

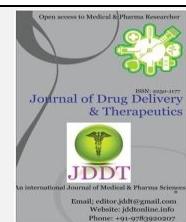


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Research Article

# PHARMACOLOGICAL EVALUATION OF SOLANUM VIARUM DUNAL LEAVES EXTRACT FOR ANALGESIC AND ANTIPYRETIC ACTIVITIES

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### ABSTRACT

The family Solanaceae consists of many plants, one of them is *Solanum viarum* Dunal. This plant contains chemical constituents like Solasodine which is found in many plants of Solanaceae family. The Solasodine have many medicinal properties and used as cardiotonic, antifungal, antispermatic, antiandrogenic, immunomodulatory, anticancer, anti-inflammatory, antinociceptive and as antipyretic. The study was carried out to ascertain analgesic and antipyretic activity of ethanolic extract of *Solanum viarum* Dunal leaves. The ethanolic extract of *Solanum viarum* Dunal leaves at 100 and 200mg/kg oral single dose treatment show a significant difference ( $p<0.0001$ ) in reaction time in terms of analgesic activity before and after treatments comparable to standard drug Diclofenac (10mg/kg body weight) and also reduced the elevated body temperature induced by Brewer's yeast. The extract also shows significant ( $p<0.0001$ ) decrease in elevated body temperature at 100 and 200mg/kg comparable to standard drug Paracetamol (150mg/kg body weight).

**Keywords** *Solanum viarum* Dunal, Analgesic activity, Antipyretic activity.

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### INTRODUCTION

Injuries and diseases co-exist with pain and fever. The drugs that relief pain and lower the elevated body temperature are known as analgesic and antipyretic which comes under the category of non-steroidal anti-inflammatory drugs or NSAIDS. These drugs prevent the synthesis of prostaglandins by inhibiting cyclooxygenase enzyme (COX) and relief pain and lower the elevated body temperature, but prostaglandins are also essential for synthesis of various components which causes GI mucosal defence. Hence NSAIDS are responsible for various gastrointestinal complications like perforation, obstructions, peptic ulcers, and bleeding. These complication are not occurs with selective COX-2 inhibitors but COX-2 inhibitors also cause cardiovascular and renal complications. Narcotic analgesics are the drugs used in the management of chronic pain but they possess various side effects like,

sedation, addiction, tolerance, psychological dependency, constipation, respiratory depression and mainly social abuse. Furthermore, only 50% of existing analgesics contributing relief from pain in approx 30% of the patients, for minimize these adverse events, exploration for newer analgesic and antipyretic drugs is required. Natural products play important role in managing various type of diseases due to their medicinal properties. Approx 25% of synthetic compounds are directly or indirectly based on medicinal plants. Medicinal plants possess lower side effects, traditional uses and they are also found in abundance, they provide appropriate source for discovering the newer drugs to manage pain and fever.

*Solanum viarum* Dunal is commonly known as tropical soda apple belongs to family Solanaceae. It also has various synonyms like *Solanum chloranthum*, *Solanum khasianum*, *Solanum viridiflorum* etc. *Solanum viarum*

described as a broad leaf herb, subshrub or shrub. In India, it is considered as a "woody herb", generally perennial, occurs in warm climate, remains green over the winter. They grow from 3-6 feet tall; leaves and stem are lined with thorn like prickles up to 1 inch (2.5cm long). The leaves are 2 to 8 inches (6-20cm) long x 2 to 6 inches (6-15cm) wide. Its inflorescence is a 1 to 3 flowered cyme. The fruits are globular berries, typically about 0.8 to 1 inch (2-3cm) in diameter at maturity, but viable seed develop in ripe fruits as small as 0.4 inch (1cm) in diameter. It contains chemical constituents like Solasodine, Caffeoylquinic acid (CQA) derivatives, 5-caffeooyl and 3-malonyl-5-caffeooyl-[4-(1beta-[6-(5-caffeooyl)quinate] glucopyranosyl)], quinic acid.

