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EVALUATION OF CENTRAL AND PERIPHERAL ANALGESIC ACTIVITIES OF *SOLANUM MELONGENA* ETHANOLIC LEAF EXTRACT IN EXPERIMENTAL ANIMALS.

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Analgesic, *Solanum melongena*, (*S. melongena*) Writhing, Tail flick, Hot plate, Aspirin, Pethidine, Naloxone

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ABSTRACT: The aim of the study was to evaluate the central and peripheral analgesic activities of *Solanum melongena* ethanolic leaf extract in experimental animals. The *Solanum melongena* leaves were air dried at room temperature and were ground to a fine powder. Ethanolic extract was obtained by percolating the dried powder with 95% ethanol. Oral toxicity test was done according to OECD guidelines. For evaluation of central analgesic activity hot plate and tail flick methods were performed. These methods were carried out in healthy albino rats (*Rattus norvegicus*) of either sex weighing 100-200 gm. Thirty animals were used in each method. They were divided into five groups with six animals in each group for both methods. *Solanum melongena* ethanolic leaf extracts (500mg/kg) was used as test drug and Pethidine (5mg/kg) was used as the standard drug in these methods. For evaluation of peripheral analgesic activity, acetic acid induced writhing test was performed in albino mice. Total 18 healthy albino mice of either sex weighing 20–30 gm were used. They were divided into three groups with six animals in each group. In this method *Solanum melongena* ethanolic leaf extract (500mg) was used as test drug and Aspirin 100mg/kg was used as the standard drug. *Solanum melongena* ethanolic leaf extract showed significant ($p<0.01$) analgesic activity, both central and peripheral when compared to the control.

INTRODUCTION: Pain has been defined as "unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage." It is a subjective experience which cannot be objectively defined or quantified satisfactorily [1]. Pain may be acute or chronic. Acute pain may be due to wounds, irritants, burns or ischemia and chronic pain maybe due to arthritis, cancer and neuropathies. In acute pain the cause is well defined whereas in chronic pain cause may not be well defined [2]. An analgesic is a drug that selectively relieves pain by acting on the CNS or on peripheral pain mechanisms without significantly altering consciousness [3].

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The traditional medicine refers to a broad range of ancient, natural health care practices including folk/tribal practices, as well as Ayurveda, Sidha, Amchi and Unani. These practices incorporated ancient beliefs and were passed on from one generation to another by oral tradition and/or guarded literature [4].

It is well known that traditional herbal medicine existed before the application of modern scientific method to health care and even today majority of the world population depends on herbal health care practices [5]. The wide use of medicinal plants for various ailments has been due to the presence of secondary metabolites and essential oils of therapeutic value. Easy availability, being economical, effective, and safe are the advantages of medicinal plants for their widespread use [6].

Solanum melongena Linn. (garden egg) is an economic flowering plant belonging to the family Solanaceae. Members are mostly herbaceous plants, fruit is berry and seeds have large

endosperm and are grown mainly for food and medicinal purposes [7]. Brinjal, eggplant or aubergine (*Solanum melongena* Linn.) is widely cultivated as vegetables in both temperate and tropical areas, especially in Asia [8]. It is widely distributed in India for its fruit [9]. Various parts of the plant are useful in the treatment of inflammatory conditions, cardiac debility, neuralgias, ulcer of nose, cholera, bronchitis and asthma. Rural people of Karnataka use the fresh juice of brinjal leaves against fever [10].

A bioflavonoid glycoside named solanoflavone is present in the leaves and fruits of *S. melongena* [11]. Some of the alkaloids present are tropane, pyrrolidine, steroid alkaloids and glycoalkaloids [12]. Besides, having many traditional uses, *S. melongena* is reported to exhibit many important pharmacological actions. The present study was carried out to evaluate the central and peripheral analgesic activities of *S. melongena* ethanolic leaf extract in experimental animals.

