



## Antinociceptive activity of methanol extract of leaves of *Solanum sisymbriifolium* in heat and chemical-induced pain

Tania Nasrin<sup>1</sup>, Mahia Khandaker<sup>2</sup>, Saleha Akter<sup>3</sup>, Mohammad Zafar Imam<sup>1\*</sup>

<sup>1</sup>Department of Pharmacy, Stamford University Bangladesh, 51 Siddeswari Road, Dhaka 1217, Bangladesh.

<sup>2</sup>Department of Biotechnology, Bangabandhu Sheikh Mujibur Rahman Agricultural University, Salna, Gazipur 1706, Bangladesh.

<sup>3</sup>Department of Pharmacy, Primeasia University, HBR Tower, Banani, Dhaka 1213, Bangladesh.

### ARTICLE INFO

#### Article history:

Received on: 20/03/2017

Accepted on: 19/05/2017

Available online: 30/11/2017

#### Key words:

*Solanum sisymbriifolium*,  
Solanaceae, antinociceptive,  
medicinal plant, pain.

### ABSTRACT

*Solanum sisymbriifolium* Lamk. (Solanaceae) is a perennial prickly herb traditionally used in folk medicine to treat different ailments. This study evaluated the methanol extract of *S. sisymbriifolium* leaf (MSS) (100, 200, and 400 mg/kg; p.o.) for analgesic activity using heat- and chemical-induced pain models such as hot plate, tail immersion, formalin-induced licking and acetic acid-induced writhing. Interaction with the opioid receptor system was verified using naloxone to antagonize the effect of MSS, if any. MSS demonstrated significant and dose-dependent antinociceptive activity, though moderate, in both hot plate and tail immersion test ( $p < 0.05$ ). Naloxone reversed the antinociceptive effect in both tests. MSS produced profound antinociceptive effect in formalin test and acetic acid-induced writhing at 400 mg/kg dose. These results imply that the antinociceptive effect of MSS is mainly due to its central effect and peripheral effects also contribute to some extent. These results provide preliminary evidence of antinociceptive activity of *S. sisymbriifolium* leaves and the potential of the plant in treating different painful conditions.

### INTRODUCTION

*Solanum sisymbriifolium* Lamk. (Solanaceae) is a densely prickly perennial herb commonly known as sticky nightshade. The plant is traditionally used in the treatment of stomachache, remitting fever, hysteria (Uddin, 2016), respiratory tract infections, central nervous system (CNS) disorders and diarrhea (Ibarrola *et al.*, 2000; Ferro *et al.*, 2005). This plant is also used as diuretic, antihypertensive (Gonzales Torrez, 1992), emenagogue and fertility regulator (Martinez-Crovetto, 1981). Pharmacological investigations of different parts of *S. sisymbriifolium* have reported hypotensive (Ibarrola *et al.*, 2000), analgesic (Shilpi *et al.*, 2005), neuropharmacological and anti-diarrheal activity (Apu *et al.*, 2013). Phytochemical analyses confirmed isolation of a number of pharmacologically active compounds from the plant including solamine, solasodine and solasodine (Mazumdar, 1984), neolignan, designated as

sisymbriifolin, and carpesterol together with  $\beta$ -sitosterol and its  $\beta$ -D-glucoside, cuscohygrine, (Evans and Somanabandhu, 1980; Ferro *et al.*, 2005), solacaproine, solamargine, and  $\beta$ -solamarine (Ferro *et al.*, 2005) and isonuatigenin-3-O- $\beta$ -solatriose (Ibarrola *et al.*, 2000). Solasodine, a major alkaloid, isolated from the plant has demonstrated variety of biological activities including antifungal (Kusano *et al.*, 1987), cytotoxic (Nakamura *et al.*, 1996), hepatoprotective (Lin *et al.*, 1988), antinociceptive (Basu and Lahiri, 1977; Pandurangan *et al.*, 2010), anti-inflammatory (Pandurangan *et al.*, 2011), anticonvulsant, CNS depressant (Chauhan *et al.*, 2011) and antiatherosclerotic activity (Dixit *et al.*, 1992). Solasodine is effective in skin tumor treatment (Cham *et al.*, 1987; Cham *et al.*, 1991). Nuatigenosido isolated from this plant has been reported to have cardiovascular effect (Ibarrola *et al.*, 2006). The use of this plant in folk medicine in different ailments and analgesic report of whole plant extract by Shilpi *et al.* (2005) in acetic acid-induced writhing motivated this study to evaluate the methanol extract of *S. sisymbriifolium* (MSS) leaf in different peripheral and central pain models in mice to find out whether the leaf is the major contributor in the effect as well the possible pathways involved in the analgesic effect.