Solasodine is aglycone part of glycoalkaloids (nitrogen analogue of saponins). Solasodine having 27 carbon

atoms (cholestane skeleton) and it can be converted into dihydropregnolone. Dihydropregnolone is an important intermediate in synthesis of many steroid drugs like progesterone and cortisone.<sup>1</sup>

## MATERIAL AND METHODS

Diclofenac, Paracetamol and Brewer's yeast, were purchased from Yarrow Chem Products Mumbai, and other chemicals were used of laboratory grade.

### Collection and Identification of Plant

The *Solanum viarum* Dunal leaves were collected from Naukuchiatal road site of Bhimtal region District Nainital. The specimen was identified and authenticated by Botanical Survey of India (BSI) NRC Dehradun.



**Figure 1: Solanum viarum Dunal**

### Preparation of extract of *Solanum viarum* Dunal

Shade dried leaves of *Solanum viarum* Dunal were ground to fine powder in an electric grinder and sieved. 150 gm of dried powder were extracted with 1500ml of ethanol. It was subjected to reflux for 2 cycles, which was further evaporated to dryness to obtain ethanolic extract. The percentage yield of extract was 30.19% w/w with respect to the original air dried powder was obtained.<sup>12</sup> The extract was finally stored in air tight container, in dry place for further use in experiment.

### Experimental Animals

Healthy Wistar rats (200-250gm) of either sex were used for this study. They were acclimated to laboratory environment for 7 days before the beginning of the experiment, with alternative light-dark cycle of 12 hrs and were allowed free access to standard dry pellet diet and water ad libitum. Animals were fasted overnight with free access to water preceding the experiment. The study was performed according to the **Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA)** guidelines.<sup>2,3</sup>

### Preliminary Phytochemical Tests

The ethanolic extract of *Solanum viarum* Dunal leaves were tested for different phytoconstituents like alkaloids,

saponin, flavonoids, proteins, phenolic compounds, tannins, terpenoids and steroids.<sup>4,5</sup>

### Acute Oral Toxicity Studies

Acute oral toxicity study was carried out for ethanolic extract of *Solanum viarum* Dunal leaves using Acute Toxic class method as described in OECD (Organization of Economic Co-Operation and Development) guidelines no. 423 on female Wistar rats.

### Analgesic activity

#### Hot Plate Method

The paws of mice and rats are particularly responsive to heat at a temperature which not damaging the skin. The responses include withdrawal of the paws, jumping and licking of the paws. The Wistar rats (either sex) weighing between 200-250gm were divided into four groups each group having six animals. The animals were weighed and numbered appropriately. The group first considered as control group and received only distilled water and second group considered as standard group and received Diclofenac sodium 10mg/kg. Third and fourth groups received *Solanum viarum* Dunal leaf extract (T<sub>1</sub> 200mg/kg and T<sub>2</sub> 400mg/kg) respectively and the animals were positioned on the hot plate and the time until either licking or jumping occurs is noted down by a stop-watch for 0, 30, 60, 120 and 180 minutes. Fifteen

second cut off time was taken to avoid the damage of paw skin<sup>6</sup>

### Tail flick method

The application of thermal radiation to the tail of an animal provokes the tail withdrawal. The withdrawal of tail from the heat source, referred to as "tail flick latency".

Wistar rats having weight between 200-250gm were placed into four groups and each group having six animals. The first group was considered as control group and received distilled water and second one considered as standard group and received Diclofenac sodium 10mg/kg. Third and fourth groups received *Solanum viarum* Dunal leaf extract (T<sub>1</sub> 200mg/kg and T<sub>2</sub> 400mg/kg) respectively. The rat tail was located on analgesiometer that was previously maintained at 55<sup>0</sup>c and nociceptive response latency of time flicking of tail was recorded 0, 30, 60, 120 and 180 minutes. Usually withdrawal time is about 2-10 sec and the cut off time is 10 sec.<sup>7</sup>

### Antipyretic activity

#### Brewer's yeast induced pyrexia in rats

Antipyretic activity on Wistar rats was performed with Brewer's yeast induced pyrexia. The rats (weight 200-250gm) were divided into four groups each containing six animals. Firstly basal rectal temperature was taken by inserting 1-2cm of digital thermometer in rat rectum. After taking the basal rectal temperature, intraperitoneally 15% of Brewer's yeast injection in normal saline was injected to induce pain at a dose of 10ml/kg of body weight. Later than 18hrs of injection, rats which showed a rise in temperature of at least 1<sup>0</sup>c were taken for the study. Animals were treated with test and standard drugs after 18 hrs of yeast injection and temperature of rat's rectum was measured for 1, 2, 3 and 4 hrs after treatment.<sup>8</sup>

We can represent percentage reduction in rectal temperature as;

$$= \frac{Y-X}{Y-Z} \times 100 \quad \text{eq.1}$$

Where,

Z represents initial rectal temperature (in<sup>0</sup>c).