MATERIALS AND METHODS: The study was carried out in the department of pharmacology at Assam Medical College in 2006. Fresh *S. melongena* leaves were collected within Dibrugarh district of Assam, in the months from March to May 2006. The leaf samples were identified and confirmed at the Dept. of Life Sciences, Dibrugarh University. The leaves were air dried at room temperature and were ground to a fine powder. Ethanolic extract was obtained by percolating the dried powder with 95% ethanol [13]. All the animals used in the study were taken care of under ethical consideration with approval from the institutional ethics committee (Registration no.-634/02/a/ CPCSEA), Assam Medical College.

Toxicity studies: *S. melongena* ethanolic leaf extract (SME) was subjected to acute oral toxicity [14]. Mortality in the acute oral toxicity test was not seen in the limit test up to dose 2000 mg/kg. For testing central analgesic activity: The central analgesic activity of *S. melongena* ethanolic leaf extract was tested by Hotplate [15] and Tail flick method [16]. These methods were carried out in healthy albino rats (*Rattus norvegicus*) of either sex weighing 100-200 gm obtained from the Central Animal House, Assam Medical College, Dibrugarh. The animals were fasted overnight and during the experiment had water *ad libitum*. Thirty animals were used in each method. They were divided into five groups with six animals in each group for both methods.

TABLE 1: SHOWING THE EXPERIMENTAL DESIGN FOR HOT PLATE AND TAIL FLICK METHODS

Group	Treatment
Group–I	3% gum acacia (5 ml/kg S.C.)
Group–II	Naloxone (1 mg/kg S.C.)
Group–III	SME (500 mg/kg S.C.)
Group–IV	SME (500 mg/kg S.C.) + Naloxone (1 mg/kg S.C.)
Group–V	Pethidine (5 mg/kg S.C.)

Reaction time to thermal pain was recorded with the use of Eddy's hot plate. Reaction time was obtained by dropping the animals on a hot plate maintained at $55^0 \pm 0.5^0$ C. The rats reacted to the thermal stimuli by jumping, licking of fore limbs or squeaking. The time taken between the dropping of the rat on the hot plate and first jump was taken as reaction time. A cut off time of 15 sec observed to prevent injury. The reaction time was noted at pre drug, 15, 30, 60, 90, 120, 150 and 180 min after drug and vehicle administration.

The tail flick latencies (reaction time) of the animals were assessed by analgesiometer (Elite). Basal reaction time to radiant heat was taken by placing the tip (last 2 cm) of the tail on the radiant heat source. Tail withdrawal from the heat (flicking response) was taken as the end point. A cut off period of 10 sec was observed to prevent damage to the tail. The tail flick latencies were recorded at pre-drug, 15, 30, 60, 90, 120, 150 and 180 min after vehicle and drugs administration. Pethidine was taken as standard drug [17] while Naloxone 1 mg/kg [18] was used to determine the mechanism of action.

Peripheral analgesic activity: The peripheral analgesic activity of *S. melongena* ethanolic leaf extract was tested by using Glacial Acetic Acid Induced Writhing Test [19].

Total 18 healthy albino mice of either sex weighing 20–30 gm were used for the study. The animals were fasted overnight. They were divided into three groups with six animals in each group. One hour after administration of the drugs, induction of writhing was done in mice by giving intra-peritoneal injection of acetic acid at a dose of 10 ml/kg body weight. The number of writhing

responses were counted and recorded for 20 minutes. The percentage protection was noted. Here, Aspirin was used as the standard drug at the dose of 100 mg/kg per orally.

TABLE 2: SHOWING THE EXPERIMENTAL DESIGN FOR GLACIAL ACID INDUCED WRITHING TEST

Group	Treatment
Group I	3% gum acacia 5 ml/kg P.O.
Group II	SME 500 mg/kg. P.O.
Group III	Aspirin 100 mg/kg P.O.

Statistical analysis: The data were subjected to statistical analysis using one way ANOVA followed by Dunnet's multiple comparison test. *p* values <0.05 were considered significant.

RESULTS: The present study showed that *S. melongena* ethanolic leaf extract produced significant (p <0.01) central analgesic activity in both hot plate and tail flick methods. The reaction time in both the methods was significantly increased by the extract. The *S. melongena* ethanolic leaf extract (500mg/kg) showed significant (p <0.01) peripheral analgesic activity when compared to the control. There was significant reduction of writhing movements.