\* Corresponding Author

Mohammad Zafar Imam, Department of Pharmacy, Stamford University Bangladesh, 51 Siddeswari Road, Dhaka 1217, Bangladesh.  
Fax: +88-02-9355967-176; E-mail: [zafarimam@gmail.com](mailto:zafarimam@gmail.com).

## MATERIALS AND METHODS

### Plant material and extraction

The leaves of *S. sisymbriifolium* were collected from Natore of Rajshahi Division, Bangladesh in January, 2011. Sarder Nasir Uddin, Senior Scientific Officer, Bangladesh National Herbarium identified the samples (DACB: 35424). Powdered dried leaves (58 g) were extracted with 350 ml of methanol by Soxhlet apparatus at 50°C for 36 h. Filtration was done using a sterile cotton filter, then the solvent was removed by rotary evaporator and 9.02 gm extract (Yield 15.55%) was obtained. This extract was used for the phytochemical screening and animal studies.

### Chemicals and drugs

Methanol (Merck, Germany), morphine sulphate (Gonoshasthaya Pharmaceuticals Ltd.), naloxone (Sigma, USA), diclofenac sodium (Square Pharmaceuticals Ltd.), formalin (Merck, Germany) and acetic acid (Merck, Germany).

### Animals

Swiss albino male mice weighing 20-25 gm were used in the study (Animal Resources Branch of the International Center for Diarrhoeal Disease Research, Bangladesh (icddr,b)). The mice were housed in cages in group and had access to food and water *ad libitum*. Room temperature of the animal house was 25 ± 2°C and relative humidity was 55-60%. 12 h light and 12 h dark cycle were maintained during the 14 day acclimatization period and throughout the experimental period. The Swiss Academy of Medical Sciences and the Swiss Academy of Sciences developed *Ethical Principles and Guidelines for Scientific Experiments on Animals* (1995) were followed for the animal welfare.

### Drugs and treatments

Morphine sulphate, used as a positive standard, at the dose of 5 mg/kg body weight (b.w.) was injected intraperitoneally (i.p.) 15 min prior to hot plate, tail immersion and formalin test while diclofenac sodium was injected (i.p.) at the dose of 10 mg/kg dose in acetic acid-induced writhing test. Vehicle controlled group was gavaged 0.9% saline water (vehicle) at the dose of 10 ml/kg. MSS was administered by oral gavage to mice at three different doses i.e., 100, 200, and 400 mg/kg b.w. I.P. injection of naloxone at 2 mg/kg dose was given 15 min before administering morphine or MSS in appropriate route to anticipate any possible involvement of MSS-opioid receptor interaction.

### Phytochemical screening

Following standard qualitative phytochemical procedure described by Ghani (2003) alkaloids, carbohydrates, flavonoids, glucosides, glycosides, proteins, reducing sugars, saponins and steroids were tested in MSS.

### Acute toxicity test

Three different mice groups (n = 5) received MSS orally at 500, 1000 and 2000 mg/kg dose. Animals were closely observed

for the next 72 h for any abnormality in behavior, any allergic response, morbidity and mortality (Walker *et al.*, 2008).

