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ANALGESIC ACTIVITY OF ETHANOLIC ROOT EXTRACT OF SYZYGIUM CERASOIDEUM (MYRTACEAE)

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ABSTRACT

Syzygium cerasoideum, an Indian species, is ethnomedically used in various pathologic states of human body. The plant is traditionally used as antirheumatic, hypoglycemic, rubefacient, and astringent as well as it is rubbed over painful joints. Hence this research was carried out to establish the data support for scientific evidence as an analgesic potential of root of Syzygium cerasoideum. The ethanolic root extract of Syzygium cerasoideum was chosen for pharmacological screening as an analgesic activity in swiss albino mice. The analgesic effect was measured in mice using the acetic acid-induced writhing test and the radiant heat tail-flick method. In the acetic acid-induced writhing test in mice, the extract at 250 and 500 mg/kg doses level showed 41.76% ($p<0.001$) and 58.29% ($p<0.001$) inhibition of writhing, respectively. In radiant heat tail-flick method, the root extract produced 43.88% ($p<0.001$) and 64.81% ($p<0.001$) increase in reaction time 30 min after p.o. administration at the 250 and 500 mg/kg doses level, respectively. The roots of Syzygium cerasoideum revealed the significant analgesic activity.

Keywords: *Syzygium cerasoideum, analgesic, acetic acid, writhing, tail flick*

INTRODUCTION

Syzygium cerasoideum belongs to the family Myrtaceae and is habitat throughout India primarily in Uttar Pradesh, Bihar, Orissa and Assam up to 600 m & in the Western Ghats up to 900 m. In ayurvedic medicinal system it is called as Bhumi Jambu, in folk system of medicine it is known as Rai Jaamun, Dugdugiaa; Topaakudaa (Bihar) & Peeta-jaam (Orissa). Its fruit possesses antirheumatic potential. Ariel parts of the plant are used as hypoglycaemic. Root is traditionally found to be rubefacient while bark is bitter, astringent & given in dysentery, biliousness and bronchitis. A concentrate of the root infusion is applied and rubbed over painful joints. (Indian Medicinal Plants; C. P. Khare).

Therefore it is needed to explore the analgesic activity to generate the scientific data in evidence of its use in the painful conditions.

Materials and Methods

Plant collection

The root part of fresh unadulterated Syzygium *cerasoideum* was collected from rural areas of Uttar Pradesh, India & authenticated. A fresh sample was dried at room temperature (25–30°C) for 15 days. The dried root sample was then ground in coarse powder using high capacity grinding machine in the Phytochemical Research Laboratory, Teerthanker Mahaveer College of Pharmacy, Teerthanker Mahaveer University, Moradabad, India and preserved in air tight container.

Extraction of the plant materials and sample preparation

The dried and ground root (2 kg) part of the plant was macerated with ethanol (95%) for 10 days. Then the extract was filtered and concentrated with a rotary evaporator and was subsequently defatted to get the dried extract yielding 18% root (225 g) (Nikita *et al*., 1999). For the pharmacological tests, the extract was dissolved in 0.1% CMC in normal saline solution to prepare 250 mg/kg and 500 mg/kg concentrations.

Drugs and Chemicals

Diclofenac was purchased from Saurabh chemicals ltd., India. Acetic acid was used from Rankem, Ranbaxy, India.

Experimental animals

Swiss albino mice weighing 20-30 g were used in this study. They were obtained from the Animal house, Teerthanker Mahaveer College of Pharmacy, TMU, Moradabad, India. The animals were housed in polyvinyl cages with not more than six animals per cage and maintained under standard laboratory conditions (temperature 25 ± 2^0C) and a 12/12 h dark/light cycle and received feed, and water *ad libitum*. To keep the hydration rate constant, food and water were stopped 12 h before the experiments. Experiments on animals were performed strictly in accordance with the guidelines provided by the Institutional Animal Ethics Committee.

Analgesic activity

Acetic acid induced writhing method

The peripheral analgesic activity of root extract of *Syzygium cerasoideum* was measured by the acetic acid induced writhing test in mice (Saha and Ahmed, 2009; Koster *et al*., 1959). The abdominal writhing was induced by intraperitoneal injection of acetic acid solution (0.7%) at a dose of 0.1 ml/10 g of body weight to each mouse, a model of visceral pain. Diclofenac at oral dose of 50 mg/kg was used as standard analgesic agent. The extract was administered at 250 and 500 mg/kg body weight. The extract, standard drug and control (normal saline solution, 1 ml/kg) were orally administered 1 h prior to the injection of acetic acid. The number of writhing was calculated for 10 min after the application of acetic acid.

