Research Article

Analgesic Activity of Sathikkai Podi- a Siddha Drug

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ABSTRACT
The present study was aimed at evaluation of the analgesic activity of **Sathikkai podi** in mice. The results of hot plate model indicated that the total extract of Sathikkai podi (sp) shows a significant increases ($p< 0.01$) in reaction time at 3,4 and 6 hours comparable to the reference drug Pentazocin. The tail immersion and hot plate test reveal that this has high analgesic activity. The biochemical parameters never show any untoward changes during study period. Hence the drug is very safe as a pain killer for long term use also for Migraine.

Keywords: Sathikkai podi- siddha drug , analgesic.

INTRODUCTION

Migraine is a syndrome clinically manifested in attacks which dominant symptom is unilateral, rarely generalized, recurrent headache, and occasionally days. According to different sources, it is considered that about 10-15% of world population suffers from some type of this syndrome. Migraine is most frequently clinically revealed in the age of 30-40 therefore in the most productive period with significant share in treatment costs and a great influence to the working ability of those patients[1]. The WHO places Migraine as one of the 20 most disability medical illness on the planet. In India 15-20% of people suffer from Migraine[2]. All the symptoms of Migraine is analogous with Oruthalai vatha petham in the text, Yugi vaithiya chintamani[3]. The Siddha drug Sathikkai podi has been tried for Migraine. Gunapadam-Mooligai vaguppu- part-1 describes a preparation quoted as Sathikkai podi (SP) is therapeutically preferred for Migraine.[4] The analgesic activity of Sathikkai podi (SP) is proved in preclinical studies done by Eddy's hotplate method and Writhing test. Prolonged usage of vasoconstrictors leads to complication such as
Gangrene. Due to this, still majority of the human race preferred analgesic and anti-inflammatory drugs to relief Migrainous pain.

MATERIALS AND METHODS

Drugs and chemicals

Acetic acid, and CMC, all from Sigma-Aldrich Chemicals were the chemicals used. The standard drugs aspirin and Pentazocin was procured from the local market. All the other chemicals and drugs used were of analytical grade.

Stock solution preparation

The test drug SathikkaiPodi 200mg of fine powder form was accurately weighed using electronic balance and mixed thoroughly with 5ml of 2% Carboxy Methyl Cellulose (CMC) solution to achieve 40mg/ml stock solution as a suspension and this was used for further study.

Animals

Albino mice (24–28 g) either sex were obtained from the animal house of animal housing facility of department of pharmacology, Vels University, Chennai. Animals were maintained at standard laboratory conditions and fed with standard feeding pellets (Sai durga foods, Bangalore)[5]. Prior to treatment, the animals were fasted for 10 and 12 h respectively. However, water was made available ad libitum. (Approval number: XIII/VELS/PCOL/18/2000/CPCSEA/IAEC/08.08.2012).

Experimental Methods

Acute toxicity safety Study

Acute oral toxicity test for the Sathikkai Podi was carried out as per OECD Guidelines 425[6]. As with other sequential test designs, care was taken to ensure that animals are available in the appropriate size and age range for the entire study. The test substance is administered in a single dose by gavage using a stomach tube or a suitable intubation cannula. The fasted body weight of each animal is determined and the dose is calculated according to the body weight. After the substance has been administered, food was withheld for a further 2 hours in mice. The animals were observed continuously for the first 4 h and then each hour for the next 24 h and at 6 hourly intervals for the following 48 h after administering of the test drug, to observe any death or changes in general behaviour and other physiological activities. Single animals are dosed in sequence usually at 48 h intervals.

However, the time interval between dosing is determined by the onset, duration, and severity of toxic signs. Treatment of an animal at the next dose was delayed until one is confident of survival of the previously dosed animal. General behavior, respiratory pattern, cardiovascular signs, motor activities, reflexes, change in skin and fur, mortality and the body weight changes were monitored daily. The time of onset, intensity, and duration of these signs, if any, was recorded.

Evaluation of analgesic activity by Eddy's Hotplate method

The hot-plate test method was employed to assess the analgesic activity. The temperature of the cylinder was set at 55 ± 0.5^0C. The experimental mice were divided into four groups. Each mouse acted as its own control. Prior to treatment, the reaction time of each mouse (licking of the forepaws or jumping response) was done at 0 and 10min interval. The average of the two readings was obtained as the initial reaction time. The reaction time following the administration of the Sathikkai Podi (100, 200, 400mg/kg, p.o.), Pentazocin (5mg/kg) and Saline (p.o.), was measured at 30, 60, 90 and 120 minutes after a latency period of 30 mins. The pain inhibition percentage was calculated according to the following formula:[7]

Pain inhibition percentage = $((T_1-T_0)/T_0) \times 100$

T_1 is post-drug latency and T_0 is predrug latency.

Writhing test

The antinociceptive property of Sathikkai Podi was tested using the model of writhing response in mice. Swiss albino mice of either sexes weighing 20-30 g were used. The writhing syndrome was elicited by an intra peritoneal injection of 0.7% acetic acid at the dose of 0.1ml/10 g body weight. For the test group of animals Sathikkai Podi at the dose level of 100, 200, 400mg/kg, p.o. and for control group vehicle saline and Aspirin 100mg/kg was orally administered into the mice 30 min before acetic acid and the number of writhes was noted for 15 min beginning 5 min after acetic acid injection[8].