### Antinociceptive tests

#### Hot plate test

The test was performed following previously described method (Imam *et al.*, 2012). Mice were fasted overnight with water given *ad libitum*. The animals were treated with morphine or MSS or vehicle and were placed on hot plate maintained at a temperature of 55 ± 1°C. To avoid any tissue damage in the paw of the mice 20 s was considered as cut off period. The response to the thermal stimuli as forepaw licking, withdrawal of the paw(s) or jumping was documented at 30, 60, 90, and 120 min after treatment.

#### Tail immersion test

Mice were pretreated with morphine or MSS and ~2 cm of the tail was immersed in warm water maintained at 52 ± 1°C. The latency period at 30, 60, 90, and 120 min after treatment were documented (Toma *et al.*, 2003). In this test, 20s was considered as cut off period to avoid tail tissue damage.

#### Formalin test

Formalin (20 µl of 1.35% formalin) was injected into the sub-plantar region of the right hind paw of mice 30 min after MSS treatment and 15 min after injection of morphine. Paw licking was considered as nociceptive response and was documented at 0-5 min (early phase) and 15-25 min (late phase) after formalin injection (Coelho *et al.*, 2005).

#### Acetic acid-induced writhing test

Morphine or MSS was administered in mice and then 0.7% acetic acid was injected i.p. after 15 and 30 min respectively (10 ml/kg) to induce writhing. The number of writhing was documented for 10 min starting after 5 min post treatment (Vogel, 2007).

### Statistical analysis

The results are presented as mean ± standard error of mean (SEM). The statistical analyses of the results were performed using ANOVA (SPSS 11.5). Dunnett's or Bonferroni's test was performed as post-hoc test as appropriate. Differences between groups were considered significant at a level of  $p < 0.05$ .

## RESULTS

### Phytochemical screening

Preliminary phytochemical screening of MSS detected the presence of alkaloids, glycosides, carbohydrates and saponins.

### Acute toxicity

Oral administration of MSS up to 2000 mg/kg did not show any mortality, allergic manifestations or abnormality in behavior during the 72 h observation period in mice.

### Hot Plate test

MSS at 200 and 400 mg/kg significantly increased the latency to the thermal stimulus ( $p < 0.01$ ) dose dependently. MSS at 400 mg/kg dose produced strong antinociception. The effect of morphine at 5 mg/kg dose was highly significant ( $p < 0.001$ ). The effects of morphine and MSS were reversed by naloxone (Table 1).

### Tail immersion test

The antinociceptive activity of MSS and standard drug morphine on the tail immersion test are given in Table 1. MSS at all three doses showed significant increase in latency and at 400 mg/kg dose showed highest increase in latency ( $< 0.001$ ) which was reversed by naloxone. The effect of morphine was

highly significant ( $p < 0.001$ ) and strongest among the treatment groups.

### Formalin test

MSS at all doses (100, 200, and 400 mg/kg) reduced both early and late phase of paw licking induced by formalin (Table 2). However, the reduction in licking was significant ( $p < 0.05$ ) only for morphine and MSS at 400 mg/kg doses.

### Acetic acid-induced writhing

Oral administration of MSS at 100, 200, and 400 mg/kg doses reduced acetic acid-induced writhing compared to the control group (Table 2). However, the reduction was significant only at 400 mg/kg dose ( $p < 0.05$ ) and interestingly the effect was much stronger than that of diclofenac sodium.

**Table 1:** The antinociceptive effect of *S. sisymbriifolium* leaf, morphine, and reversal effect of naloxone in hot plate and tail immersion test.