Y represents rectal temperature after 18hrs of administration of yeast (in<sup>0</sup>c).

X represents rectal temperature after administration of extract (in<sup>0</sup>c).

### RESULT

Hot plate test- The result of analgesic activity of the ethanolic extract of the leaves of *Solanum viarum* Dunal by Hot plate method are shown in Table 1 and graphically presented as Fig 1. The rats of control group (treated with normal saline) did not show any difference in reaction time during conduction of hot plate test. The rats treated with standard drug Diclofenac were showed

significant (p<0.0001) increase in reaction time and the rats treated with ethanolic extract of *Solanum viarum* Dunal leaves were also showed significant (p<0.0001) increase in reaction time. The highest reaction time for the higher concentration extract treated (T<sub>2</sub> 200mg/kg) group was 8.0 second at 180 minutes while it was 7.8 second at 180 minutes for lower concentration extract treated (T<sub>1</sub> 100mg/kg) group and for standard drug treated group it was 8.1 second at 180 minutes. Both the extracts were found to cause time-dependently prolongation of hot plate latency. The longest latency was obtained at 180 minutes post administration of the extract or the reference drug. The standard drug diclofenac (10mg/kg) was more potent than the extracts at all time levels at 200mg/kg. The leaves extract showed significant result at 60, 90, 120 and 180 min in compare to control. No significant difference was observed between the extract and diclofenac treated groups.

Fig 1 shows diclofenac elicit significant analgesic activity within 30 minutes after administration and analgesic activity gradually increased with time. Similarly, the extract also shows significant analgesic activity within 30 minutes and activity also gradually increases with time.

Tail Flick test- The result of analgesic activity of the ethanolic extract of the leaves of *Solanum viarum* Dunal by Tail Flick method are shown in Table 2 and graphically presented as Fig 2. Rats of control group did not show any significant difference in tail flick latency throughout the reaction time. The rats of standard group (treated with diclofenac) were showed a significant (p<0.0001) difference in reaction time between before and after administration of diclofenac. The maximum tail flick latency observed was 7.1 second at 180 minutes with higher concentration of extract (T<sub>2</sub> 200mg/kg) while for standard drug the tail flick latency was 7.0 second at 180 minutes. The tail flick latency for T<sub>1</sub> (100mg/kg) was 6.8 second at 180 minutes. The T<sub>2</sub> show 0.1 second of increment in reaction time in comparison to standard drug.

Fig 2 The T<sub>1</sub> and T<sub>2</sub> show significant analgesic activity within 30 min of administration and gradually increase with time.

Brewer's yeast induced pyrexia test- The result of antipyretic activity of the ethanolic extract of the leaves of *Solanum viarum* Dunal by Brewer's yeast induced pyrexia test are shown in Table 3 and graphically presented as Fig 3. The control group showed elevation in body temperature after administration of Brewer's yeast. The rats of extract treated group (T<sub>2</sub> 200mg/kg) showed 38<sup>0</sup>c elevation in body temperature after 18hrs of Brewer's yeast injection which was become 35<sup>0</sup>c after 4 hrs of T<sub>2</sub> administration.

Fig. 3 illustrate Standard drug paracetamol 150mg/kg and both the test drugs orally showed significant (P<0.0001) difference in body temperature in 1, 2, 3, and 4 hr of time interval respectively.

