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Acute Toxicity Studies and *In-vitro* Antioxidant Potential of *Solanum indicum*

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ABSTRACT

Solanum indicum (*Solanaceae*) is traditionally used treatment of cough, asthma, sexual disorders and diarrhoea. Efficacy of traditional medicine was determined using the in-vitro antioxidant activity of the plant extract. Toxicological codicil of the drug was performed following OECD guidelines 423 with slight modifications. *Solanum indicum* extract administered to the rats by oral gavage at 500, 1000, 1500 & 2000 mg/kg body weight daily up to 28 days to male and female Sprague Dawley rats. Oral toxicity studies substantiate, no treatment-related death or toxic *indicia* were observed. It revealed that the *Solanum indicum* extract could be well tolerated up to the dose 2000 mg/kg body weight and could be classified as Category 5 drug.)

Keywords: *Solanum indicum*, Phytochemistry, Antioxidant, Acute toxicity, DPPH, H_2O_2

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INTRODUCTION

Solanum indicum (Synonym: *Solanum anguivi*) family *Solanaceae*, (**Figure 1)** is known in traditional system of medicine as Poison Berry, *Brihati* (Ayurvedic), *Kateli* (Unani), and *Jangli bhata* (Hindi).[1] It is a shrub up to l0 ft high, branches herbaceous. Stem and branches often have prickles. Prickles are sharp, usually mildly recurved, slightly hooked, and have a compressed broad base. The stalk is fleshy, and the whole plant is covered with minute stellate brown hairs. Leaves are stellate and tomentose. Leaves have ovate shape, sparsely prickly on both sides, and measure about 5–15 cm × 2.5–7.5 cm. Leaves are lined with hairs that have a bulbous base on the upper surface. Petioles are prickly and about 1.3–2.5 cm long. Flowers occur as racemose, extra-axillary cymes. Flowers are bluish- purple with yellow stamens around 1 to 1.5 cm in dia. Pedicels are 6–13 mm long, and prickly. The calyx is 3 mm long, with triangular teeth. Corolla is about 8 mm long, pale, purple, clothed outside with darker, purple; lobes are 5 mm long, deltoid, ovate, and acute. The fruit is a globose, smooth berry about an inch in dia, green with white lining when young and becomes yellow when ripe. Sometimes it has a few stellate hairs at the apex. Seeds are small, many, and discoid.[2,3] S. indicum is distributed across India as well as in the earth's tropical and subtropical zones.

This herb plays a unique role in the management of several disabilities, based on traditional Ayurvedic medicine. The different products of this shrub (fruits, leaves, roots) used by traditional practitioners in the cure of appetite loss and eating disorders, autoimmune conditions, hay fever, cough, asthma, sexual dysfunctions, stomach pain and worm infestation, pain, temperature, and inflammation.[4,5] S. indicum widely used in Chinese folk medicine as anti-inflammatory and wound-healing agents, and as an analgesic for toothache, rhinitis and breast cancer. [6] The fruits, leaves and root of this herb contain wax, fatty acid, alkaloids etc. [7]Phytochemical research on S. indicum reveals that it includes a number of plant metabolites steroids (indiosides A–F, isoanguivine, protodioscin) [8], steroidal alkaloids (solamargine, solasonine), coumarin (scopoletin)[9], amide (N-(p-trans-coumaroyl)-tyramine), and sesquiterpenes (solavetivone, solafuranone)[10,11]. Considering the scarce information available on the composition of Brihati, the purpose of this study was to characterize the antioxidant content and acute toxicity of herb.

Figure 1 Parts of *Solanum indicum* plant (whole plant, leaf, flower and fruit).

MATERIAL AND METHODS

Collection and Authentication of plant material:

Solanum indicum (Fam. Solanaceae) dried whole plant were collected from local market Khari Baoli, Delhi and authenticated by Dr. H B Singh (NESCAIR, New Delhi). The plants were dried in shade, powdered and stored in air tight containers for further studies.

