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COMPARATIVE ANALGESIC ACTIVITY OF SELECTED *SOLANUM* SPECIES

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ABSTRACT

Synthetic analgesic drugs have prominent side effects like gastritis, gastric ulcer, kidney disorder and cardiac arrhythmias. The genus *Solanum* has been primarily used for various therapeutic effects, mainly analgesics, in the indigenous system of medicine. The current research aimed to investigate and compare the analgesic activities of methanolic extracts of leaves of *Solanum indicum*, *Solanum surattense* and *Solanum torvum*. Using acetic acid induced writhing method and hot plate method, the analgesic activity was evaluated. Significant anti-nociceptive effects were observed on both animal models after the application of different doses of the extracts of *Solanum* species. The results exhibited that MESI, MESS and MEST at a dose of 200 and 400 mg/kg produced analgesic effects equivalent to diclofenac (10 mg/kg). However the extracts at 400 mg/kg exhibited more pronounced analgesic activity. The results of this study demonstrated that the analgesic effects of all the three species were significant to each other and validate the traditional use of the plants of this Genus for the treatment of pain.

Keywords: *Solanum* species, Analgesic activity, Acetic acid-induced writhings, Medicinal Plants, Pain, Methanolic extract

INTRODUCTION

As stated by the International Association for the Study of Pain, pain is an unwanted psychological and disturbing sensation, linked with probable or real tissue damage or is produced in some periods of these types of pains (Bonica, 1990). Pain basically helps the person to get away from harmful conditions, to guard an injured part of body as it recovers, and to prevent similar exploit further (Lynn *et al.*, 1984). If not, may lead to harmful conditions like tumour, physical trauma, operational treatments, harmful chemical stimulation, etc. (Alieu, 2007). As most pain relief medications have developed severe side effects on the body's functioning like sweating, nervousness, vomiting and tremor (Raquibul *et al.*, 2010). There is, therefore, an extreme need for appropriate another treatment of pain with no side effects. It is suspected that naturally occurring secondary metabolites in plants are an important source of possible pain relief. Many drugs are used for relieving the pain. Morphine (Smet, 1997) and aspirin (Shu, 1998) are used as pain killers since ages. Pain caused due to stimulation of the nociceptor is said to be nociceptive pain (Rajagopal, 2006). A variety of diverse pathways centrally modulate the pain, including dopaminergic, descending noradrenergic, opiate and serotonergic systems (Chaudhari *et al.*, 2012).

Since a number of researchers have tested the analgesic properties of plant extracts and their phytoconstituents, a number of plants have been reported to possess analgesic properties viz. *Bowdichia virgilioids* (Thomazzi *et al.*, 2010), *Capparis ovate* (Arslan *et al.*, 2010), *Lavandula officinalis* (Heidari *et al.*, 2000), *Solanum melongena* (Dashti Rahmatabadi *et al.*, 2009), *Apium graveolens*

(Nasri *et al.*, 2009), *Glaucium grandiflorum* (Morteza-Semnani *et al.*, 2002).

Owing to their numerous pharmacological functions, such as anti-inflammatory, analgesic and antipyretic, etc. secondary metabolites like steroids, flavanoids, alkaloids, terpenoids and glycosides have gained importance. The genus *Solanum* is found to be one of the largest and most complex genera among the Angiosperms and the most characteristic and principal genus of the family Solanaceae (Yokose *et al.*, 2004). Plants of this genus represent a wide variety of secondary metabolites with various biological activities, which from an economic, agricultural and pharmaceutical perspective, make them very valuable (Hanumanthappa *et al.*, 2012; Bhakta, 2004). It is known that several of these species have numerous medicinal uses. In the Ayurveda system of medicine, *Solanum indicum*, widely recognized as *Badi Bhatkataiya* (Hindi) and Brihati in Sanskrit, is used both as a single drug and alongwith other medicines. Roots, berries, seeds and leaves are found to be valuable in number of diseases like bronchitis, asthma, dry cough, dysuria, leukoderma, cardiac weakness and pruritis (Bhattacharya & Banaushadhi, 1982; Zadra *et al.*, 2012). *Solanum surattense* also known as Thorny Nightshade or Yellow Berried Nightshade has versatile medicinal properties such as Anti-inflammatory, Anthelmintic, Antiepileptic, Antileprotic, Antitussive and Analgesic. *Solanum torvum* commonly known as Turkey Berry, is used for asthma, inflammation, and analgesic, antibacterial, antipyretic, antifungal and antiviral properties.