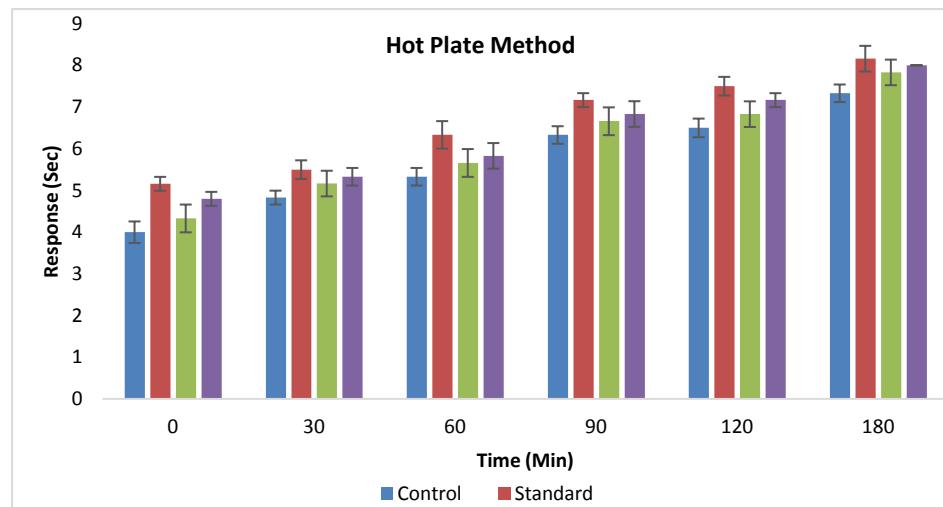


Figure 2: Analgesic Activity by Hot Plate Method [standard- Diclofenac (10mg/kg), T<sub>1</sub>- *Solanum viarum* Dunal Ethanolic Extract(100mg/kg), T<sub>2</sub>-*Solanum viarum* Dunal Ethanolic Extract(200mg/kg)]

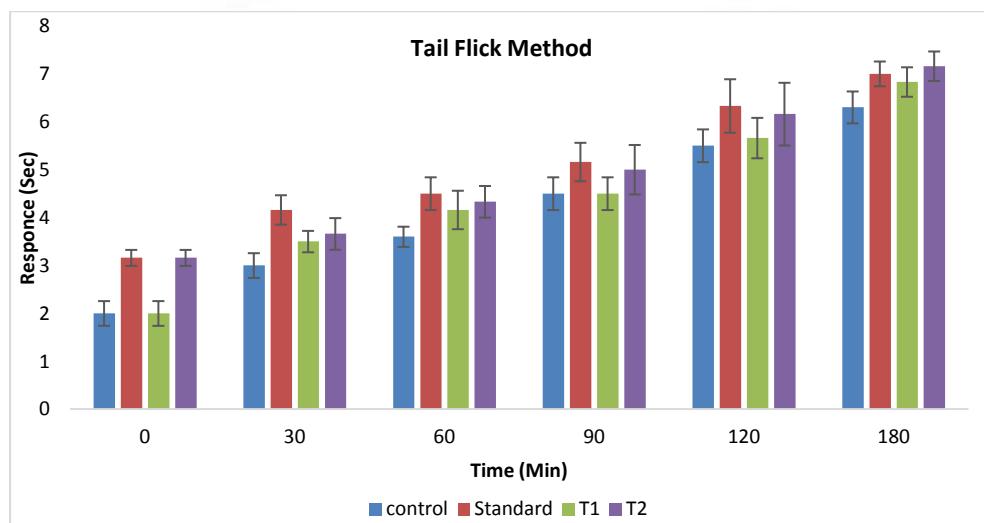


Figure 3: Analgesic Activity by Tail Flick Method in Rats [standard- Diclofenac (10mg/kg), T<sub>1</sub>-*Solanum viarum* Dunal Ethanolic Extract (100mg/kg) T<sub>2</sub>-*Solanum viarum* Dunal Ethanolic Extract (200mg/kg)]

