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Research Article

ANALGESIC ACTIVITY OF LEAVES EXTRACTS OF *SAMANEA SAMAN* MERR., AND *PROSOPIS CINERARIA* DRUCE.

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ABSTRACT

Current study was designed to explore the analgesic effects of methanol extracts of the leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce., using tail immersion test. The painful reactions in mice were produced by thermal stimuli through dipping the tail tips of mice into hot water. Methanol extracts of the leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce., were administered intraperitoneally at the dose of 100mg /kg body weight. Pethidine 50mg/Kg intraperitoneally was used as standard analgesic drug. The tail flick latency delay was measured at 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0 hour after the intraperitoneal administration. Both extracts produce analgesic effects when compare with pethidine.

KEYWORDS: Analgesic activity, *Samanea saman* Merr., *Prosopis cineraria* Druce., tail immersion test.

INTRODUCTION

Samanea saman Merr., and *Prosopis cineraria* Druce., are medicinal plants of Pakistan and India belong to the family Mimosaceae[1]. *Samanea saman* Merr., is a folk remedy for colds, diarrhoea, headache, intestinal ailments, and stomach ache[2]. Leaves are used in diarrhea[3]. Inner bark decoction is used for the treatment of colds and diarrhea[3]. Seeds of *Samanea saman* Merr., are chewed for sore throat[4,5]. Antifungal[6] and antioxidant[7] activities are reported from *Samanea saman* Merr. Leaves possess antiemetic[8], antibacterial[9] and insecticidal[10] activities. Bark possesses hepatoprotective activity[11]. Pods possess antibacterial and antifungal activity[12]. Alkaloids, glycosides and terpenes are reported from *Samanea saman* Merr[13]. Leaves contain flavonoids, glycosides, saponins, steriods, tannins, and terpenoids[14]. Pods indicated the presence of alkaloids, flavonoids, saponins, steroids and tannins[12].

The leaves of *Prosopis cineraria* Druce., are used in cataract, dyspepsia, earache and toothache. The stem bark possesses abortifacient and laxative properties. It is used to treat anxiety, asthma, bronchitis, fever, dysentery, dyspepsia[15] and rheumatism[16]. Flowers are used as an anti-diabetic agent and to prevent abortion[17]. Root is antidysenteric[16]. *Prosopis cineraria* Druce., possesses antitumor activity[18]. Antibacterial[19], anthelmintic[20], antipyretic[21], antioxidant, hypoglycemic and hypolipidemic activities[22] are reported from stem bark. Literature survey of *Prosopis cineraria* Druce., revealed the presence of alkaloids[23], fatty acids[24], glycosides and sterols[25] whereas glucosides are reported form flowers and flavones from seeds[16].

The tail immersion test is used for evaluating central antinociceptive activity by responding to the pain stimuli conducting through neuronal pathways[26]. The purpose of the present study is to investigate analgesic activity of the leaves (methanol extracts) of *Samanea saman* Merr., and *Prosopis cineraria* Druce., in Swiss albino mice using tail immersion test. The stem bark[24] and roots[27] of *Prosopis cineraria* Druce., are reported to possess analgesic activity. The analgesic potential of leaves (aqueous extract) by acetic acid induced writhing test has already studied[28]. Here we evaluate methanol extract by using tail immersion test to further confirm its central analgesic effect. The analgesic effect of *Samanea saman* Merr., is reported first time.

MATERIALS AND METHODS

Plant Sample Collection and Identification

Leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce., were collected in summer 2012 from Karachi, Pakistan and compared with already deposited voucher specimen of *Samanea saman* Merr., (K-97-13) and *Prosopis cineraria* Druce.,(K-97-05).

Plant Extraction

Leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce., were dried under shade and soaked in methanol for a week. The extracts were filtered then concentrated using rotary evaporator at 40°C.