Chemical reagents:

All the chemicals used in this study were obtained from Hi-Media Laboratories Pvt. Ltd. (Mumbai, India), Sigma-Aldrich Chemical Co. (Milwaukee, WI, USA), and SD Fine-Chem. Ltd. (Mumbai, India). All the chemicals used in this study were of analytical grade

Preparation of extracts:

One kg of the air dried, powdered drug was blended in 95% ethanol (solvent: drug ratio 2:1), macerated for one week at room temperature and filtered. The residue was mixed with fresh 95% ethanol and macerated for another week. Both ethanolic extracts were collected, filtered through no. 1 Whatman filter paper, and concentrated under reduced pressure and dried in air and kept sealed in a refrigerator until used. The dried extract was sequentially macerated at room temperature in different polar solvents {petroleum ether, chloroform, methanol, and water) and concentrated under reduced pressure. The extracts (SPE, SCE, SME, and SWE) collected in air tight amber colored container and kept at -2°C until further use.

Preliminary Phytochemical Study

For the identification of various phytochemical constituents, the different extracts were subjected to qualitative tests as per the standard procedure. [12,13]

Antioxidant Activity Assessment

In-Vitro Antioxidant Activity conducted on *Solanum indicum* extracts was DPPH (2, 2-diphenyl-picryl-hydrazine) test as per Silva[14] and H_2O_2 assay as per Yang[15] using ascorbic acid as standard. All the studies were carried out in triplicate.

Experimental animals

For acute oral toxicology assessment, (total of 65), age (6 weeks) and weight (129.1 to 140.2 gm) matched female Sprague Dawley (SD) pathogen-free rats were used. Fifteen female rats were used for an acute oral toxicity test. The toxicity tests were carried out according to Organization for Economic Cooperation and Development (OECD) test guideline, specifically OECD Guideline 423 for the acute oral toxicity test[16] with slight modifications. All animals were procured and housed in animal house maintained under standard hygienic conditions. Animals were acclimatised to the laboratory environment for seven days ahead of the experiments. The animals were allowed free to access commercial rat pellet diet (Lipton India Ltd, Mumbai, India) and water *ad libitum*. The bedding materials of the enclosure were changed every day. All the experimental trial was carried out in conformity with the CPCSEA guidelines. The study design was approved by IAEC PBRI (IAEC/PN-209).

Acute toxicity

Animals were randomly divided in the groups (n=3), a control group (Group A) and dose levels (200, 1000 and 2000 mg drug extracts / kg body weight). Extract was given once by oral gavage at a weight of 10 mL/kg body weight. The control animals have been treated with distilled water in the same volume. Animals were observed for three hours after dose administration changes in behaviour. The rats were weighed, and visual observations for mortality, behavioural pattern (salivation, fur, lethargy, and sleep), changes in physical appearance, injury, pain, and any signs of illness were conducted once daily during of 24 and 48 hours.

Statistical Analysis:

The results were expressed as mean ± SEM (n = 5). Data acquired as of hematology analysis, serum biochemistry, as well as the body and organ weight measurements were articulated as mean + SD and evaluated by unpaired t test (2-tailed P value) to compare the mean of the treated group of each sex with the control. Data were analysed using Student's t-test, and results were considered significant when $p < 0.05$.

RESULTS

Preliminary Phytochemical Analysis

The study results showed a spectrum of secondary metabolites (**Table 1**). It was also determined that extracts of *S. indicum* contained a high concentration of secondary metabolites like Terpenoids, Saponins Flavonoids, Glycosides, Phytosterols, etc., all of which were reported to have antioxidant as well as physiological properties.