The *Solanum* species contains glycoalkaloids, which are potent analgesic and antinociceptive in action. Further

Solanum species have been reported to inhibit COX enzymes. A number of studies have shown that plants possessing inhibitory activity against the COX enzymes are used to treat pain. *Solanum* species are commonly available species throughout India and has been proved in traditional literature as a useful plant for different diseases. Till date no scientific data is available on comparative analgesic activity of these species.

Since no scientific evidence is available to justify these species' comparative analgesic activities, the present work have been designed to compare the analgesic activities of the leaf extracts of *S. indicum*, *S. surattense* and *S. torvum*.

MATERIALS AND METHODS

Plant material and extraction

The herbal samples for the planned study have been amassed from Tirumala Hills, Tirupathi District, Andhara Pradesh, India and certified by Dr K Madhava Chetty, Asst. Professor, Dept. of Botany, Sri Venkateswara University, Tirupati, Andhara Pradesh, India. Washed the collected leaves using distilled water, dried in the shade, powdered and stored at 4°C till further use. Prepared the crude extracts using methanol as solvent. The extraction was done at room temperature. Filtered the extracts through Whatmann No. 1 filter paper and dried by means of rotary vacuum evaporator to give a concentrated extract. The extracts were dried with the help of drier and stored in air tight container for further use.

Animals

Swiss albino mice of either sex weighing 22±5g were employed in the present study. The approval for protocol was given by institutional ethical committee under reg. No. 1181/PO/ReBia/s/08/CPCSEA. The research was performed as per CPCSEA's rules and regulations for animal well-being including free access to fed and water along with exposure to natural cycle of light and dark.

Drugs and Chemicals

Diclofenac potassium (Standard drug), Glacial acetic acid and other chemicals were of analar quality and diluted in sterile saline.

Analgesic activity

Acetic acid-induced writhing test

Based on the procedure described in Aoki *et al.*, (2006), the acetic-acid writhing test was carried out. Groups of Mice (n=6), were given 200 & 400 mg/kg, methanolic extract of leaves of *Solanum indicum*, *Solanum surattense* and *Solanum torvum*, p.o. and diclofenac 10 mg/kg, *i.p.*, as positive control and 1 mL distilled water as vehicle

control group. 0.1 mL acetic acid (0.6%) was administered after 30 minutes to mice with *i.p* injection. Abdominal contractions of animals were then recorded for 30 minutes following acetic acid injection and the following formula was used to calculate the Percentage Analgesic Activity (PAA)

$$PAA = ((C - C_D) / C_D) \times 100$$

Where C = mean number of contractions in animals treated with various doses of methanolic extract of *Solanum indicum*, *Solanum surattense* and *Solanum torvum* and diclofenac

C_D = mean number of contractions in animals acted as negative control.

Hot Plate method

The Hot plate test was performed according to the procedure reported in Damaj *et al.*, (1999). Anti-nociceptive effect of methanolic extract of leaves of *Solanum Indicum*, *Solanum Surattense* and *Solanum Torvum*, p.o. and Diclofenac 10 mg/kg, *i.p.*, was investigated using hot plate test in swiss albino mice. Each mice is to be placed at a temperature of 55±2°C on the hot plate, and the response time like licking of paw or jump response is to be recorded. The same procedure was applied to the animals of each group and the latency time was measured and compared to control group. The given formula was used to determine the Percentage Analgesic Activity (PAA).

$$PAA = ((L_a - L_b) / L_b) \times 100$$

L_a = Latency time after treatment with drug or extract

L_b = Latency time before treatment with drug or extract
The response time is to be observed before and after 15, 30, 45, 60 and 90 minutes of treatment.