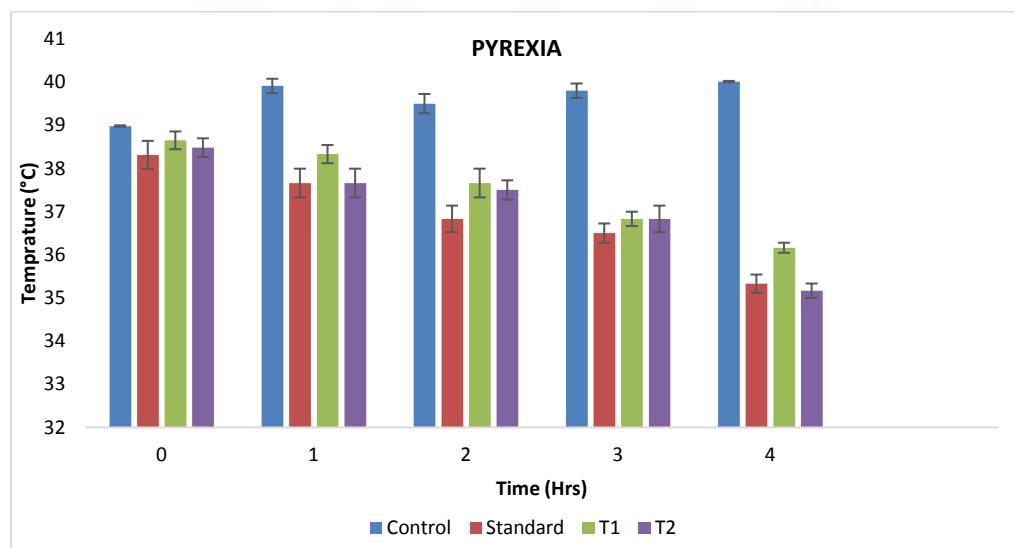


Figure 4: Antipyretic Activity by Brewer's Yeast Induced Pyrexia Method in Rats [standard- Paracetamol (150mg/kg), T<sub>1</sub>- *Solanum viarum* Dunal Ethanolic Extract(100mg/kg), T<sub>2</sub>- *Solanum viarum* Dunal Ethanolic Extract(200mg/kg)]

## Effect on analgesia

### Analgesic effect by hot plate method

Table 1: Values are expressed as mean  $\pm$  SEM (N=6), standard p<0.0001 significant with respect to the control, and in test 2 p<0.0001 significant with respect to the control group by one way ANOVA test.

Groups	Dose	Reaction time in sec					
		0 min	30 Min	60 min	90 min	120 Min	180 min
Control	10 ml/kg	4 $\pm$ 0.2582	4.83 $\pm$ 0.166	5.33 $\pm$ 0.2108	6.33 $\pm$ 0.2108	6.5 $\pm$ 0.2236	7.33 $\pm$ 0.2106
Standard Diclofenac sod	10 mg/kg	5.16 $\pm$ 0.166	5.5 $\pm$ 0.2236	6.33 $\pm$ 0.2108	7.16 $\pm$ 0.2108	7.5 $\pm$ 0.2236	8.16 $\pm$ 0.3073
Test drug (T <sub>1</sub> )	200 mg/kg	4.33 $\pm$ 0.333	5.16 $\pm$ 0.307	5.66 $\pm$ 0.333	6.66 $\pm$ 0.333	6.83 $\pm$ 0.307	7.83 $\pm$ 0.3073
Test drug (T <sub>2</sub> )	400 mg/kg	4.8 $\pm$ 0.1667	5.33 $\pm$ 0.210	5.83 $\pm$ 0.3073	6.83 $\pm$ 0.3073	7.16 $\pm$ 0.166	8

### Analgesic effect by tail flick method

Table 2: Values are expressed as mean  $\pm$  SEM (N=6), standard p<0.0001 significant with respect to the control, by one way ANOVA test.

Groups	Dose	Reaction time in sec					
		0 min	30 Min	60 Min	90 min	120 Min	180 min
Control	10 ml/kg	2 $\pm$ 0.2582	3 $\pm$ 0.2582	3.6 $\pm$ 0.2108	4.5 $\pm$ 0.341	5.5 $\pm$ 0.341	6.3 $\pm$ 0.333
Standard Diclofenac sod.	10 mg/kg	3.16 $\pm$ 0.166	4.16 $\pm$ 0.307	4.5 $\pm$ 0.3416	5.16 $\pm$ 0.401	6.33 $\pm$ 0.557	7 $\pm$ 0.258
Test drug (T <sub>1</sub> )	200 mg/kg	2 $\pm$ 0.2582	3.5 $\pm$ 0.223	4.16 $\pm$ 0.4014	4.5 $\pm$ 0.3416	5.66 $\pm$ 0.421	6.83 $\pm$ 0.307
Test drug (T <sub>2</sub> )	400 mg/kg	3.16 $\pm$ 0.166	3.66 $\pm$ 0.33	4.33 $\pm$ 0.33	5 $\pm$ 0.5164	6.16 $\pm$ 0.654	7.16 $\pm$ 0.307