	Treatment	Dose (mg/kg)	Latency period (sec)				
			30 min	45 min	60 min	90 min	120 min
Hot plate test	Vehicle	-	2.20 ± 0.07	2.36 ± 0.06	2.37 ± 0.14	1.99 ± 0.05	2.59 ± 0.09
	Morphine	5 (i.p.)	11.63 ± 0.13***	8.56 ± 0.22***	9.41 ± 0.20***	8.05 ± 0.17***	4.56 ± 0.18*
	MSS	100	1.95 ± 0.13	3.15 ± 0.19	3.37 ± 0.21	2.53 ± 0.12	2.02 ± 0.23
	MSS	200	2.17 ± 0.12	4.30 ± 0.16*	4.32 ± 0.12*	4.05 ± 0.23**	3.83 ± 0.04
	MSS	400	3.26 ± 0.16*	4.44 ± 0.26**	4.54 ± 0.25**	5.16 ± 0.21***	4.05 ± 0.22*
	NLX	2 (i.p.)	1.95 ± 0.16	2.62 ± 0.11	2.85 ± 0.11	3.54 ± 0.14	2.00 ± 0.09
	NLX + Morphine	2 + 5	3.54 ± 0.19 <sup>a</sup>	4.23 ± 0.14 <sup>a</sup>	4.06 ± 0.22 <sup>a</sup>	3.06 ± 0.22 <sup>a</sup>	2.79 ± 0.13 <sup>a</sup>
	NLX + MSS	2 + 100	2.60 ± 0.06	2.10 ± 0.15	2.74 ± 0.21	3.60 ± 0.18 <sup>b</sup>	2.68 ± 0.17
	NLX + MSS	2 + 200	2.43 ± 0.16	2.18 ± 0.16 <sup>c</sup>	2.39 ± 0.20 <sup>c</sup>	2.19 ± 0.16 <sup>c</sup>	3.24 ± 0.17
	NLX + MSS	2 + 400	2.49 ± 0.19	2.86 ± 0.21 <sup>d</sup>	2.53 ± 0.18 <sup>d</sup>	3.58 ± 0.21 <sup>d</sup>	2.63 ± 0.20 <sup>d</sup>
Tail immersion test	Vehicle	-	2.03 ± 0.09	2.15 ± 0.05	2.35 ± 0.09	3.35 ± 0.15	2.41 ± 0.11
	Morphine	5 (i.p.)	8.00 ± 0.25***	13.93 ± 0.96***	12.41 ± 0.53***	8.15 ± 0.14***	2.42 ± 0.09
	MSS	100	3.32 ± 0.12	3.37 ± 0.15	3.79 ± 0.10	5.00 ± 0.24*	4.67 ± 0.24*
	MSS	200	4.69 ± 0.14***	4.93 ± 0.26	5.52 ± 0.20**	6.33 ± 0.08***	5.44 ± 0.22**
	MSS	400	6.09 ± 0.26***	5.28 ± 0.10	5.61 ± 0.21**	6.42 ± 0.25***	6.63 ± 0.44***
	NLX	2 (i.p.)	4.44 ± 0.11	3.40 ± 0.16	3.29 ± 0.16	3.99 ± 0.11	3.84 ± 0.09
	NLX + Morphine	2 + 5	3.28 ± 0.10 <sup>a</sup>	4.79 ± 0.17 <sup>a</sup>	4.54 ± 0.14 <sup>a</sup>	4.04 ± 0.18 <sup>a</sup>	3.52 ± 0.22
	NLX + MSS	2 + 100	3.86 ± 0.07	5.17 ± 0.12 <sup>b</sup>	5.39 ± 0.16 <sup>b</sup>	6.02 ± 0.46	4.92 ± 0.40
	NLX + MSS	2 + 200	3.03 ± 0.17 <sup>c</sup>	2.41 ± 0.16 <sup>c</sup>	2.30 ± 0.10 <sup>c</sup>	2.41 ± 0.07 <sup>c</sup>	2.85 ± 0.13 <sup>c</sup>
	NLX + MSS	2 + 400	3.68 ± 0.09 <sup>d</sup>	3.76 ± 0.14 <sup>d</sup>	4.72 ± 0.09	3.40 ± 0.10 <sup>d</sup>	3.05 ± 0.11 <sup>d</sup>

Each value is presented as the mean ± SEM (n = 5). MSS = Methanol extract of *S. sisymbriifolium* leaves; NLX = Naloxone. \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$  compared with the control group (Dunnett's test). <sup>a</sup>  $p < 0.001$  compared with the morphine group; <sup>b</sup>  $p < 0.05$  compared with the MSS 100 group; <sup>c</sup>  $p < 0.05$  compared with the MSS 200 group; <sup>d</sup>  $p < 0.01$  compared with the MSS 400 group (Bonferroni's test).