Animals

Male Swiss albino mice (17–23 g) were obtained from the Animal house of Aga Khan University and hospital, Karachi, Pakistan. During the acclimatization period (1 week), the animals were supplied with a standard commercial diet and water *ad libitum* and kept in room temperature. The experimental procedures were carried out in accordance with the ethical guidelines for investigations of experimental pain in conscious animals given by Zimmermann (1983)[29]. All mice were equally divided into four groups of seven mice each and transferred into different cages with their identification mark. The first group received subcutaneous 0.9% saline, second group received pethidine (50mg/kg i.p.) as standard analgesic drug whereas remaining two groups treated with methanol extracts of leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce., (100 mg/kg i.p. each).

Acute Systemic Toxicity Test

The acute systemic toxicity of methanol extracts of leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce., in Swiss albino mice suggested that 100mg/kg body weight of each extract is safe for intraperitoneal administration[30].

Analgesic Activity

The central analgesic activity of *Samanea saman* Merr., and *Prosopis cineraria* Druce., were evaluated by tail immersion test. This test was performed according to the technique of Janssen *et al.,* (1963)[31] which later on adapted by Ramabadran *et al.,* (1989)[32].

The lower two-third of the tail was marked and immersed in a water bath having temperature of 55±0.5°C. The time in seconds until the tail was withdrawn from the water was defined as the reaction time. The reaction time was measured

at 0.5,1.0, 1.5, 2.0, 2.5 and 3.0 hour after the intraperitoneal (i.p.) administration of vehicle, test group (*Samanea saman* Merr., and *Prosopis cineraria* Druce., at the dose of 100mg/kg body weight) and standard (pethidine,50mg/kg), with the reaction time of zero minutes being the start of the test. While measurements were being made, animals were immobilized. Inhibition of pain (%) or pain threshold was calculated as follows:

Pain threshold = (Treated mean – Control mean/ Control mean) x 100

Statistical Analysis

Analgesic activity was expressed as mean ± standard error of mean. The statistical significance of the difference was determined by an unpaired Student's *t*-test. The values P<0.01 and P<0.05 are statistically significant and more significant vs. control.

Table: Effects of the methanolic extracts of *Samanea saman* and *Prosopis cineraria* on pain threshold of mice in tail immersion test

Treatment	Post treatment time (seconds) TFLD±SEM (% inhibition of pain)						Average % analgesia
	0.5hr	1hr	1.5hr	2hr	2.5hr	3hr	
Control	1.20±0.2	1.0±0.3	1.60±0.4	1.20±0.2	1.10±0.4	1.2±0.3	--------
Pethidine (50mg/kg i.p.)	22.52±0.13** (94.67)	22.57±0.23** (95.56)	23.52±0.46** (93.19)	22.2±0.63** (94.59)	21.92±0.07** (94.98)	21.57±0.20* (94.43)	94.57
SS (100mg/kg i.p.)	23.4±0.68 (94.87)	23.9±0.68 (95.81)	24.58±0.03 (93.49)	28.69±0.70** (95.81)	25.2±0.60* (95.63)	22.25±0.70** (94.60)	95.03
PC (100mg/kg i.p.)	24±0.23 (95.0)	28.12±0.25 (96.44)	28.9±0.23 (94.46)	30.2±0.61** (96.02)	27.2±0.23 (95.95)	20.36±0.20 (94.10)	95.32

PC= *Prosopis cineraria*, SS= *Samanea saman* ; Tail withdrawal reflex in seconds ; TFLD = Tail Flick Latency Difference, n=7 for each group, *p<0.01 and **p<0.05 are statistically significant and more significant vs. control followed by unpaired students' *t* –test.