Statistical study

The findings are stated as mean ± S.E.M. The statistical study was done using one way analysis of variance (ANOVA). By post hoc analysis using Tukey's test, group differences were determined. The differences with values of P<0.05 were considered significant for all tests.

RESULT AND DISCUSSION

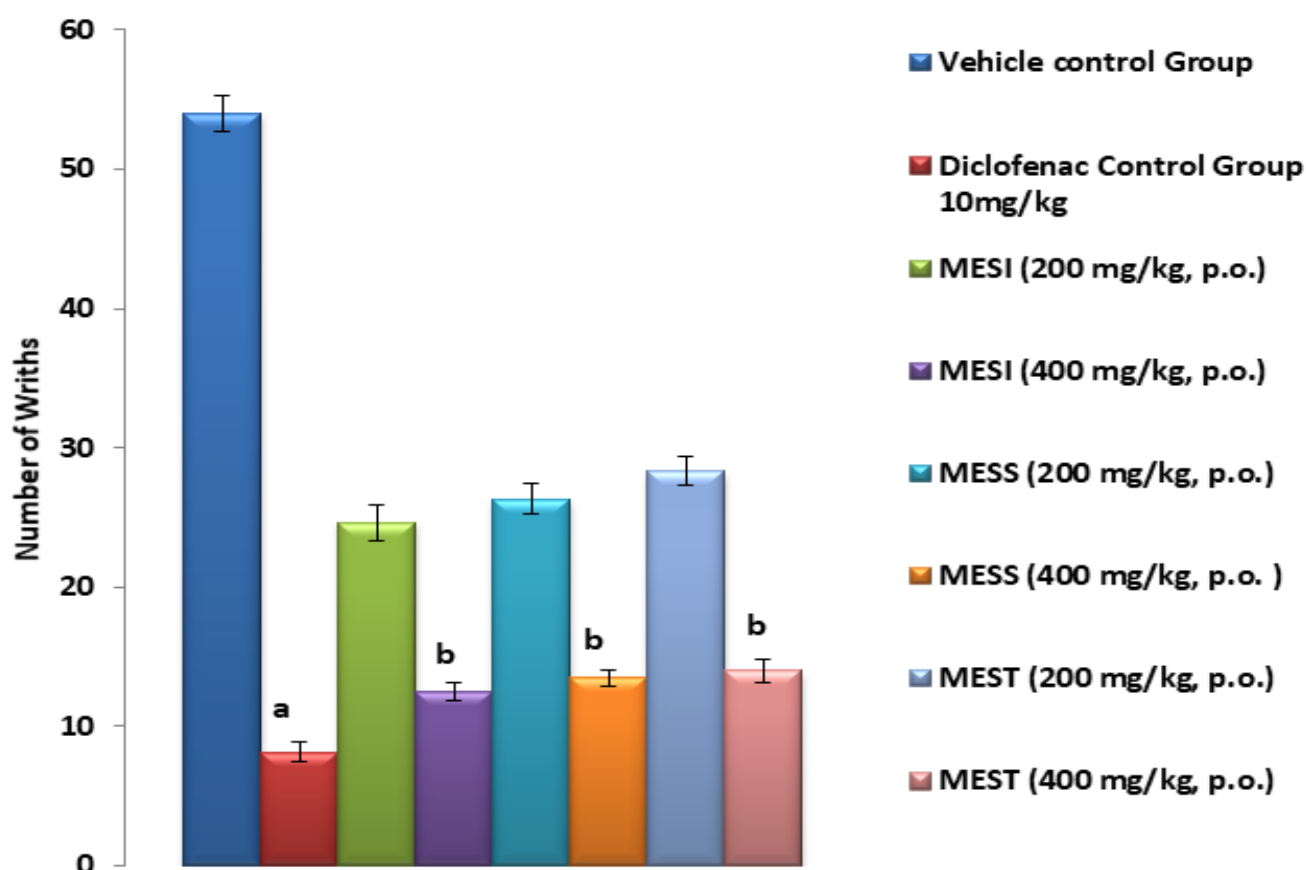
Analgesic activity

Acetic Acid Induced writhing test

In this procedure, all the tested extracts, significantly (p < 0.0001) showed dose related decrease in count of writhes, after 30 min of acetic acid injection (0.6% v/v), relative to control. Observations for the method are depicted in figure

