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ANALGESIC ACTIVITY OF AQUEOUS EXTRACT OF SPERMACOCE HISPIDA IN MICE

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ABSTRACT

Aim: To evaluate the analgesic activity of aqueous extract of *S. hispida* on thermal and chemical method induced pain in mice.
Materials and methods: 48 Adult albino mice (Swiss strain) weighing 25-30 gm were selected. 24 animals were allocated to each experimental model, in each model there were 4 groups. The control group received vehicle (10 ml /kg, p.o), standard group aspirin (300 mg /kg, p.o) and test groups received dried aqueous extract of *S. hispida* (100 mg /kg, 200 mg /kg p.o. respectively) 1 hr prior to acute study. The drugs were administered orally one hour before placing the animal over the hot plate or one before injecting 0.6% acetic acid.
Results: All the tested doses of *S. hispida* on acute administration significantly delayed the reaction time in hot-plate method and reduced number of writhing in chemical method.
Conclusion: The present study has shown that *S. hispida* has analgesic activity in mice.

KEYWORDS: Hot plate method, Chemical method, *S. hispida*, analgesic activity

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INTRODUCTION

Pain is "an unpleasant sensory and emotional experience normally associated with tissue damage or described in terms of such damage." Pain is a disabling accompaniment of many medical conditions. Pain control is one of the most important therapeutic priorities. Analgesics are drugs that selectively relieve pain by acting on the central nervous system (CNS) or peripheral pain mechanisms without altering consciousness employed agents for symptomatic relief of pain[1]. Opioids act both centrally as well as peripherally. Nausea, Constipation, and diminished acuity are among the most commonly encountered adverse effects associated with opioid analgesic use. Abuse liability of the drug is a major drawback. Patients are likely to develop tolerance to the analgesic effect[2]. NSAIDs provide effective management of pain and inflammation, but are associated with formation of peptic ulcer and an increased risk of peptic ulcer haemorrhage and perforations[3]. These drugs act only peripherally. They can cause acute or chronic renal damage following repeated use. Hence, there is a need for better analgesics which could effectively relieve pain without causing much of adverse effects. Ayurvedic medicine is essentially promotive and preventive in therapeutic approach. Many Ayurvedic medicines are used for treating pain. Among them *S. hispida* (Rubiaceae), is one and is popularly known as "Nattaiccuri" in Tamil or "Shaggy button weed" in English. It is widely distributed in the Western Ghats of Kerala and in Maruthamalai forest, which is an extension of Western Ghats in Tamil Nadu[4]. The seed extract of the plant has been used as a remedy for the treatment of internal injuries of nerves and kidney. It is suggested that it removes signs of old age, purify blood and improve vitality, and has been used by the tribal's living in the forest regions in the Western Ghats of Kerala since ancient times . It has been also reported that *S. hispida* is an effective natural drug for the treatment of Diabetic[5], hypertension[6], Hepatoprotective[7], Gastric problems[8], anti-inflammatory[9] & antioxidant properties[10]. As for analgesic activity, no conclusive data is available. Hence it was decided to evaluate the analgesic effect of *S. hispida* on the thermal and chemical method induced pain in mice.

MATERIALS AND METHODS

Animals

The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC) of Chettinad Hospital and Research Institute, Chettinad University, Chennai, India. Inbreed albino mice (Swiss strain) weighing between 25-30 gm of either sex were used for the study. They were housed in clean polypropylene cages and maintained at room temperature between 27-31 ºC with 12:12 hr light and dark cycle. They had free access to food and water. Animals were divided into 2 sets for each model. Each set consisting of 4 groups with 6 animals in each group. The animals were used according to the CPCSEA guidelines for the use and care of experimental animals

Drugs

Aqueous extract – the leaves of *S. hispida* was dried under the shade, powdered and extracted in water by percolation method[11].
Standard drug: Aspirin
Control: 1% gum acacia

Experimental design

The animals were kept fasting for 4 hrs before commencing experiments with free access to water. The animals were divided into 4 groups with 6 animals in each group. Control group received gum acacia (10 ml/kg p.o). Standard group received Aspirin (300 mg /kg p.o). Test groups received an aqueous extract of *S. hispida* 100 mg and 200 mg /kg p.o (made suspension with 1% gum acacia) respectively. The animals were observed for the number of death after 24 hrs. The analgesic activity of the test drug was evaluated using the following experimental models.

Evaluation of analgesic activity

Thermal method

Eddy's Hot plate method

Hot plate method is used to evaluate analgesics acting through CNS. The pain

stimulus is heat (55ºC ± 1ºC).Thermal pain reflex is evoked due to foot pad contact with heated surface. Animals will be placed individually on the hot plate. Analgesiometer maintained at 55ºC ± 1ºC. the time in seconds taken by the animal for the reaction either by licking the paw or jumping or rising the limbs whichever will be observed first will be taken as the end point (reaction time). Reaction time will be noted at the 0 min, 30 min, 60 min and 90 min after the drug administration. A cut off time at 15 seconds will be fixed to avoid damage to the paw[12] (Table 1).