Radiant heat tail-flick method

The central analgesic activity of the root extract was studied by measuring drug-induced changes in the sensitivity of the pre-screened (reaction time: 2-4 sec) mice to heat stress applied to their tails by using a analgesiometer. The current intensity passing through the naked nichrome wire was maintained at 5 ampere. The distance between the heat source and the tail skin was 1.5 cm and cut-off reaction time was fixed at 10 sec to avoid any tissue damage. Morphine was used to compare the analgesic effect of the plant extract. The extract was orally administered at 250 and 500 mg/kg body weight. Morphine was administered sub-cutaneously at a dose of 2 mg/kg body weight.

Statistical analysis

Data was analyzed by one-way ANOVA followed by Dunnett's test and *p* value *of* 0.05 was considered statistically significant.

Results

Analgesic activity

Acetic acid induced writhing method

The root extract of the plant *Syzygium cerasoideum* at the doses of 250 and 500 mg/kg b.w. and diclofenac 50 mg/kg b.w induced a significant ($p<0.001$) decrease in the number of writhes when compared to control untreated groups. The two doses tested (250 and 500 mg/kg) produced significant ($p<0.001$) analgesic activity **(Table 1)**.

Radiant heat tail-flick method

In the radiant heat tail-flick test, the root extract prolonged the heat stress tolerance capacity of the mice, indicating the possible involvement of a higher center (Whittle, 1964). In radiant heat tail-flick test, the root extract produced 43.88% ($p<0.001$) and 64.81% ($p<0.001$) elongation of the reaction time to tail flicking 30 min after oral doses of 250 and 500 mg/kg body weight respectively. After 60 min the extract caused 30.81% ($p<0.001$) and 46.44% ($p<0.001$) increase in reaction time to tail flicking of 250 and 500 mg/kg body weight respectively and after 120

min the extract caused 13.34% and 19.69% (p<0.01) increase in reaction time to tail flicking of 250 and 500 mg/kg body weight respectively. Morphine caused 78.88% (p<0.001), 54.00% (p<0.001) and 25.13% (p<0.001) increase in reaction time to tail flicking after 30, 60 and 120 min respectively when used as a reference drug at 2 mg/kg body weight **(Table 2)**

Table 1. Effects of *Syzygium cerasoideum* extract (SCE) on acetic acid induced writhing response in mice.

Group	Dose (mg/kg, p.o.)	Writhing[a]	Percentage (%) of inhibition
Control	-	21.17 ± 0.477	-
SCE	250	12.33 ± 0.333***	41.76
SCE	500	8.83 ± 0.703***	58.29
Diclofenac	50	7.67 ± 0.494***	63.77

[a]Each data represents the mean writhing number ± SEM (n = 6)

****p*<0.001 compared with the control group (Dunnett's test)

Table 2. Effects of *Syzygium cerasoideum*extract (SCE) on radiant heat tail-flick response in mice.

Group	Dose (mg/kg)	Reaction time (sec)	60 min (% elongation)	120 min (% elongation)
Control	-	4.50 ± 0.24	4.62 ± 0.18	4.97 ± 0.23
SCE	500	7.22 ± 0.39*** (64.81)	6.55 ± 0.25*** (46.44)	5.93 ± 0.21** (19.69)
Morphine	2	8.15 ± 0.86*** (78.88)	7.15 ± 0.31*** (54.00)	6.20 ± 0.12*** (25.13)

[a]Each data represents the mean reaction time (sec) ± SEM (n = 6)

****p*<0.001, ***p*<0.01 compared with the control group (Dunnett's test)

Discussion

Pain is associated with the pathophysiology of various clinical conditions such as arthritis, cancer and vascular diseases. Many natural products are used in traditional medical systems to relieve the symptoms from pain and inflammation (Kaplan *et al*., 2007; Marrassini *et al*., 2010).

Results from the present study shows that the ethanolic root extract of *Syzygium cerasoideum* has a potent analgesic effect against chemical pains provoked by acetic acid and a good activity against mechanic pain induced by heat.

In the acetic acid-induced writhing test, local peritoneal receptors are postulated to be partly involved in the abdominal writhing response and the mechanism of the reaction to this nociceptive stimulus seems to be related to the prostanoid system (Nguemfo *et al*., 2007). The constriction response of abdomen produced by acetic acid is a sensitive procedure for peripheral analgesic agents, and has also been associated with prostanoids in general, for example, increased levels of PGE2 and PGF2*α* in peritoneal fluids (Ronaldo *et al*., 2000; Deraedt *et al*., 1980) as well as lipoxygenase products (Levini *et al*., 1984; Dhara *et al*., 2000). The extract of *Syzygium cerasoideum* and diclofenac exhibit marked inhibitory effect on the writhing response induced by acetic acid. These results strongly suggest that the extract possesses peripheral analgesic activity and its mechanism of action may be mediated through inhibition of local peritoneal receptors or arachidonic acid pathways, involving cyclo-oxygenases and/or lipoxygenases.

Conclusion

This study has shown that the ethanolic root extract of *Syzygium cerasoideum* possesses significant analgesic effect that may be mediated through inhibition of cell mediators such as bradykinin, and prostaglandins. These results support the traditional use of this plant in some painful conditions.

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