Table 1: Analgesic activity by acetic acid induced writhing in mice

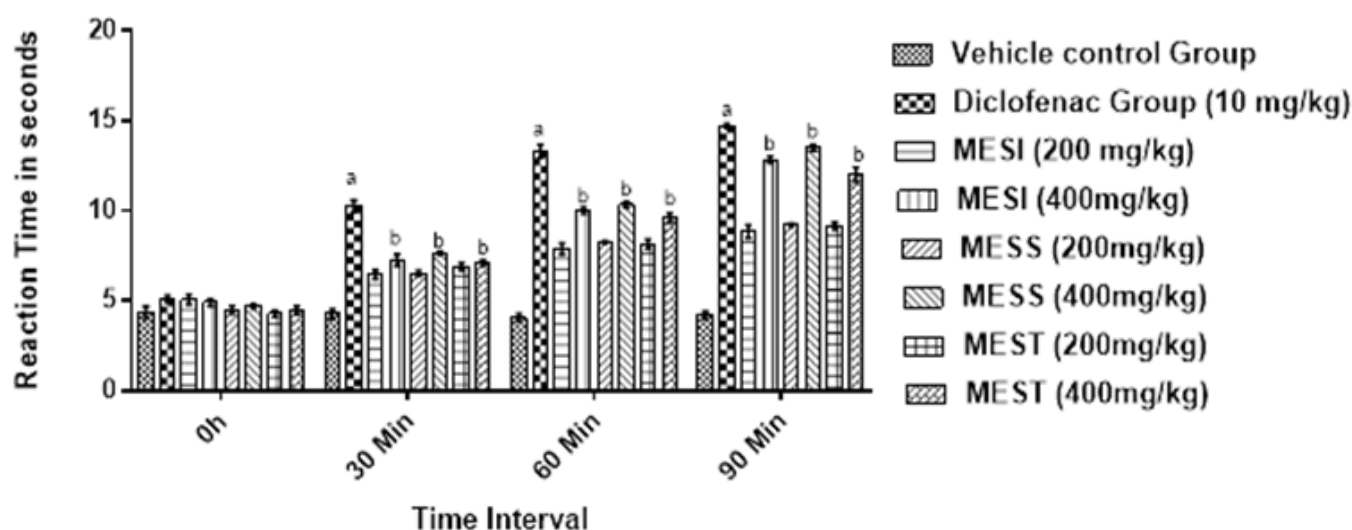
Group	Dose (mg/kg)	No. of writhes in 30 min (mean \pm SEM)	Inhibition (%)
Vehicle	54 \pm 1.26
Diclofenac	10 mg/kg	8.17 \pm 0.70	84.87
MESI	200 mg/kg	24.67 \pm 1.33	54.31
MESI	400 mg/kg	12.50 \pm 0.67	76.85
MESS	200 mg/kg	26.33 \pm 1.08	51.24
MESS	400 mg/kg	13.50 \pm 0.62	75
MEST	200 mg/kg	28.33 \pm 1.05	47.54
MEST	400 mg/kg	14 \pm 0.82	74.07

**Figure 1:** Effects of methanolic extract of leaves of *Solanum indicum*, *Solanum surattense* and *Solanum torvum* on acetic acid induced writhing

Each reading is the mean \pm SEM for 6 mice, a $P < 0.0001$; b $P < 0.0001$ in comparison to the control Group. Using One-way ANOVA, data was analyzed followed by Tukey's test.