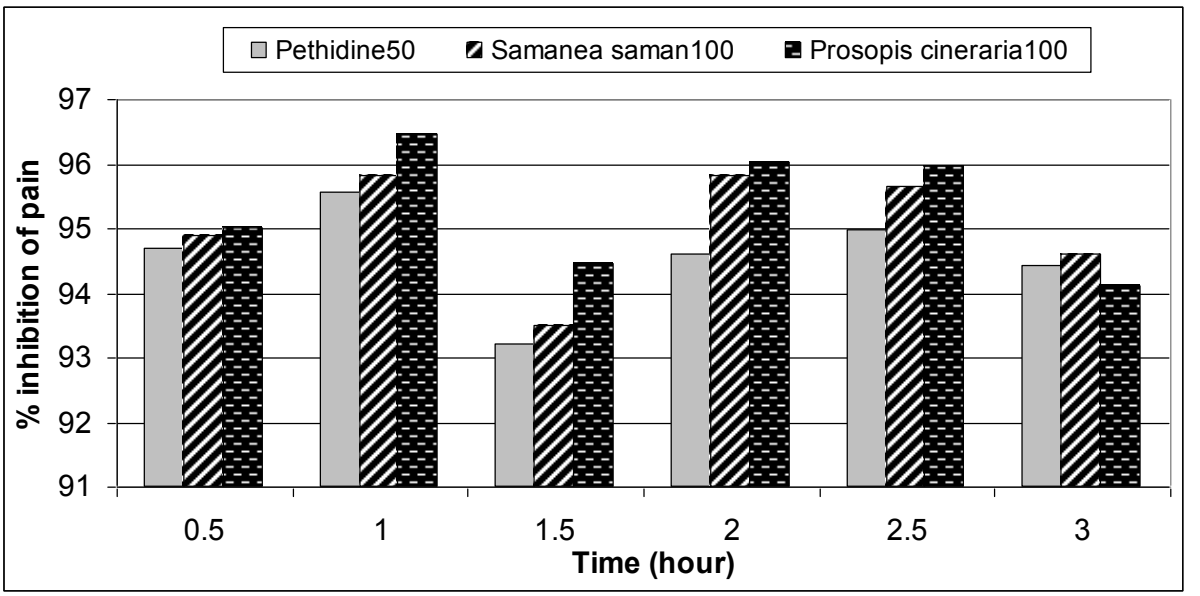

Figure: Analgesic effect of *Samanea saman* and *Prosopis cineraria.*

RESULTS AND DISCUSSION

The methanol extracts of *Samanea saman* Merr., and *Prosopis cineraria* Druce., inhibited tail flick response at 0.5hr in mice. This tail flick latency delay was increased in linear fashion till 1hr and then decreased (table). The inhibitory effects of the extract became pronounced between 0.5 and 2 h post-dosing and reached a maximum of 28.69 sec and 30.2 sec ($p < 0.05$) in case of *Samanea saman* Merr., and *Prosopis cineraria* Druce., respectively. In case of pethidine tail flick latency delay was increased till 1hr and afterward decreases. The leaves extract of *Samanea saman* Merr., and *Prosopis cineraria* Druce., in a dose of 100 mg/kg showed anti-nociceptive activity when compared with pethidine (figure).

The tail immersion test is used for evaluating centrally acting analgesics[33] and is more sensitive to opioid receptor agonists[34].This test consists of a thermal stimulus and increase in the reaction time is used for evaluating central antinociceptive activity[35]. The tail flick response is believed to be a spinally mediated reflex[27]. So, it differentiates between central and peripheral analgesics[36]. Opioid agents exhibit their analgesic effects both via supraspinal (μ_1, κ_3, δ_1, σ_2) and spinal (μ_2, κ_1 ,δ_2) receptors[37,38]. Pethidine produces analgesia by stimulating mu(μ), delta(δ) and kappa(κ) opioid receptors present in spinal cord and brain stem[39]. As this test model is for evaluating centrally acting analgesic effect so, it may be said that the methanol extracts of leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce., possess central analgesic effect. However, more centrally acting analgesic models are further needed to confirm this effect.

One possible reason of this central analgesic effect may be the presence of alkaloids and terpenes[40] already reported in leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce.

The present investigation suggested the central analgesic effects of leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce. However, further studies are required to obtain effective compound(s) from the methanolic extracts of the leaves of *Samanea saman* Merr., and *Prosopis cineraria* Druce., and clarify the possible mechanism of action. The exact mechanism and the bioactive principles responsible for these actions remain to be explained.

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