**Table 2:** The antinociceptive effect of *S. sisymbriifolium* leaf extract and morphine in formalin-induced paw licking and acetic acid-induced writhing test in mice.

Treatment	Dose (mg/kg)	Formalin-induced licking of the hind paw			Acetic acid-induced writhing		
		Early phase (0-5 min)	% Inhibition	Late phase (15-30 min)	% Inhibition	Number of writhing	% Inhibition
Vehicle	10	163.67 ± 9.30	-	153.67 ± 12.1	-	28.5 ± 1.29	-
Morphine	5	50.00 ± 3.28*	69.45	0.00 ± 0.00*	100.00	NT	NT
Diclofenac sodium	10	NT	NT	NT	NT	6.3 ± 1.27*	77.89
MSS	100	143.00 ± 6.64	12.63	139.00 ± 7.88	9.55	21.2 ± 0.93	25.61
MSS	200	138.67 ± 6.80	15.28	110.00 ± 6.03	28.12	16.9 ± 0.98	40.70
MSS	400	102.00 ± 6.70*	37.68	60.30 ± 8.26*	60.76	2.7 ± 0.77*	90.53

Each value is presented as the mean ± SEM (n = 5). ). MSS = Methanol extract of *S. sisymbriifolium* leaves; NT = not tested. \*  $p < 0.05$  compared with the control group (Dunnett's test).

## DISCUSSION

The results of the present study indicate moderate but significant antinociceptive activity of MSS in particular at 400 mg/kg dose. The effect was more profound in heat-induced pain models. It is believed that hot plate method demonstrates the supraspinal reflex mediated by  $\mu_1$ - and  $\mu_2$ -opioid receptors whereas the tail immersion test monitors the spinal reflex involving  $\mu_2$ - and  $\delta$ -opioid receptors (Arslan and Bektas, 2010). These methods are, therefore, useful for screening molecules effective in spinal and supraspinal region. The increase in latency in these two tests by MSS indicates the modulation of central nervous system pain signaling. This hypothesis is further supported by the reversal of antinociception of MSS at all doses by naloxone in both hot plate and tail immersion test. Reversal of antinociceptive effect of MSS by naloxone raises the possibility of involvement of opioid receptor mediated effect at the spinal and supraspinal level which is predominant in case of morphine in both tests. Formalin-induced paw licking is a well-accepted chemical induced pain model that works in two divergent phases; early phase neurogenic pain due to direct stimulation of the sensory afferent fibers followed by inflammatory pain due to action of different inflammatory mediators (Parada *et al.*, 2001; Le Bars *et al.*, 2001). The effect of formalin can be consistently inhibited by typical analgesic and anti-inflammatory drugs like indomethacin, diclofenac sodium and morphine (Tjolsen *et al.*, 1992). The results of our present study have shown that MSS reduced the number of paw licking significantly in neurogenic and inflammatory pain phases ( $p < 0.05$ ). Acetic acid-induced release of prostaglandins, serotonin, bradykinin, histamine, TNF (some common endogenous mediators) in the peripheral tissue fluid is associated with the development of pain and writhing (Ikeda *et al.*, 2001). The profound antinociceptive effect of MSS at 400 mg/kg dose in acetic acid-induced writhing test, therefore, implies that MSS may be involved in the inhibition of inflammatory mediators like cyclooxygenase, lipoxygenase and others which results in the interruption of signal transduction in primary afferent nociceptors. Solasodine which have already been shown antinociceptive, anti-inflammatory and CNS depressant activity may play important role in MSS's antinociceptive effect along with other phytochemicals (Basu and Lahiri, 1997; Pandurangan *et al.*, 2010; Pandurangan *et al.*, 2011; Chauhan *et al.*, 2011). The results of the present study underpin the preliminary basis of traditional use of *S. sisymbriifolium* in some painful conditions. It also presents the possibility of inhibition of inflammatory mediators as well as modulation of opioid system by compounds present in MSS. However, further research with isolated compounds is required to better understand the principal chemical entity/entities that contribute to the effect, the mechanisms involved and optimization of the preparation to be used.