Statistical data

Data were presented as mean ± S.E.M. Statistical differences between control and treated groups were tested by one way ANOVA followed by dunnet's test.

RESULTS AND DISCUSSION

Sathikkai Podi did not show acute toxicity up to the maximum dose of 2g/kg and the weight of the mice. It is important to carry out toxicological studies in animal species in order to demonstrate its lack of toxicity. Thermal induced nociception indicates narcotic involvement. Thermal nociceptive tests are more sensitive to opioid μ receptors and non-thermal tests are to opioid κ receptors. Basal reaction time is recorded as mentioned in the method using hot plate. Here the reaction may be hind paw licking or jump response.

Hind paw licking appears within 4-6 sec and after 2-3 sec jumping was shown by the test animals. The hot plate test of nociception screens for substances with central nervous system activity. Sathikkai Podi significantly ($P<0.01$) increased the reaction time of animals towards the thermal source in a dose-dependent manner. In hot plate test Sathikkai Podi showed a pain inhibition percentage at the maximum level of 62% at 90th minute after drug administration whereas Standard drug showed 72% in mice.

The intraperitoneal injection of acetic acid produces an abdominal writhing response due to sensitization chemo-sensitive nociceptors by prostaglandins. Increased level of prostanoids, particularly PGE2 and PGF2 as well as lipoxygenase products have been found in the peritoneal fluid after intraperitoneal injection of acetic acid. The analgesic activity of Sathikkai Podi was determined by writhing test.

In acetic acid induced writhing test aspirin 300mg/kg orally was used as reference compound. The result showed that in control

animal mean number of writhes induced by intraperitoneal ingestion of acetic acid was 56 writhes which was reduced to 49, 44 and 32 in animals with 100, 200mg/kg and 400mg/kg oral doses of the Sathikkai Podi respectively. The results of writhes test proved highly significant when compared with aspirin that produced 28 writhes. Aspirin leads to a relief from pain by suppressing the formation of pain inducing substances in the peripheral tissues. Prostaglandin and bradykinin were suggested to play an important role in the pain process.
The percentage inhibition of writhes with different doses of Sathikkai Podi was 12.69, 20.87, and 41.68, whereas with aspirin it was 62.09%. The analgesic effect of the Sathikkai Podi may therefore be due either to its action on visceral receptors sensitive to acetic acid, to the inhibition of the production of algogenic substances or the inhibition at the central level of the transmission of painful messages.

CONCLUSION

These results support the traditional use of Sathikkai Podi in some painful conditions and gastro intestinal complaints. The Sathikkai Podi potently and significantly prolonged reaction time in mice subjected to thermal stimuli, indicative of an analgesic effect, comparable with the opioid agonist pentazocin.

Table 1: Dose finding experiment and its behavioral Signs of Toxicity

No	Dose mg/kg	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1.	2000	+	-	-	+	-	+	+	-	-	-	-	-	-	+	-	-	-	-	-	-
2	4000	+	-	-	-	-	+	-	+	-	-	-	-	-	+	-	-	-	-	+	-

1. Alertness 2. Aggressiveness 3. Pile erection 4. Grooming 5. Gripping 6. Touch Response 7. Decreased Motor Activity 8. Tremors 9. Convulsions 10. Muscle Spasm 11. Catatonia 12. Muscle relaxant 13. Hypnosis 14. Analgesia 15.Lacrimation 16. Exophthalmos 17. Diarrhoea 18. Writhing 19. Respiration 20. Mortality