TABLE 3: SHOWING THE ANALGESIC ACTIVITY OF *SOLANUM MELONGENA* ETHANOLIC LEAF EXTRACT ON THERMALLY INDUCED PAIN IN ALBINO RATS; REACTION TIME IN SEC (MEAN ± SEM)

Group	Drug, Dose (mg/kg) S.C.	Pre Drug Reaction Time (in sec) (Mean ± Sem)	Time (in minutes)						
			15	30	60	90	120	150	180
Group-I	3% gum acacia (5ml/kg)	5.40 ± 0.07	5.30 ± 0.06	5.10 ±0.03	5.50 ±0.08	5.70 ±0.09	6.10 ±0.09	5.60 ±0.09	5.55 ±0.09
Group-II	Naloxone (1mg/kg)	5.40 ±0.14	4.10 ± 0.16[b]	2.89 ± 0.11[b]	3.00 ± 0.14[b]	3.18 ± 0.21[a]	3.40 ± 0.17[b]	3.60 ± 0.14[b]	4.10 ± 0.14[b]
Group-III	SME (500mg/kg)	5.68 ±0.20	6.47 ± 0.19[b]	7.04 ± 0.20[b]	8.02 ± 0.29[b]	11.25 ± 0.60[b]	9.34 ± 0.70[b]	8.58 ± 0.50[b]	6.97 ± 0.39[b]
Group-IV	SME (500mg/kg) +Naloxone(1mg/kg)	6.08 ±0.23	6.57 ± 0.18[b]	6.88 ± 0.15[b]	7.82 ± 0.32[b]	8.42 ± 0.36[b]	8.30 ± 0.13[b]	7.90 ± 0.24[b]	7.20 ± 0.38[b]
Group-V	Pethidine 5mg/kg	5.45 ±0.10	6.80 ±0.38b	7.57 ±0.30b	10.10 ± 0.58b	12.39 ± 0.83b	9.23 ± 0.16b	7.70 ± 0.26b	6.90 ± 0.34b
One way ANOVA	F	2.63	24.37	86.66	68.09	44.20	26.59	49.39	74.29
	df	25, 4	25, 4	25, 4	25, 4	25, 4	25, 4	25, 4	25, 4
	p	> 0.05	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01

n = 6 in each group; a: p < 0.05, b : p <0.01 when compared to the Control; ANOVA followed by Dunnet's Multiple Comparison Test.

TABLE 4: SHOWING THE ANALGESIC ACTIVITY OF *SOLANUM MELONGENA* ETHANOLIC LEAF EXTRACT ON TAIL FLICK RESPONSE IN ALBINO RATS; REACTION TIME IN SEC (MEAN ± SEM)

Group	Drug, Dose (mg/kg) S.C.	Pre Drug Reaction Time (in sec) (Mean ± Sem)	Time (in minutes)						
			15	30	60	90	120	150	180
Group–I	3% gum acacia (5ml/kg)	3.80 ±0.18	3.60 ±0.12	3.40 ±0.10	3.90 ±0.09	4.30 ±0.15	4.30 ±0.12	4.24 ±0.12	4.00 ±0.12
Group–II	Naloxone (1mg/kg)	3.30 ±0.08	3.00 ±0.05[b]	2.37 ±0.03[b]	2.92 ±0.27[b]	3.00 ±0.27[a]	3.06 ±0.28[a]	3.11 ±0.27[b]	3.19 ±0.07[a]
Group–III	SME (500mg/kg)	3.70 ±0.22	4.49 ±0.28[b]	4.77 ±0.25[b]	5.18 ±0.23[b]	6.20 ±0.47[b]	5.99 ±0.51[b]	5.77 ±0.22[b]	4.75 ±0.24[a]
Group–IV	SME (500mg/kg) +Naloxone (1 mg/kg)	3.60 ±0.18	3.96 ±0.20[b]	3.98 ±0.15[a]	4.70 ±0.12[a]	5.53 ±0.10[b]	5.50 ±0.10[a]	5.30 ±0.38[a]	4.79 ±0.22[a]
Group–V	Pethidine 5mg/kg	3.80 ±0.07	4.60 ±0.17[b]	4.66 ±0.17[b]	4.86 ±0.24[a]	7.85 ±0.40[b]	7.67 ±0.39[b]	7.28 ±0.38[b]	4.81 ±0.38[a]
One way ANOVA	F	1.73	130.00	39.06	20.66	34.07	29.52	43.97	12.72
	df	25, 4	25, 4	25, 4	25, 4	25, 4	25, 4	25, 4	25, 4
	p	> 0.05	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.05