## Effect on pyrexia

### Antipyretic effect by brewer's yeast induced pyrexia

Table 3: Values are expressed as mean  $\pm$  SEM (N=6), standard p<0.0001 significant with respect to the control, by one way ANOVA test.

Groups	Dose	Reaction time in hrs				
		0hr	1hr	2hr	3hr	4hr
Control	10 ml/kg	38.98 $\pm$ 0.01667	39.91 $\pm$ 0.166	39.5 $\pm$ 0.2236	39.8 $\pm$ 0.1667	40.01 $\pm$ 0.016
Standard Paracetamol	150 mg/kg	38.31 $\pm$ 0.327	37.66 $\pm$ 0.333	36.83 $\pm$ 0.307	36.5 $\pm$ 0.2236	35.33 $\pm$ 0.212
Test drug (T <sub>1</sub> )	200 mg/kg	38.65 $\pm$ 0.2062	38.33 $\pm$ 0.210	37.66 $\pm$ 0.333	36.83 $\pm$ 0.166	36.16 $\pm$ 0.117
Test drug (T <sub>2</sub> )	400 mg/kg	38.48 $\pm$ 0.2167	37.66 $\pm$ 0.333	37.5 $\pm$ 0.2236	36.83 $\pm$ 0.307	35.16 $\pm$ 0.166

## DISCUSSION

Currently available drug regimens for management of analgesic, antipyretic and anti-inflammatory activity have certain drawbacks and therefore there is a need for safer and more effective drugs. The use of traditional medicine and medicinal plants in most developing countries, as a normative basis for the maintenance of good health has been widely observed.

The study indicated that *Solanum viarum* Dunal leaves extract has analgesic and antipyretic activities. The analgesic activity was studied by using thermal test (hot plate and tail flick method). The thermal tests were selected to evaluate analgesic activity of the extract because temperature induces pain and this pain can be utilized to study the analgesic efficacy of the extract. The tail of the animal are very sensitive to heat or thermal stimuli, tail flick method was used for the evaluation of analgesic activity of drug. In hot plate

method, a plate was heated on constant temperature produces two behavioural responses (that can be measured in terms of their reaction times), namely paw licking and jumping. Both are considered to be supraspinally integrated responses.<sup>9</sup> The extract produced a prolongation of time latency in all the tests.<sup>10</sup> It is well known that most analgesic drugs possess antipyretic activity. The antipyretic activity of the extract was determined by yeast induce pyrexia method. In the present study, rise of temperature after 18hrs of subcutaneous yeast injection was above 38<sup>0</sup>c. There was a significant difference between the initial mean basal temperature of the different groups and the mean temperature of pyrexia rats. Rectal temperature of pyrexia rats were lowered significantly with the test drug and standard drug. Standard drug paracetamol is more potent than the test extract<sup>11</sup> No toxicity was seen in the test drug treated groups after 24hrs of experiment. So the test drug is a safer antipyretic agent.

## CONCLUSION

Based on the result of this study, it was concluded that leaf extract of *Solanum viarum* Dunal have analgesic and antipyretic activities when used orally at a dose of 100 and 200mg/kg. Phytochemical analysis has been done. The data collectively indicate the leaf extract of *Solanum viarum* Dunal possesses analgesic and

antipyretic activities which is probably mediated by both central and peripheral inhibitory mechanism as well as via inhibition of prostaglandins synthesis. In conclusion, this study demonstrated that the leaf of *Solanum viarum* Dunal has marked analgesic and antipyretic activities. The present study offered of scientific evidence to the traditional use of *Solanum viarum* Dunal as analgesic, antipyretic agent.

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