Table 2: Effect of Sathikkai Podi on pain induced by hot plate method

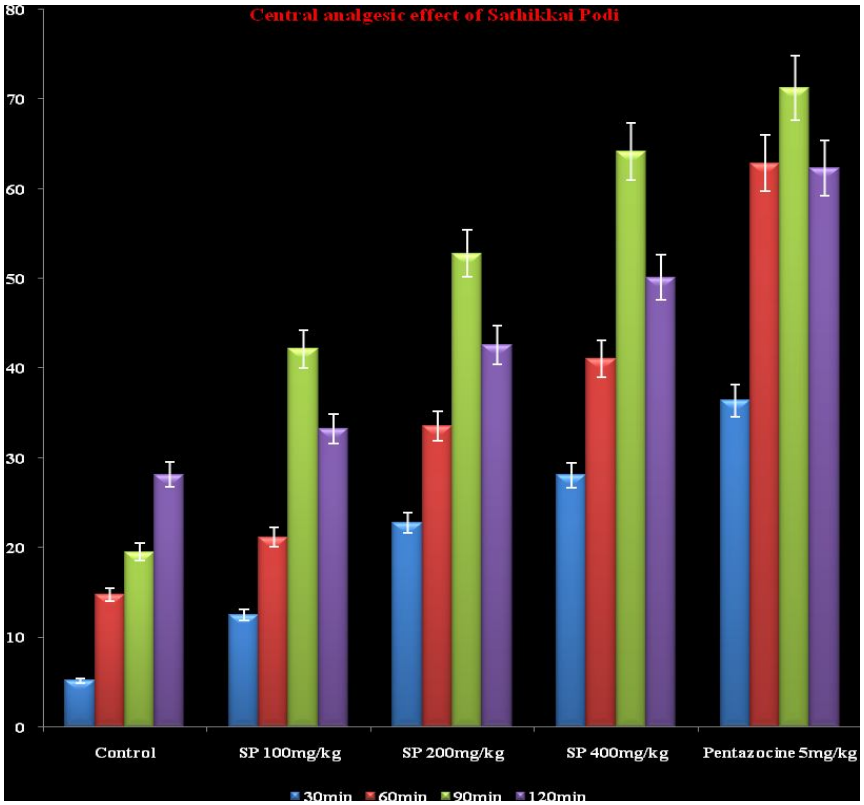
Treatment	Dose	Reaction time in sec. before drug	% increase in reaction time after drug treatment			
			30min	60min	90min	120min
Control	Saline 2ml/kg	3.4±0.04	5.2±0.35	14.8±0.42	19.55±0.70	28.15±0.51
Sathikkai Podi	100mg/kg	3.0±0.03	12.5±0.40**	21.19±1.27	42.15±2.86**	33.25±1.42
Sathikkai Podi	200mg/kg	3.2±0.05	22.8±0.65**	33.56±1.51**	52.82±3.00**	42.63±1.32**
Sathikkai Podi	400mg/kg	3.5±0.05	28.1±1.31**	41.05±1.69**	64.15±3.08**	50.12±1.28**
Pentazocine	5mg/kg	3.2±0.06	36.4±2.15**	62.86±3.00**	71.28±4.11**	62.33±2.56**

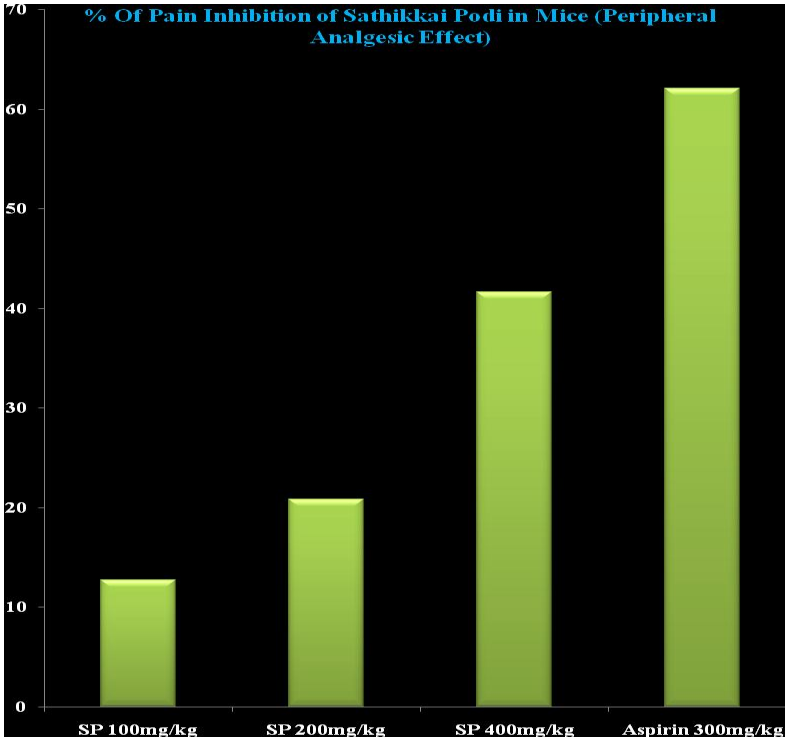
Values expressed in mean ±SEM, Significant **P<0.01 (n=6)

Table 3: Effect of Sathikkai Podi on writhing response in mice

Treatment	Dose (mg/kg)	Number of writhes	Inhibition (%)
Control	Saline 2ml/kg	56.38±5.2	-----
Sathikkai Podi	100mg/kg	49.22±5.05	12.69
Sathikkai Podi	200mg/kg	44.61±4.62	20.87
Sathikkai Podi	400mg/kg	32.88±4.19	41.68
Acetyl salicylic acid	100mg/kg	21.37±3.54	62.09

Values are expressed as Mean±S.E.M. Drug and test compounds were given orally 30 min before 0.3% acetic acid injection.
**P<0.01; significantly different from the control group (N=6).


Central analgesic effect of Sathikkai Podi
80
70
60
50
40
30
20
10
0
Control
SP 100mg/kg
SP 200mg/kg
SP 400mg/kg
Pentazocine 5mg/kg
30min
60min
90min
120min


% Of Pain Inhibition of Sathikkai Podi in Mice (Peripheral Analgesic Effect)
70
60
50
40
30
20
10
0
SP 100mg/kg
SP 200mg/kg
SP 400mg/kg
Aspirin 300mg/kg

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