## ACKNOWLEDGEMENT

**Financial support and sponsorship:** None.

**Conflict of Interests:** There are no conflicts of interest.

## REFERENCES

- Apu AS, Matin M, Bhuyan SH, Hossain MF, Ireem K. Study of analgesic, neuropharmacological and anti-diarrheal activities of ethanol extract of *Solanum sisymbriifolium* fruits. *Pharmacologia*, 2013; 4:164-169.
- Arslan R, Bektas N. Antinociceptive effect of methanol extract of *Capparis ovata* in mice. *Pharm Biol*, 2010; 48:1185-1190.
- Basu A, Lahiri SC. Some pharmacological actions of solasonine. *Indian J Exp Biol*, 1977; 15:285-289.
- Cham BE, Daunter B, Evans RA. Topical treatment of malignant and premalignant skin lesions by very low concentrations of a standard mixture (BEC) of solasodine glycosides. *Cancer Lett*, 1991; 59:183-192.
- Cham BE, Gilliver M, Wilson L. Antitumor effects of glycoalkaloids isolated from *Solanum sodomaeum*. *Planta Med*, 1987; 53:34-36.
- Chauhan K, Sheth N, Ranpariya V, Parmar S. 2011. Anticonvulsant activity of solasodine isolated from *Solanum sisymbriifolium* fruits in rodents. *Pharm Biol*, 2011; 49:194-199.
- Coelho LP, Reis PA, Castro FL, Gayer CRM, Lopes CS, Silva MCC, Sabino KCC, Todeschini AR, Coelho MGP. 2005. Antinociceptive properties of ethanolic extract and fractions of *Pterodon pubescens* Benth seeds. *J Ethnopharmacol*, 2005; 98:109-116.
- Dixit VP, Verma M, Mathur NT, Mathur R, Sharma S. Hypocholesterolaemic and antiatherosclerotic effects of solasodine (C27H43O2N) in cholesterol fed rabbits. *Phytother Res*, 1992; 6:270-273.
- Evans WC, Somanabandhu A. 1980. Nitrogen-containing non-steroidal secondary metabolites of *Solanum*, *Cyphomandra*, *Lycianthes* and *Margaranthus*. *Phytochem*, 1980; 19:2351-2356.
- Ferro EA, Alvarenga NL, Ibarrola DA, Helli6n-Ibarrola MC, Ravelo AG. A new steroidal saponin from *Solanum sisymbriifolium* roots. *Fitoterapia*, 2005; 76:577-579.
- Ghani A. 2003. Medicinal Plants of Bangladesh: Chemical Constituents and Uses. 2<sup>nd</sup> Ed. The Asiatic Society of Bangladesh, Dhaka, Bangladesh.
- Gonzales Torrez DM. 1992. Catalog of Medicinal Plants (with Useful Food Values) Used in Paraguay. Asuncion, El Pais.
- Ibarrola DA, Helli6n-Ibarrola MC, Alvarenga NL, Ferro EA, Hatakeyama N, Shibuya N, Yamazaki M, Momose Y, Yamamura S, Tsuchida K. Cardiovascular action of Nuatigenosido from *Solanum sisymbriifolium*. *Pharm Biol*, 2006; 44:378-381.
- Ibarrola DA, Helli6n-Ibarrola MC, Montalbetti Y, Heinichen O, Alvarenga N, Figueredo A, Ferro EA. Isolation of hypotensive compounds from *Solanum sisymbriifolium* Lam. *J Ethnopharmacol*, 2000; 70:301-307.
- Ikeda Y, Ueno A, Naraba H, Oh-ishi S. Involvement of vanilloid receptor VR1 and prostanoids in the acid acid-induced writhing responses of mice. *Life Sci*, 2001; 69:2911-2919.
- Imam MZ, Nahar N, Akter S, Rana MS. Antinociceptive activity of methanol extract of flowers of *Impatiens balsamina*. *J Ethnopharmacol*, 2012; 142:804-810.
- Kusano G, Takahashi A, Sugiyama K, Nozoe S. Antifungal properties of *Solanum* alkaloids. *Chem Pharm Bull*, 1987; 35:4862-4867.
- Le Bars D, Gozariu M, Cadden SW. Animal models of nociception. *Pharmacol Rev*, 2001; 53:597-652.
- Lin CN, Chung MI, Gan KH. Novel antihepatotoxic principles of *Solanum incanum*. *Planta Med*, 1988; 54:222.
- Martinez-Crovetto R. Fertility-regulating plants used in popular medicine in Northeastern Argentina. *Parodiana*, 1981; 1:97-117.
- Mazumdar BC. Steroidal saponin in two wild species of *Solanum*. *Sci Cult*, 1984; 50:122-123.
- Nakamura T, Komori C, Lee Y, Hashimoto F, Yahara S, Nohara T, Ejima A. Cytotoxic activities of *Solanum* steroidal glycosides. *Biol Pharm Bull*, 1996; 19:564-566.

