*
5	Group V (DoseIII)	3.13 ± 0.85	3.74 ± 0.88	5.41 ± 0.8*	7.53 ± 0.96**

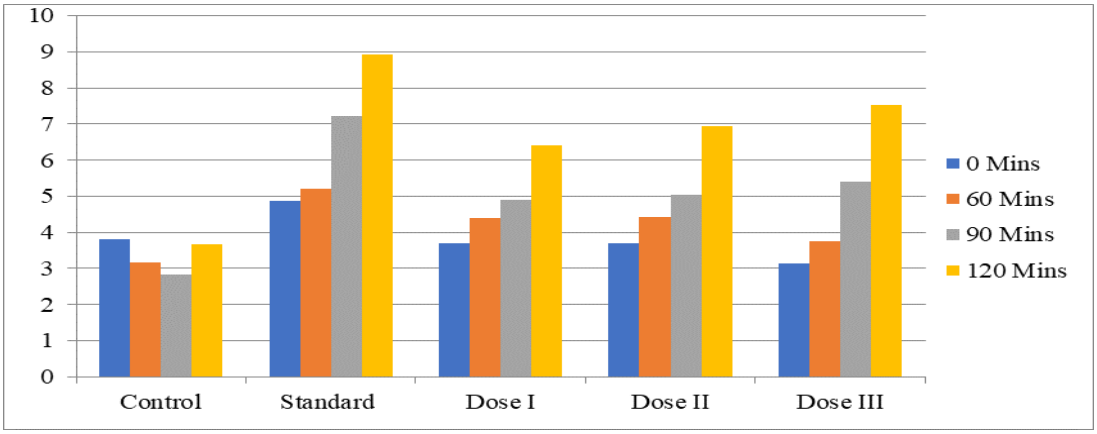

Fig : 1. Analgesic activity of Naga Parpam

4. Discussion:

The analgesic activity of Naga parpam was evaluated by the Tail immersion method. Naga parpam exhibited statistically significant analgesic activity by increasing the reaction time of Wistar albino rats compared to Group I (control group – Ghee treated group) at all time points. With the control group at 60 minutes,90 minutes ($P<0.05$), and 120 minutes ($p<0.01$) in the tail immersion method. These results show that the test drug possesses a significant analgesic activity (shown Table no:3)

Analgesic drugs act on the central and peripheral nervous system to relieve the pain without affecting consciousness. Centrally acting analgesic drugs alter the physiological response to pain and raise the threshold for pain (Opioid drugs produce analgesia by binding to specific G- protein-coupled receptors in the brain and spinal cord). Peripherally acting analgesics inhibit the impulse generation at the chemoreceptor site of pain which inhibits the prostaglandins formation and sensitis of the peripheral nerve ending [7,8]. The initial phase of pain arises from the direct stimulation of nociceptors and primary nerve fibers sue to the release of substances like bradykinin and tachykinins. Opioid analgesics are effective in this phase [9].

Pentazocine is a opioid analgesics it is used to treat moderate to severe pain. Pentazocine group of drugs are below to the morphine and act as on CNS through Brain and Spinal cord. It used to decreases post operative pain and analgesic requirement in patients in operative theater [10].

Jain, N.K. et al., demonstrate the analgesic activity of Zinc-Naproxen Complex in experimental animals. Compared with naproxen treated group the Zinc-Naproxen complex was found to have grater analgesic activity in thermal stimuli in mice. In this study proved that the Nagam (Zinc) has potent analgesic activity [11].

Nitin G Sutar et al., validate the methanol extract and petroleum ether extract of *Pergularia daemia* .L leaves analgesic activity in vivo experimental animal model, it results shows that the methanol extract of *pergularia daemia* treated group has potent analgesic activity by delaying time taken for flicking of the tail out of water (55^{o}C) [12].

Ahmad M et al., evaluate the analgesic activity in rats by using termal stimuli . Eugenol deperated from *Abutilin indicum* .L it shows increased tail flicking (Thermal stimuli) time in rats [13].

In this study of analgesic models using thermal stimuli, the Tail immersion method is considered to be a selective drug acting centrally. It is possible that the test drug Naga Parpam acted on centrally acting analgesics. So its activity might involve opioid receptors.

So, the test drug traditionally prepared Naga parpam contributes to attenuating the management of piles and fistula associated with pain. Herbal and metallic preparations have certain advantages compared to allopathic preparations. These advantages include greater stability over time, sustained availability, lower required doses, ease of storage, and minimal adverse effects.

5. Conclusion

In this present study, the test drug Naga Parpam exhibited promising analgesic activity in Wistar albino rats through a dose-dependent manner. Naga Parpam could be used to prevent adverse effects associated with currently

available analgesics. Further studies are needed to establish the analgesic activity in various mechanical and Chemical induced models. The result of the present study provides further scope for the development of a new palatable dosage form, exact molecular mechanism of action, and also tested clinically for better efficacy.

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Conflict of interest: Nil

Ethical approval :

The study was approved by the IAEC (Institutional Animal Ethics Committee) of the National Institute of Siddha, Chennai-47. (**IAEC No: NIS/IAEC-22/R02/16112021/20)**.

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