Table 2: Analgesic activity by hot plate method in mice

Group	Dose (mg/kg)	Reaction time in seconds at time (minutes) (mean \pm SEM)			
		0	30	60	90
Vehicle control	4.35 \pm 0.32	4.27 \pm 0.26	4.08 \pm 0.22	4.2 \pm 0.19
Diclofenac	10 mg/kg	5.11 \pm 0.18	10.25 \pm 0.35	13.32 \pm 0.37	14.72 \pm 0.13
MESI	200 mg/kg	5.08 \pm 0.29	6.47 \pm 0.24	7.88 \pm 0.31	8.83 \pm 0.36
MESI	400 mg/kg	4.9 \pm 0.21	7.27 \pm 0.32	10.02 \pm 0.19	12.83 \pm 0.18
MESS	200 mg/kg	4.53 \pm 0.23	6.53 \pm 0.16	8.25 \pm 0.06	9.2 \pm 0.09
MESS	400 mg/kg	4.7 \pm 0.13	7.65 \pm 0.09	10.37 \pm 0.17	13.52 \pm 0.18
MEST	200 mg/kg	4.28 \pm 0.19	6.9 \pm 0.21	8.15 \pm 0.27	9.15 \pm 0.20
MEST	400 mg/kg	4.48 \pm 0.22	7.1 \pm 0.18	9.6 \pm 0.26	12.02 \pm 0.42

**Figure 2:** Evaluation of anti-nociceptive effects of methanolic extracts of leaves of *Solanum indicum*, *Solanum surattense* and *Solanum torvum* in hot plate

Each value is the mean \pm SEM for 6 mice, a $P < 0.0001$; b $P < 0.0001$ compared to control Group. Data were analyzed by using One-way ANOVA followed by Tukey's test.

1. The methanolic extracts of leaves of *Solanum indicum*, *Solanum surattense* and *Solanum torvum* reported a significant decrease in count of writhes at doses of 200 and 400 mg/kg respectively. The greatest writhing retardation was detected at 400 mg/kg for the methanol extracts of the three species, MESI, MESS and MEST (76.85%, 75%, 74.07%) which was equivalent with standard diclofenac at 10 mg/kg i.p (84.87%)

Hot Plate method

Dose-dependent analgesic activity was expressed by all the extracts of MESI, MESS and MEST. Figure 2 shows the results for hot plate method. Compared to control, methanol extracts at doses of 200, 400 mg/kg, depicted a remarkable outcome ($p < 0.0001$) at 60 and 90 min readings. At a dose of 10 mg/kg i.p., diclofenac had a significant effect ($p < 0.0001$). Significant effect

($p < 0.0001$) was evaluated with the extracts at the dose of 400 mg/kg in comparison to control at 90 minute reading. The extracts MEST, MESI, MESS with 400 mg/kg drastically improved the latency time by 12.02, 12.83 and 13.52 s at 90 minutes, respectively.

CONCLUSION

The current research depicts the analgesic activity of MESI, MESS and MEST in each of the two models, hot plate model and the acetic acid induced writhing model. Mice were protected in case of both hot and chemically generated toxic stimuli by all the extracts. Acetic acid, administered i.p, raised the prostaglandin levels i.e. PGE₂ and PGF_{2 α} . Abdominal constrictions in mice were coupled with prostaglandin mediated stimulation of peritoneal nociceptors (Bose *et al.*, 2007; Sengar *et al.*, 2015). The analgesic effects revealed by the extracts can be because of prostaglandin levels being inhibited.

The hot plate method was used broadly to monitor compounds expressing pain relieving effect by central mechanism, in which increase in the pain tolerance of mice for heat is determined. Since, the reaction by mice to toxic thermal stimuli is supra-spinally mediated in the hot plate method (Wani *et al.*, 2021), So, the analgesic effects of MESI, MESS and MEST in hot plate method possibly be because of their association with different receptors found in supra-spinal sites.

Our results shows that among all the three *Solanum* species' extracts, the extracts at a dose of 400 mg/kg exhibited significant analgesic activity followed by 200 mg/kg dose. The findings confirmed the demand for the conventional use of these species in treating pain. More experimental work is required to separate the phytoconstituents from the active extracts expressing prominent analgesic activity. Moreover, research is also required for the mechanism responsible for the activity, which will guarantee its clinical values.

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