Chemical method

Acetic acid induced writhing test

Freshly prepared 0.6% acetic acid solution in the volume of 10 ml /kg was administered intraperitoneally to each animal of all the groups. In this study, drugs were administered orally 60 min prior to the administration of acetic acid. Onset and the number of writhes were counted for 15 min. Percentage of reduction in writhing syndrome was calculated and compared with control group[13] (Table 2).

STATISTICAL ANALYSIS

All data were expressed as SEM and analyzed using one way ANOVA and Turkey multiple comparison test. $P < 0.05$ was considered as significant.

RESULTS

Table 1

Analgesic Activity of Aqueous extract of S. Hispida on Mice by using Hot Plate Method

Treatment	Dose	Reaction time in sec			
		0 min	30 min	60 min	90 min
Control (Normal Saline)	10 ml/kg	1.96 ± 0.14	2.16 ±0.84	2.16± 0.71	2.01± 0.06
Standard (Aspirin)	300 mg/kg	2.08± 0.04	2.10 ±0.08	2.48 ±0.06*	2.77± 0.13
Aqueous extract of *S. hispida*	100 mg/kg	2.13± 0.07	2.45 ±0.08**	2.80± 0.05**	3.51 ±0.08**
Aqueous extract of *S. hispida*	200 mg/kg	2.23± 0.10	2.98 ±0.03**	3.50± 0.02**	4.08± 0.16**

Values shown are mean ± SEM (n= 6). * P < 0.05 compared with control, ** P < 0.05 compared with Standard

Table 2

Analgesic Activity of Aqueous extract of S. hispida on mice by using Chemical Method

Treatment	Dose	Time of onset of writhing (min)	Number of wriths in 15 min
Control (Normal Saline)	10 ml/kg	4.22 ± 0.61	48.00 ± 2.05
Standard (Aspirin)	300 mg/kg	5.25 ± 0.31*	30.66 ± 3.41*
Aqueous extract of *S. hispida*	100 mg/kg	7.78 ± 0.57**	21.66 ± 1.18**
Aqueous extract of *S. hispida*	200 mg/kg	6.33 ± 0.35**	23.16 ± 3.37**

Values shown are mean ± SEM (n= 6). * P < 0.05 compared with control, ** P < 0.05 compared with Standard.

DISCUSSION

Pain is a direct response to an untoward event associated with tissue damage, such as injury, inflammation or cancer. In addition to the conventional analgesic drugs, many plant products and ritual therapies have been used for thousands of years. Among the medicinal plants *S. hispida* has been used as a remedy for the treatment of internal injuries of nerves and kidney, diabetic, hypertension, hepatoprotective, gastric problems and anti-inflammatory activity. As it reported as a remedy for internal injuries, it is not known

whether it will have analgesic action. If it has analgesic activity, it will contribute to the treatment of pain. Therefore, the purpose of this study was to evaluate the analgesic effect of *S. hispida* in mice using animal models. In this study, two animal models, hot plate method and chemical method in mice were used. The time in seconds taken by the animal for the reaction either by licking the paw or jumping was considered as reaction time. The reaction time was noted for analgesic activity. An increase in reaction time or reduction in number of writhings evidences analgesic activity. The results of present study indicate that the aqueous extract of *S. hispida* exhibited maximum analgesic activity at 30, 60, 90 min. at both the doses 100 mg /kg and 200 mg /kg (p.o), and it was significant when compared with control group and with standard ($P < 0.05$) in thermal method. There was significant reduction in the number of abdominal constrictions with *S. hispida* at doses 100 mg /kg and 200 mg /kg compared to standard drug aspirin. In the present study, the aqueous extract of *S. hispida* was found to possess good analgesic activity at both the doses. Any injury or tissue damage is associated with pain and inflammation. Analgesics can act on peripheral or central nervous system[14]. Peripherally acting analgesics act by inhibiting the cyclooxygenase (COX) enzyme that is responsible for synthesis of Prostaglandins (PGs), PGs are the main mediators of pain[15], while centrally acting analgesics not only raise the threshold for pain, but also alter the physiological response to pain and suppress the patient's anxiety and apprehension[16]. Pain and inflammation are an essential prelude to the repair process. The extract showed the significant analgesic activity when compared with standard drug aspirin. This analgesic activity could be inhibition of COX enzyme[9], the preliminary photochemical study revealed the presence of alkaloids, carbohydrates, phytosterols, tannins; flavonoids may be responsible for inhibition of COX enzyme. It helps to undertake further studies on the isolation and identification of specific phyto-constituents[17]. On the basis of these findings, it may be inferred that *S. hispida* is an effective agent for analgesic activity.

CONCLUSION

In our study, the analgesic activity of *S. hispida* was found to be superior to that of the standard drug aspirin. We believe that *S. hispida* has the potential to be used as an adjuvant in the treatment of pain. Further studies may help to elucidate the possible mechanisms of action of *S. hispida*.

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