Pandurangan A, Khosa RL, Hemalatha S. 2011. Anti-inflammatory activity of an alkaloid from *Solanum trilobatum* on acute and chronic inflammation models. *Nat Prod Res*, 2011; 25:1132-1141.

Pandurangan A, Khosa RL, Hemalatha S. Antinociceptive activity of steroid alkaloids isolated from *Solanum trilobatum* Linn. *J Asian Nat Prod Res*, 2010; 12:691-695.

Parada CA, Tambeli CH, Cunha FQ, Ferreira SH. The major role of peripheral release of histamine and 5-hydroxytryptamine in formalin-induced nociception. *Neurosci*, 2001; 102:937-944.

Shilpi JA, Rouf R, Sarker MAM, Qamrunnahar, Ferdous MM, Uddin SJ. Antinociceptive activity of methanol extract of *Solanum sisymbriifolium* Lamk. *Pak J Biol Sci*, 2005; 8:1123-1125.

Tjolsen A, Berge OG, Hunskaa S, Rosland JH, Hole K. The formalin test: An evaluation of the method. *Pain*, 1992; 51:5-17.

Toma W, Graciosa JS, Hiruma-Lima CA, Andrade FDP, Vilegas W, Brita ARMS. Evaluation of the analgesic and antiedematogenic activities of *Quassia amara* bark extract. *J Ethnopharmacol*, 2003; 85:19-23.

Uddin SN. 2006. Traditional uses of ethnomedicinal plants of the Chittagong Hill Tracts. Bangladesh National Herbarium, Dhaka, Bangladesh.

Vogel HG. 2007. Drug Discovery and Evaluation: Pharmacological Assays. Springer, Berlin, H.G.

Walker CIB, Trevisan G, Rossato MF, Franciscato C, Pereira ME, Ferreira J, Manfron MP. Antinociceptive activity of *Mirabilis jalapa* in mice. *J Ethnopharmacol*, 2008; 120:169-175.

**How to cite this article:**

Nasrin T, Khandaker M, Akter S, Imam MZ. Antinociceptive activity of methanol extract of leaves of *Solanum sisymbriifolium* in heat and chemical-induced pain. *J App Pharm Sci*, 2017; 7 (11): 142-146.