n = 6 in each group; a: p < 0.05, b: p <0.01 when compared to the Control; ANOVA followed by Dunnet's Multiple Comparison Test.

TABLE 5: SHOWING THE ANALGESIC ACTIVITY OF *SOLANUM MELONGENA* ETHANOLIC LEAF EXTRACT ON GLACIAL ACETIC ACID INDUCED WRITHING RESPONSE IN ALBINO MICE

Group	Drug Dose (mg/kg) P.O.	Number of Writhing Movements (Mean ± SEM) 20 minutes	Percentage of Protection S.C. (%)
Group–I (Control)	5ml/kg	72.33 ± 5.23	-
Group–II (Test)	500mg/kg	13.50 ± 2.53a	81.34
Group–III (Standard)	100mg/kg	10.67 ± 1.80a	85.25
One Way ANOVA	F	256.80	
	df	15, 2	
	p	<0.01	

n = 6 in each group; a : p < 0.01 when compared to control; ANOVA followed by Dunnet's multiple comparison test.

DISCUSSION: The study shows that *Solanum melongena* ethanolic leaf extract produced significant analgesic activity in hot-plate method, tail flick test and acetic acid induced writhing test. Hot-plate and tail flick methods are models of nociception that involve central mechanism of analgesic action. Acetic acid induced writhing test is a model of nociception that mainly involves peripheral mechanism of analgesic action. Our results suggest that *S. melongena* ethanolic leaf extract possesses both central and peripheral mechanisms of analgesic activity.

In both the hotplate and tail flick methods the analgesic action of SME was partially antagonized by Naloxone. This is thought to be due to involvement of endogenous opioid peptides in the mediation of anti-nociceptive response of SME. As the analgesic effect was reduced partially after Naloxone, some other non-opioid mechanisms may be involved. *Solanum melongena* is a plant with many medicinal properties. The medicinal properties of the plant are derived from its chemical constituents [20].

The leaves of *S. melongena* contain flavonoids, alkaloids, tannins and steroids [10]. In an earlier study, the alkaloidal extract of *S. melongena* was found to produce significant analgesic effect [21]. A number of flavonoids have been reported to produce analgesic activity [22]. Also there are few reports on the role of tannins in analgesic activity. Hence, in the present study the analgesic activity of *S. melongena* leaves may be attributed to the presence of alkaloids, flavonoids and tannins. *S. melongena* leaf extract significantly raised the pain threshold in the tests used to evaluate the central analgesic activity. Naloxone (1 mg/kg) was able to partially antagonize the central analgesic effect of SME suggesting that opioid receptors and some non-opioid mechanisms may be involved.

Aspirin offers relief from inflammatory pain by suppressing the formation of pain substances in the peripheral tissues, where prostaglandins and bradykinin were suggested to play an important role in the pain process [23]. Therefore, it is likely that *S. melongena* ethanolic leaf extract exerts its peripheral analgesic activity in acetic acid-induced writhing test by antagonizing the action of pain mediating substances or suppressing the formation of these substances.

The results of the present study suggest that *S. melongena* ethanolic leaf extract produces significant central and peripheral analgesic activity at the dose of 500 mg/kg. After observing the results of the study, it would not be unwise to carry out further studies to confirm the true potential of this plant, for its analgesic activity, so that it may be clinically applicable and commercially viable.

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