Table 1 **Preliminary Phytochemical Analysis of *Solanum indicum extracts.***

S. No.	Phytochemical category	* SPE	SCE	SME	SWE
1.	Carbohydrate	_	_	+	+
2.	Alkaloids	_	+	+	+
3.	Glycosides	_	_	_	_
4.	Coumarin glycosides	_	+	+	+
5.	Flavanoids & Phenolic Compounds	_	_	+	+
6. .	Saponin	+	+	_	_
7.	Tannin	+	+	+	+
8.	Steroids	+	+	+	+
9.	Protein	_	_	+	+
10.	Amino acid	_	_	+	+
11.	Fats & Oils	_	+	_	_

* SPE: *S. indicum* Pet ether extract; SCE: *S. indicum* chloroform extract; SME : *S. indicum* methanol extract; SWE: *S. indicum* water extract + =Present , - = Absent

Antioxidant Activity Assessment

Mostly because of the complex nature of phytochemicals, the antioxidant effects of plant products must be measured by incorporating two or more different in vitro assays to acquire satisfactory data. Each of these tests is based on one feature of the antioxidant activity, such as the ability to scavenge free radicals, or the metal ion chelation. The results are presented in **Table 2** and **3.** Overall, our study indicates that the high antioxidant properties of *Solanum indicum* extract and may inhibit cellular lipid peroxidation and ameliorate other oxidative damage caused by free radicals[17].

Table 2: DPPH free radical activity of *Solanum indicum* extracts.

S. No.	Concentration (in µg/ml)	%Inhibition				
		*AA	SPE	SCE	SME	SWE
1.	10	51.0479	19.45854	24.02707	43.82403	36.04061
2.	20	51.94611	21.99662	26.22673	46.86971	38.74788
3.	30	52.69461	25.21151	28.4264	49.06937	41.28596
4.	40	54.64072	27.24196	30.45685	52.11506	43.65482
5.	50	55.68862	29.10321	32.3181	54.48393	46.70051
6.	60	57.48503	31.47208	34.17936	57.52961	50.42301
7.	70	59.28144	33.50254	38.40948	59.89848	52.45347
8.	80	60.92814	35.8714	41.96277	63.95939	54.31472
9.	90	64.22156	38.91709	44.33164	66.15905	57.022
10.	100	67.96407	41.79357	47.20812	69.20474	59.56007

* AA: Ascorbic acid; SPE: *S. indicum* Pet ether extract; SCE: *S. indicum* chloroform extract; SME : *S. indicum* methanol extract; SWE: *S. indicum* water extract

Table 3 : Comparative H_2O_2 Inhibition Potential of *Solanum indicum* (SI extracts).

S. No.	Concentration (in µg/ml)	% Inhibition				
		*AA	SPE	SCE	SME	SWE
1.	10	51.0479	19.45854	24.02707	43.82403	36.04061
2.	20	51.94611	21.99662	26.22673	46.86971	38.74788
3.	30	52.69461	25.21151	28.4264	49.06937	41.28596
4.	40	54.64072	27.24196	30.45685	52.11506	43.65482
5.	50	55.68862	29.10321	32.3181	54.48393	46.70051
6.	60	57.48503	31.47208	34.17936	57.52961	50.42301
7.	70	59.28144	33.50254	38.40948	59.89848	52.45347
8.	80	60.92814	35.8714	41.96277	63.95939	54.31472
9.	90	64.22156	38.91709	44.33164	66.15905	57.022
10.	100	67.96407	41.79357	47.20812	69.20474	59.56007

* AA: Ascorbic acid; SPE: *S. indicum* Pet ether extract; SCE: *S. indicum* chloroform extract; SME : *S. indicum* methanol extract; SWE: *S. indicum* water extract

Acute oral toxicity

In the present investigation, we assessed the likely toxicity and 50% lethal dose (LD50) of Extract following a regiment of solitary oral dose to female rodents. Following the gavage administration of 2000 mg SI preparation/kg to rats. No deaths in any animals were observed during the experimental period. No test substance-related effects were evident concerning clinical signs, body weight changes, and necropsy findings .These results suggest that acute exposure to DRE does not cause toxic effects, and its LD50 value is considered to be greater than 2000 mg/kg in rats.

CONCLUSION

In conclusion, the DRE was well tolerated, lack of mortality and neither produced overt signs of clinical toxicity (loss of hair, behavioral changes, impairments in feed intake and body weight gain. Further studies in repeated doses (sub-acute and chronic) must be performed to prove its safety.

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